AMICI Documentation

Release 0.23.0

The AMICI developers

Mar 07, 2024

ABOUT

Version: 0.23.0
Source code: https://github.com/AMICI-dev/amici

CHAPTER

ONE

ABOUT AMICI

AMICI provides a multi-language (Python, C++, Matlab) interface to the *SUNDIALS* solvers *CVODES* (for *ODE*s) and *IDAS* (for *DAE*s). AMICI allows the user to read differential equation models specified as *SBML* or *PySB* and automatically compiles such models into Python modules, C++ libraries or *.mex* simulation files (Matlab).

In contrast to the (no longer maintained) sundialsTB Matlab interface, all necessary functions are transformed into native C++ code, which allows for a significantly faster simulation.

Beyond forward integration, the compiled simulation file also allows for forward sensitivity analysis, steady state sensitivity analysis and adjoint sensitivity analysis for likelihood-based output functions.

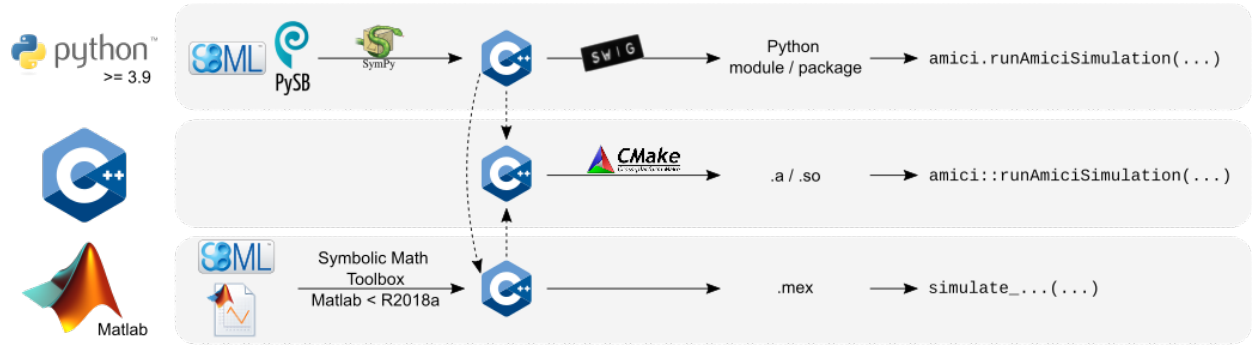
The interface was designed to provide routines for efficient gradient computation in parameter estimation of biochemical reaction models but it is also applicable to a wider range of differential equation constrained optimization problems.

1.1 Features

- *SBML* import
- *PySB* import
- Generation of C++ code for model simulation and sensitivity computation
- Access to and high customizability of *CVODES* and *IDAS* solver
- Python, C++, Matlab interface
- Sensitivity analysis
  - forward
  - steady state
  - adjoint
  - first- and second-order (second-order Matlab-only)
- Pre-equilibration and pre-simulation conditions
- Support for discrete events and logical operations

1.2 Interfaces & workflow

The AMICI workflow starts with importing a model from either *SBML* (Matlab, Python), *PySB* (Python), or a Matlab definition of the model (Matlab-only). From this input, all equations for model simulation are derived symbolically and C++ code is generated. This code is then compiled into a C++ library, a Python module, or a Matlab *.mex* file and is then used for model simulation.



The functionality of the Python, Matlab and C++ interfaces slightly differ, as shown in the following table:

Feature \ Interface	Python	C++	Matlab
SBML import	yes (*details*)	no	yes (<=R2017b)
PySB import	yes	no	no
DAE import	no	no	yes
Forward sensitivities	yes	yes	yes
Adjoint sensitivities	yes	yes	yes
Steadystate sensitivities	yes	yes	yes
Second-order sensitivities	no	no	yes
Events	yes	yes	yes
preequilibration	yes	yes	yes
presimulation	yes	yes	no

CHAPTER

TWO

AVAILABILITY

2.1 Source code

The AMICI source code is available as

- tar archive
- zip archive
- Git repository on GitHub

If AMICI was downloaded as an archive, it needs to be unpacked. If AMICI was obtained via cloning the Git repository, no further unpacking is necessary.

2.1.1 Obtaining AMICI via the Git version control system

In order to always stay up-to-date with the latest AMICI versions, simply pull it from our Git repository and recompile it when a new version is available. For more information about Git, check out their website.

The Git repository can currently be found at https://github.com/AMICI-dev/AMICI and clone is done via:

```
git clone https://github.com/AMICI-dev/AMICI.git AMICI
```

2.2 Python package

A Python package is available on PyPI.

2.3 Installation instructions

Installation instructions are available for

- *Python*
- *C++*
- *Matlab*

CHAPTER

THREE

LICENSE CONDITIONS

3.1 AMICI

AMICI is released under the 3-Clause BSD License (BSD-3-Clause) with the following terms:

Redistribution and use in source and binary forms, with or without modification, are permitted provided that the following conditions are met:

1. Redistributions of source code must retain the above copyright notice, this list of conditions and the following disclaimer.
2. Redistributions in binary form must reproduce the above copyright notice, this list of conditions and the following disclaimer in the documentation and/or other materials provided with the distribution.
3. Neither the name of the copyright holder nor the names of its contributors may be used to endorse or promote products derived from this software without specific prior written permission.

3.2 AMICI Logo

The AMICI logo is released under the Creative Commons CC0 1.0 Universal (CC0 1.0) license with the terms given in `documentation/gfx/LICENSE.md`.

3.3 Dependencies

- Parts of the *SUNDIALS* solver suite are redistributed under the BSD 3-Clause License (BSD-3-Clause) with terms given in `ThirdParty/sundials/LICENSE`
- Parts of *SuiteSparse* are redistributed under the various licenses with the terms given in `ThirdParty/SuiteSparse/LICENSE.txt`
- *gsl-lite* is redistributed under the MIT License (MIT) with the terms given in `ThirdParty/gsl/gsl/gsl-lite.hpp`
- *xml2struct* and *struct2xml* are redistributed under the BSD 2-Clause License (BSD-2-Clause) with terms given in `matlab/auxiliary/xml2struct/license.txt` and `matlab/auxiliary/struct2xml/license.txt`
- *CalcMD5* is redistributed under the BSD 2-Clause License (BSD-2-Clause) with terms given in `matlab/auxiliary/CalcMD5/license.txt`

CHAPTER

FOUR

HOW TO CITE AMICI

Citable DOI for the latest AMICI release:

There is a list of publications using AMICI. If you used AMICI in your work, we are happy to include your project, please let us know via a Github issue.

When using AMICI in your project, please cite

- Fröhlich, F., Weindl, D., Schälte, Y., Pathirana, D., Paszkowski, Ł., Lines, G.T., Stapor, P. and Hasenauer, J., 2021. AMICI: High-Performance Sensitivity Analysis for Large Ordinary Differential Equation Models. Bioinformatics, btab227, DOI:10.1093/bioinformatics/btab227.

```
@article{frohlich2020amici,
  title={AMICI: High-Performance Sensitivity Analysis for Large Ordinary␣
↪Differential Equation Models},
  author={Fr{\"o}hlich, Fabian and Weindl, Daniel and Sch{\"a}lte, Yannik and␣
↪Pathirana, Dilan and Paszkowski, {\L}ukasz and Lines, Glenn Terje and Stapor,␣
↪Paul and Hasenauer, Jan},
  journal = {Bioinformatics},
  year = {2021},
  month = {04},
  issn = {1367-4803},
  doi = {10.1093/bioinformatics/btab227},
  note = {btab227},
  eprint = {https://academic.oup.com/bioinformatics/advance-article-pdf/doi/10.1093/
↪bioinformatics/btab227/36866220/btab227.pdf},
}
```

When presenting work that employs AMICI, feel free to use one of the icons in documentation/gfx/, which are available under a CC0 license:

CHAPTER

FIVE

REFERENCES

List of publications using AMICI. Total number is 83.

If you applied AMICI in your work and your publication is missing, please let us know via a new GitHub issue.

CHAPTER

SIX

BACKGROUND

This section is to be extended.

6.1 Publications on various features of AMICI

Some mathematical background for AMICI is provided in the following publications:

- Fröhlich, F., Kaltenbacher, B., Theis, F. J., & Hasenauer, J. (2017). **Scalable Parameter Estimation for Genome-Scale Biochemical Reaction Networks.** PLOS Computational Biology, 13(1), e1005331. doi:10.1371/journal.pcbi.1005331.
- Fröhlich, F., Theis, F. J., Rädler, J. O., & Hasenauer, J. (2017). **Parameter estimation for dynamical systems with discrete events and logical operations.** Bioinformatics, 33(7), 1049-1056. doi:10.1093/bioinformatics/btw764.
- Terje Lines, Glenn, Łukasz Paszkowski, Leonard Schmiester, Daniel Weindl, Paul Stapor, and Jan Hasenauer. 2019. **Efficient Computation of Steady States in Large-Scale ODE Models of Biochemical Reaction Networks.** *IFAC-PapersOnLine* 52 (26): 32–37. DOI: 10.1016/j.ifacol.2019.12.232.
- Stapor, Paul, Fabian Fröhlich, and Jan Hasenauer. 2018. **Optimization and Profile Calculation of ODE Models Using Second Order Adjoint Sensitivity Analysis.** *Bioinformatics* 34 (13): i151–i159. DOI: 10.1093/bioinformatics/bty230.
- Lakrisenko, Polina, Paul Stapor, Stephan Grein, Łukasz Paszkowski, Dilan Pathirana, Fabian Fröhlich, Glenn Terje Lines, Daniel Weindl, and Jan Hasenauer. 2022. **Efficient Computation of Adjoint Sensitivities at Steady-State in ODE Models of Biochemical Reaction Networks.** *bioRxiv* 2022.08.08.503176. DOI: 10.1101/2022.08.08.503176.
- L. Contento, P. Stapor, D. Weindl, and J. Hasenauer, "A more expressive spline representation for SBML models improves code generation performance in AMICI," bioRxiv, 2023, DOI: 10.1101/2023.06.29.547120.

Note: Implementation details of the latest AMICI versions may differ from the ones given in the references manuscripts.

6.2 Third-Party numerical algorithms used by AMICI

AMICI uses the following packages from SUNDIALS:

- CVODES:

  The sensitivity-enabled ODE solver in SUNDIALS. Radu Serban and Alan C. Hindmarsh. *ASME 2005 International Design Engineering Technical Conferences and Computers and Information in Engineering Conference*. American Society of Mechanical Engineers, 2005. PDF

- IDAS

AMICI uses the following packages from SuiteSparse:

- Algorithm 907: **KLU** A Direct Sparse Solver for Circuit Simulation Problems. Timothy A. Davis, Ekanathan Palamadai Natarajan, *ACM Transactions on Mathematical Software*, Vol 37, Issue 6, 2010, pp 36:1-36:17. PDF
- Algorithm 837: **AMD**, an approximate minimum degree ordering algorithm, Patrick R. Amestoy, Timothy A. Davis, Iain S. Duff, *ACM Transactions on Mathematical Software*, Vol 30, Issue 3, 2004, pp 381-388. PDF
- Algorithm 836: **COLAMD**, a column approximate minimum degree ordering algorithm, Timothy A. Davis, John R. Gilbert, Stefan I. Larimore, Esmond G. Ng *ACM Transactions on Mathematical Software*, Vol 30, Issue 3, 2004, pp 377-380. PDF

Others:

- SuperLU_MT

  "A general purpose library for the direct solution of large, sparse, nonsymmetric systems of linear equations" (https://crd-legacy.lbl.gov/~xiaoye/SuperLU/#superlu_mt). SuperLU_MT is optional and is so far only available from the C++ interface.

CHAPTER

SEVEN

CHANGELOG

7.1 v0.X Series

7.1.1 v0.23.0 (2024-03-07)

Features

- SBML `InitialAssignment` are no longer absorbed into other model expressions, but are available as parameters or expressions (`w`) in the amici model by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2304, https://github.com/AMICI-dev/AMICI/pull/2305, https://github.com/AMICI-dev/AMICI/pull/2345, https://github.com/AMICI-dev/AMICI/pull/2359
- Upgraded to SuiteSparse 7.6 by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2316
- Model expressions `w` are now split into static and dynamic expressions, and only evaluated as needed by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2303
- Exposed additional solver settings:
  - `Solver.setMaxConvFails()`: maximum number of non-linear solver convergence failures
  - `Solver.setMaxNonlinIters()`: maximum number of non-linear solver iterations
  - `Solver.setMaxStepSize()`: maximum step size
  - `Solver.setConstraints()`: for setting (non)negativity/positivity constraints on state variables

  by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2335, https://github.com/AMICI-dev/AMICI/pull/2360, https://github.com/AMICI-dev/AMICI/pull/2340
- Improved output for debugging simulation failures: `ReturnData.{xdot,J}` now contain the respective values from the timepoint of failure, not the last output timepoint. NaN/Inf warnings now always include the timepoint at which the issue occurred. Note that C++ stacktraces are now only logged for debug builds. by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2349, https://github.com/AMICI-dev/AMICI/pull/2347, https://github.com/AMICI-dev/AMICI/pull/2366
- Updated dataframes import/export to include parameter values and scales by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/2351

Fixes

- CMake: Updated BLAS detection and some minor fixes by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2318 and https://github.com/AMICI-dev/AMICI/pull/2357
- Deterministic ordering of source files in generated `CMakeLists.txt` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2322

- Fixed size check in `Model::setStateIsNonNegative` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2332
- Fixed uncaught C++ exception in `runAmiciSimulation` that may crash Python in case of invalid values for standard deviations by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2338
- Fixed missing import in `amici/petab/petab_import.py` by @plakrisenko in https://github.com/AMICI-dev/AMICI/pull/2342
- Fixed `ReturnDataView AttributeError: messages` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2341
- Added a missing return code constant `LSETUP_FAIL` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2353
- Fixed in-place building of model wheels by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2352
- Made is-zero-checks compatible with the upcoming sympy>1.12 by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2350
- Fixed issues with paths containing blanks for sundials by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2361
- Added `amici.petab.conditions` to the API documentation by @PaulJonasJost in https://github.com/AMICI-dev/AMICI/pull/2364
- Improved type annotations in swig-wrappers by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2344, https://github.com/AMICI-dev/AMICI/pull/2365

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.22.0...v0.23.0

7.1.2 v0.22.0 (2024-02-23)

Features

- PEtab import: User option to fail if model needs to be compiled by @dilpath in https://github.com/AMICI-dev/AMICI/pull/2289

  The `force_compile` argument is now **deprecated**. Use `compile_` instead.

- Model import now adds a `.gitignore` file to the model output directory by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2301

Fixes

- **Fixed a bug that may have caused wrong simulation results for certain SBML models that contain `rateOf`-expressions** by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2291
- More informative error message for `ReturnDataView.by_id` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2295
- Fixed `ENABLE_AMICI_DEBUGGING=TRUE` not working with MSVC by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2296
- Fixed MANIFEST.in warning by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2297
- (performance) Skip unnecessary toposorting in `DEModel._collect_heaviside_roots` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2299
- (performance) Fix redundant calls to `Model::fdwdx` from `Model_ODE::fJ` (only relevant for dense and banded solvers) by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2298

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.21.2...v0.22.0

7.1.3 v0.21.2 (2024-02-06)

- Fixed `Solver` copyctor issues with swig4.2 that resulted in installation errors by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2276
- Fixed error when calling `amici.ExpData()` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2280
- Fixed invalid-type-error when loading an antimony model from file by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2281

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.21.1...v0.21.2

7.1.4 v0.21.1 (2024-01-17)

Fixed package configuration for PyPI upload. No further changes.

7.1.5 v0.21.0 (2024-01-16)

Deprecations

- Moved PEtab-related functionality from `amici.petab_*` to the petab-subpackage `amici.petab.*`. The old public functions are still available but will be removed in a future release. by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2205, https://github.com/AMICI-dev/AMICI/pull/2211, https://github.com/AMICI-dev/AMICI/pull/2252

Features

- Handle events occurring at fixed timepoints without root-finding. This avoids event-after-reinitialization errors in many cases a brings a slight performance improvement. by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2227
- Added `PetabProblem` class for handling PEtab-defined simulation conditions, making it easier to perform customized operations based on PEtab-defined simulation conditions. by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2255
- code-gen: Simplified `switch` statements, leading to reduced file sizes and faster compilation for certain models. by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2240
- Made `Model` and `ModelPtr` deepcopyable by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2247
- Made `Solver` and `SolverPtr` deepcopyable by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2245
- Added a debugging helper `get_model_for_preeq` for debugging simulation issues during pre-equilibration. by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2250
- Added `SwigPtrView` fields to `dir()` outputs by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2244
- Use proper labels for in plotting functions if IDs are available in `ReturnData`. by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2249
- Added `ExpData::clear_observations` to set all measurements/sigmas to NaN by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2258

Fixes

- Fixed AMICI hiding all warnings. Previously, importing `amici` resulted in all warnings being hidden in the rest of the program. by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2243
- CMake: Fixed model debug builds by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2222

- Fixed CMake potentially using incorrect Python library for building model extension by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2220
- CMake: fixed cxx flag check by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2225
- Fixed potential out-of-bounds read in `Model::checkFinite` for matlab-imported models by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2232
- Fixed piecewise/Heaviside handling by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2234
- Deterministic order of event assignments by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2242
- Proper error message in case of unsupported state-dependent sigmas by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2239
- Fixed swig shadow warning + other linting issues by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2261
- Fixed `SwigPtrView.__getattr__` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2259
- `simulate_petab`: Avoid warning when simulating with default parameters by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2265

Documentation

- Updated Python package installation instructions for Arch Linux by @willov in https://github.com/AMICI-dev/AMICI/pull/2212
- Updated `ExpData` documentation by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2254
- Documented simulation starting time `t0` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2263
- Updated PEtab example by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2255

...

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.20.0...v0.21.0

7.1.6 v0.20.0 (2023-11-23)

Fixes

- Fixed CMake `cmake_minimum_required` deprecation warning by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2183
- Fixed misleading preequilibration failure messages by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2181
- Removed setuptools<64 restriction by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2180
- Fixed ExpData equality operator for Python by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2194
- Enabled deepcopy for ExpData(View) by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2196
- Allowed subsetting simulation conditions in simulate_petab by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2199
- Set CMake CMP0144 to prevent warning by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2209

Features

- Possibility to evaluate and plot symbolic expressions based on simulation results by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2152
- Easier access to timepoints via ExpDataView by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2193

- Nicer `__repr__` for ReturnDataView by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2192

Documentation

- Added installation instructions for Arch Linux by @stephanmg in https://github.com/AMICI-dev/AMICI/pull/2173
- Updated reference list by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2172
- Installation guide: optional requirements by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2207

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.19.0...v0.20.0

7.1.7 v0.19.0 (2023-08-26)

Features

- SBML import now supports `rateOf` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2120
- Added `Model.{get,set}SteadyStateComputationMode` (analogous to `SteadyStateSensitivityMode`) which allows to choose how steady state is computed. by @plakrisenko in https://github.com/AMICI-dev/AMICI/pull/2074

  Note: The default `SteadyStateSensitivityMode` changed from `newtonOnly` to `integrateIfNewtonFails`.
- SBML import: Allow hardcoding of numerical values by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2134
- Added `antimony2amici` for more convenient antimony import (simplifies working with raw ODEs, see documentation) by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2142
- Added `AMICI_TRY_ENABLE_HDF5` environment variable to control whether to search for HDF5 or not by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2148

Fixes

- Fixed SBML import for events with trigger functions depending on parameters that are initial assignment targets by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2145
- Fixed SBML import for event-assigned parameters with non-float initial assignments by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2156
- Fixed `unistd.h` dependency of `hdf5.cpp` that led to compilation failures on Windows by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2154
- Set CMake policies for cmake 3.27 by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2162
- Fixed a `lib/` vs `lib64/` issue, leading to `SUNDIALSConfig.cmake`-not-found issues on some systems by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2165
- CMake: fixed scope of `-DHAS_BOOST_CHRONO` which may have lead to a mix of `boost::chrono::thread_clock` and `std::clock` being used in programs using amici, and potentially segmentation faults by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2163

Performance:

- Combined code for sparse model functions and their index files for slightly faster compilation of small models by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2159
- Removed complex / complex long KLU functions for slightly faster amici package installation by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2160

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.18.1...v0.19.0

7.1.8 v0.18.1 (2023-06-26)

Fixes:

- Fixed pysb pattern matching during PEtab import by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/2118
- Fixed `sp.Matrix` errors with `numpy==1.25` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2124
- Readme: added info containers by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2125
- Fixed deprecation warnings by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2122 https://github.com/AMICI-dev/AMICI/pull/2131
- Fixed logging typo in SBML import by @dilpath in https://github.com/AMICI-dev/AMICI/pull/2126
- Added minimum version for `pandas` by @dilpath in https://github.com/AMICI-dev/AMICI/pull/2129

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.18.0...v0.18.1

7.1.9 v0.18.0 (2023-05-26)

Features:

- More efficient handling of splines in SBML models by @paulstapor, @lcontento, @dweindl in https://github.com/AMICI-dev/AMICI/pull/1515
- Partial support of current PEtab2.0 draft, including support for PySB models by @dweindl, @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1800

Fixes:

- **Fixed incorrect forward sensitivities for models with events with state-dependent trigger functions** by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2084
- Model import: Don't create spl.h and sspl.h for models without splines by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2088
- SBML import - faster processing of SpeciesReference IDs by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2094
- Update swig ignores by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/2098
- CMake: Fixed choosing SWIG via `SWIG` env variable by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2100
- CMake: Try FindBLAS if no other information was provided by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2104
- Fixed cblas error for models without solver states in combination with forward sensitivities by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2108
- Fixed compilation error for models with events and xdot=0 by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2111
- Fixed import error for models with events and 0 states by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2112

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.17.1...v0.18.0

7.1.10 v0.17.1 (2023-05-10)

This release fixes two bugs:

- One bug introduced in v0.17.0, that causes an `ImportError` on macOS (https://github.com/AMICI-dev/AMICI/issues/2075).
- An AttributeError in petab_import_pysb with petab>=0.2.0 https://github.com/AMICI-dev/AMICI/pull/2079

7.1.11 v0.17.0 (2023-05-09)

AMICI v0.17.0 requires Python>=3.9 and a C++17 compatible compiler

Features

- DAE support in SBML by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/2017
- SBML import: flatten SBML-comp models by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2063
- Added sllh computation back to `petab_objective.simulate_petab` by @dilpath in https://github.com/AMICI-dev/AMICI/pull/1548
- CMake-based Python extension builds by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1992

Fixes

- Fixed CPU time tracking with multi-threading (partially) by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2023
- Fixed HDF5 ambiguous overload by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2031
- Fixed varying cmake libdir lib(64)/ by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2033
- Fixed Equilibration cpu time computation by @plakrisenko in https://github.com/AMICI-dev/AMICI/pull/2035
- CMake: add header files to library sources for generated models by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2047
- CMake: Handle header-dependency of swig files by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2046
- Don't try to detect conservation laws for models with Species-AssignmentRules by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2056
- Smith benchmark and SBML initialization fix by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/2034
- SBML import: Fixed check for required packages by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2064
- Nan observables by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/2065
- Fixed check for discontinuities for conservation law computation by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2068
- Specify visualization dependencies by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2070
- Fixed sympy symbol name clashes during PEtab import by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2069
- Fixed ReturnData::{preeq_wrms,posteq_wrms} with FSA and check_sensi_steadystate_conv_=True by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2071

Extended / updated documentation, for example:

- Jax example notebook by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1996
- Updated Windows/MSVC installation instructions by @Podde1 in https://github.com/AMICI-dev/AMICI/pull/2053

New Contributors

- @Podde1 made their first contribution in https://github.com/AMICI-dev/AMICI/pull/2053

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.16.1...v0.17.0

7.1.12 v0.16.1 (2023-02-24)

Fixes:

- Additional package names for finding blas via pkg-config by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1959
- Changed default interpolation type from hermite to polynomial by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1960
- PySB import: Change default simplify to work with multiprocessing by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1961
- Add –no-validate to amici_import_petab @dweindl in https://github.com/AMICI-dev/AMICI/pull/1963
- Fix get_model for direct import of swig interface by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1969
- Fix PytestReturnNotNoneWarning in test_conserved_quantities_demartino.py by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1968
- Fix MSVC builds / remove -W* flags by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1972
- Add option to use IDs when plotting trajectories by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1974
- Fix assignmentRules2observables - skip non-assignment-rule targets by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1973
- Use std::clock for measuring solver time by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1982 (*Note that this uses cpu-time consumed by all threads*)
- Fix narrowing-conversion-warning by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1983
- PEtab import: allow specifying default values for output parameters by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1987
- Print stacktraces only with debug logging level by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1985
- Change default ReturnData::status to AMICI_NOT_RUN by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1984
- Reduce time-tracking overhead by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1988
- Fix equilibraton status discrepancy by @plakrisenko in https://github.com/AMICI-dev/AMICI/pull/1991
- Pass model_name to _create_model_output_dir_name by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1994
- CMake: Build with OpenMP support if available by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2000
- Fix SuiteSparse Makefiles for compiler-paths by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2003

- CMake: Build with HDF5 support if available by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1999
- CMake: Fix reading version file on Windows by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2001
- CMake: raise minimum required version to 3.15 by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2002
- Fix/extend runtime logging by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/2005
- Fix error logging in steadystate solver by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/2008
- Don't pass `-py3` to swig after 4.1.0 by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/2010
- SWIG __repr__s for different templated vector classes by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/2009
- Matlab: If mex fails, print mex arguments by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2013
- Simplify OpenBLAS installation on Windows by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2016
- Remove model name prefix in generated model files by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2015
- …

Documentation:

- Restructure sphinx doc by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1978
- Instructions for AMICI with singularity by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1964
- Illustrate options for potentially speeding up model import/simulation by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1965
- …

Dependencies:

- Updated SuiteSparse to v7.0.1 by @dweindl in https://github.com/AMICI-dev/AMICI/pull/2018

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.16.0…v0.16.1

7.1.13 v0.16.0 (2023-01-25)

Features

- Python 3.11 compatibility by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1876
- AMICI now runs on binder (https://mybinder.org/v2/gh/AMICI-dev/AMICI/develop?labpath=binder%2Foverview.ipynb) by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1935, https://github.com/AMICI-dev/AMICI/pull/1937, https://github.com/AMICI-dev/AMICI/pull/1939
- More informative `Solver.__repr__` and `ExpData.__repr__` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1928 and @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1948
- `simulate_petab` returns the generated/used `ExpData`s by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1933
- Model module is now accessible from model instance by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1932
- Added `plot_jacobian` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1930
- Now logs all nested execution times as debug by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1947

- Always check for finite initial states, not only with `Model.setAlwaysCheckFinite(True)` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1955

Fixes

- `ReturnDataView.status` now returns `int` instead of `float` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1929
- Updated simulation status codes by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1931
- Skip irrelevant frames in stacktraces by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1934
- Fixed compiler warning (matlab) by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1954

Documentation:

- Added a notebook demonstrating common simulation failures and show how to analyze / fix them by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1946
- various minor fixes / updates

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.15.0...v0.16.0

7.1.14 v0.15.0 (2023-01-11)

Features

- Improved logging by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1907

  For Python: Don't print messages to stdout, but collect them in ReturnData and forward them to python logging, making it easier to filter specific messages or to disable output completely. Messages are also available via `ReturnData.messages`.

  breaking change for C++ interface: Messages aren't printed to stdout by default, but are collected in `ReturnData`. The user has to decide what to do with them.
- MultiArch docker build by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1903
- Added cmake target for cmake-format by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1909
- Updated clang-format style, fixed clang-format target by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1908
- Subsetting `ReturnData` fields by ID via `ReturnDataView.by_id` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1911 https://github.com/AMICI-dev/AMICI/pull/1916

Fixes

- PEtab import: fixed handling of fixed parameters for rule targets by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1915
- Fixed compiler warnings for matlab interface by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1919
- Fixed pandas DeprecationWarning for Series.iteritems() by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1921
- Fixed circular import in amici.petab_import_pysb by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1922
- Fixed 'operator ==' swig warning by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1923
- Prevent swig4.0.1 segfault by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1924

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.14.0...v0.15.0

7.1.15 v0.14.0 (2022-11-23)

Features:

- Added optional functionality to apply C99 math optimization to generated C++ code by @dweindl and @lcontento in https://github.com/AMICI-dev/AMICI/pull/1377, https://github.com/AMICI-dev/AMICI/pull/1878
- Added option to treat fixed parameters as constants in PEtab import

  by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1877
- Added equality operator for ExpData

  by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1881
- Updated base image for Dockerfile to Ubuntu 22.04/Python 3.10

  by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1896

Fixes:

- Fixed deprecation warnings by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1873, https://github.com/AMICI-dev/AMICI/pull/1893
- Fixes/updates to GitHub actions by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1885, https://github.com/AMICI-dev/AMICI/pull/1893, https://github.com/AMICI-dev/AMICI/pull/1889, https://github.com/AMICI-dev/AMICI/pull/1891
- Added hdf5 search directories for arm64 architecture (M1/M2 macs)

  by @Doresic in https://github.com/AMICI-dev/AMICI/pull/1894
- Fixed missing return in generated non-void functions

  by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1892
- Fixed import failure for pre-compiled models

  by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1897

Documentation:

- Update reference list by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1874, https://github.com/AMICI-dev/AMICI/pull/1884

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.13.0...v0.14.0

7.1.16 v0.13.0 (2022-10-04)

- Fixed extraction of common subexpressions by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1865
- Added function to convert `ReturnData::status` flags to string by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1864

And further contributions by @dweindl, @FFroehlich

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.12.0...v0.13.0

7.1.17 v0.12.0 (2022-08-26)

Features:

- Support for event observables via the Python interface by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1845
- Treat non-estimated parameters as constants during SBML-PEtab import by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1810
- Updated SUNDIALS to v5.8.0 by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1836
- Option to extract common subexpressions by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1852, https://github.com/AMICI-dev/AMICI/pull/1856 **not available in this release, use v0.13.0**
- Parallelize matrix simplification by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1778
- Validate PEtab problems before attempting import by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1842
- Improved type annotations for the swig interface by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1860

Fixes:

- Fixed an issue with potentially infinite loops during conservation law processing by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1833
- Fixed potential deadlocks during parallel simplification by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1844
- Fix resetting `ReturnData::numstepsB` when re-using Solver by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1841

And further contributions by @dilpath, @dweindl, @FFroehlich

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.11.32...v0.12.0

7.1.18 v0.11.32 (2022-07-15)

Fixes:

- Fixed `ImportErrors` during package installation with recent setuptools by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1830

7.1.19 v0.11.31 (2022-07-12)

Fixes:

- Fixed `ParameterMapping.__getitem__` to either return a `ParameterMappingForCondition` or a new `ParameterMapping`, but not a list by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1826

7.1.20 v0.11.30 (2022-07-07)

Features:

- Allow overriding model name during PySB import by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1801
- Added **repr** for parameter mapping classes by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1799
- More informative warning messages for NaNs/Infs by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1798
- Moved `sim_steps` increment by @plakrisenko in https://github.com/AMICI-dev/AMICI/pull/1806
- Re-arranged application of parameters from `ExpData` to avoid initial sensitivities error by @dilpath in https://github.com/AMICI-dev/AMICI/pull/1805
- Checking for unused parameters in `simulate_petab` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1816
- Add `create_parameter_mapping` kwarg forwarding by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1820

Other

- Remove `constant_species_to_parameters` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1809

Fixes

- Fixed handling of SBML models given as `pathlib.Path` in `petab_import.import_model_sbml by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1808
- Fixed missing CPU time reset by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1814
- Raise in `simulate_petab` with `scaled_parameters=True problem_parameters=None` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1819

…

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.11.29…v0.11.30

7.1.21 v0.11.29 (2022-05-06)

7.2 What's Changed

Features:

- Performance: Limit newton step convergence check by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1780
- More informative NaN/Inf warnings by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1640
- SBML import can now handle initial events by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1789

Fixes:

- Avoid error if no measurements in PEtab problem; fixed type handling in PEtab parameter mapping by @dilpath in https://github.com/AMICI-dev/AMICI/pull/1783
- Fixed substitution of expressions in root and stau by @dilpath in https://github.com/AMICI-dev/AMICI/pull/1784

- Workaround for PEtab problems with state-dependent noise models by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1791

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.11.28...v0.11.29

7.2.1 v0.11.28 (2022-04-08)

New features:

- Added `Solver.setSteadyStateToleranceFactor` and `Solver.setSteadyStateSensiToleranceFactor` to specify a steady state tolerance factor by @dilpath in https://github.com/AMICI-dev/AMICI/pull/1758

  NOTE: This also relaxed the default steady state (sensitivity) tolerances by a factor of 100.

- Added support for `pathlib.Path` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1769
- Allow specifying initial timepoint with `ExpData` by @dilpath in https://github.com/AMICI-dev/AMICI/pull/1776

Performance:

- Speedup for models with conservation laws by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1765
- Improved efficiency of newton step convergence check by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1775

Fixes:

- Fixed deprecation warning for pandas.DataFrame.append in `rdatas_to_measurement_df` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1770
- Fixed Rule-target handling in PEtab import by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1753

Removed functionality:

- Removed long deprecated `sbml2amici` arguments `modelName` and `constantParameters` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1774

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.11.27...v0.11.28

7.2.2 v0.11.27 (2022-04-04)

New features:

- Checking condition number when computing sensitivities via Newton by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1730
- Removed SPBCG solver by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1729
- Added Newton step convergence checks to steadystate solver by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1737
- Removed legacy options/members `amioption.newton_preeq` and `Solver::r... by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1744
- Added `ReturnData::cpu_time_total` to track total time spent in `runAmiciSimulation` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1743
- SBML import: Alternative algorithm for identifying conservation laws by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1748
- Use `amici.AmiciVersionError` to indicate version mismatch by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1764

Performance:

- Optional parallel computation of derivatives during model import by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1740
- Sparsify jacobian by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1766
- Speedup conservation law computation by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1754
- Exploit stoichiometric matrix in pysb import by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1761
- Speedup edata construction from petab problems by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1746

Fixes:

- Fixed `get_model_settings` that would to setting incorrect initial states and initial state sensitivities for models with parameter-dependent initial states by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1751
- Use correct tolerances for convergence check in Newton solver by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1728
- Harmonized convergence checks by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1731
- Made sundials' KLU_INDEXTYPE match actual klu index type by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1733
- Fixed `Model::setStateIsNonNegative` logic that would raise exceptions in cases where it shouldn't by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1736
- Fixed undefined reference to dladdr by @kristianmeyerr in https://github.com/AMICI-dev/AMICI/pull/1738
- Fixed HDF5 OSX intermediate group creation errors by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1741
- Fixed recent cmake-based build issues due to changed sundials library directory by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1756
- Updated Windows installation instructions by @paulflang in https://github.com/AMICI-dev/AMICI/pull/1763

… and other contributions by @FFroehlich, @dweindl

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.11.26…v0.11.27

7.2.3 v0.11.26 (2022-03-14)

New features:

- Import of BioNetGenLanguage (BNGL) models by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1709
- Added support for observable-dependent sigmas by @dweindl, @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1692
- Added support for pysb local functions by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1666
- Added experimental support for conservation laws for non-constant species to SBML import: conservation laws for non-constant species by @stephanmg, @dweindl in https://github.com/AMICI-dev/AMICI/pull/1669 Enable this feature by setting environment variable `AMICI_EXPERIMENTAL_SBML_NONCONST_CLS` to any value
  - Allow using states eliminated by conservation laws to be used in root functions by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1677

  - Added support for parameter-dependent conservation laws by @dweindl, @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1678

- Added optional caching for symbolic simplifications in ODE export by @dilpath in https://github.com/AMICI-dev/AMICI/pull/1672
- Added CLI option `--no-sensitivities` to `amici_import_petab` by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1688

Fixes:

- SBML import: Raise in case of nested observables by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1690
- Sympy 1.10 compatibility by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1694

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.11.25...v0.11.26

7.2.4 v0.11.25 (2022-02-09)

- Fixed a bug where `Model::setStateIsNonNegative(Model::getStateIsNonNegative())` would raise an exception in case conservation laws were enabled - by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1648
- Fixed a bug where `Model::setStateIsNonNegative` would be ignored in certain model expressions - by @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1650
- Fixed a bug where special function parsing inside `min()` and `max()` would not be parsed correctly - by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1655
- Fixed a numpy dependency issues for Mac+ARM systems - by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1657
- Fixed convergence check in Newton method - by @plakrisenko in https://github.com/AMICI-dev/AMICI/pull/1663
- Add `AMICI_CXX_OPTIONS` to pass libamici-specific compiler options during CMake-based builds - by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1664
- Fixed various warnings and updated documentation - by @dweindl

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.11.24...v0.11.25

7.2.5 v0.11.24 (2022-02-01)

Features:

- Introduced environment variable `AMICI_DLL_DIRS` to control DLL directories on Windows (useful for setting BLAS library directory, as required by Python>=3.8) by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1637
- Dropped Python3.7 support by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1635
- Include header files in CMake targets for better IDE integration by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1639

Fixes:

- Fixed an issue in PEtab import where all-integer parameters would previously result in a TypeError by @stephanmg in https://github.com/AMICI-dev/AMICI/pull/1634

- Fixed tempdir deletion issues for test suite on Windows by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1636
- Added functions to provide state IDs/names for x_solver by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1638
- Fixed docs on RTD by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1643

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.11.23...v0.11.24

7.2.6 v0.11.23 (2022-01-11)

Features:

- Added overload for Model::setParameterScale with vector by @dilpath in https://github.com/AMICI-dev/AMICI/pull/1614
- Removed assert_fun argument from gradient checking, improve output by @dweindl, @FFroehlich in https://github.com/AMICI-dev/AMICI/pull/1609
- Added get_expressions_as_dataframe by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1621
- Added `id` field to ExpData and ReturnData by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1622
- Included condition id in dataframes by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1623

Fixes:

- C++: Fixed SUNMatrixWrapper ctor for size 0 matrices by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1608
- Python: Handle TemporaryDirectory cleanup failures on Windows by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1617
- Python: pysb.Model.initial_conditions throws a DeprecationWarning by @PaulJonasJost in https://github.com/AMICI-dev/AMICI/pull/1620
- Fixed wrong array size in warnings by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1624

NOTE: AMICI 0.11.23 requires numpy<1.22.0

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.11.22...v0.11.23

7.2.7 v0.11.22 (2021-12-02)

- **Require sympy>=1.9,pysb>=1.13.1* by @FFroehlich, @dweindl in https://github.com/AMICI-dev/AMICI/pull/1599
- Fixed sympy deprecation warning by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1600
- Updated Windows installation instructions for Python>=3.8 by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1597
- Fixed plot labels by @dweindl in https://github.com/AMICI-dev/AMICI/pull/1598

Full Changelog: https://github.com/AMICI-dev/AMICI/compare/v0.11.21...v0.11.22

7.2.8 v0.11.21 (2021-11-21)

Fixes:

- Fixed a bug in recursion depth computation for model expressions. This may have resulted in incorrect sensitivities for models with expressions nested more than 2 levels. (#1595)
- Fixed improper handling of Piecewise functions in PySB import which may have produced incorrect simulation results. (#1594)
- Fixed changed googletest reference which broke the CMake-based build if tests were enabled (#1592)

New:

- It's now possible to build AMICI using Ninja (#1593)

7.2.9 v0.11.20 (2021-11-12)

New:

- Changed parameter mappings such that unassigned values have non-nan default values. This fixes erroneous evaluation of `llh` as `NaN` in some situations (#1574)
- Added support for Python 3.10 (#1555)

Fixes:

- Fixed a bug when simulation start time was not transferred when copying a solver instance (#1573)
- Fixed a bug which led to incorrect sensitivies for models with multiple assignment rules or rate rules (#1584)

Other:

- Update CI and documentation settings (#1569, #1527, #1572, #1575, #1579, #1580, #1589, #1581)
- Extend set of validated benchmark models that is checked during CI (#1571, #1577)
- Fixed string formatting in derivative checks (#1585)
- Added helper methods to save and restore model instance-only settings (#1576)

7.2.10 v0.11.19 (2021-10-13)

New:

- Added support for observable transformations (lin/log/log10) (#1567). Thereby supporting additional noise distributions in combination with least squares solvers.

Fixes:

- Fixed a bug when Newton sensitivity computation was activated despite specifying newton_steps == 0. The error occurs when simulation converges to a steadystate but simulation sensitivities are not converged according to convergence criteria. In that case simulation returned failure, but the newton rootfinding "finds" a steadystate even before the iteration check, leading to the erroneous computation of sensitivities via Newton/IFT. For singular jacobians this means the overall simulation still fails, but a different, more informative error message is displayed. (#1541)
- Fixed a bug where argument "outdir" in ODEExporter.**init** would not be used (#1543)

Other:

- Improve checking support for SBML extensions (#1546)

- SBML import: Use more descriptive IDs for flux expressions (#1551)
- Optimized SUNMatrixWrapper functions (#1538)
- C++: Changed test suite from CppUTest to gtest (#1532)
- Add CITATION.cff (#1559)
- Updated documentation (#1563, #1554, #1536)
- Removed distutils dependency (#1557)
- Require sympy<1.9

7.2.11 v0.11.18 (2021-07-12)

New:

- Allow specifying maximum integration time via `amici::Solver::setMaxTime()` (#1530)
- Py: Add `failfast` and `num_threads` argument to `simulate_petab` (#1528, #1524)
- Enable typehints / static type checking for AMICI-generated model modules (#1514) (`amici.ModelModule`, available with Python>=3.8)

Fixes:

- Python: Fix unused argument `generate_sensitivity_code` in `pysb2amici` (#1526)
- Python: Fix C(++) stdout redirection which could have let to deadlocks in exotic situations (#1529)
- Py: Fixed deprecation warning (#1525)
- Py: Proper typehints for SWIG interface (#1523), enabling better static type checking and IDE integration (available with Python>=3.9)
- C++: Fixed clang compiler warning (#1521)
- C++: Fix inherited variadic ctor in exception class (#1520)
- PEtab: More informative output for unhandled species overrides (#1519)
- Return SbmlImporter from PEtab model import (#1517)

7.2.12 v0.11.17 (2021-05-30)

Fixes:

- Fix “maybe-uninitialized” compiler warning (#1495)
- Fix substitution of expressions in `drootdt_total (#1512)
- C++: Fix serialization and == operator (#1493)
- C++: Avoid `w` in `root` and `stau` headers (refactor) (#1503)

Documentation:

- Updated OpenBLAS Windows installation instructions (#1496)
- Updated how-to-cite to Bioinformatics paper (#1499)
- Updated list of papers using AMICI (#1509)

Other:

- Remove sllh computation from `petab_objective.simulate_petab` (#1498)
- Add **main**.py to Python package to provide info on AMICI installation via `python -m amici` (#1500)

7.2.13 v0.11.16 (2021-04-13)

Fixes:

- Fixed serialization bug (#1490)

New:

- Construction of condition specific plist for parameter mappings (#1487, #1488)
- **Add support for error residuals** (#1489)

7.2.14 v0.11.15 (2021-03-31)

Fixes:

- Fixed initial state sensitivities in adjoint preequilibration (#1468)
- Fixed various model import / parameter mapping issues (#1469, #1473, #1475)

New:

- New AMICI releases will automatically trigger releases at https://biosimulators.org/simulators/amici/latest
- Transparent logo

7.2.15 v0.11.14 (2021-03-16)

New features:

- **Python import now supports SBML Events** (#1443)
- Implement support for compilation without sensitivities (#1454)

Fixes:

- Issue #1446: Check whether constant parameters are valid targets (#1450)
- Issue #1422: Fix Steadystate solver failing if preequilibration starts in steadystate (#1461)
- Issue #1401: Ensure diagnostics variables in ReturnData are always of expected length (#1438, #1447)
- Fix FIM approximation for parameter dependent sigma (#1441)
- Fix invalid SBML in PEtab/PySB import (#1433)
- Fix: No context for inspect.getouterframes (#1432)

Documentation:

- Added this CHANGELOG
- Added feature request issue template (#1437)
- Updated reference list (#1430)
- Overhauled experimental conditions notebook (#1460)

CI:

- Test Matlab interface on GHA (#1451)
- Include componentTags in SBML test suite output (#1462)
- Split SBML semantic test suite into multiple jobs (#1452)
- Fix Crauste ref val, fixes #1458 (#1459)

Misc:

- Various cleanup (#1465, #1448, #1455)
- Micro-optimize SUNMatrixWrapper::transpose (#1439)
- Remove constant triggers from roots in Heaviside (#1440)

7.2.16 v0.11.13 (2021-02-20)

Breaking changes:

- AMICI requires Python>=3.7
- Updated package installation (PEP517/518): Creating source distributions requires https://github.com/pypa/build (#1384) (but now handles all package building dependencies properly)

Features:

- More flexible state reinitialization (#1417)

Updated dependencies:

- Upgrade to sundials 5.7.0 (#1392)

Fixes:

- Python: account for heaviside functions in expressions (#1382)
- Python: allow loading of existing models in import_petab_problem (#1383)
- Python: Don't override user-provided compiler/linker flags (#1389)
- Python: PEtab import reinitialization fixes (#1417)
- Python: Fix PEtab observables for pysb models (#1390)
- Python: Substitute expressions in event condition expressions (#1404)
- Python: Unspecified initial states in PEtab conditions table default to SBML initial value (#1397)
- C++: Fix timepoint out of bounds access (#1402)
- C++: Fix exported CMake config (#1388)
- Fixed Dockerfile: add python3-venv (#1398, #1408)

Other:

- Slim exported swig interface (#1425)
- Updated documentation
  - Getting started tutorial (#1423)
  - List supported SBML test tags (#1428)
  - Add AMICI C++/Python/Matlab feature comparison (#1409)
  - …

- Various minor CI improvements
- …

7.2.17 v0.11.12 (2021-01-26)

Features:

- Add expression IDs and names to generated models (#1374)

Fixes:

- Raise minimum sympy version to 1.7.1 (Closes #1367)
- Fix species assignment rules in reactions (#1372)
- Fix id vector for DAEs (#1376)

Docs:

- Update how-to-cite (#1378)

7.2.18 v0.11.11 (2020-12-15)

Python

- Restore support for species references (#1358)
- Add support for noise models in pysb (#1360)
- Proper handling of discontinuities in the ODE rhs (#1352)
- Fix directly calling AMICI from snakemake (#1348)
- Extend mathml function support, particularly for numerical arguments (#1357)
- Restore support for sympy 1.6 (#1356)

C++

- Fix some compiler related warnings (#1349, #1362)
- Fix a rare segfault for adjoint sensitivities (#1351)

CI

- Move windows tests to GHA (#1354)
- Pin breathe to 4.24.1

Docker

- Update ubuntu to 20.04

7.2.19 v0.11.10 (2020-11-30)

Bugfix release that restores compatibility with sympy 1.7

7.2.20 v0.11.9 (2020-11-29)

Python

- General improvements to SBML import (#1312, #1316, #1315, #1322 , #1324 #1333, #1329)
- Small bugfixes and improvements (#1321)
- Improve derivative computation for instances of `power` (#1320)

C++

- Fix FIM and residual computation for models with parameter dependent sigma. (#1338)
- Disable chi2/residual/FIM computation for non-gaussian objective functions. (#1338)
- Bugfix for integration failure during adjoint solve (#1327)

Doc

- Update references (#1331, #1336)

CI

- Update OpenBLAS for windows (#1334)

7.2.21 v0.11.8 (2020-10-21)

Python

- Fix pysb-petab support (#1288)
- Fix ExpData constructor overloading (#1299)
- Fix support for positivity enforcement (#1306)
- **Refactor SBML import, adds support for parameter rate rules and initial assignments** (#1284, #1296, #1304)
- Improve model generation for models with many parameters (#1300)
- Add support for PEtab based synthetic data generation (#1283)

C++

- Make HDF5 an optional dependency (#1285)

Doc

- General Improvements to Documentation (#1289, #1291, #1292, #1293, #1294, #1286, #1277, #1281)

CI

- Add python 3.9 support test (#1282)
- Allow manual triggering of GitHub actions (#1287)
- Remove appveyor config (#1295)
- Update GHA env and path management (#1302)

7.2.22 v0.11.7 (2020-09-22)

Python

- Improve and extend available objective functions (#1235)
- Fix processing of compartment definitions (#1223)
- Fix replacement of reserved symbols (#1265)
- Use Hierarchical Derivatives for Expressions (#1224, #1246)
- Fix duplicate running of swig (#1216)
- Overload python interface functions for amici.{Model,Solver,ExpData} and amici.{Model,Solver,ExpData}Ptr (#1271)

C++

- Fix and extend use of sparse matrix operations (#1230, #1240, #1244, #1247, #1271)
- **Fix application of maximal number of steps**, MaxNumStep parameter now limit total number of steps, not number of steps between output times. (#1267)

Doc

- Move all Documentation to RTD (#1229, #1241)
- General Improvements to Documentation (#1225, #1227, #1219, #1228, #1232, #1233, #1234, #1237, #1238, #1239, #1243, #1253, #1255, #1262)

CI

- Better check for doc building (#1226)
- Add more gradient checks (#1213)
- Update GHA to Ubuntu 20.04 (#1268)

7.2.23 v0.11.6 (2020-08-20)

Python

- Bugfix for piecewise functions (#1199)
- Refactor swigging - generate one single wrapper (#1213)

C++

- Fix warnings: account for zero indexing in nan/inf error (#1112)

Doc

- Update Windows build instructions (#1200, #1202)
- Update README: Projects using AMICI (#1209)
- Add CODE_OF_CONDUCT.md (#1210)
- Update documentation for Python interface (#1208)

CI

- Create sdist on GHA using swig4.0.1 (#1204) (Fixing broken pypi package)
- Fix links after repository move
- Speed-up swig build: disable all languages except python (#1211)
- Fix doc generation on readthedocs (#1196)

7.2.24 v0.11.5 (2020-08-07)

General

- Move repo to new organization (#1193)
- Update Bibliography

Python

- Fix bug for energyPySB models (#1191)

CI

- Fix release deployment (#1189)

7.2.25 v0.11.4 (2020-08-06)

Python

- Skip unnecessary expressions in pysb models (#1185)
- MSVC compiler support (this time for real… #1152)

CI

- Implement MSVC tests (#1152)
- Rename and group GitHub actions (#1186)
- Fix release deployment (#1186)

7.2.26 v0.11.3 (2020-08-06)

Python

- Fix simplification for pysb models (#1168)
- Pass verbosity flags to pysb network generation (#1173)
- Enable experimental pysb-petab support (#1175)
- Add installation instructions for Fedora (#1177)
- Implement support for SBML rate-references (#1180)

C++

- Refactoring (#1162, #1163)

CI

- Move majority of tests to Github Actions (#1166, #1160)
- Improve reporting of skipped tests in SBML testsuite (#1183)

7.2.27 v0.11.2 (2020-07-17)

Python

- Speed up model import, compilation (#1123, #1112)
- Improve/Add steady-state solver documentation (#1102)
- Improve extension import (#1141)
- Bugfixes SBML import (#1135, #1134, #1145, #1154)
- Fixed issue that prevented simplification (#1158)

C++

- Bugfixes (#1121, #1125, #1131, #1132, #1136)
- Enable openMP by default (#1118)
- Improve memoy footprint for simulations with replicates (#1153)
- Improve steady-state solver and add option to to adjoint-steadystate hybrid (#1143, #1099, #1129, #1146)

CI

- Store build artifacts from github actions (#1138)

7.2.28 v0.11.1 (2020-06-05)

Python

- Upgrade to sympy 1.6.0, which is now required minimum version (#1098, #1103)
- Speed up model import
  - Speed-up computation of sx0, reduce file size (#1109)
  - Replace terribly slow sympy.MutableDenseMatrix.is_zero_matrix by custom implementation (#1104)
- speedup dataframe creation in `get*AsDataFrame` (#1088)
- Allow caching edatas for simulate_petab (#1106)
- Fix wrong deprecation warning (Fixes #1093)
- Fix segmentation faults in NewtonSolver under certain conditions (#1089, #1090, #1097)
- fix wrong power function call in `unscale_parameter` (#1094)
- Fix MathML conversion (#1086)
- Fix deepcopy of SymPy objects (#1091)

Matlab

- handle empty rdata->{pre|post}eq_numlinsteps (Closes #1113), which previously made the matlab interface unusable
- Fix generation of compileMexFile.m for matlab compilation of python code (#1115)

C++

- Reduce memory requirements and speedup compilation of large models (#1105)
- Place generated code into own namespace (#937) (#1112)
- Fix several msvc compiler warnings (#1116) (Note that MSVC support is still experimental) **breaking change for users of C++ interface**
- Fix swig warning: ensure base class ContextManager is known before use (Fixes #1092) (#1101)

CI

- Don't install/run valgrind on travis CI (done with github actions… (#1111)

7.2.29 v0.11.0 (2020-05-10)

Python:

- **Implement support for variable compartments (#1036)**
- Better handling of constant species (#1047)
- **Better handling of C++ enums, this makes `amici.SensitivityMethod_forward` available as `amici.SensitivityMethod.forward` (#1042)**
- Improve installation routines (#1055, #1056, #1058, #1076)
- Add option to reduce memory usage (#1044)
- **Fix handling of symbolic expressions in nested rules (#1081, 1069)**

Library:

- Update Sundials to 5.2.0 (#1039)
- Update SuiteSparse to 5.4.0 (#1040)
- Refactor use of ReturnData, now completely created post-hoc (#1002)
- **Fix propagation of reinitialization in ExpData constructor (#1041)**
- **Fix issue where InternalSensitivityParameter was sometimes not set (#1075)**
- **Fix or disable certain combinations of equilibraition, presimulation and adjoint sensitivity analysis**

CI:

- Move from Codacy to Sonarcloud (#1065)
- Run SBML Testsuite when appropriate (#1058)

7.2.30 v0.10.21 (2020-04-04)

Library:

- Fix: Handle paths with blanks in build scripts
- Feature: Add function to write amici::Solver settings to HDF5 (#1023)
- Fix: typehints (#1018, #1022)
- Refactor: Move creation of parameter mapping for objective<->simulation to classes (#1020)

CI:

- Refactor: Cleanup and reorganize tests (#1026)
- Fix: benchmark problem test should fail on missing files (Closes #1015)

7.2.31 v0.10.20 (2020-03-18)

- Fixed (re)initialization of sensitivities if ExpData::fixedParametersPreequilibration is set (#994)
- Fixed sensitivities for parameters in sigma expressions for Python/SBML in case provided expression was not just a single parameter ID
- Enable parallel compilation of model files from Python (#997) based on AMICI_PARALLEL_COMPILE enviroment variable
- Fixed computation of log-likelihood for log10-normal distributed noise
- Added `reinitializeFixedParameterInitialStates` to ExpData (#1000) (**breaking change**: overrides settings in `amici::Model`)
- Python model import now verifies that chosen model name is a valid identifier (Closes #928)
- Made w available in ReturnData (Closes #990) (#992)
- Fixed setting of log level when passing boolean values to verbose (#991)
- Documentation now on ReadTheDocs https://amici.readthedocs.io/en/
- Use proper state/observable names in plotting functions (#979)
- PEtab support:
  - Adapt to most recent PEtab (0.1.5)
  - Extended support for import of PEtab models
  - Added support for computing cost function based on PEtab problem
  - Implemented handling of species in condition table
  - petab_import.import_model now provides reproducible parameter list (Closes #976)
  - Fix python import error in import_petab_problem: Add absolute paths to python path, invalidate caches and reload (#970)
  - Added example notebook
- CI: PEtab test suite integrated in CI workflow
- Added AMICI dockerfile and image deployment to dockerhub (#948)
- Removed mention of 'mex' in warning/error ids (#968)
- More informative errors on SWIG interface import failures (#959)

7.2.32 v0.10.19 (2020-02-13)

Python:

- Fix logo display on pypi
- Fix deadlocks in multithreaded python environments when using openMP parallelization

Matlab:

- Fix compilation errors due to switch to C++14

7.2.33 v0.10.18 (2020-02-11)

General:

- AMICI now comes with a logo
- implement getName function for models
- Updated documentation / examples

Python:

- Enable MSVC compilation of Python extensions (#847)
- Always recompile clibs and extensions (Closes #700)
- Extended PEtab support (Running
- enable multithreading in swig (#938)
- Fixes pysb (#902) (#907)

C++

- Build optimized AMICI and sundials by default (Closes #934)

Matlab:

- Fix(matlab) Compile CalcMD5 on demand (Fixes #914)
- Don't pass empty include strings to mex
- Fix Matlab compilation error if AMICI or model path contains blanks

CI:

- Running additional test models

… and various minor fixes/updates

7.2.34 v0.10.17 (2020-01-15)

- **added python 3.8 support, dropped python 3.6 support** (#898)
- Added logging functionality (#900)
- Fixes PySB import (#879, #902)
- Fixes symbolic processing (#899)
- Improved build scripts (#894,
- Improved petab support (#886, #888, #891)

- CI related fixes (#865, #896)

7.2.35 v0.10.16 (2019-12-11)

- **Sparsify dwdp to reduce computation time for adjoints (#858)**
- Fix(matlab) update example name example_dae_events->example_calvetti (Closes #866)
- Fix nullptr deferencing for simulations with events when no measurements are provided (Fixes #866)
- Fix accessing empty vector during adjoint state event update (Closes #866)
- Fix pysb_import (fixes #878)

7.2.36 v0.10.15 (2019-12-03)

Bugfix release due to incorrect sensitivities w.r.t. sigmas introduced in 0.10.14.

No other changes.

7.2.37 v0.10.14 (2019-12-02)

NOTE: For Python-imported SBML-models this release may compute incorrect sensitivities w.r.t. sigma. Bug introduced in 0.10.14, fixed in 0.10.15.

Python:

- Don't require use of ModelPtr.get to call ExpData(Model)
- Fix import in generated model Python package
- Setup AMICI standalone scripts as setuptools entrypoints
- Simplify symbolic sensitivity expressions during Python SBML import Fixes Infs in the Jacobian when using Hill-functions with states of 0.0.
- Extended Newton solver #848 The changes that allow performing Newton tests from the paper: G. T. Lines, Ł. Paszkowski, L. Schmiester, D. Weindl, P. Stapor, and J. Hasenauer. Efficient computation of steady states in large-scale ODE models of biochemical reaction networks. accepted for Proceedings of the 8th IFAC Conference on Foundations of Systems Biology in Engineering (FOSBE), Valencia, Spain, October 2019.
- Use SWIG>=4.0 on travis to include PyDoc in sdist / pypi package (#841)
- **Fix choice of likelihood formula; failed if observable names were not equal to observable IDs**
- Fix(sbml-import) Compartment IDs in right-hand side of Rules are not replaced and lead to undefined identifiers in c++ files
- Fix invalid logging level
- Speed up sympy simplification (#871)

C++:

- Performance: Avoid unnecessary repeated function calls for SUNMatrixWrapper dimensions
- Add AmiciApplication class as context for handling so far global settings. This allows for example setting custom logging functions for concurrent AMICI runs, e.g. in multi-thread applications (Closes #576).

Misc:

- Setup performance test on github actions (#853)

- Update documentation and FAQ for CBLAS requirement and others
- Update reference list

7.2.38 v0.10.13 (2019-10-09)

- BREAKING CHANGE: Renaming {get|set}tNewtonPreequilibration to {get|set}Preequilibration (Closes #720)
- Make wurlitzer non-optional requirement for AMICI python package (Fixes missing AMICI errors when running from jupyter notebooks)
- Compute initial state for Model::getInitialStates if not already set (Fixes #818)
- Make swig generate pydoc comments from doxygen comments #830 (Closes #745) to provide Python docstrings for C++ wrapper functions
- feature(cmake) Add option to disable compiler optimizations for wrapfunctions.cpp (Fixes #828) (#829)
- Change SBML test suite to pytest to allow for parallel test execution… (#824)
- Fix(cmake): -E option is not available in all sed versions. Neither is the equivalent -r. Use –regexp-extended instead (Closes #826)
- Refactor(python) Move PEtab import code from command line script… (#825)
- Fix(core) Fix regular expressions for intel compiler (Closes #754) (#822)
- Update workflow figure to include PySB (Closes #799)
- Fix compiler warnings

7.2.39 v0.10.12 (2019-09-28)

- Fix handling of species specified in PEtab condition table (#813)
- Fix some Visual C++ issues, update cppcheck handling, cleanup (VisualC++ still not fully supported)
- Minor fixups (#801)
- Create SBML test suite result files for upload to http://sbml.org/Facilities/Database/ (#798)

7.2.40 v0.10.11 (2019-08-31)

- Fixed setting initial conditions for preequilibration (#784)
- Fixed species->parameter conversion during PEtab import (#782)
- Set correct Matlab include directories in CMake (#793)
- Extended and updated documentation (#785, #787)
- Fix various SBML import issues
- Run SBML test suite using github actions instead of travisCI (#789)

7.2.41 v0.10.10 (2019-08-07)

- Simplify/fix AMICI installation
  - If available use environment modules to detect dependencies
  - Add SWIG installation script
- Update list of publication
- Update documentation
  - Update doc for SWIG build and custom SWIG location.
  - Add AMICI interface overview / workflow figure and show in README
  - Document environment variables for model/core compilation (Closes #737)
- Added handling of abs function, since there seem to be problems with case sensitivity (#713) Closes #770

Detaills: * cmake: Use package_ROOT environment variables * fix(cmake) Fix finding version.txt * cmake: Auto-detect loaded MKL environment module * cmake: Use new FindPython3 modules where possible * fix(python) Restore python3.6 compatibility * Inside venv, use pip instead of pip3 which should point to the correct version * fix(python) Workaround for missing ensurepip during venv creation [ci skip] * feature(python) Use MKL from environment modules to provide cblas * fix(python) Fix define_macros not being passed to setuptools for Extension * fix(python) Fix define_macros not being passed to setuptools for clibs * Do not always add 'cblas' library since users may want to override that by a cblas-compatible library with a different name (closes #736) * Update HDF5 path hints; use shared library if static is not available. * Check for HDF5_BASE from environment module * Fix system-dependent sundials library directory (Fixes #749) (#750) * Handle OSTYPE==linux in scripts/buildBNGL.sh (Fixes #751) * Add SWIG download and build script * Improve finding swig executable and allow user override via SWIG environment variable * Provide installation hints if no SWIG found (Closes #724) * Allow overriding cmake executable with environment variables in build scripts (Closes #738)

7.2.42 v0.10.9 (2019-07-24)

Fixup for missing version bump in v0.10.8 release. No code changes compared to v0.10.8.

7.2.43 v0.10.8 (2019-07-24)

Changes in this release:

All:

- Updated / extended documentation
- Fix reuse of `Solver` instances (#541)

C++:

- Check for correct AMICI version for model in CMake
- Add reporting of computation times (#699)

Python:

- Fix manifest file (#698)
- Fix initial amounts/concentrations in SBML import

… and various other minor fixes/improvements

7.2.44 v0.10.7 (2019-05-01)

Python

- fix unset noise distribution when automatically generating observables in case None are passed (#691)

7.2.45 v0.10.6 (2019-04-19)

C++

- Add SuperLUMT support (#681)
- Sparsified dJydy (#686)
- Enabled support of impulse-free events for DAE models (#687) - thanks to Sebastien Sten for providing a testcase for this

Python

- Enabled support for piecewise functions in SBML import (#662)
- Fix numeric type when constructing ExpData from Dataframes (#690)
- Fix dynamic override in PETab

7.2.46 v0.10.5 (2019-04-08)

Bugfix release

Doc

- Update documentation of Windows installation

C++

- Fix missing source files in CMakeLists.txt (#658)
- Set CMake policies to prevent warnings (Closes #676) (#677)
- Start using gsl::span instead of raw pointers (#393) (#678)

Python

- PySB parsing fix (#669)
- Fix failure to propagate BLAS_LIBS contents (#665)
- Require setuptools at setup (#673)
- Updated PEtab import to allow for different noise models

7.2.47 v0.10.4 (2019-03-21)

Features / improvements:

- Implement ReturnData and ExpData wrappers as more efficient views (#657)
- Add list of references using AMICI (#659)
- Custom llh (normal/laplace, lin/log/log10) (#656)

Bugfixes:

- Speedup and fix travis build

7.2.48 v0.10.3 (2019-03-13)

Features / improvements:

- adds the option for early termination on integration failures for runAmiciSimulations
- improve runtime of `SUNMatrixWrapper::mutliply`
- expose finite difference routines in public API
- enable parallel compilation of clib source files

Bugfixes:

- fixed symbolic processing for unreleased pysb features

7.2.49 v0.10.2 (2019-03-07)

Features / improvements:

- extended `ExpData` interface to allow for condition specific parameters, parameter scales, parameter lists, initial conditions and initial condition sensitivities.

Bugfixes:

- fixed output values of `ReturnData::x_ss` and `ReturnData::sx_ss`

7.2.50 v0.10.1 (2019-03-04)

- travis-ci.com migration
- fix problem with has{variable} functions
- allow to import sbml model from string, not only file

7.2.51 v0.10.0 (2019-03-01)

Features / improvements:

- updated sundials to 4.1.0
- updated SuiteSparse to 5.4.0
- added generic implementations for symbolic expressions that were sparse matrix vector products

Bugfixes:

- fixed return value of `rz` when no data is provided.

7.2.52 v0.9.5 (2019-02-26)

Features / improvements:

- allow python installations without compilation of c++ extension
- improvements to ExpData <-> pandas.DataFrame interface
- allow generation of matlab models from python
- implement CLI interface for PEtab
- improve computation time for conservation laws from pysb import

Bugfixes:

- Fix sign in undamped Newton step.

Maintenance:

- use newer CI images

7.2.53 v0.9.4 (2019-02-11)

Minor fixes only:

- fix(core) Get solver diagnostics for first(last) timepoint (#588) (Closes #586)
- fix(ci) Fix autodeploy (Closes #589)

7.2.54 v0.9.3 (2019-02-07)

CRITICAL FIXES

- **fix(python) fix symbolic computations for adjoint (#583)**

Features

- feature(python) Check for matching AMICI versions when importing model (Closes #556). Set exact AMICI version as model package requirement.
- feature(core) Add option to rethrow AMICI exception (Closes #552)
- feature(python) Redirect C/C++ output in stdout is redirected (e.g. in ipython notebooks) (Closes #456)

Minor fixes

- fix(python) Fix doc and rename sys_pipes to something more meaningful
- fix(ci) Fix premature exit of scripts/runNotebook.sh
- fix(deploy) Update pyenv shims to find twine

7.2.55 v0.9.2 (2019-01-30)

Bugfixes:

- fixes a critical bug in the newton solver
- fixes multiple bugs in sbml import for degenerate models, empty stoichiometry assignments and conversion factors
- improved error messages for sbml import
- #560
- #557
- #559

7.2.56 v0.9.1 (2019-01-21)

Features / improvements:

- make pure steadystate results available as `rdata['x_ss']` and `rdata['sx_ss']`
- add option to specify integration tolerances for the adjoint problem via `atolB` and `rtolB`

Bugfixes:

- improved conservation law identification to also account for constant species.
- fixed a bug where simulation results were written into results of the second newton solver attempt
- fixed an openMP related warning

Maintenance:

- attempt to fix automatic deploy to pypi via travis

7.2.57 v0.9.0 (2019-01-18)

Features / improvements:

- Allow computation and application of conservation laws for pysb importet models. This enables use of NewtonSolver for preequilibration for models where it was previously not possible.
- Use `klu_refactor` in the sparse Newton solver instead of always using `klu_factor` and only perform symbolic factorization once (#421)
- Allow more detailed finiteness checks (#514)

Bugfixes:

- #491

Maintenance:

- Several improvements to travis log sizes and folding
- Use default copy constructor for Model by implementing class wrappers for sundials matrix types (#516)
- Reenable run of SBML testsuite

7.2.58 v0.8.2 (2019-01-07)

Features / improvements:

- Speedup symbolic processing for ODE generation in python

Bugfixes:

- Fix(python) Add missing deepcopy (introduced in 6847ba675f2088854db583199b8754aaa6e01576)
- Fix(core) Prevent parameter scaling length mismatch (#488)
- Fix(python) Set distutils dependency to current version to fix </usr/lib/python3.6/distutils/dist.py:261: UserWarning: Unknown distribution option: 'long_description_content_type'>
- fix(python) add symlink to version.txt to be included in package

Backwards-compatibility:

- Replace 'newline' by literal to restore <R2016b compatibility (Fixes #493)

Maintenance:

- Remove obsolete swig library build via cmake and related file copying
- Provide issue template for bug reports
- Providing valid SBML document to import is not optional anymore
- Update documentation and tests
- Add python version check and raise required version to 3.6 to prevent cryptic error messages when encountering f-strings

7.2.59 v0.8.1 (2018-11-25)

- [all] **critical** Fix long standing bugs in solving steadystate problems (including preequilibration) (#471)
- [all] Fix AmiVector constructor from std::vector (#471)
- [python] Reenable Solver and Model copy constructors
- Update documentation

7.2.60 v0.8.0 (2018-11-25)

- replaced symengine by sympy for symbolic processing in python *which fixes several critical bugs* that were due to bugs in symengine (#467)

7.2.61 v0.7.13 (2018-11-18)

- fixes a critical bug in objective function computation for models compiled using `sbml2amici` and `pysb2amici` that was introduced in v0.7.12
- fixes a critical bug in sensitivity computation when`model.reinitializeFixedParameterInitialStates` was set to true
- readds the python interface to the ExpData copy constructor that was inadvertently removed in 0.7.12 and streamlines the respective convenience wrapper to provide access to the full range of constructors.

7.2.62 v0.7.12 (2018-11-17)

- fixed a critical bug in `amici.constructEdataFromDataFrame`
- enabled multithreaded simulation of multiple experiments (requires compilation with openMP)
- modularized sbml import and added pysb import

7.2.63 v0.7.11 (2018-10-15)

- [python] Added numpy and python wrappers that provide a more user friendly python API
- [python] Enable import of SBML models with non-float assignment rules
- [python] Enable handling of exceptions in python
- [python] Enable nativ python access to std::vector data-structures
- [core] Provide an API for more fine-grained control over sensitivity tolerances and steady-state tolerances
- [core] Provide an API to specify non-negative state variables (this feature is still preliminary)

7.2.64 v0.7.10 (2018-08-29)

- Fixed python SBML import `log()` issues (#412)

7.2.65 v0.7.9 (2018-08-24)

- fixes MATLAB compilation of models
- adds option to perform steady state sensitivity analysis via FSA
- condition dependent intitial conditions are now newly set after preequilibration is done

7.2.66 v0.7.8 (2018-08-19)

- bugfixes for the ExpData interface
- created build configuration that enables debugging of c++ extensions on os x
- fixed python sbml import when stoichiometry is empty

7.2.67 v0.7.7 (2018-08-17)

Fixes a couple of bugs just introduced in v0.7.6

7.2.68 v0.7.6 (2018-08-13)

Important: **Use AMICI v0.7.7 due to https://github.com/ICB-DCM/AMICI/pull/403/commits/3a495d3db2fdbba70c2b0d52a3d465**

Bug fixes:

- Python import: Fix log10 issues in observables (#382)
- Matlab: Fix broken model compilation (#392)
- Fixed simulation for models without observables (#390)
- Fixed potential matlab memory leaks (#392)

Breaking C++ API changes:

- Revised ExpData interface (#388)

7.2.69 v0.7.5 (2018-07-30)

Features/enhancements:

- Add computation of residuals, residuals sensitivity, Fisher information matrix (#223)
- More efficient conversion of std::vector to numpy ndarray (#375)
- Allow specifying timepoints in ExpData (#370)

Minor fixes:

- Condition parameters in ExpData now only temporarily override Model parameters (#371)
- Ensure non-negative states for Newton solver (#378)

7.2.70 v0.7.4 (2018-07-27)

Features/enhancements:

- Check SBML model validity (#343)
- Allow per-parameter setting of amioptions::pscale from matlab interface (#350)
- Documentation

Major fixes:

- Don't compile main.cpp into python model module which broke modules if amici was compiled without libhdf5 (#363)

Minor fixes:

- Fix compiler warnings (#353)
- Plotting, SBML example mode, …

7.2.71 v0.7.3 (2018-07-13)

Features:

- Added symbol names to python-wrapped models and make available via Model.getParameterNames(), model.getStateNames(), ...
- Extended Python interface example

Python package available via pypi: https://pypi.org/project/amici/0.7.3/

7.2.72 v0.7.2 (2018-07-03)

Features:

- Python package: more flexible HDF5 library localization
- Extended CI: python tests, preequilibration tests, run in venv

Major bugfixes:

- Fix python sbml model import / compilation error (undefined function)
- Fix model preequilibration

Minor fixes:

- Various fixes for mingw compilation of python source distribution
- Cmake compatibility with < 3.8 restored

7.2.73 v0.7.1 (2018-06-12)

Features:

- Allow specifying sigma-parameters from Python interface

Major bugfixes:

- Fix dsigma_y/dp and downstream sensitivity errors

7.2.74 v0.7.0 (2018-06-09)

- Major revision of documentation
- Improved Python interface
- More comprehensive Python interface example
- Fixed sensitivity computation in Python-generated models
- Various other bug fixes

WARNING:

- For models with sigma-parameters and dsigma_y/dp != 0, dsigma_y/dp was computed incorrectly. This propagates to all dependent sensitivities. This applies also to some older releases and has been fixed in v0.7.1.

7.2.75 v0.6.0 (2018-05-22)

Implement experimental support for python via swig. Python interface is now usable, but API will still receive some updates in the future.

WARNING:

- There is a bug in sensitivity computation for Python-generated models
- Matlab C++ compilation will fail due to undefined M_PI -> Please use v0.7.0

7.2.76 v0.5.0 (2018-03-15)

Main new features are:

- Reimplemented support for DAE equations
- Added newton solver for steady state calculation and preequilibration
- Better caching for recompilation of models
- Blas support to allow compilation of large models with many observables
- Improved SBML support
- Added c++ interface
- Added support for second order adjoint computation
- Rewrote large parts of the code as proper c++11 code to allow easier code maintanance
- Substantially extended testing in continuous integration to assure code quality

7.2.77 v0.4.0 (2017-05-15)

- First citable version of AMICI (via zenodo integration).
- Better support for standalone compilation
- Improved SBML import scripts
- General Code Cleanup

7.2.78 v0.3.0 (2016-09-05)

This update comes with many improvements, bug fixes and several new features. Most notably:

1. AMICI should now run on older versions of MATLAB (back to R2014a)
2. AMICI now compiles using older versions of Visual Studio
3. AMICI now also supports second order adjoint sensitivities (full (via the o2flag = 1 and as a vector product via o2flag = 2)
4. AMICI now supports more SBML, SBML v2 and rate rules

7.2.79 0.2.1 (2016-05-09)

Bugfix release. This release also includes some changes that should improve the performance on the new R2016a release of MATLAB.

7.2.80 v0.2 (2016-03-17)

This update comes with many improvements to the computation time for both compilation and simulation. Moreover several new features were included:

1. Hessian Vector products for second order forward sensitivities
2. Correct treatment of parameter/state dependent discontinuities for both forward and adjoint sensitivities

7.2.81 v0.1 (2015-11-05)

This is the initial release of the toolbox

CHAPTER

EIGHT

GLOSSARY

BNGL
: BioNetGenLanguage is a language for modular, structure-based modeling of biochemical reaction networks.

CVODES
: CVODES is a solver for stiff and non-stiff *ODE* systems with sensitivity analysis capabilities and is used by AMICI. It is part of the *SUNDIALS* solver suite.

DAE
: Differential-Algebraic Equation

fixed parameters
: In AMICI, *fixed parameters* are parameters with respect to which no sensitivities are computed. They usually correspond to experimental conditions. For fixed parameters, different values can be set for *preequilibration*, *presimulation* and simulation.

IDAS
: IDAS is a solver *DAE* systems with sensitivity analysis capabilities and is used by AMICI. It is part of the *SUNDIALS* solver suite.

ODE
: Ordinary Differential Equation

PEtab
: PEtab is a format for specifying parameter estimation problems. It is based on an *SBML* model and tab-separated value files specifying the observation model and experimental conditions.

preequilibration
: Simulating or solving the dynamical system for the steadystate.

presimulation
: Simulation for a fixed time before the regular simulation. Can be used to specify pretreatments.

PySB
: PySB is a tool for specifying rule-based systems biology models as Python code.

SBML
: The Systems Biology Markup Language is a commonly used format for specifying systems biology models.

SUNDIALS
: SUNDIALS: SUite of Nonlinear and DIfferential/ALgebraic equation Solvers. Provides the *CVODES* and *IDAS* solvers used by AMICI.

SWIG
: SWIG is a tool that creates interfaces for C(++) code to a variety of languages. Much of the AMICI Python interface is generated by SWIG.

CHAPTER

NINE

CONTRIBUTING

9.1 Contributing to AMICI

We are happy about contributions to AMICI in any form, be it new functionality, documentation, bug reports, or anything else.

If you would to contribute to AMICI, a good start is looking for issues tagged `good first issue` or `help wanted`. For other ideas or questions, just post an issue.

For code contributions, please read our developer's guide first.

9.2 Code of Conduct

9.2.1 Our Pledge

In the interest of fostering an open and welcoming environment, we as contributors and maintainers pledge to making participation in our project and our community a harassment-free experience for everyone, regardless of age, body size, disability, ethnicity, sex characteristics, gender identity and expression, level of experience, education, socio-economic status, nationality, personal appearance, race, religion, or sexual identity and orientation.

9.2.2 Our Standards

Examples of behavior that contributes to creating a positive environment include:

- Using welcoming and inclusive language
- Being respectful of differing viewpoints and experiences
- Gracefully accepting constructive criticism
- Focusing on what is best for the community
- Showing empathy towards other community members

Examples of unacceptable behavior by participants include:

- The use of sexualized language or imagery and unwelcome sexual attention or advances
- Trolling, insulting/derogatory comments, and personal or political attacks
- Public or private harassment
- Publishing others' private information, such as a physical or electronic address, without explicit permission
- Other conduct which could reasonably be considered inappropriate in a professional setting

9.2.3 Our Responsibilities

Project maintainers are responsible for clarifying the standards of acceptable behavior and are expected to take appropriate and fair corrective action in response to any instances of unacceptable behavior.

Project maintainers have the right and responsibility to remove, edit, or reject comments, commits, code, wiki edits, issues, and other contributions that are not aligned to this Code of Conduct, or to ban temporarily or permanently any contributor for other behaviors that they deem inappropriate, threatening, offensive, or harmful.

9.2.4 Scope

This Code of Conduct applies both within project spaces and in public spaces when an individual is representing the project or its community. Examples of representing a project or community include using an official project e-mail address, posting via an official social media account, or acting as an appointed representative at an online or offline event. Representation of a project may be further defined and clarified by project maintainers.

9.2.5 Enforcement

Instances of abusive, harassing, or otherwise unacceptable behavior may be reported by contacting the project team at froehlichfab@gmail.com. All complaints will be reviewed and investigated and will result in a response that is deemed necessary and appropriate to the circumstances. The project team is obligated to maintain confidentiality with regard to the reporter of an incident. Further details of specific enforcement policies may be posted separately.

Project maintainers who do not follow or enforce the Code of Conduct in good faith may face temporary or permanent repercussions as determined by other members of the project's leadership.

9.2.6 Attribution

This Code of Conduct is adapted from the Contributor Covenant, version 1.4, available at https://www.contributor-covenant.org/version/1/4/code-of-conduct.html

For answers to common questions about this code of conduct, see https://www.contributor-covenant.org/faq

CHAPTER

TEN

PYTHON INTERFACE

10.1 Installing the AMICI Python package

10.1.1 Short guide

Installation of the AMICI Python package has the following prerequisites:

- Python>=3.9
- *SWIG*>=3.0
- CBLAS compatible BLAS library (e.g., OpenBLAS, CBLAS, Atlas, Accelerate, Intel MKL)
- a C++17 compatible C++ compiler and a C compiler (e.g., g++>=9.1, clang>=12, Intel C++ compiler, mingw)

If these requirements are fulfilled and all relevant paths are setup properly, AMICI can be installed using:

```
pip3 install amici
```

If this worked, you can now import the Python module via:

```
import amici
```

If this does not work for you, please follow the full instructions below.

10.1.2 Installation on Linux

Ubuntu 22.04

Install the AMICI dependencies via `apt` (this requires superuser privileges):

```
sudo apt install libatlas-base-dev swig

# optionally for HDF5 support:
sudo apt install libhdf5-serial-dev

 # optionally for boost support (thread-specific CPU times, extended math functions,␣
↪serialization)
 libboost-chrono-dev libboost-math-dev libboost-serialization-dev
```

Install AMICI:

```
pip3 install amici
```

Fedora 32

Install the AMICI dependencies via `apt` (this requires superuser privileges):

```
sudo dnf install blas-devel swig
```

Install AMICI:

```
pip3 install amici
```

Arch Linux

Install the AMICI dependencies via `pacman` (this requires superuser privileges):

```
sudo pacman -S python swig openblas gcc hdf5 boost-libs
```

Export the bash variables `BLAS_CFLAGS` and `BLAS_LIBS` to point to where BLAS was installed, e.g.:

```
export BLAS_CFLAGS="-I/usr/include/openblas/"
export BLAS_LIBS="-lopenblas"
```

Install AMICI:

```
pip3 install amici
```

Alternatively:

1. Check if packages are already installed with the required versions for AMICI installation.

```
sudo pacman -Si python swig openblas gcc hdf5 boost-libs
```

2. Upgrade installed packages if required mininum versions are not satisfied for AMICI installation.

```
sudo pacman -Su python swig openblas gcc hdf5 boost-libs
```

3. Export the bash variables `BLAS_CFLAGS` and `BLAS_LIBS` to point to where BLAS was installed, e.g.:

```
export BLAS_CFLAGS="-I/usr/include/openblas/"
export BLAS_LIBS="-lopenblas"
```

4. Install AMICI:

```
pip3 install amici
```

10.1.3 Installation on OSX

Install the AMICI dependencies using homebrew:

```
brew install swig

# optionally for HDF5 support:
brew install hdf5

# optionally for parallel simulations:
brew install libomp
# followed by either `brew link openmp` once,
# or `export OpenMP_ROOT=$(brew --prefix)/opt/libomp"` where `OpenMP_ROOT` will have to␣
↪be set during every re-installation of AMICI or any new model import

# optionally for boost support (thread-specific CPU times, extended math functions,␣
↪serialization)
brew install boost && export BOOST_ROOT=$(brew --prefix)/opt/boost
# followed by either `brew link boost` once,
# or `export BOOST_ROOT=$(brew --prefix)/opt/boost"` where `BOOST_ROOT` will have to be␣
↪set during every re-installation of AMICI or any new model import
```

Install AMICI:

```
pip3 install amici
```

10.1.4 Installation on Windows

Some general remarks:

- Consider using the Windows Subsystem for Linux (WSL) and follow the instructions for installation on linux.
- Install all libraries in a path not containing white spaces, e.g. directly under C:.
- Replace the following paths according to your installation.
- Slashes can be preferable to backslashes for some environment variables.
- See also [#425](https://github.com/AMICI-dev/amici/issues/425) for further discussion.

Using the Microsoft Visual Studio

We assume that Visual Studio (not to be confused with Visual Studio Code) is already installed. Using Visual Studio Installer, the following components need to be included:

- Microsoft Visual C++ (MSVC). This is part of multiple packages, including Desktop Development with C++.
- Windows Universal C Runtime. This is an individual component and installs some DLLs that we need.

OpenBLAS

There are prebuilt OpenBLAS binaries available, but they did not seem to work well here. Therefore, we recommend building OpenBLAS from scratch. This requires an installation of CMake. CMake can be installed from https://cmake.org/download/ (system-wide), or via `pip install cmake` (in the current Python environment).

To build OpenBLAS, download the following scripts from the AMICI repository:

- https://github.com/AMICI-dev/AMICI/blob/master/scripts/installOpenBLAS.ps1
- https://github.com/AMICI-dev/AMICI/blob/master/scripts/compileBLAS.cmd

The first script needs to be called in Powershell, and it needs to call `compileBLAS.cmd`, so you will need to modify line 11:

    cmd /c "scriptscompileBLAS.cmd $version"

Additionally, in `compileBLAS.cmd` make sure that you point to your Visual Studio installation on line 3. Newer installations could be located under `C:\Program Files\Microsoft Visual Studio\...\VC\Auxiliary\Build\vcvars64.bat`.

so that it matches your directory structure. This will download OpenBLAS and compile it, creating

    C:\BLAS\OpenBLAS\lib\openblas.lib C:\BLAS\OpenBLAS\bin\openblas.dll

You will also need to define two environment variables:

```
BLAS_LIBS="-LIBPATH:C:/BLAS/OpenBLAS/lib openblas.lib"
BLAS_CFLAGS="-IC:/BLAS/OpenBLAS"
```

One way to do that is to run a PowerShell script with the following commands:

```
[System.Environment]::SetEnvironmentVariable("BLAS_LIBS", "-LIBPATH:C:/BLAS/OpenBLAS/lib␣
↪openblas.lib", [System.EnvironmentVariableTarget]::User)
[System.Environment]::SetEnvironmentVariable("BLAS_LIBS", "-LIBPATH:C:/BLAS/OpenBLAS/lib␣
↪openblas.lib", [System.EnvironmentVariableTarget]::Process)
[System.Environment]::SetEnvironmentVariable("BLAS_CFLAGS", "-IC:/BLAS/OpenBLAS/include/
↪openblas", [System.EnvironmentVariableTarget]::User)
[System.Environment]::SetEnvironmentVariable("BLAS_CFLAGS", "-IC:/BLAS/OpenBLAS/include/
↪openblas", [System.EnvironmentVariableTarget]::Process)
```

The call ending in `Process` sets the environment variable in the current process, and it is no longer in effect in the next process. The call ending in `User` is permanent, and takes effect the next time the user logs on.

Now you need to make sure that all required DLLs are within the scope of the `PATH` variable. In particular, the following directories need to be included in `PATH`:

    C:\BLAS\OpenBLAS\bin C:\Program Files (x86)\Windows Kits\10\Redist\ucrt\DLLs\x64

The first one is needed for `openblas.dll` and the second is needed for the Windows Universal C Runtime.

If any DLLs are missing in the `PATH` variable, Python will return the following error upon `import amici`:

    ImportError: DLL load failed: The specified module could not be found.

Almost all of the DLLs are standard Windows DLLs and should be included in either Windows or Visual Studio. But, in case it is necessary to test this, here is a list of some DLLs required by AMICI (when compiled with MSVC):

- `openblas.dll`
- `python37.dll`
- `MSVCP140.dll`

- KERNEL32.dll
- VCRUNTIME140_1.dll
- VCRUNTIME140.dll
- api-ms-win-crt-convert-l1-1-0.dll
- api-ms-win-crt-heap-l1-1-0.dll
- api-ms-win-crt-stdio-l1-1-0.dll
- api-ms-win-crt-string-l1-1-0.dll
- api-ms-win-crt-runtime-l1-1-0.dll
- api-ms-win-crt-time-l1-1-0.dll
- api-ms-win-crt-math-l1-1-0.dll

MSVCP140.dll, VCRUNTIME140.dll, and VCRUNTIME140_1.dll are needed by MSVC (see Visual Studio above). KERNEL32.dll is part of Windows and in C:\Windows\System32. The api-ms-win-crt-XXX-l1-1-0.dll are needed by openblas.dll and are part of the Windows Universal C Runtime.

Note: Since Python 3.8, the library directory needs to be set either from Python:

```
import os
# directory containing `openblas.dll`
os.add_dll_directory("C:\\BLAS\\OpenBLAS\\bin")
import amici
```

or via the environment variable AMICI_DLL_DIRS="C:\BLAS\OpenBLAS\bin".

10.1.5 Further topics

Installation of development versions

To install development versions which have not been released to PyPI yet, you can install AMICI with pip directly from GitHub using:

```
pip3 install -e git+https://github.com/AMICI-dev/amici.git@develop#egg=amici\&
↪subdirectory=python/sdist
```

Replace develop by the branch or commit you want to install.

Note that this will only work on Windows if you have enabled developer mode, because symlinks are not supported by default (more information).

Light installation

In case you only want to use the AMICI Python package for generating model code for use with Matlab or C++ and don't want to bothered with any unnecessary dependencies, you can run

```
pip3 install --install-option --no-clibs amici
```

Note: Following this installation, you will not be able to simulate the imported models in Python.

Note: If you run into an error with above installation command, install all AMICI dependencies listed in setup.py manually, and try again. (This is because `pip --install-option` is applied to *all* installed packages, including dependencies.)

Custom installation

Installation of the AMICI Python package can be customized using a number of environment variables:

Variable	Purpose	Example
`SWIG`	Path to the *SWIG* executable	`SWIG=$HOME/bin/swig4.0`
`CC`	Setting the C(++) compiler	`CC=/usr/bin/g++`
`CFLAGS`	Extra compiler flags used in every compiler invocation	
`BLAS_CFLAGS`	**Compiler flags for, e.g. BLAS** include directories	
`BLAS_LIBS`	Flags for linking BLAS	
`ENABLE_GCOV_COVERAGE`	Set to build AMICI to generate code coverage information	`ENABLE_GCOV_COVERAGE=TRUE`
`ENABLE_AMICI_DEBUGGING`	Set to build AMICI with debugging symbols	`ENABLE_AMICI_DEBUGGING=TRUE`
`AMICI_PARALLEL_COMPILE`	Set to the number of parallel processes to be used for C(++) compilation (defaults to 1)	`AMICI_PARALLEL_COMPILE=4`
`AMICI_TRY_ENABLE_HDF5`	Whether to build AMICI with HDF5-support if possible. Default: `ON`	`AMICI_TRY_ENABLE_HDF5=OFF`

Installation under Anaconda

To use an Anaconda installation of Python https://www.anaconda.com/distribution/, Python>=3.7), proceed as follows:

Since Anaconda provides own versions of some packages which might not work with AMICI (in particular the `gcc` compiler), create a minimal virtual environment via:

```
conda create --name ENV_NAME pip python
```

Here, replace `ENV_NAME` by some name for the environment.

To activate the environment, run:

```
source activate ENV_NAME
```

(and `conda deactivate` later to deactivate it again).

SWIG must be installed and available in your `PATH`, and a CBLAS-compatible BLAS must be available. You can also use conda to install the latter locally, using:

```
conda install -c conda-forge openblas
```

To make AMICI use openblas, set the following environment variable:

```
export BLAS_LIBS=-lopenblas
```

`BLAS_LIBS` needs to be set during installation of the AMICI package, as well as during any future model import.

To install AMICI, now run:

```
pip install amici
```

The `pip` option `--no-cache` may be helpful here to make sure the installation is done completely anew.

Now, you are ready to use AMICI in the virtual environment.

Note: Anaconda on Mac

If the above installation does not work for you, try installing AMICI via:

```
CFLAGS="-stdlib=libc++" CC=clang CXX=clang pip3 install --verbose amici
```

This will use the `clang` compiler.

You will have to pass the same options when compiling any model later on. This can be done by inserting the following code before model import:

```
import os
os.environ['CC'] = 'clang'
os.environ['CXX'] = 'clang'
os.environ['CFLAGS'] = '-stdlib=libc++'
```

(For further discussion see https://github.com/AMICI-dev/AMICI/issues/357)

Optional Boost support

Boost is an optional C++ dependency only required for special functions (including e.g. gamma derivatives) in the Python interface. Boost can be installed via package managers via

```
apt-get install libboost-math-dev
```

or

```
brew install boost
```

As only headers are required, also a source code download suffices. The compiler must be able to find the module in the search path.

10.2 Examples

Various example notebooks.

10.2.1 Getting Started in AMICI

This notebook is a brief tutorial for new users that explains the first steps necessary for model simulation in AMICI, including pointers to documentation and more advanced notebooks.

Model Compilation

Before simulations can be run, the model must be imported and compiled. In this process, AMICI performs all symbolic manipulations that later enable scalable simulations and efficient sensitivity computation. The first step towards model compilation is the creation of an SbmlImporter instance, which requires an SBML Document that specifies the model using the Systems Biology Markup Language (SBML).

For the purpose of this tutorial, we will use `model_steadystate_scaled.xml`, which is contained in the same directory as this notebook.

[1]:
```
import amici

sbml_importer = amici.SbmlImporter("model_steadystate_scaled.xml")
```

Next, we will compile the model as python extension using the amici.SBMLImporter.sbml2amici method. The first two arguments of this method are the name of the model, which will also be the name of the generated python module, and the model directory, which defines the directory in which the model module will be placed. Compilation will take a couple of seconds.

[2]:
```
model_name = "model_steadystate"
model_dir = "model_dir"
sbml_importer.sbml2amici(model_name, model_dir)
```

Loading the model module

To run simulations, we need to instantiate amici.Model and amici.Solver instances. As simulations require instances matching the imported model, they have to be imported from the generated model module.

[3]:
```
# load the model module
model_module = amici.import_model_module(model_name, model_dir)
# instantiate model
model = model_module.getModel()
# instantiate solver
solver = model.getSolver()
```

The model allows the user to manipulate model related properties of simulations. This includes the values of model parameters that can be set by using amici.Model.setParameterByName. Here, we set the model parameter `p1` to a value of `1e-3`.

[4]:
```
model.setParameterByName("p1", 1e-3)
```

In contrast, the solver instance allows the specification of simulation related properties. This includes setting options for the SUNDIALS solver such as absolute tolerances via amici.Solver.setAbsoluteTolerance. Here we set the absolute integration tolerances to `1e-10`.

[5]:
```
solver.setAbsoluteTolerance(1e-10)
```

Running Model Simulations

Model simulations can be executed using the amici.runAmiciSimulations routine. By default, the model does not contain any timepoints for which the model is to be simulated. Here we define a simulation timecourse with two timepoints at `0` and `1` and then run the simulation.

[6]:
```
# set timepoints
model.setTimepoints([0, 1])
rdata = amici.runAmiciSimulation(model, solver)
```

Simulation results are returned as ReturnData instance. The simulated SBML species are stored as `x` attribute, where rows correspond to the different timepoints and columns correspond to different species.

[7]:
```
rdata.x
```

[7]:
```
array([[0.1       , 0.4       , 0.7       ],
       [0.98208413, 0.51167992, 0.10633388]])
```

All results attributes are always ordered according to the model. For species, this means that the columns of `rdata.x` match the ordering of species in the model, which can be accessed as amici.Model.getStateNames

[8]:
```
model.getStateNames()
```

[8]:
```
('x1', 'x2', 'x3')
```

This notebook only explains the basics of AMICI simulations. In general, AMICI simulations are highly customizable and can also be used to simulate sensitivities. The ExampleSteadystate notebook in this folder gives more detail about the model employed here and goes into the basics of sensitivity analysis. The ExampleEquilibrationLogic notebook, builds on this by using a modified version of this model to give detailed insights into the methods and options to compute steady states before and after simulations, as well as respective sensitivities. The ExampleExperimentalConditions example notebook, goes into the details of how even more complex experimental setups, such as addition of drugs at predefined timepoints, can be simulated in AMICI. Finally, the petab notebook explains how standardized definitions of experimental data and conditions in the PEtab format can be imported in AMICI.

10.2.2 SBML import, observation model, sensitivity analysis, data export and visualization

This is an example using the [model_steadystate_scaled.sbml] model to demonstrate:

- SBML import
- specifying the observation model
- performing sensitivity analysis

- exporting and visualizing simulation results

[1]:
```
# SBML model we want to import
sbml_file = "model_steadystate_scaled_without_observables.xml"
# Name of the model that will also be the name of the python module
model_name = "model_steadystate_scaled"
# Directory to which the generated model code is written
model_output_dir = model_name

import libsbml
import amici
import numpy as np
import matplotlib.pyplot as plt
```

The example model

Here we use `libsbml` to show the reactions and species described by the model (this is independent of AMICI).

[2]:
```
sbml_reader = libsbml.SBMLReader()
sbml_doc = sbml_reader.readSBML(sbml_file)
sbml_model = sbml_doc.getModel()
dir(sbml_doc)

print("Species: ", [s.getId() for s in sbml_model.getListOfSpecies()])

print("\nReactions:")
for reaction in sbml_model.getListOfReactions():
    reactants = " + ".join(
        [
            "%s %s"
            % (
                int(r.getStoichiometry()) if r.getStoichiometry() > 1 else "",
                r.getSpecies(),
            )
            for r in reaction.getListOfReactants()
        ]
    )
    products = " + ".join(
        [
            "%s %s"
            % (
                int(r.getStoichiometry()) if r.getStoichiometry() > 1 else "",
                r.getSpecies(),
            )
            for r in reaction.getListOfProducts()
        ]
    )
    reversible = "<" if reaction.getReversible() else ""
    print(
        "%3s: %10s %1s->%10s\t\t[%s]"
        % (
            reaction.getId(),
```

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```
            reactants,
            reversible,
            products,
            libsbml.formulaToL3String(reaction.getKineticLaw().getMath()),
        )
    )
```

```
Species:  ['x1', 'x2', 'x3']

Reactions:
 r1:       2 x1  ->        x2          [p1 * x1^2]
 r2:   x1 +  x2  ->        x3          [p2 * x1 * x2]
 r3:         x2  ->      2 x1          [p3 * x2]
 r4:         x3  ->  x1 +  x2          [p4 * x3]
 r5:         x3  ->                    [k0 * x3]
 r6:             ->        x1          [p5]
```

Importing an SBML model, compiling and generating an AMICI module

Before we can use AMICI to simulate our model, the SBML model needs to be translated to C++ code. This is done by `amici.SbmlImporter`.

[3]:
```
# Create an SbmlImporter instance for our SBML model
sbml_importer = amici.SbmlImporter(sbml_file)
```

In this example, we want to specify fixed parameters, observables and a σ parameter. Unfortunately, the latter two are not part of the SBML standard. However, they can be provided to `amici.SbmlImporter.sbml2amici` as demonstrated in the following.

Constant parameters

Constant parameters, i.e. parameters with respect to which no sensitivities are to be computed (these are often parameters specifying a certain experimental condition) are provided as a list of parameter names.

[4]:
```
constant_parameters = ["k0"]
```

Observables

Specifying observables is beyond the scope of SBML. Here we define them manually.

If you are looking for a more scalable way for defining observables, then checkout PEtab. Another possibility is using SBML's `AssignmentRules <https://sbml.org/software/libsbml/5.18.0/docs/formatted/python-api/classlibsbml_1_1_assignment_rule.html>`__ to specify model outputs within the SBML file.

[5]:
```
# Define observables
observables = {
    "observable_x1": {"name": "", "formula": "x1"},
    "observable_x2": {"name": "", "formula": "x2"},
    "observable_x3": {"name": "", "formula": "x3"},
    "observable_x1_scaled": {"name": "", "formula": "scaling_x1 * x1"},
```

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```
    "observable_x2_offsetted": {"name": "", "formula": "offset_x2 + x2"},
    "observable_x1withsigma": {"name": "", "formula": "x1"},
}
```

σ parameters

To specify measurement noise as a parameter, we simply provide a dictionary with (preexisting) parameter names as keys and a list of observable names as values to indicate which sigma parameter is to be used for which observable.

[6]:
```
sigmas = {"observable_x1withsigma": "observable_x1withsigma_sigma"}
```

Generating the module

Now we can generate the python module for our model. `amici.SbmlImporter.sbml2amici` will symbolically derive the sensitivity equations, generate C++ code for model simulation, and assemble the python module. Standard logging verbosity levels can be passed to this function to see timestamped progression during code generation.

[7]:
```
import logging

sbml_importer.sbml2amici(
    model_name,
    model_output_dir,
    verbose=logging.INFO,
    observables=observables,
    constant_parameters=constant_parameters,
    sigmas=sigmas,
)
```

```
2024-03-07 23:08:57.836 - amici.sbml_import - INFO - Finished importing SBML
↪            (6.97E-02s)
2024-03-07 23:08:57.905 - amici.sbml_import - INFO - Finished processing SBML␣
↪observables            (6.34E-02s)
2024-03-07 23:08:57.913 - amici.sbml_import - INFO - Finished processing SBML event␣
↪observables      (1.85E-06s)
2024-03-07 23:08:57.962 - amici.de_model - INFO - Finished computing xdot
↪            (7.83E-03s)
2024-03-07 23:08:57.974 - amici.de_model - INFO - Finished computing x0
↪            (5.78E-03s)
2024-03-07 23:08:57.991 - amici.de_model - INFO - Finished computing w
↪            (1.07E-02s)
2024-03-07 23:08:59.213 - amici.de_export - INFO - Finished generating cpp code
↪            (1.21E+00s)
2024-03-07 23:09:14.563 - amici.de_export - INFO - Finished compiling cpp code
↪            (1.53E+01s)
```

Importing the module and loading the model

If everything went well, we can now import the newly generated Python module containing our model:

[8]:
```
model_module = amici.import_model_module(model_name, model_output_dir)
```

And get an instance of our model from which we can retrieve information such as parameter names:

[9]:
```
model = model_module.getModel()

print("Model name:      ", model.getName())
print("Model parameters:", model.getParameterIds())
print("Model outputs:   ", model.getObservableIds())
print("Model states:    ", model.getStateIds())
```

```
Model name:       model_steadystate_scaled
Model parameters: ('p1', 'p2', 'p3', 'p4', 'p5', 'scaling_x1', 'offset_x2', 'observable_
↪x1withsigma_sigma')
Model outputs:    ('observable_x1', 'observable_x2', 'observable_x3', 'observable_x1_
↪scaled', 'observable_x2_offsetted', 'observable_x1withsigma')
Model states:     ('x1', 'x2', 'x3')
```

Running simulations and analyzing results

After importing the model, we can run simulations using `amici.runAmiciSimulation`. This requires a `Model` instance and a `Solver` instance. Optionally you can provide measurements inside an `ExpData` instance, as shown later in this notebook.

[10]:
```
# Create Model instance
model = model_module.getModel()

# set timepoints for which we want to simulate the model
model.setTimepoints(np.linspace(0, 60, 60))

# Create solver instance
solver = model.getSolver()

# Run simulation using default model parameters and solver options
rdata = amici.runAmiciSimulation(model, solver)
```

[11]:
```
print(
    "Simulation was run using model default parameters as specified in the SBML model:"
)
print(dict(zip(model.getParameterIds(), model.getParameters())))
```

```
Simulation was run using model default parameters as specified in the SBML model:
{'p1': 1.0, 'p2': 0.5, 'p3': 0.4, 'p4': 2.0, 'p5': 0.1, 'scaling_x1': 2.0, 'offset_x2':␣
↪3.0, 'observable_x1withsigma_sigma': 0.2}
```

Simulation results are provided as `numpy.ndarrays` in the returned dictionary:

[12]:
```
# np.set_printoptions(threshold=8, edgeitems=2)
for key, value in rdata.items():
    print("%12s: " % key, value)
```

```
         ts:  [ 0.          1.01694915  2.03389831  3.05084746  4.06779661  5.08474576
 6.10169492  7.11864407  8.13559322  9.15254237 10.16949153 11.18644068
12.20338983 13.22033898 14.23728814 15.25423729 16.27118644 17.28813559
18.30508475 19.3220339  20.33898305 21.3559322  22.37288136 23.38983051
24.40677966 25.42372881 26.44067797 27.45762712 28.47457627 29.49152542
30.50847458 31.52542373 32.54237288 33.55932203 34.57627119 35.59322034
36.61016949 37.62711864 38.6440678  39.66101695 40.6779661  41.69491525
42.71186441 43.72881356 44.74576271 45.76271186 46.77966102 47.79661017
48.81355932 49.83050847 50.84745763 51.86440678 52.88135593 53.89830508
54.91525424 55.93220339 56.94915254 57.96610169 58.98305085 60.        ]
          x:  [[0.1        0.4        0.7       ]
[0.57995052 0.73365809 0.0951589 ]
[0.55996496 0.71470091 0.0694127 ]
[0.5462855  0.68030366 0.06349394]
[0.53561883 0.64937432 0.05923555]
[0.52636487 0.62259567 0.05568686]
[0.51822013 0.59943346 0.05268079]
[0.51103767 0.57935661 0.05012037]
[0.5047003  0.56191592 0.04793052]
[0.49910666 0.54673518 0.0460508 ]
[0.49416809 0.53349812 0.04443205]
[0.48980687 0.52193767 0.04303399]
[0.48595476 0.51182731 0.04182339]
[0.48255176 0.50297412 0.04077267]
[0.47954511 0.49521318 0.03985882]
[0.47688833 0.48840304 0.03906254]
[0.47454049 0.48242198 0.03836756]
[0.47246548 0.47716502 0.0377601 ]
[0.47063147 0.47254128 0.03722844]
[0.46901037 0.46847202 0.03676259]
[0.46757739 0.46488881 0.03635397]
[0.46631065 0.46173207 0.03599523]
[0.46519082 0.45894987 0.03568002]
[0.46420083 0.45649684 0.03540285]
[0.4633256  0.45433332 0.03515899]
[0.4625518  0.45242457 0.03494429]
[0.46186768 0.45074016 0.03475519]
[0.46126282 0.44925337 0.03458856]
[0.46072804 0.44794075 0.03444166]
[0.46025521 0.44678168 0.03431212]
[0.45983714 0.44575804 0.03419784]
[0.45946749 0.44485388 0.03409701]
[0.45914065 0.44405514 0.03400802]
[0.45885167 0.44334947 0.03392946]
[0.45859615 0.44272595 0.03386009]
[0.45837021 0.44217497 0.03379883]
[0.45817043 0.44168805 0.03374473]
[0.45799379 0.44125772 0.03369693]
[0.4578376  0.44087738 0.03365471]
[0.45769949 0.44054121 0.0336174 ]
[0.45757737 0.44024405 0.03358444]
[0.45746939 0.43998137 0.03355531]
[0.45737391 0.43974917 0.03352956]
```

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```
[0.45728948 0.43954389 0.03350681]
[0.45721483 0.43936242 0.0334867 ]
[0.45714882 0.43920198 0.03346892]
[0.45709045 0.43906014 0.03345321]
[0.45703884 0.43893474 0.03343932]
[0.4569932  0.43882387 0.03342704]
[0.45695285 0.43872584 0.03341618]
[0.45691717 0.43863917 0.03340658]
[0.45688561 0.43856254 0.0333981 ]
[0.45685771 0.43849478 0.0333906 ]
[0.45683304 0.43843488 0.03338397]
[0.45681123 0.4383819  0.0333781 ]
[0.45679194 0.43833507 0.03337292]
[0.45677488 0.43829365 0.03336833]
[0.4567598  0.43825703 0.03336428]
[0.45674646 0.43822466 0.0333607 ]
[0.45673467 0.43819603 0.03335753]]
         x0:  [0.1 0.4 0.7]
       x_ss:  [nan nan nan]
         sx:  None
        sx0:  None
      sx_ss:  None
          y:  [[0.1        0.4        0.7        0.2        3.4        0.1       ]
[0.57995052 0.73365809 0.0951589  1.15990103 3.73365809 0.57995052]
[0.55996496 0.71470091 0.0694127  1.11992992 3.71470091 0.55996496]
[0.5462855  0.68030366 0.06349394 1.092571   3.68030366 0.5462855 ]
[0.53561883 0.64937432 0.05923555 1.07123766 3.64937432 0.53561883]
[0.52636487 0.62259567 0.05568686 1.05272975 3.62259567 0.52636487]
[0.51822013 0.59943346 0.05268079 1.03644027 3.59943346 0.51822013]
[0.51103767 0.57935661 0.05012037 1.02207533 3.57935661 0.51103767]
[0.5047003  0.56191592 0.04793052 1.00940059 3.56191592 0.5047003 ]
[0.49910666 0.54673518 0.0460508  0.99821331 3.54673518 0.49910666]
[0.49416809 0.53349812 0.04443205 0.98833618 3.53349812 0.49416809]
[0.48980687 0.52193767 0.04303399 0.97961374 3.52193767 0.48980687]
[0.48595476 0.51182731 0.04182339 0.97190952 3.51182731 0.48595476]
[0.48255176 0.50297412 0.04077267 0.96510352 3.50297412 0.48255176]
[0.47954511 0.49521318 0.03985882 0.95909022 3.49521318 0.47954511]
[0.47688833 0.48840304 0.03906254 0.95377667 3.48840304 0.47688833]
[0.47454049 0.48242198 0.03836756 0.94908097 3.48242198 0.47454049]
[0.47246548 0.47716502 0.0377601  0.94493095 3.47716502 0.47246548]
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```

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```

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         sz:  None
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    ssigmaz:  None
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      s2llh:  None
          J:  [[-2.04603669  0.57163267  2.        ]
[ 0.69437133 -0.62836733  2.        ]
[ 0.21909801  0.22836733 -3.        ]]
       xdot:  [-1.08967281e-05 -2.64534209e-05 -2.92761862e-06]
```

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       chi2:  nan
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0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0. 0.
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[0.21183485 0.1028168  0.17871267 0.06862424 0.03431212 0.1       ]
[0.21145019 0.10248805 0.17830322 0.06839569 0.03419784 0.1       ]
[0.21111037 0.10219795 0.17794155 0.06819402 0.03409701 0.1       ]
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 [0.21010325 0.10133992 0.17686999 0.06759766 0.03379883 0.1       ]
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 [0.20898505 0.10039033 0.17568079 0.06693784 0.03346892 0.1       ]
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     preeq_t:  nan
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preeq_numstepsB:  0.0
preeq_status:  [[0 0 0]]
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preeq_cpu_timeB:  0.0
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    posteq_t:  nan
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posteq_numstepsB:  0.0
posteq_status:  [[0 0 0]]
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posteq_cpu_timeB:  0.0
    numsteps:  [  0 100 144 165 181 191 200 207 213 218 223 228 233 237 241 245 249 252
 255 258 261 264 266 269 272 275 278 282 286 290 293 296 299 303 307 311
 314 317 321 325 328 333 337 340 342 344 346 348 350 352 354 356 358 359
 360 361 362 363 364 365]
 numrhsevals:  [  0 114 160 193 212 227 237 248 255 260 267 272 277 282 287 292 296 300
 303 306 309 312 315 318 322 325 329 333 337 342 345 348 352 358 365 369
 372 376 381 385 389 395 400 403 405 407 409 411 413 415 417 419 421 422
 424 426 427 428 429 430]
numerrtestfails:  [0 1 1 3 3 4 4 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 6␣
↪6 6
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```
 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6]
numnonlinsolvconvfails:  [0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0␣
↪0 0 0 0 0 0
 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0]
       order:  [0 5 5 5 5 5 4 5 4 5 4 4 4 4 4 4 5 5 5 5 5 5 5 5 4 4 5 5 5 4 4 4 5 5 5 4 4
 4 4 5 5 4 5 5 5 5 5 5 5 4 4 4 4 4 4 4 4 4 4 4 4 4]
    cpu_time:  1.321999999999998
   numstepsB:  None
numrhsevalsB:  None
numerrtestfailsB:  None
numnonlinsolvconvfailsB:  None
   cpu_timeB:  0.0
cpu_time_total:  2.012
    messages:  <Swig Object of type 'std::vector< amici::LogItem > *' at 0x7f23489855f0;␣
↪[] >
      t_last:  60.0
```

[13]:
```
# In particular for interactive use, ReturnDataView.by_id() and amici.evaluate provides␣
↪a more convenient way to access slices of the result:
# Time trajectory of observable observable_x1
print(f"{rdata.by_id('observable_x1')=}")
# Time trajectory of state variable x2
print(f"{rdata.by_id('x2')=}")
```

```
rdata.by_id('observable_x1')=array([0.1       , 0.57995052, 0.55996496, 0.5462855 , 0.
↪53561883,
       0.52636487, 0.51822013, 0.51103767, 0.5047003 , 0.49910666,
       0.49416809, 0.48980687, 0.48595476, 0.48255176, 0.47954511,
       0.47688833, 0.47454049, 0.47246548, 0.47063147, 0.46901037,
       0.46757739, 0.46631065, 0.46519082, 0.46420083, 0.4633256 ,
       0.4625518 , 0.46186768, 0.46126282, 0.46072804, 0.46025521,
       0.45983714, 0.45946749, 0.45914065, 0.45885167, 0.45859615,
       0.45837021, 0.45817043, 0.45799379, 0.4578376 , 0.45769949,
       0.45757737, 0.45746939, 0.45737391, 0.45728948, 0.45721483,
       0.45714882, 0.45709045, 0.45703884, 0.4569932 , 0.45695285,
       0.45691717, 0.45688561, 0.45685771, 0.45683304, 0.45681123,
       0.45679194, 0.45677488, 0.4567598 , 0.45674646, 0.45673467])
rdata.by_id('x2')=array([0.4       , 0.73365809, 0.71470091, 0.68030366, 0.64937432,
       0.62259567, 0.59943346, 0.57935661, 0.56191592, 0.54673518,
       0.53349812, 0.52193767, 0.51182731, 0.50297412, 0.49521318,
       0.48840304, 0.48242198, 0.47716502, 0.47254128, 0.46847202,
       0.46488881, 0.46173207, 0.45894987, 0.45649684, 0.45433332,
       0.45242457, 0.45074016, 0.44925337, 0.44794075, 0.44678168,
       0.44575804, 0.44485388, 0.44405514, 0.44334947, 0.44272595,
       0.44217497, 0.44168805, 0.44125772, 0.44087738, 0.44054121,
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       0.43863917, 0.43856254, 0.43849478, 0.43843488, 0.4383819 ,
       0.43833507, 0.43829365, 0.43825703, 0.43822466, 0.43819603])
```
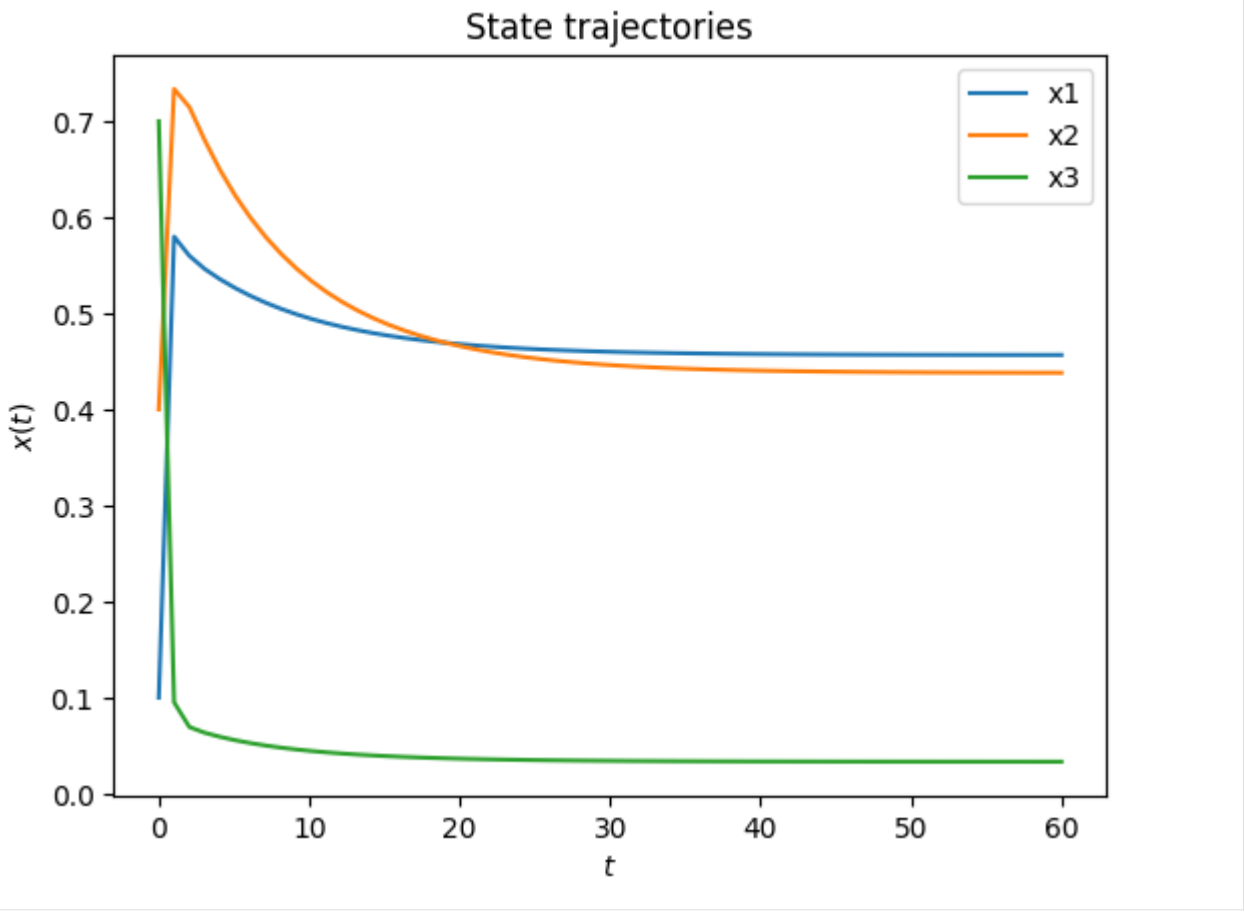
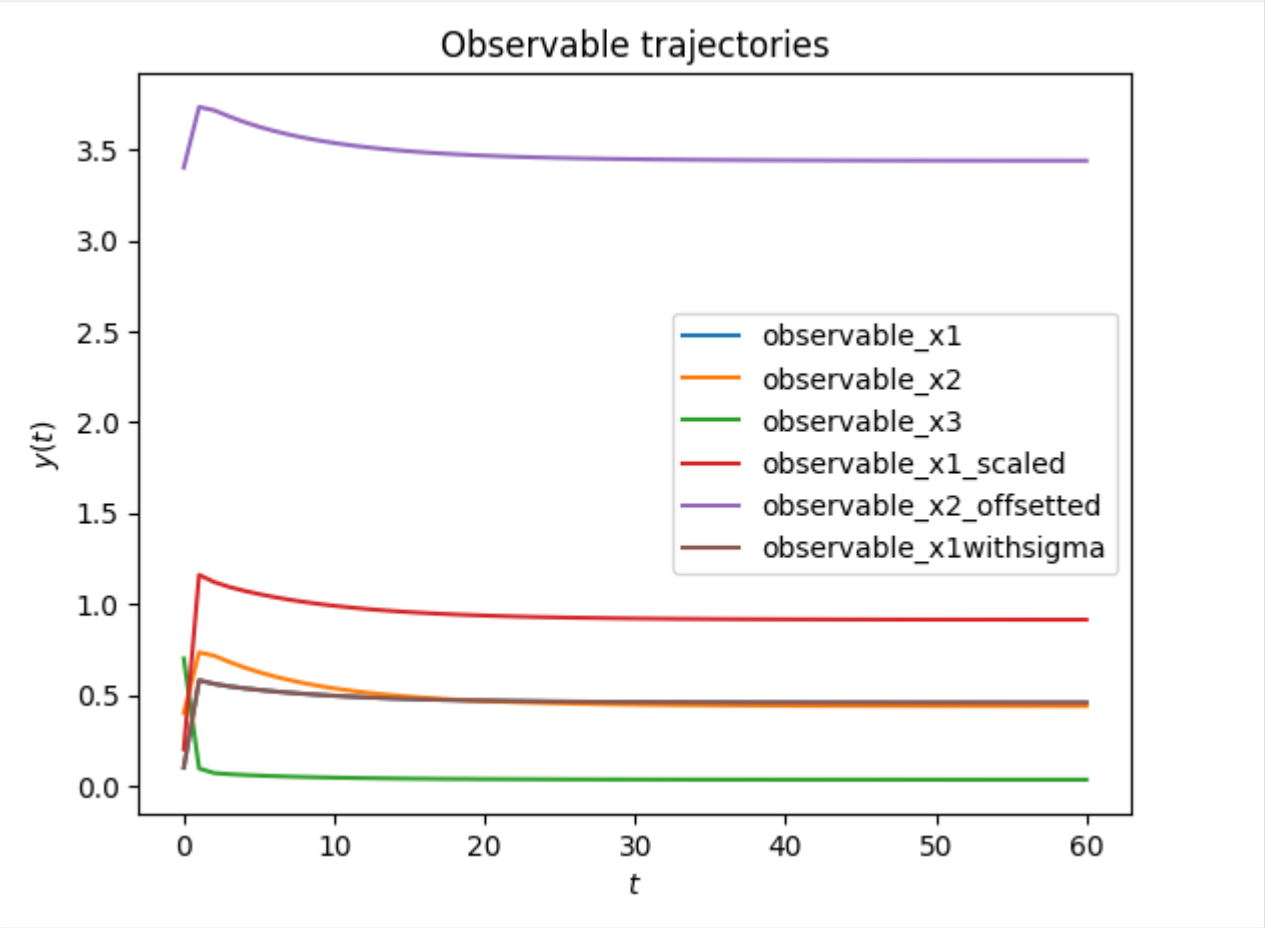

Plotting trajectories

The simulation results above did not look too appealing. Let's plot the trajectories of the model states and outputs them using `matplotlib.pyplot`:

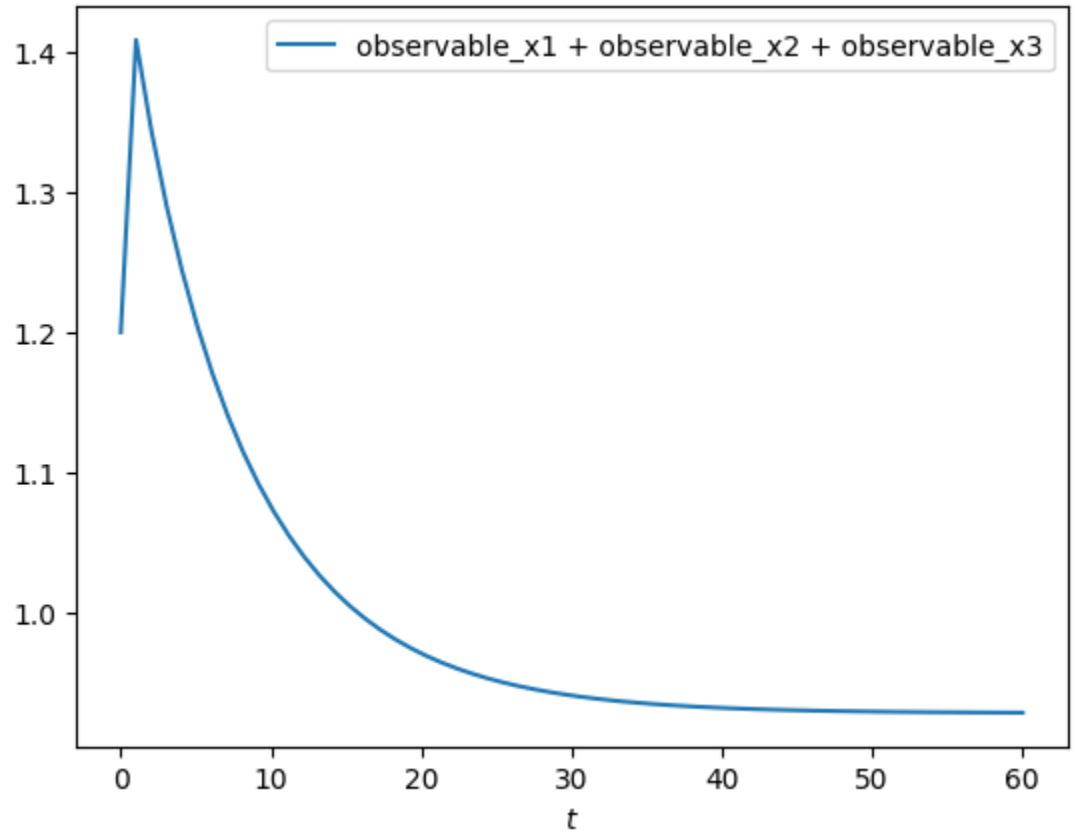
[14]:
```
import amici.plotting

amici.plotting.plot_state_trajectories(rdata, model=None)
amici.plotting.plot_observable_trajectories(rdata, model=None)
```





We can also evaluate symbolic expressions of model quantities using `amici.numpy.evaluate`, or directly plot the results using `amici.plotting.plot_expressions`:

[15]:
```
amici.plotting.plot_expressions(
    "observable_x1 + observable_x2 + observable_x3", rdata=rdata
)
```



Computing likelihood

Often model parameters need to be inferred from experimental data. This is commonly done by maximizing the likelihood of observing the data given to current model parameters. AMICI will compute this likelihood if experimental data is provided to `amici.runAmiciSimulation` as optional third argument. Measurements along with their standard deviations are provided through an `amici.ExpData` instance.

[16]:
```
# Create model instance and set time points for simulation
model = model_module.getModel()
model.setTimepoints(np.linspace(0, 10, 11))

# Create solver instance, keep default options
solver = model.getSolver()

# Run simulation without experimental data
rdata = amici.runAmiciSimulation(model, solver)

# Create ExpData instance from simulation results
edata = amici.ExpData(rdata, 1.0, 0.0)

# Re-run simulation, this time passing "experimental data"
rdata = amici.runAmiciSimulation(model, solver, edata)

print("Log-likelihood %f" % rdata["llh"])
```

```
Log-likelihood -86.361751
```

Simulation tolerances

Numerical error tolerances are often critical to get accurate results. For the state variables, integration errors can be controlled using `setRelativeTolerance` and `setAbsoluteTolerance`. Similar functions exist for sensitivities, steadystates and quadratures. We initially compute a reference solution using extremely low tolerances and then assess the influence on integration error for different levels of absolute and relative tolerance.

[17]:
```
solver.setRelativeTolerance(1e-16)
solver.setAbsoluteTolerance(1e-16)
solver.setSensitivityOrder(amici.SensitivityOrder.none)
rdata_ref = amici.runAmiciSimulation(model, solver, edata)


def get_simulation_error(solver):
    rdata = amici.runAmiciSimulation(model, solver, edata)
    return np.mean(np.abs(rdata["x"] - rdata_ref["x"])), np.mean(
        np.abs(rdata["llh"] - rdata_ref["llh"])
    )


def get_errors(tolfun, tols):
    solver.setRelativeTolerance(1e-16)
    solver.setAbsoluteTolerance(1e-16)
    x_errs = []
    llh_errs = []
    for tol in tols:
        getattr(solver, tolfun)(tol)
        x_err, llh_err = get_simulation_error(solver)
        x_errs.append(x_err)
        llh_errs.append(llh_err)
    return x_errs, llh_errs


atols = np.logspace(-5, -15, 100)
atol_x_errs, atol_llh_errs = get_errors("setAbsoluteTolerance", atols)

rtols = np.logspace(-5, -15, 100)
rtol_x_errs, rtol_llh_errs = get_errors("setRelativeTolerance", rtols)

fig, axes = plt.subplots(1, 2, figsize=(15, 5))


def plot_error(tols, x_errs, llh_errs, tolname, ax):
    ax.plot(tols, x_errs, "r-", label="x")
    ax.plot(tols, llh_errs, "b-", label="llh")
    ax.set_xscale("log")
    ax.set_yscale("log")
    ax.set_xlabel(f"{tolname} tolerance")
    ax.set_ylabel("average numerical error")
```

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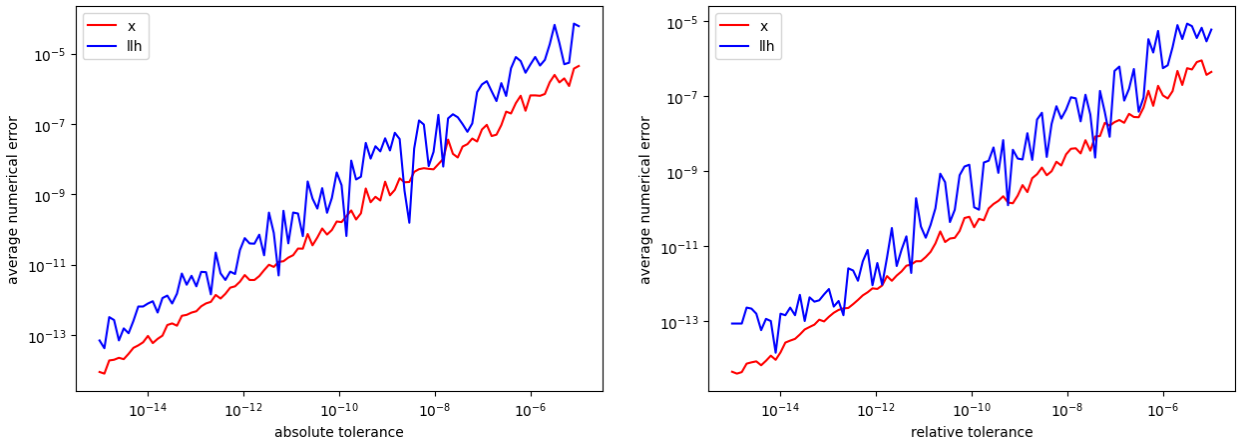
```
    ax.legend()


plot_error(atols, atol_x_errs, atol_llh_errs, "absolute", axes[0])
plot_error(rtols, rtol_x_errs, rtol_llh_errs, "relative", axes[1])

# reset relative tolerance to default value
solver.setRelativeTolerance(1e-8)
solver.setRelativeTolerance(1e-16)
```



Sensitivity analysis

AMICI can provide first- and second-order sensitivities using the forward- or adjoint-method. The respective options are set on the Model and Solver objects.

Forward sensitivity analysis

[18]:
```
model = model_module.getModel()
model.setTimepoints(np.linspace(0, 10, 11))
model.requireSensitivitiesForAllParameters()  # sensitivities w.r.t. all parameters
# model.setParameterList([1, 2])                          # sensitivities
# w.r.t. the specified parameters
model.setParameterScale(
    amici.ParameterScaling.none
)  # parameters are used as-is (not log-transformed)

solver = model.getSolver()
solver.setSensitivityMethod(
    amici.SensitivityMethod.forward
)  # forward sensitivity analysis
solver.setSensitivityOrder(
    amici.SensitivityOrder.first
)  # first-order sensitivities

rdata = amici.runAmiciSimulation(model, solver)
```

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```
# print sensitivity-related results
for key, value in rdata.items():
    if key.startswith("s"):
        print("%12s: " % key, value)
```

```
          sx:  [[[ 0.00000000e+00  0.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00]]

 [[-2.00747250e-01  1.19873139e-01 -9.44167985e-03]
  [-1.02561396e-01 -1.88820454e-01  1.01855972e-01]
  [ 4.66193077e-01 -2.86365372e-01  2.39662449e-02]
  [ 4.52560294e-02  1.14631370e-01 -3.34067919e-02]
  [ 4.00672911e-01  1.92564093e-01  4.98877759e-02]
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  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00]]

 [[-2.23007240e-01  1.53979022e-01 -1.26885280e-02]
  [-1.33426939e-01 -3.15955239e-01  9.49575030e-02]
  [ 5.03470377e-01 -3.52731535e-01  2.81567412e-02]
  [ 3.93630714e-02  1.10770683e-01 -1.05673869e-02]
  [ 5.09580304e-01  4.65255489e-01  9.24843702e-02]
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  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00]]

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  [-1.60981967e-01 -4.00490452e-01  7.54810648e-02]
  [ 4.87746419e-01 -3.76014315e-01  2.30919334e-02]
  [ 4.28733680e-02  1.15473583e-01 -6.63571687e-03]
  [ 6.05168647e-01  7.07226039e-01  1.23870914e-01]
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  [ 4.66407064e-01 -3.87612079e-01  1.76410128e-02]
  [ 4.52451104e-02  1.19865712e-01 -4.73313094e-03]
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```

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  [ 4.69732048e-02  1.22961727e-01 -3.35899442e-03]
  [ 7.68998995e-01  1.10844286e+00  1.70889328e-01]
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  [ 4.82793652e-02  1.24952071e-01 -2.30991637e-03]
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  [ 4.92546648e-02  1.26089711e-01 -1.50412006e-03]
  [ 9.06806543e-01  1.42334018e+00  2.04522708e-01]
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  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00]]

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  [ 4.99612484e-02  1.26581014e-01 -8.85891342e-04]
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  [ 1.07443160e+00  1.78183962e+00  2.39710937e-01]
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  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00]
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```
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[nan nan nan]
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[nan nan nan]
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[nan nan nan]]
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[1.  1.  1.  1.  1.  0.2]]
         sy:  [[[ 0.00000000e+00  0.00000000e+00  0.00000000e+00  0.00000000e+00
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 [ 4.66193077e-01 -2.86365372e-01  2.39662449e-02  9.32386154e-01
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 [ 4.52560294e-02  1.14631370e-01 -3.34067919e-02  9.05120589e-02
   1.14631370e-01  4.52560294e-02]
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```
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  [ 4.87746419e-01 -3.76014315e-01  2.30919334e-02  9.75492839e-01
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  [ 4.52451104e-02  1.19865712e-01 -4.73313094e-03  9.04902208e-02
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  [ 6.90798449e-01  9.20396633e-01  1.49475827e-01  1.38159690e+00
```

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```
    9.20396633e-01  6.90798449e-01]
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  [ 4.47070326e-01 -3.94304029e-01  1.32107437e-02  8.94140651e-01
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  [ 4.69732048e-02  1.22961727e-01 -3.35899442e-03  9.39464097e-02
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  [ 7.68998995e-01  1.10844286e+00  1.70889328e-01  1.53799799e+00
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  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  5.27091252e-01
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  [ 4.82793652e-02  1.24952071e-01 -2.30991637e-03  9.65587304e-02
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  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  5.18989205e-01
    0.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  0.00000000e+00
    1.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  0.00000000e+00
    0.00000000e+00  0.00000000e+00]]

 [[-1.87672774e-01  1.77588334e-01 -3.38318222e-03 -3.75345548e-01
    1.77588334e-01 -1.87672774e-01]
  [-2.33807210e-01 -5.86081383e-01  2.89236334e-02 -4.67614420e-01
   -5.86081383e-01 -2.33807210e-01]
  [ 4.16201399e-01 -3.99295277e-01  7.06598588e-03  8.32402797e-01
   -3.99295277e-01  4.16201399e-01]
  [ 4.92546648e-02  1.26089711e-01 -1.50412006e-03  9.85093296e-02
    1.26089711e-01  4.92546648e-02]
  [ 9.06806543e-01  1.42334018e+00  2.04522708e-01  1.81361309e+00
    1.42334018e+00  9.06806543e-01]
```

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```
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  5.11829985e-01
    0.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  0.00000000e+00
    1.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  0.00000000e+00
    0.00000000e+00  0.00000000e+00]]

 [[-1.83320440e-01  1.78410042e-01 -2.47240692e-03 -3.66640879e-01
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  [-2.44690164e-01 -6.09568485e-01  2.25774266e-02 -4.89380329e-01
   -6.09568485e-01 -2.44690164e-01]
  [ 4.04061655e-01 -3.99063012e-01  4.97908386e-03  8.08123310e-01
   -3.99063012e-01  4.04061655e-01]
  [ 4.99612484e-02  1.26581014e-01 -8.85891342e-04  9.99224969e-02
    1.26581014e-01  4.99612484e-02]
  [ 9.67473970e-01  1.55589415e+00  2.17895305e-01  1.93494794e+00
    1.55589415e+00  9.67473970e-01]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  5.05500234e-01
    0.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  0.00000000e+00
    1.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  0.00000000e+00
    0.00000000e+00  0.00000000e+00]]

 [[-1.79620591e-01  1.78640114e-01 -1.75822439e-03 -3.59241183e-01
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  [-2.53540123e-01 -6.27448857e-01  1.75019839e-02 -5.07080247e-01
   -6.27448857e-01 -2.53540123e-01]
  [ 3.93704970e-01 -3.97656641e-01  3.35895484e-03  7.87409940e-01
   -3.97656641e-01  3.93704970e-01]
  [ 5.04492282e-02  1.26586733e-01 -4.13401240e-04  1.00898456e-01
    1.26586733e-01  5.04492282e-02]
  [ 1.02322336e+00  1.67481439e+00  2.29524046e-01  2.04644672e+00
    1.67481439e+00  1.02322336e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  4.99901907e-01
    0.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  0.00000000e+00
    1.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  0.00000000e+00
    0.00000000e+00  0.00000000e+00]]

 [[-1.76478441e-01  1.78430281e-01 -1.19867662e-03 -3.52956882e-01
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  [-2.60686971e-01 -6.40868686e-01  1.34365068e-02 -5.21373942e-01
   -6.40868686e-01 -2.60686971e-01]
  [ 3.84873835e-01 -3.95414931e-01  2.10369522e-03  7.69747670e-01
   -3.95414931e-01  3.84873835e-01]
  [ 5.07601805e-02  1.26231631e-01 -5.46465317e-05  1.01520361e-01
    1.26231631e-01  5.07601805e-02]
  [ 1.07443160e+00  1.78183962e+00  2.39710937e-01  2.14886320e+00
    1.78183962e+00  1.07443160e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  4.94949118e-01
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    0.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  0.00000000e+00
    1.00000000e+00  0.00000000e+00]
  [ 0.00000000e+00  0.00000000e+00  0.00000000e+00  0.00000000e+00
    0.00000000e+00  0.00000000e+00]]]
     ssigmay:  [[[0. 0. 0. 0. 0. 0.]
  [0. 0. 0. 0. 0. 0.]
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  [0. 0. 0. 0. 0. 0.]
  [0. 0. 0. 0. 0. 0.]
  [0. 0. 0. 0. 0. 0.]
  [0. 0. 0. 0. 0. 0.]
  [0. 0. 0. 0. 0. 1.]]

 [[0. 0. 0. 0. 0. 0.]
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  [0. 0. 0. 0. 0. 0.]
  [0. 0. 0. 0. 0. 1.]]

 [[0. 0. 0. 0. 0. 0.]
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 [0. 0. 0. 0. 0. 0.]
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 [0. 0. 0. 0. 0. 0.]
 [0. 0. 0. 0. 0. 1.]]]
     sigmaz:  None
```

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```
          sz:  None
         srz:  None
     ssigmaz:  None
        sllh:  [nan nan nan nan nan nan nan nan]
       s2llh:  None
      status:  0
        sres:  [[0. 0. 0. 0. 0. 0. 0. 0.]
 [0. 0. 0. 0. 0. 0. 0. 0.]
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 [0. 0. 0. 0. 0. 0. 0. 0.]
 [0. 0. 0. 0. 0. 0. 0. 0.]
```

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 [0. 0. 0. 0. 0. 0. 0. 0.]
 [0. 0. 0. 0. 0. 0. 0. 0.]
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 [0. 0. 0. 0. 0. 0. 0. 0.]
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 [0. 0. 0. 0. 0. 0. 0. 0.]
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 [0. 0. 0. 0. 0. 0. 0. 0.]
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 [0. 0. 0. 0. 0. 0. 0. 0.]
 [0. 0. 0. 0. 0. 0. 0. 0.]
 [0. 0. 0. 0. 0. 0. 0. 0.]
 [0. 0. 0. 0. 0. 0. 0. 0.]
 [0. 0. 0. 0. 0. 0. 0. 0.]
 [0. 0. 0. 0. 0. 0. 0. 0.]]
```

Adjoint sensitivity analysis

[19]:

```
# Set model options
model = model_module.getModel()
p_orig = np.array(model.getParameters())
p_orig[
    list(model.getParameterIds()).index("observable_x1withsigma_sigma")
] = 0.1  # Change default parameter
model.setParameters(p_orig)
model.setParameterScale(amici.ParameterScaling.none)
model.setTimepoints(np.linspace(0, 10, 21))

solver = model.getSolver()
solver.setMaxSteps(10**4)  # Set maximum number of steps for the solver

# simulate time-course to get artificial data
rdata = amici.runAmiciSimulation(model, solver)
edata = amici.ExpData(rdata, 1.0, 0)
edata.fixedParameters = model.getFixedParameters()
# set sigma to 1.0 except for observable 5, so that p[7] is used instead
# (if we have sigma parameterized, the corresponding ExpData entries must NaN, otherwise␣
↪they will override the parameter)
edata.setObservedDataStdDev(
    rdata["t"] * 0 + np.nan,
    list(model.getObservableIds()).index("observable_x1withsigma"),
)

# enable sensitivities
solver.setSensitivityOrder(amici.SensitivityOrder.first)  # First-order ...
```

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```
solver.setSensitivityMethod(
    amici.SensitivityMethod.adjoint
)  # ... adjoint sensitivities
model.requireSensitivitiesForAllParameters()  # ... w.r.t. all parameters

# compute adjoint sensitivities
rdata = amici.runAmiciSimulation(model, solver, edata)
# print(rdata['sigmay'])
print("Log-likelihood: %f\nGradient: %s" % (rdata["llh"], rdata["sllh"]))
```

```
Log-likelihood: -912.475467
Gradient: [ 1.59238067e+01 -2.42680973e+01 -3.69602159e+01  3.08634183e+00
  1.00176912e+02  1.84460069e+00  2.84182727e+00  1.57272745e+04]
```

Finite differences gradient check

Compare AMICI-computed gradient with finite differences

[20]:
```
from scipy.optimize import check_grad


def func(x0, symbol="llh", x0full=None, plist=[], verbose=False):
    p = x0[:]
    if len(plist):
        p = x0full[:]
        p[plist] = x0
    verbose and print("f: p=%s" % p)

    old_parameters = model.getParameters()
    solver.setSensitivityOrder(amici.SensitivityOrder.none)
    model.setParameters(p)
    rdata = amici.runAmiciSimulation(model, solver, edata)

    model.setParameters(old_parameters)

    res = np.sum(rdata[symbol])
    verbose and print(res)
    return res


def grad(x0, symbol="llh", x0full=None, plist=[], verbose=False):
    p = x0[:]
    if len(plist):
        model.setParameterList(plist)
        p = x0full[:]
        p[plist] = x0
    else:
        model.requireSensitivitiesForAllParameters()
    verbose and print("g: p=%s" % p)

    old_parameters = model.getParameters()
```

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```
    solver.setSensitivityMethod(amici.SensitivityMethod.forward)
    solver.setSensitivityOrder(amici.SensitivityOrder.first)
    model.setParameters(p)
    rdata = amici.runAmiciSimulation(model, solver, edata)

    model.setParameters(old_parameters)

    res = rdata["s%s" % symbol]
    if not isinstance(res, float):
        if len(res.shape) == 3:
            res = np.sum(res, axis=(0, 2))
    verbose and print(res)
    return res


epsilon = 1e-4
err_norm = check_grad(func, grad, p_orig, "llh", epsilon=epsilon)
print("sllh: |error|_2: %f" % err_norm)
# assert err_norm < 1e-6
print()

for ip in range(model.np()):
    plist = [ip]
    p = p_orig.copy()
    err_norm = check_grad(
        func, grad, p[plist], "llh", p, [ip], epsilon=epsilon
    )
    print("sllh: p[%d]: |error|_2: %f" % (ip, err_norm))

print()
for ip in range(model.np()):
    plist = [ip]
    p = p_orig.copy()
    err_norm = check_grad(func, grad, p[plist], "y", p, [ip], epsilon=epsilon)
    print("sy: p[%d]: |error|_2: %f" % (ip, err_norm))

print()
for ip in range(model.np()):
    plist = [ip]
    p = p_orig.copy()
    err_norm = check_grad(func, grad, p[plist], "x", p, [ip], epsilon=epsilon)
    print("sx: p[%d]: |error|_2: %f" % (ip, err_norm))

print()
for ip in range(model.np()):
    plist = [ip]
    p = p_orig.copy()
    err_norm = check_grad(
        func, grad, p[plist], "sigmay", p, [ip], epsilon=epsilon
    )
    print("ssigmay: p[%d]: |error|_2: %f" % (ip, err_norm))
```

```
sllh: |error|_2: 23.769330

sllh: p[0]: |error|_2: 0.002076
sllh: p[1]: |error|_2: 0.004618
sllh: p[2]: |error|_2: 0.019564
sllh: p[3]: |error|_2: 0.000825
sllh: p[4]: |error|_2: 0.090860
sllh: p[5]: |error|_2: 0.000280
sllh: p[6]: |error|_2: 0.001050
sllh: p[7]: |error|_2: 23.769147

sy: p[0]: |error|_2: 0.002974
sy: p[1]: |error|_2: 0.002717
sy: p[2]: |error|_2: 0.001308
sy: p[3]: |error|_2: 0.000939
sy: p[4]: |error|_2: 0.006106
sy: p[5]: |error|_2: 0.000000
sy: p[6]: |error|_2: 0.000000
sy: p[7]: |error|_2: 0.000000

sx: p[0]: |error|_2: 0.001033
sx: p[1]: |error|_2: 0.001076
sx: p[2]: |error|_2: 0.000121
sx: p[3]: |error|_2: 0.000439
sx: p[4]: |error|_2: 0.001569
sx: p[5]: |error|_2: 0.000000
sx: p[6]: |error|_2: 0.000000
sx: p[7]: |error|_2: 0.000000

ssigmay: p[0]: |error|_2: 0.000000
ssigmay: p[1]: |error|_2: 0.000000
ssigmay: p[2]: |error|_2: 0.000000
ssigmay: p[3]: |error|_2: 0.000000
ssigmay: p[4]: |error|_2: 0.000000
ssigmay: p[5]: |error|_2: 0.000000
ssigmay: p[6]: |error|_2: 0.000000
```

```
ssigmay: p[7]: |error|_2: 0.000000
```

[21]:
```
eps = 1e-4
op = model.getParameters()


solver.setSensitivityMethod(
    amici.SensitivityMethod.forward
)  # forward sensitivity analysis
solver.setSensitivityOrder(
    amici.SensitivityOrder.first
)  # first-order sensitivities
model.requireSensitivitiesForAllParameters()
solver.setRelativeTolerance(1e-12)
rdata = amici.runAmiciSimulation(model, solver, edata)


def fd(x0, ip, eps, symbol="llh"):
    p = list(x0[:])
    old_parameters = model.getParameters()
    solver.setSensitivityOrder(amici.SensitivityOrder.none)
    p[ip] += eps
    model.setParameters(p)
    rdata_f = amici.runAmiciSimulation(model, solver, edata)
    p[ip] -= 2 * eps
    model.setParameters(p)
    rdata_b = amici.runAmiciSimulation(model, solver, edata)

    model.setParameters(old_parameters)
    return (rdata_f[symbol] - rdata_b[symbol]) / (2 * eps)


def plot_sensitivities(symbol, eps):
    fig, axes = plt.subplots(4, 2, figsize=(15, 10))
    for ip in range(4):
        fd_approx = fd(model.getParameters(), ip, eps, symbol=symbol)

        axes[ip, 0].plot(
            edata.getTimepoints(), rdata[f"s{symbol}"][:, ip, :], "r-"
        )
        axes[ip, 0].plot(edata.getTimepoints(), fd_approx, "k--")
        axes[ip, 0].set_ylabel(f"sensitivity {symbol}")
        axes[ip, 0].set_xlabel("time")

        axes[ip, 1].plot(
            edata.getTimepoints(),
            np.abs(rdata[f"s{symbol}"][:, ip, :] - fd_approx),
            "k-",
        )
        axes[ip, 1].set_ylabel("difference to fd")
        axes[ip, 1].set_xlabel("time")
        axes[ip, 1].set_yscale("log")
```

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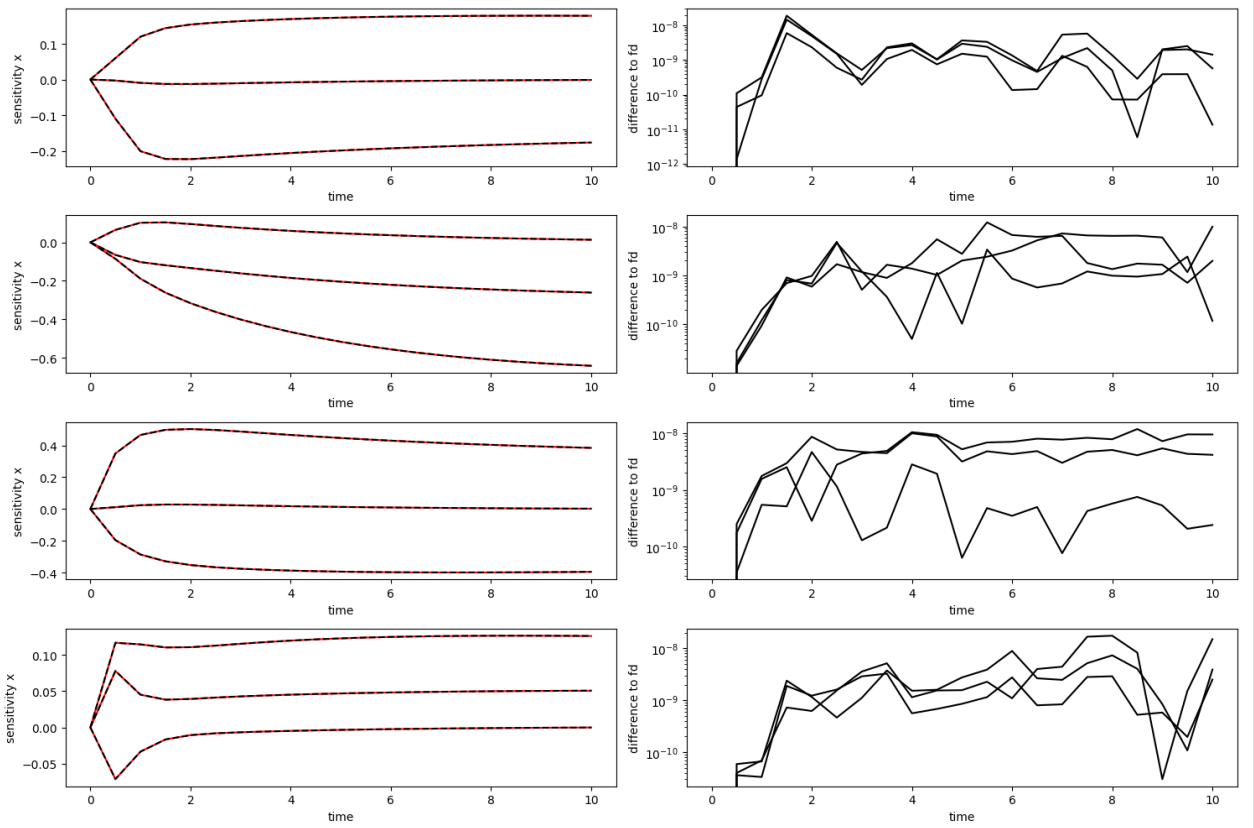
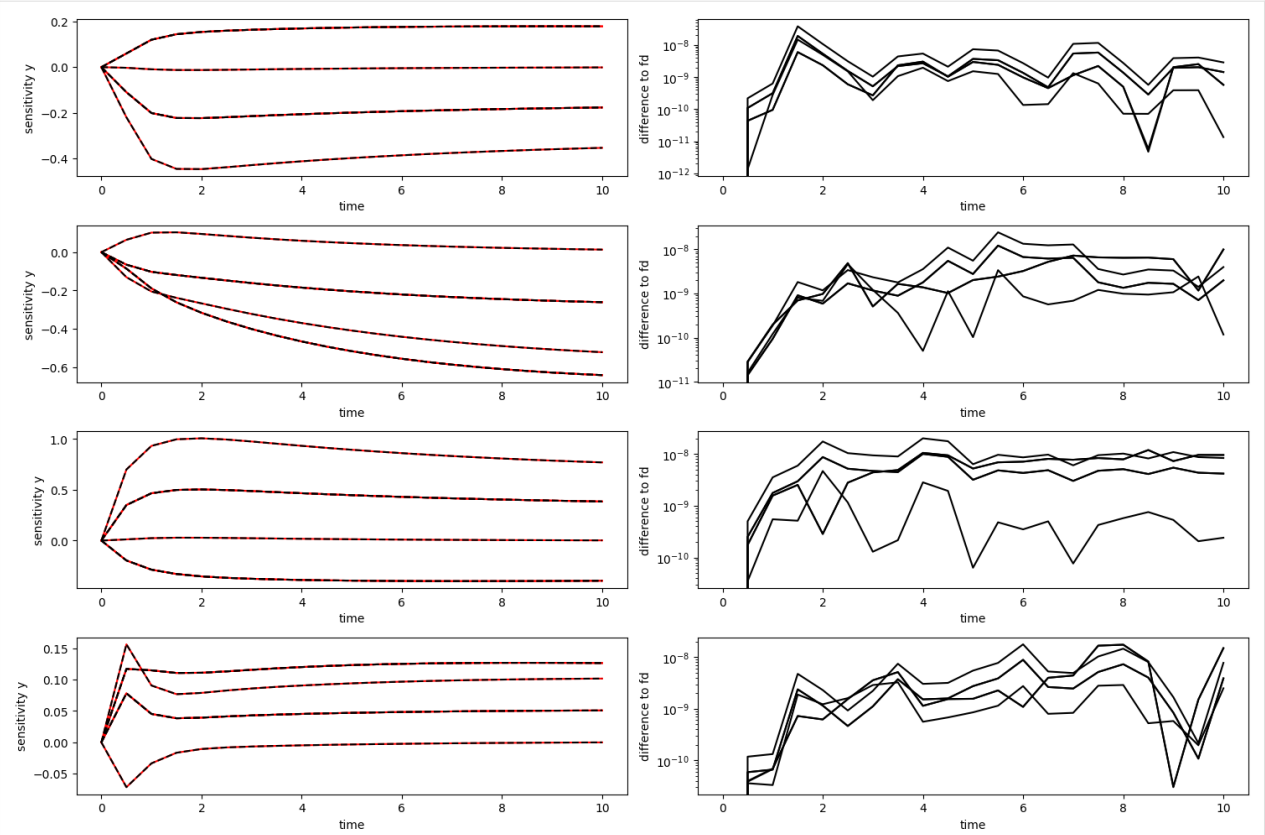
```
    plt.tight_layout()
    plt.show()
```

[22]:
```
plot_sensitivities("x", eps)
```



[23]:
```
plot_sensitivities("y", eps)
```



Export as DataFrame

Experimental data and simulation results can both be exported as pandas Dataframe to allow for an easier inspection of numeric values

[24]:
```
# run the simulation
rdata = amici.runAmiciSimulation(model, solver, edata)
```

[25]:
```
# look at the ExpData as DataFrame
df = amici.getDataObservablesAsDataFrame(model, [edata])
df
```

[25]:

	condition_id	time	datatype	t_presim	k0	k0_preeq	k0_presim	p1	p2	\
0		0.0	data	0.0	1.0	NaN	NaN	1.0	0.5	
1		0.5	data	0.0	1.0	NaN	NaN	1.0	0.5	
2		1.0	data	0.0	1.0	NaN	NaN	1.0	0.5	
3		1.5	data	0.0	1.0	NaN	NaN	1.0	0.5	
4		2.0	data	0.0	1.0	NaN	NaN	1.0	0.5	
5		2.5	data	0.0	1.0	NaN	NaN	1.0	0.5	
6		3.0	data	0.0	1.0	NaN	NaN	1.0	0.5	
7		3.5	data	0.0	1.0	NaN	NaN	1.0	0.5	
8		4.0	data	0.0	1.0	NaN	NaN	1.0	0.5	
9		4.5	data	0.0	1.0	NaN	NaN	1.0	0.5	
10		5.0	data	0.0	1.0	NaN	NaN	1.0	0.5	
11		5.5	data	0.0	1.0	NaN	NaN	1.0	0.5	

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```
12                6.0     data       0.0  1.0       NaN        NaN  1.0  0.5
13                6.5     data       0.0  1.0       NaN        NaN  1.0  0.5
14                7.0     data       0.0  1.0       NaN        NaN  1.0  0.5
15                7.5     data       0.0  1.0       NaN        NaN  1.0  0.5
16                8.0     data       0.0  1.0       NaN        NaN  1.0  0.5
17                8.5     data       0.0  1.0       NaN        NaN  1.0  0.5
18                9.0     data       0.0  1.0       NaN        NaN  1.0  0.5
19                9.5     data       0.0  1.0       NaN        NaN  1.0  0.5
20               10.0     data       0.0  1.0       NaN        NaN  1.0  0.5

     p3  ...  observable_x3  observable_x1_scaled  observable_x2_offsetted  \
0   0.4  ...      2.021088              2.260618                 3.875483
1   0.4  ...      0.127412              2.427724                 3.870299
2   0.4  ...      0.273618              1.044879                 4.099415
3   0.4  ...      1.037871              1.467580                 3.461660
4   0.4  ...     -0.546966              0.346188                 2.437839
5   0.4  ...     -0.066667              1.935784                 4.260718
6   0.4  ...      0.566809             -0.014514                 3.374442
7   0.4  ...      0.092011              0.556910                 3.084864
8   0.4  ...     -1.187218              0.223393                 2.698267
9   0.4  ...     -1.499219              1.196472                 3.239905
10  0.4  ...     -0.765725              2.848015                 3.788577
11  0.4  ...      0.542465              1.666798                 3.680870
12  0.4  ...     -1.668326              1.603380                 5.833866
13  0.4  ...     -0.783678              1.741354                 4.446379
14  0.4  ...      1.805791              1.953009                 4.616472
15  0.4  ...     -0.221432             -0.392911                 4.981600
16  0.4  ...     -0.651046              0.028690                 3.500305
17  0.4  ...      0.292404              1.982981                 2.790731
18  0.4  ...      0.430141              1.551267                 4.376032
19  0.4  ...     -1.025568              0.667944                 2.684654
20  0.4  ...     -0.444338              1.486089                 3.670681

    observable_x1withsigma  observable_x1_std  observable_x2_std  \
0                -1.274507                1.0                1.0
1                 0.939544                1.0                1.0
2                -0.666911                1.0                1.0
3                 1.360615                1.0                1.0
4                 0.123733                1.0                1.0
5                 0.076251                1.0                1.0
6                 0.637662                1.0                1.0
7                -0.009104                1.0                1.0
8                -0.468465                1.0                1.0
9                 0.447092                1.0                1.0
10               -0.069605                1.0                1.0
11                1.378979                1.0                1.0
12               -1.189779                1.0                1.0
13                1.899144                1.0                1.0
14                0.929198                1.0                1.0
15               -0.299463                1.0                1.0
16                0.973614                1.0                1.0
17                2.156537                1.0                1.0
```

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```
18                0.424894                1.0                1.0
19                0.866506                1.0                1.0
20                0.834081                1.0                1.0

    observable_x3_std  observable_x1_scaled_std  observable_x2_offsetted_std  \
0                 1.0                        1.0                          1.0
1                 1.0                        1.0                          1.0
2                 1.0                        1.0                          1.0
3                 1.0                        1.0                          1.0
4                 1.0                        1.0                          1.0
5                 1.0                        1.0                          1.0
6                 1.0                        1.0                          1.0
7                 1.0                        1.0                          1.0
8                 1.0                        1.0                          1.0
9                 1.0                        1.0                          1.0
10                1.0                        1.0                          1.0
11                1.0                        1.0                          1.0
12                1.0                        1.0                          1.0
13                1.0                        1.0                          1.0
14                1.0                        1.0                          1.0
15                1.0                        1.0                          1.0
16                1.0                        1.0                          1.0
17                1.0                        1.0                          1.0
18                1.0                        1.0                          1.0
19                1.0                        1.0                          1.0
20                1.0                        1.0                          1.0

    observable_x1withsigma_std
0                          NaN
1                          NaN
2                          NaN
3                          NaN
4                          NaN
5                          NaN
6                          NaN
7                          NaN
8                          NaN
9                          NaN
10                         NaN
11                         NaN
12                         NaN
13                         NaN
14                         NaN
15                         NaN
16                         NaN
17                         NaN
18                         NaN
19                         NaN
20                         NaN

[21 rows x 35 columns]
```

[26]:
```
# from the exported dataframe, we can actually reconstruct a copy of the ExpData instance
reconstructed_edata = amici.getEdataFromDataFrame(model, df)
```

[27]:
```
# look at the States in rdata as DataFrame
amici.getResidualsAsDataFrame(model, [edata], [rdata])
```

[27]:

	condition_id	time	t_presim	k0	k0_preeq	k0_presim	p1	p2	p3	p4	\
0	NaN	0.0	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
1	NaN	0.5	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
2	NaN	1.0	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
3	NaN	1.5	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
4	NaN	2.0	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
5	NaN	2.5	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
6	NaN	3.0	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
7	NaN	3.5	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
8	NaN	4.0	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
9	NaN	4.5	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
10	NaN	5.0	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
11	NaN	5.5	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
12	NaN	6.0	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
13	NaN	6.5	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
14	NaN	7.0	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
15	NaN	7.5	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
16	NaN	8.0	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
17	NaN	8.5	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
18	NaN	9.0	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
19	NaN	9.5	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	
20	NaN	10.0	0.0	1.0	NaN	NaN	NaN	NaN	NaN	NaN	

	...	p5_scale	scale_scale	offset_scale	sigma_scale	observable_x1	\
0	...	NaN	NaN	NaN	NaN	0.231304	
1	...	NaN	NaN	NaN	NaN	0.405791	
2	...	NaN	NaN	NaN	NaN	0.464433	
3	...	NaN	NaN	NaN	NaN	0.959938	
4	...	NaN	NaN	NaN	NaN	0.522949	
5	...	NaN	NaN	NaN	NaN	0.084360	
6	...	NaN	NaN	NaN	NaN	0.251932	
7	...	NaN	NaN	NaN	NaN	0.413383	
8	...	NaN	NaN	NaN	NaN	0.139943	
9	...	NaN	NaN	NaN	NaN	1.836517	
10	...	NaN	NaN	NaN	NaN	0.158962	
11	...	NaN	NaN	NaN	NaN	0.271506	
12	...	NaN	NaN	NaN	NaN	0.576614	
13	...	NaN	NaN	NaN	NaN	0.266088	
14	...	NaN	NaN	NaN	NaN	0.042584	
15	...	NaN	NaN	NaN	NaN	1.791547	
16	...	NaN	NaN	NaN	NaN	0.532636	
17	...	NaN	NaN	NaN	NaN	0.042179	
18	...	NaN	NaN	NaN	NaN	1.865994	
19	...	NaN	NaN	NaN	NaN	0.251895	
20	...	NaN	NaN	NaN	NaN	2.078912	

	observable_x2	observable_x3	observable_x1_scaled	\

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```
0        0.174521       1.321088              2.060618
1        0.000717       0.064078              1.348989
2        1.071453       0.177194              0.115266
3        2.444217       0.961795              0.326781
4        1.195239       0.616660              0.774882
5        0.047067       0.132968              0.829673
6        0.754031       0.503077              1.108255
7        0.738710       0.030505              0.525810
8        0.936120       1.246712              0.849168
9        0.366389       1.556872              0.133396
10       1.326881       0.821685              1.793833
11       1.869243       0.488065              0.620969
12       1.342562       1.721286              0.565402
13       1.081795       0.835307              0.710755
14       2.255376       1.755392              0.929349
15       1.183464       0.270691              1.410046
16       0.210303       0.699249              0.982310
17       0.224134       0.245179              0.977751
18       0.274684       0.383826              0.551463
19       0.721146       1.071039              0.326756
20       1.284101       0.489024              0.496190

    observable_x2_offsetted  observable_x1withsigma
0                  0.475483               13.745070
1                  0.185620                4.001765
2                  0.366128               12.469834
3                  0.268992                7.902157
4                  1.277997                4.368013
5                  0.561968                4.768053
6                  0.307521                0.907918
7                  0.581245                5.504638
8                  0.953036               10.047454
9                  0.397609                0.844463
10                 0.163896                5.966960
11                 0.068137                8.560643
12                 2.232264               17.087684
13                 0.855150               13.838446
14                 1.034917                4.173678
15                 1.409071                8.080306
16                 0.063799                4.681134
17                 0.765503               16.539221
18                 0.827151                0.750079
19                 0.857354                3.691564
20                 0.135100                3.391322

[21 rows x 28 columns]
```

[28]:
```
# look at the Observables in rdata as DataFrame
amici.getSimulationObservablesAsDataFrame(model, [edata], [rdata])
```

[28]:
```
   condition_id  time    datatype  t_presim   k0  k0_preeq  k0_presim   p1  \
0           0.0   0.0  simulation       0.0  1.0       NaN        NaN  1.0
```

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```
1                0.5  simulation       0.0  1.0       NaN        NaN  1.0
2                1.0  simulation       0.0  1.0       NaN        NaN  1.0
3                1.5  simulation       0.0  1.0       NaN        NaN  1.0
4                2.0  simulation       0.0  1.0       NaN        NaN  1.0
5                2.5  simulation       0.0  1.0       NaN        NaN  1.0
6                3.0  simulation       0.0  1.0       NaN        NaN  1.0
7                3.5  simulation       0.0  1.0       NaN        NaN  1.0
8                4.0  simulation       0.0  1.0       NaN        NaN  1.0
9                4.5  simulation       0.0  1.0       NaN        NaN  1.0
10               5.0  simulation       0.0  1.0       NaN        NaN  1.0
11               5.5  simulation       0.0  1.0       NaN        NaN  1.0
12               6.0  simulation       0.0  1.0       NaN        NaN  1.0
13               6.5  simulation       0.0  1.0       NaN        NaN  1.0
14               7.0  simulation       0.0  1.0       NaN        NaN  1.0
15               7.5  simulation       0.0  1.0       NaN        NaN  1.0
16               8.0  simulation       0.0  1.0       NaN        NaN  1.0
17               8.5  simulation       0.0  1.0       NaN        NaN  1.0
18               9.0  simulation       0.0  1.0       NaN        NaN  1.0
19               9.5  simulation       0.0  1.0       NaN        NaN  1.0
20              10.0  simulation       0.0  1.0       NaN        NaN  1.0

     p2   p3  ...  observable_x3  observable_x1_scaled  \
0   0.5  0.4  ...       0.700000              0.200000
1   0.5  0.4  ...       0.191491              1.078734
2   0.5  0.4  ...       0.096424              1.160145
3   0.5  0.4  ...       0.076076              1.140799
4   0.5  0.4  ...       0.069694              1.121069
5   0.5  0.4  ...       0.066301              1.106112
6   0.5  0.4  ...       0.063733              1.093741
7   0.5  0.4  ...       0.061506              1.082720
8   0.5  0.4  ...       0.059495              1.072561
9   0.5  0.4  ...       0.057653              1.063076
10  0.5  0.4  ...       0.055960              1.054183
11  0.5  0.4  ...       0.054400              1.045829
12  0.5  0.4  ...       0.052960              1.037978
13  0.5  0.4  ...       0.051629              1.030598
14  0.5  0.4  ...       0.050399              1.023660
15  0.5  0.4  ...       0.049259              1.017136
16  0.5  0.4  ...       0.048203              1.011000
17  0.5  0.4  ...       0.047224              1.005231
18  0.5  0.4  ...       0.046315              0.999804
19  0.5  0.4  ...       0.045471              0.994700
20  0.5  0.4  ...       0.044686              0.989898

    observable_x2_offsetted  observable_x1withsigma  observable_x1_std  \
0                  3.400000                0.100000                1.0
1                  3.684679                0.539367                1.0
2                  3.733287                0.580072                1.0
3                  3.730652                0.570399                1.0
4                  3.715836                0.560535                1.0
5                  3.698751                0.553056                1.0
6                  3.681963                0.546871                1.0
```

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```
7                   3.666109                0.541360                1.0
8                   3.651302                0.536280                1.0
9                   3.637515                0.531538                1.0
10                  3.624681                0.527091                1.0
11                  3.612733                0.522914                1.0
12                  3.601603                0.518989                1.0
13                  3.591229                0.515299                1.0
14                  3.581555                0.511830                1.0
15                  3.572529                0.508568                1.0
16                  3.564103                0.505500                1.0
17                  3.556234                0.502615                1.0
18                  3.548881                0.499902                1.0
19                  3.542008                0.497350                1.0
20                  3.535581                0.494949                1.0

    observable_x2_std  observable_x3_std  observable_x1_scaled_std  \
0                 1.0                1.0                       1.0
1                 1.0                1.0                       1.0
2                 1.0                1.0                       1.0
3                 1.0                1.0                       1.0
4                 1.0                1.0                       1.0
5                 1.0                1.0                       1.0
6                 1.0                1.0                       1.0
7                 1.0                1.0                       1.0
8                 1.0                1.0                       1.0
9                 1.0                1.0                       1.0
10                1.0                1.0                       1.0
11                1.0                1.0                       1.0
12                1.0                1.0                       1.0
13                1.0                1.0                       1.0
14                1.0                1.0                       1.0
15                1.0                1.0                       1.0
16                1.0                1.0                       1.0
17                1.0                1.0                       1.0
18                1.0                1.0                       1.0
19                1.0                1.0                       1.0
20                1.0                1.0                       1.0

    observable_x2_offsetted_std  observable_x1withsigma_std
0                           1.0                         0.1
1                           1.0                         0.1
2                           1.0                         0.1
3                           1.0                         0.1
4                           1.0                         0.1
5                           1.0                         0.1
6                           1.0                         0.1
7                           1.0                         0.1
8                           1.0                         0.1
9                           1.0                         0.1
10                          1.0                         0.1
11                          1.0                         0.1
12                          1.0                         0.1
```

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```
13                          1.0                          0.1
14                          1.0                          0.1
15                          1.0                          0.1
16                          1.0                          0.1
17                          1.0                          0.1
18                          1.0                          0.1
19                          1.0                          0.1
20                          1.0                          0.1

[21 rows x 35 columns]
```

[29]:
```
# look at the States in rdata as DataFrame
amici.getSimulationStatesAsDataFrame(model, [edata], [rdata])
```

[29]:
```
   condition_id  time  t_presim   k0  k0_preeq  k0_presim   p1   p2   p3   p4  \
0                0.0       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
1                0.5       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
2                1.0       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
3                1.5       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
4                2.0       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
5                2.5       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
6                3.0       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
7                3.5       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
8                4.0       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
9                4.5       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
10               5.0       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
11               5.5       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
12               6.0       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
13               6.5       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
14               7.0       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
15               7.5       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
16               8.0       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
17               8.5       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
18               9.0       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
19               9.5       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0
20              10.0       0.0  1.0       NaN        NaN  1.0  0.5  0.4  2.0

    ...  p2_scale  p3_scale  p4_scale  p5_scale  scale_scale  offset_scale  \
0   ...         0         0         0         0            0             0
1   ...         0         0         0         0            0             0
2   ...         0         0         0         0            0             0
3   ...         0         0         0         0            0             0
4   ...         0         0         0         0            0             0
5   ...         0         0         0         0            0             0
6   ...         0         0         0         0            0             0
7   ...         0         0         0         0            0             0
8   ...         0         0         0         0            0             0
9   ...         0         0         0         0            0             0
10  ...         0         0         0         0            0             0
11  ...         0         0         0         0            0             0
12  ...         0         0         0         0            0             0
13  ...         0         0         0         0            0             0
```

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```
14  ...          0         0         0         0         0         0
15  ...          0         0         0         0         0         0
16  ...          0         0         0         0         0         0
17  ...          0         0         0         0         0         0
18  ...          0         0         0         0         0         0
19  ...          0         0         0         0         0         0
20  ...          0         0         0         0         0         0

    sigma_scale        x1        x2        x3
0             0  0.100000  0.400000  0.700000
1             0  0.539367  0.684679  0.191491
2             0  0.580072  0.733287  0.096424
3             0  0.570399  0.730652  0.076076
4             0  0.560535  0.715836  0.069694
5             0  0.553056  0.698751  0.066301
6             0  0.546871  0.681963  0.063733
7             0  0.541360  0.666109  0.061506
8             0  0.536280  0.651302  0.059495
9             0  0.531538  0.637515  0.057653
10            0  0.527091  0.624681  0.055960
11            0  0.522914  0.612733  0.054400
12            0  0.518989  0.601603  0.052960
13            0  0.515299  0.591229  0.051629
14            0  0.511830  0.581555  0.050399
15            0  0.508568  0.572529  0.049259
16            0  0.505500  0.564103  0.048203
17            0  0.502615  0.556234  0.047224
18            0  0.499902  0.548881  0.046315
19            0  0.497350  0.542008  0.045471
20            0  0.494949  0.535581  0.044686

[21 rows x 25 columns]
```

10.2.3 Using PEtab

This notebook illustrates how to run model simulations based on PEtab problems with AMICI.

PEtab is a format for specifying parameter estimation problems in systems biology. It is based on SBML and TSV files. (AMICI also supports PySB-based PEtab problems, that will be covered by PEtab v2). The Python package pyPESTO provides a convenient interface for parameter estimation with PEtab problems and uses AMICI as a backend. However, AMICI can also be used directly to simulate PEtab problems. This is illustrated in this notebook.

[1]:
```
import petab

from amici import runAmiciSimulation
from amici.petab.petab_import import import_petab_problem
from amici.petab.petab_problem import PetabProblem
from amici.petab.simulations import simulate_petab
from amici.plotting import plot_state_trajectories
```

Importing a PEtab problem

We use the Boehm_JProteomeRes2014 example model from the benchmark collection:

[2]:
```
model_name = "Boehm_JProteomeRes2014"
# local path or URL to the yaml file for the PEtab problem
petab_yaml = f"https://raw.githubusercontent.com/Benchmarking-Initiative/Benchmark-
↪Models-PEtab/master/Benchmark-Models/{model_name}/{model_name}.yaml"
# load the problem using the PEtab library
petab_problem = petab.Problem.from_yaml(petab_yaml)
```

Next, we import the model to amici using `import_petab_problem`. `import_petab_problem` has many options to choose between faster importer or more flexible or faster model simulations. We import the model with default settings, and we obtain an AMICI model instance:

[3]:
```
amici_model = import_petab_problem(petab_problem, verbose=False)
```

That's it. Now, we can use the model to perform simulations.

Simulating a PEtab problem

For simple simulations, a function `simulate_petab` is available. This function will simulate the model for all conditions specified in the PEtab problem and compute the objective value (and if requested, the gradient). `simulate_petab` is mostly useful for running individual simulations. If large numbers of model simulations are required, there are more efficient means. In particular, for parameter estimation, consider using the optimized objective function provided by pyPESTO.

We use the `simulate_petab` function to simulate the model at the nominal parameters (i.e., the parameters specified in the PEtab problem in the `nominalValue` column of the parameter table):

[4]:
```
simulate_petab(petab_problem, amici_model)
```

[4]:
```
{'llh': -138.22199760826,
 'sllh': None,
 'rdatas': [<ReturnDataView(id='model1_data1', status=AMICI_SUCCESS)>],
 'edatas': [<Swig Object of type 'std::vector< amici::ExpData * >::value_type' at␣
↪0x7feef33effc0
    condition 'model1_data1' starting at t=0.0 with custom parameter scales, constants,␣
↪parameters
    16x3 time-resolved datapoints
      (48/48 measurements & 0/48 sigmas set)
    10x0 event-resolved datapoints
      (0/0 measurements & 0/0 sigmas set)
  >]}
```

Parameters can also be directly specified, both scaled and unscaled:

[5]:
```
parameters = {
    x_id: x_val
    for x_id, x_val in zip(petab_problem.x_ids, petab_problem.x_nominal_scaled)
    # Fixed parameters cannot be changed in `simulate_petab`, unless we explicitly pass
    #  a `parameter_mapping` that was generated with `fill_fixed_parameters=False`
    if x_id not in amici_model.getFixedParameterIds()
}
```

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```
simulate_petab(
    petab_problem,
    amici_model,
    problem_parameters=parameters,
    scaled_parameters=True,
)
```

[5]:
```
{'llh': -138.22199760826,
 'sllh': None,
 'rdatas': [<ReturnDataView(id='model1_data1', status=AMICI_SUCCESS)>],
 'edatas': [<Swig Object of type 'std::vector< amici::ExpData * >::value_type' at␣
↪0x7feef33ef780
    condition 'model1_data1' starting at t=0.0 with custom parameter scales, constants,␣
↪parameters
    16x3 time-resolved datapoints
      (48/48 measurements & 0/48 sigmas set)
    10x0 event-resolved datapoints
      (0/0 measurements & 0/0 sigmas set)
  >]}
```

Working with PEtab-defined simulation conditions

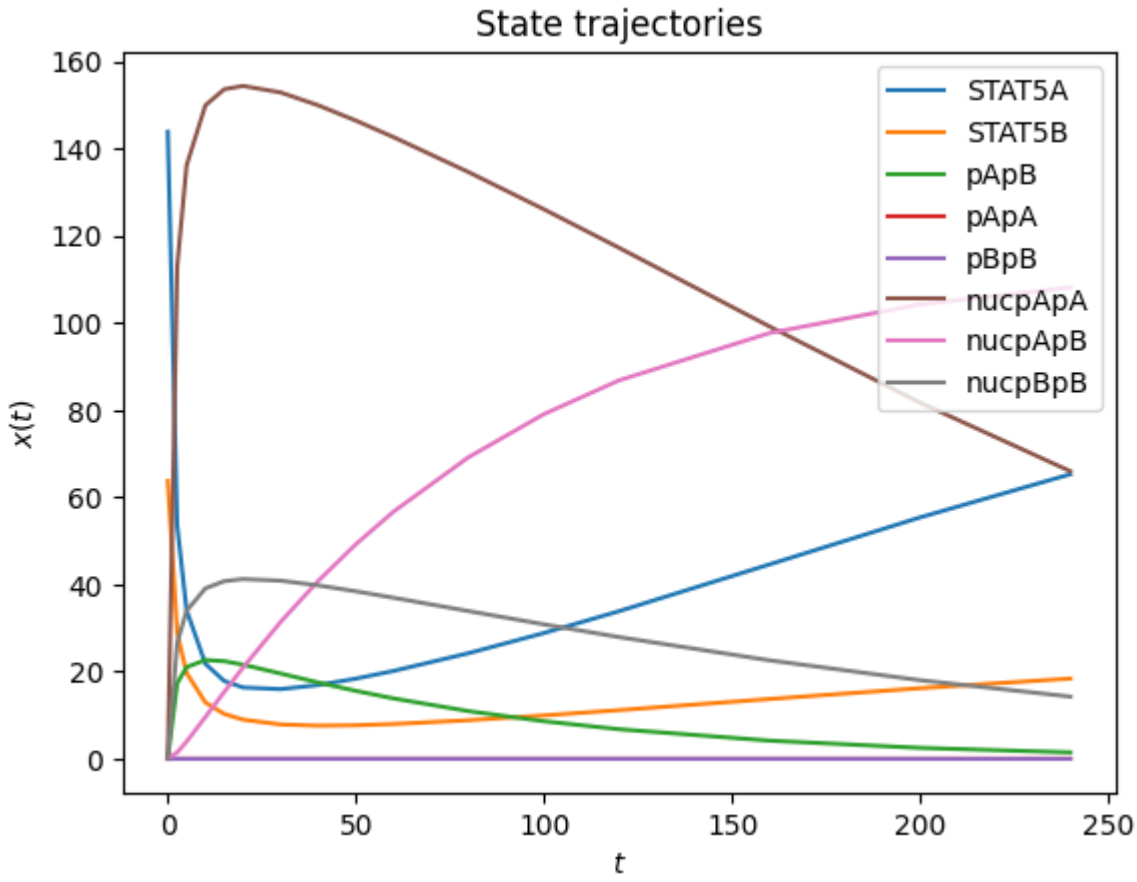
`simulate_petab` is convenient for quickly simulating PEtab-based problems, but for certain applications it may be too inflexible. For example, it is not easily possible to obtain model outputs for time points other than the measurement timepoints specified in the PEtab problem. In such a case, the `PetabProblem` class can be used to easily generate AMICI `ExpData` objects representing PEtab-defined simulation conditions:

[6]:
```
app = PetabProblem(petab_problem)

# ExpData for all conditions:
app.get_edatas()

# ExpData for a single condition:
edata = app.get_edata("model1_data1")
```

[7]:
```
rdata = runAmiciSimulation(amici_model, solver=amici_model.getSolver(), edata=edata)
rdata
```

[7]:
```
<ReturnDataView(id='model1_data1', status=AMICI_SUCCESS)>
```

[8]:
```
plot_state_trajectories(rdata)
```



For further information, check out the AMICI documentation.

10.2.4 AMICI Python example "Experimental Conditions"

In this example we will explore some more options for the initialization of experimental conditions, including how to reset initial conditions based on changing values for `fixedParameters` as well as an additional presimulation phase on top of preequilibration. This notebook is expected to run from the `python/example_presimulation` directory.

[1]:
```
# SBML model we want to import
sbml_file = "model_presimulation.xml"
# Name of the model that will also be the name of the python module
model_name = "model_presimulation"
# Directory to which the generated model code is written
model_output_dir = model_name

from pprint import pprint

import libsbml
import numpy as np

import amici.plotting
```

Model Loading

Here we load a simple model of protein phosphorylation that can be inhibited by a drug. This model was created using PySB (see `createModel.py`)

[2]:
```
sbml_reader = libsbml.SBMLReader()
sbml_doc = sbml_reader.readSBML(sbml_file)
sbml_model = sbml_doc.getModel()

print("Species:")
pprint([(s.getId(), s.getName()) for s in sbml_model.getListOfSpecies()])

print("\nReactions:")
for reaction in sbml_model.getListOfReactions():
    reactants = " + ".join(
        [
            "%s %s"
            % (
                int(r.getStoichiometry()) if r.getStoichiometry() > 1 else "",
                r.getSpecies(),
            )
            for r in reaction.getListOfReactants()
        ]
    )
    products = " + ".join(
        [
            "%s %s"
            % (
                int(r.getStoichiometry()) if r.getStoichiometry() > 1 else "",
                r.getSpecies(),
            )
            for r in reaction.getListOfProducts()
        ]
    )
    reversible = "<" if reaction.getReversible() else ""
    print(
        "%3s: %10s %1s->%10s\t\t[%s]"
        % (
            reaction.getName(),
            reactants,
            reversible,
            products,
            libsbml.formulaToL3String(reaction.getKineticLaw().getMath()),
        )
    )

print("Parameters:")
pprint([(p.getId(), p.getName()) for p in sbml_model.getListOfParameters()])
```

```
Species:
[('__s0', "PROT(kin=None, drug=None, phospho='u')"),
 ('__s1', 'DRUG(bound=None)'),
 ('__s2', 'KIN(bound=None)'),
 ('__s3', "DRUG(bound=1) ._br_PROT(kin=None, drug=1, phospho='u')"),
```

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```
 ('__s4', "KIN(bound=1) ._br_PROT(kin=1, drug=None, phospho='u')"),
 ('__s5', "PROT(kin=None, drug=None, phospho='p')")]

Reactions:
PROT_DRUG_bind:  __s0 +  __s1 <->      __s3             [-(koff_prot_drug * __s3) + kon_
↪prot_drug * __s0 * __s1]
PROT_KIN_bind:  __s0 +  __s2  ->      __s4              [kon_prot_kin * __s0 * __s2]
PROT_KIN_phospho:       __s4  -> __s2 +  __s5           [kphospho_prot_kin * __s4]
PROT_dephospho:       __s5  ->      __s0           [kdephospho_prot * __s5]
Parameters:
[('initProt', 'initProt'),
 ('initDrug', 'initDrug'),
 ('initKin', 'initKin'),
 ('pPROT_obs', 'pPROT_obs'),
 ('PROT_0', 'PROT_0'),
 ('DRUG_0', 'DRUG_0'),
 ('KIN_0', 'KIN_0'),
 ('kon_prot_drug', 'kon_prot_drug'),
 ('koff_prot_drug', 'koff_prot_drug'),
 ('kon_prot_kin', 'kon_prot_kin'),
 ('kphospho_prot_kin', 'kphospho_prot_kin'),
 ('kdephospho_prot', 'kdephospho_prot'),
 ('__obs0', 'pPROT'),
 ('__obs1', 'tPROT')]
```

[3]:
```
# Create an SbmlImporter instance for our SBML model
sbml_importer = amici.SbmlImporter(sbml_file)
```

For this example we want to specify the initial drug and kinase concentrations as experimental conditions. Accordingly, we specify them as `fixedParameters`. The meaning of `fixedParameters` is defined in the Glossary, which we display here for convenience.

[4]:
```
from IPython.display import IFrame

IFrame(
    "https://amici.readthedocs.io/en/latest/glossary.html#term-fixed-parameters",
    width=600,
    height=175,
)
```

[4]:
```
<IPython.lib.display.IFrame at 0x10ce15b50>
```

[5]:
```
fixedParameters = ["DRUG_0", "KIN_0"]
```

The SBML model specifies a single observable named pPROT which describes the fraction of phosphorylated Protein. We load this observable using amici.assignmentRules2observables.

[6]:
```
# Retrieve model output names and formulae from AssignmentRules and remove the␣
↪respective rules
observables = amici.assignmentRules2observables(
    sbml_importer.sbml,  # the libsbml model object
    filter_function=lambda variable: variable.getName() == "pPROT",
```

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```
)
print("Observables:")
pprint(observables)
```

```
Observables:
{'__obs0': {'formula': '__s5', 'name': 'pPROT'}}
```

Now the model is ready for compilation using sbml2amici. Note that we here pass `fixedParameters` as arguments to `constant_parameters`, which ensures that amici is aware that we want to have them as `fixedParameters`:

[7]:
```
sbml_importer.sbml2amici(
    model_name,
    model_output_dir,
    verbose=False,
    observables=observables,
    constant_parameters=fixedParameters,
)
# load the generated module
model_module = amici.import_model_module(model_name, model_output_dir)
```

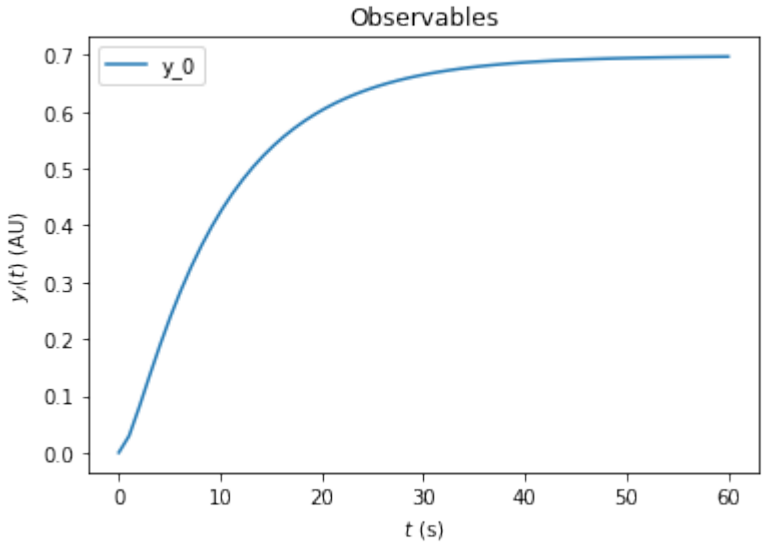
To simulate the model we need to create an instance via the `getModel()` method in the generated model module.

[8]:
```
# Create Model instance
model = model_module.getModel()

# Create solver instance
solver = model.getSolver()
```

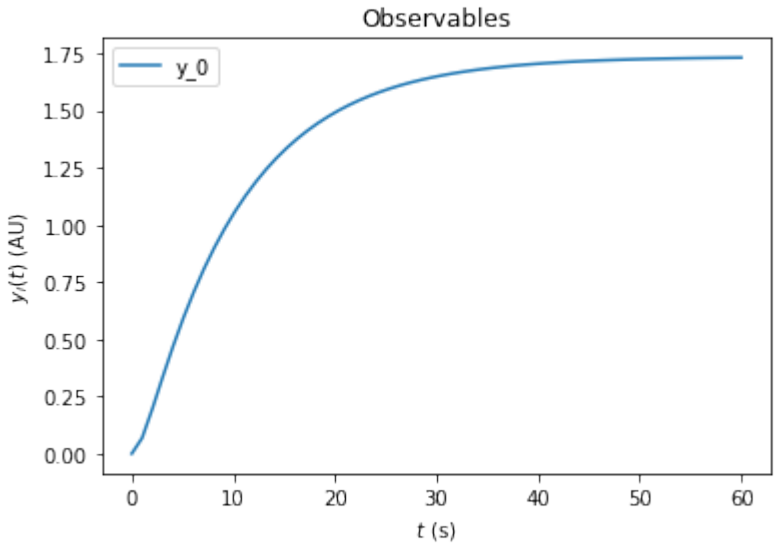
The only thing we need to simulate the model is a timepoint vector, which can be specified using the setTimepoints method. If we do not specify any additional options, the default values for `fixedParameters` and `parameters` that were specified in the SBML file will be used.

[9]:
```
# Run simulation using default model parameters and solver options
model.setTimepoints(np.linspace(0, 60, 60))
rdata = amici.runAmiciSimulation(model, solver)
amici.plotting.plotObservableTrajectories(rdata)
```



Simulation options can be specified either in the Model or in an ExpData instance. The `ExpData` instance can also carry experimental data. To initialize an `ExpData` instance from simulation results, amici offers some convenient constructors. In the following we will initialize an `ExpData` object from simulation results, but add noise with standard deviation `0.1` and specify the standard deviation accordingly. Moreover, we will specify custom values for `DRUG_0=0` and `KIN_0=2`. If `fixedParameter` is specified in an `ExpData` instance, runAmiciSimulation will use those parameters instead of the ones specified in the `Model` instance.

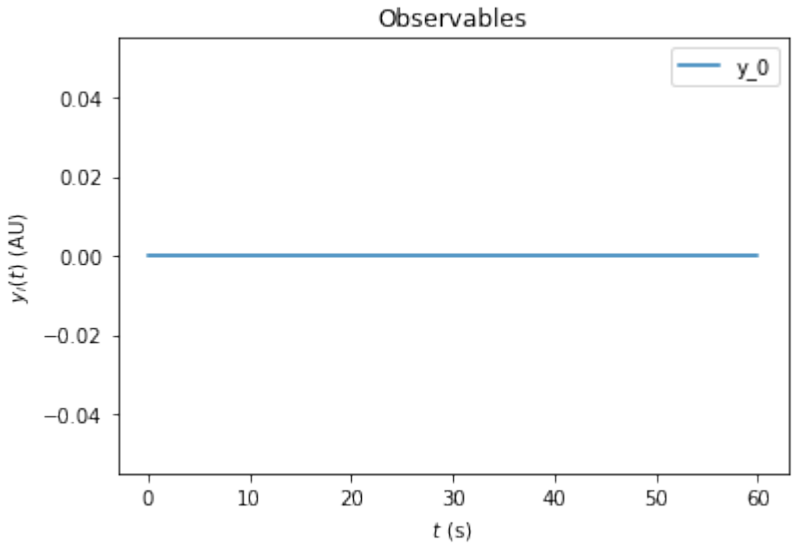
[10]:
```
edata = amici.ExpData(rdata, 0.1, 0.0)
edata.fixedParameters = [0, 2]
rdata = amici.runAmiciSimulation(model, solver, edata)
amici.plotting.plotObservableTrajectories(rdata)
```



For many biological systems, it is reasonable to assume that they start in a steady state. In this example we want to specify an experiment where a pretreatment with a drug is performed *before* the kinase is added. We assume that the pretreatment is sufficiently long such that the system reaches steadystate before the kinase is added. To implement this in amici, we can specify `fixedParametersPreequilibration` in the `ExpData` object. This automatically adds a preequilibration phase where the model is run to steadystate, before regular simulation starts. Here we set `DRUG_0=3`

and KIN_0=0 for the preequilibration. This means that there is no kinase available in the preequilibration phase.

[11]:
```
edata.fixedParametersPreequilibration = [3, 0]
rdata = amici.runAmiciSimulation(model, solver, edata)
amici.plotting.plotObservableTrajectories(rdata)
```

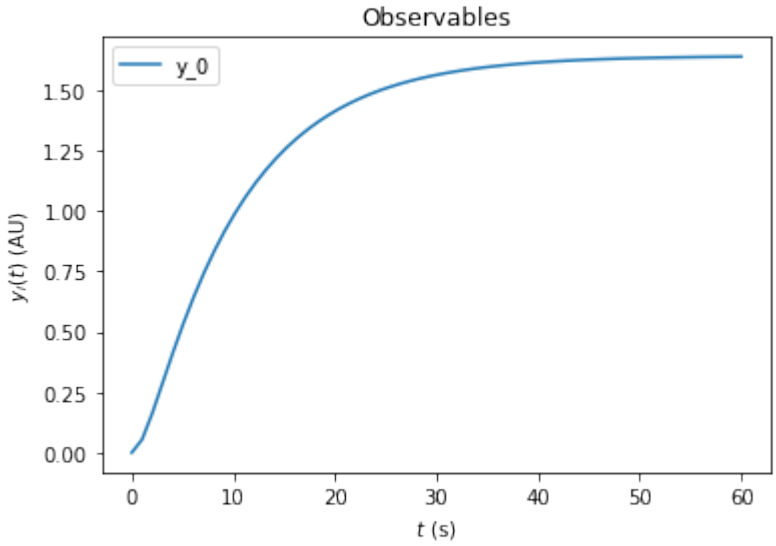


The resulting trajectory is definitely not what one may expect. The problem is that the DRUG_0 and KIN_0 set initial conditions for species in the model. By default, these initial conditions are only applied at the very beginning of the simulation, i.e., before the preequilibration. Accordingly, the fixedParameters that we specified do not have any effect. To fix this, we need to set the reinitializeFixedParameterInitialStates attribute to True, to specify that AMICI reinitializes all states that have fixedParameter-dependent initial states.

[12]:
```
edata.reinitializeFixedParameterInitialStates = True
```

With this option activated, the kinase concentration will be reinitialized after the preequilibration and we will see the expected change in fractional phosphorylation:

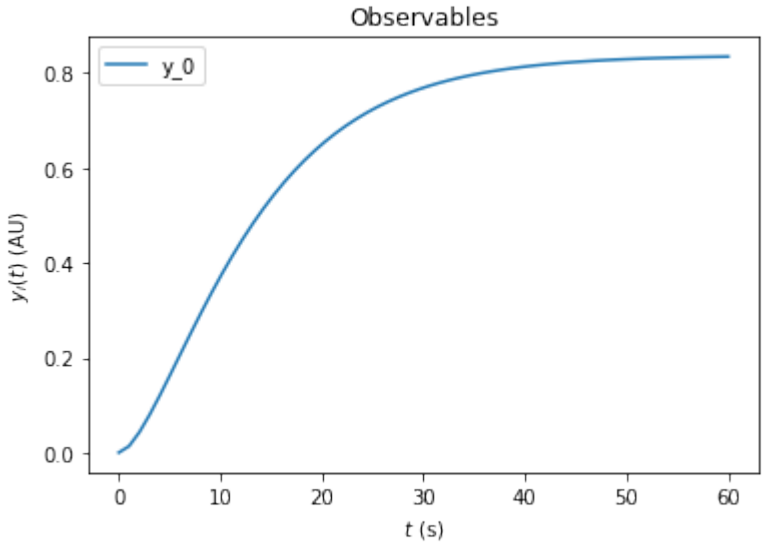
[13]:
```
rdata = amici.runAmiciSimulation(model, solver, edata)
amici.plotting.plotObservableTrajectories(rdata)
```



On top of preequilibration, we can also specify presimulation. This option can be used to specify pretreatments where the system is not assumed to reach steadystate. Presimulation can be activated by specifying `t_presim` and `edata.fixedParametersPresimulation`. If both `fixedParametersPresimulation` and `fixedParametersPreequilibration` are specified, preequilibration will be performed first, followed by presimulation, followed by regular simulation. For this example we specify `DRUG_0=10` and `KIN_0=0` for the presimulation and `DRUG_0=10` and `KIN_0=2` for the regular simulation. We do not overwrite the `DRUG_0=3` and `KIN_0=0` that was previously specified for preequilibration.

[14]:
```
edata.t_presim = 10
edata.fixedParametersPresimulation = [10.0, 0.0]
edata.fixedParameters = [10.0, 2.0]
print(edata.fixedParametersPreequilibration)
print(edata.fixedParametersPresimulation)
print(edata.fixedParameters)
rdata = amici.runAmiciSimulation(model, solver, edata)
amici.plotting.plotObservableTrajectories(rdata)
```

```
(3.0, 0.0)
(10.0, 0.0)
(10.0, 2.0)
```



10.2.5 AMICI documentation example of the steady state solver logic

This is an example to document the internal logic of the steady state solver, which is used in preequilibration and postequilibration.

Steady states of dynamical system

Not every dynamical system needs to run into a steady state. Instead, it may exhibit

- continuous growth, e.g.,

$$\dot{x} = x, \quad x_0 = 1$$

- a finite-time blow up, e.g.,

$$\dot{x} = x^2, \quad x_0 = 1$$

- oscillations, e.g.,

$$\ddot{x} = -x, \quad x_0 = 1$$

- chaotic behaviour, e.g., the Lorentz attractor

If the considered dynamical system has a steady state for positive times, then integrating the ODE long enough will equilibrate the system to this steady state. However, this may be computationally more demanding than other approaches and may fail, if the maximum number of integration steps is exceeded before reaching the steady state.

In general, Newton's method will find the steady state faster than forward simulation. However, it only converges if started close enough to the steady state. Moreover, it will not work, if the dynamical system has conserved quantities which were not removed prior to steady state computation: Conserved quantities will cause singularities in the Jacobian of the right hand side of the system, such that the linear problem within each step of Newton's method can not be solved.

Logic of the steady state solver

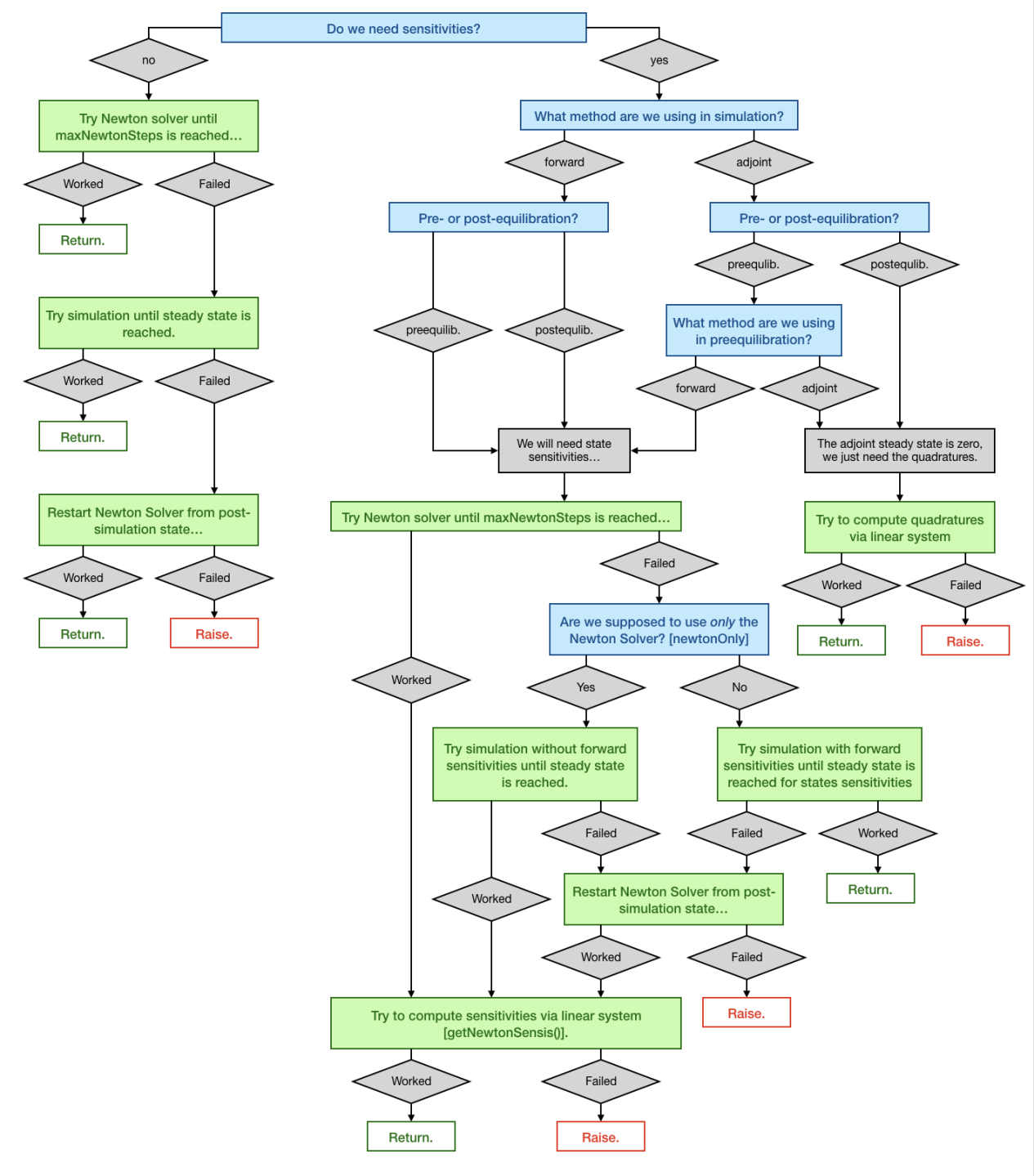
If AMICI has to equilibrate a dynamical system, it can do this either via simulating until the right hand side of the system becomes small, or it can try to find the steady state directly by Newton's method. Amici decides automatically which approach is chosen and how forward or adjoint sensitivities are computed, if requested. However, the user can influence this behavior, if prior knowledge about the dynamical is available.

The logic which AMICI will follow to equilibrate the system works as follows:

[1]:
```
from IPython.display import Image

fig = Image(
    filename="../../../documentation/gfx/steadystate_solver_workflow.png"
)
fig
```

[1]:


Do we need sensitivities?
no
yes
Try Newton solver until maxNewtonSteps is reached…
Worked
Failed
Return.
Try simulation until steady state is reached.
Worked
Failed
Return.
Restart Newton Solver from post-simulation state…
Worked
Failed
Return.
Raise.
What method are we using in simulation?
forward
adjoint
Pre- or post-equilibration?
preequilib.
postequilib.
Pre- or post-equilibration?
preequilib.
postequilib.
What method are we using in preequilibration?
forward
adjoint
We will need state sensitivities…
The adjoint steady state is zero, we just need the quadratures.
Try Newton solver until maxNewtonSteps is reached…
Failed
Are we supposed to use *only* the Newton Solver? [newtonOnly]
Worked
Yes
No
Try simulation without forward sensitivities until steady state is reached.
Failed
Worked
Restart Newton Solver from post-simulation state…
Worked
Failed
Raise.
Try simulation with forward sensitivities until steady state is reached for states sensitivities
Failed
Worked
Return.
Try to compute quadratures via linear system
Worked
Failed
Return.
Raise.
Try to compute sensitivities via linear system [getNewtonSensis()].
Worked
Failed
Return.
Raise.

The example model

We will use the example model `model_constant_species.xml`, which has conserved species. Those are automatically removed in the SBML import of AMICI, but they can also be kept in the model to demonstrate the failure of Newton's method due to a singular right hand side Jacobian.

[2]:
```
import libsbml
import amici
import os
import numpy as np

# SBML model we want to import
sbml_file = "model_constant_species.xml"

# Name of the models that will also be the name of the python module
model_name = "model_constant_species"
model_reduced_name = model_name + "_reduced"

# Directories to which the generated model code is written
model_output_dir = model_name
model_reduced_output_dir = model_reduced_name

# Read the model and give some output
sbml_reader = libsbml.SBMLReader()
sbml_doc = sbml_reader.readSBML(sbml_file)
sbml_model = sbml_doc.getModel()
dir(sbml_doc)

print("Species: ", [s.getId() for s in sbml_model.getListOfSpecies()])

print("\nReactions:")
for reaction in sbml_model.getListOfReactions():
    reactants = " + ".join(
        [
            "%s %s"
            % (
                int(r.getStoichiometry()) if r.getStoichiometry() > 1 else "",
                r.getSpecies(),
            )
            for r in reaction.getListOfReactants()
        ]
    )
    products = " + ".join(
        [
            "%s %s"
            % (
                int(r.getStoichiometry()) if r.getStoichiometry() > 1 else "",
                r.getSpecies(),
            )
            for r in reaction.getListOfProducts()
        ]
    )
    reversible = "<" if reaction.getReversible() else ""
```

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```
    print(
        "%3s: %10s %1s->%10s\t\t[%s]"
        % (
            reaction.getId(),
            reactants,
            reversible,
            products,
            libsbml.formulaToL3String(reaction.getKineticLaw().getMath()),
        )
    )
```

```
Species:  ['substrate', 'enzyme', 'complex', 'product']

Reactions:
creation:             -> substrate              [compartment * (synthesis_substrate + k_
↪create)]
binding:  substrate +  enzyme <->   complex             [compartment * (k_bind *␣
↪substrate * enzyme - k_unbind * complex)]
conversion:    complex  -> enzyme +  product            [compartment * k_convert *␣
↪complex]
decay:    product  ->                   [compartment * k_decay * product]
```

[3]:
```
# Create an SbmlImporter instance for our SBML model
sbml_importer = amici.SbmlImporter(sbml_file)

# specify observables and constant parameters
constantParameters = ["synthesis_substrate", "init_enzyme"]
observables = {
    "observable_product": {"name": "", "formula": "product"},
    "observable_substrate": {"name": "", "formula": "substrate"},
}
sigmas = {"observable_product": 1.0, "observable_substrate": 1.0}

# import the model
sbml_importer.sbml2amici(
    model_reduced_name,
    model_reduced_output_dir,
    observables=observables,
    constant_parameters=constantParameters,
    sigmas=sigmas,
)
sbml_importer.sbml2amici(
    model_name,
    model_output_dir,
    observables=observables,
    constant_parameters=constantParameters,
    sigmas=sigmas,
    compute_conservation_laws=False,
)
```

[4]:
```
# import the models and run some test simulations
model_reduced_module = amici.import_model_module(
```

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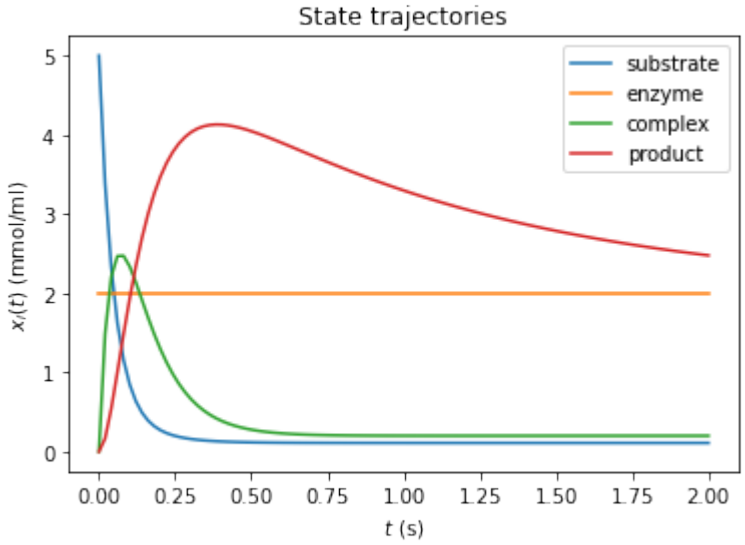
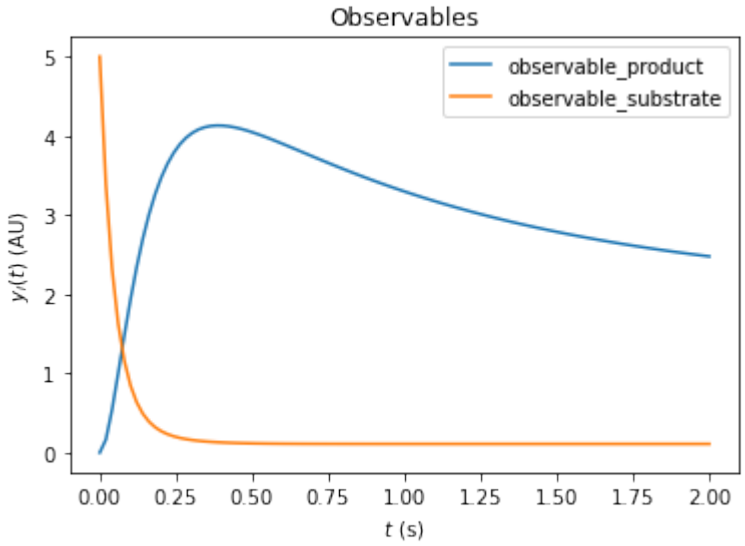
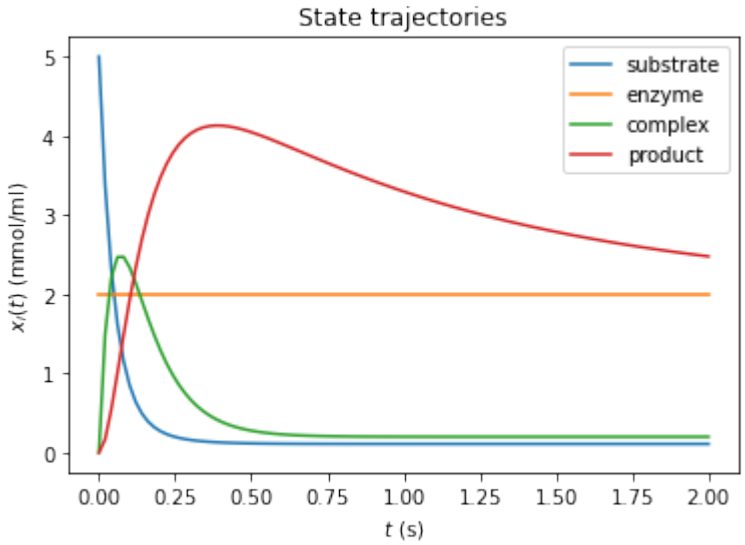
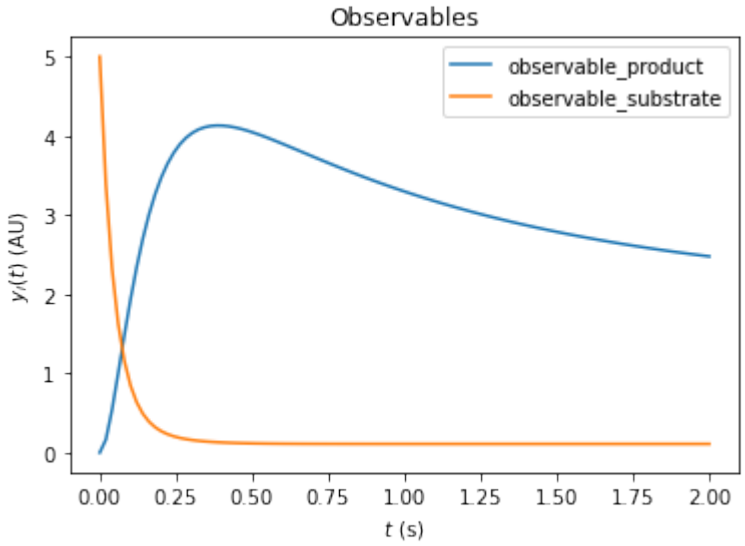
```
    model_reduced_name, os.path.abspath(model_reduced_output_dir)
)
model_reduced = model_reduced_module.getModel()

model_module = amici.import_model_module(
    model_name, os.path.abspath(model_output_dir)
)
model = model_module.getModel()


# simulate model with conservation laws
model_reduced.setTimepoints(np.linspace(0, 2, 100))
solver_reduced = model_reduced.getSolver()
rdata_reduced = amici.runAmiciSimulation(model_reduced, solver_reduced)

# simulate model without conservation laws
model.setTimepoints(np.linspace(0, 2, 100))
solver = model.getSolver()
rdata = amici.runAmiciSimulation(model, solver)

# plot trajectories
import amici.plotting

amici.plotting.plotStateTrajectories(rdata_reduced, model=model_reduced)
amici.plotting.plotObservableTrajectories(rdata_reduced, model=model_reduced)

amici.plotting.plotStateTrajectories(rdata, model=model)
amici.plotting.plotObservableTrajectories(rdata, model=model)
```




Observables
observable_product
observable_substrate
$y_i(t)$ (AU)
t (s)
0
1
2
3
4
5
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1.75
2.00


State trajectories
substrate
enzyme
complex
product
$x_i(t)$ (mmol/ml)
t (s)
0
1
2
3
4
5
0.00
0.25
0.50
0.75
1.00
1.25
1.50
1.75
2.00



Inferring the steady state of the system (postequilibration)

First, we want to demonstrate that Newton's method will fail with the unreduced model due to a singular right hand side Jacobian.

[5]:
```
# Call postequilibration by setting an infinity timepoint
model.setTimepoints(np.full(1, np.inf))

# set the solver
solver = model.getSolver()
solver.setNewtonMaxSteps(10)
solver.setMaxSteps(1000)
rdata = amici.runAmiciSimulation(model, solver)

# np.set_printoptions(threshold=8, edgeitems=2)
for key, value in rdata.items():
    print("%12s: " % key, value)
```

```
          ts:  [inf]
           x:  [[0.11       2.         0.2        2.00000002]]
          x0:  [5. 2. 0. 0.]
        x_ss:  [nan nan nan nan]
          sx:  None
         sx0:  None
       sx_ss:  None
           y:  [[2.00000002 0.11      ]]
      sigmay:  [[1. 1.]]
          sy:  None
     ssigmay:  None
           z:  None
          rz:  None
      sigmaz:  None
          sz:  None
```

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```
         srz:  None
     ssigmaz:  None
        sllh:  None
       s2llh:  None
           J:  [[-20.    0.   20.    0. ]
 [ -1.1   0.    1.1   0. ]
 [  1.    0.  -11.   10. ]
 [  0.    0.    0.   -1. ]]
        xdot:  [ 0.00000000e+00  0.00000000e+00  2.22044605e-16 -2.24170307e-08]
      status:  0.0
         llh:  nan
        chi2:  nan
         res:  [0. 0.]
        sres:  None
         FIM:  None
           w:  [[2.         2.         2.         2.00000002]]
  preeq_wrms:  nan
     preeq_t:  nan
preeq_numlinsteps:  None
preeq_numsteps:  [[0 0 0]]
preeq_numstepsB:  12.0
preeq_status:  [[0 0 0]]
preeq_cpu_time:  0.0
preeq_cpu_timeB:  0.0
 posteq_wrms:  0.5604257578208488
    posteq_t:  19.2252094591474
posteq_numlinsteps:  None
posteq_numsteps:  [[  0 417   0]]
posteq_numstepsB:  0.0
posteq_status:  [[-3  1  0]]
posteq_cpu_time:  2.315
posteq_cpu_timeB:  0.0
    numsteps:  None
 numrhsevals:  None
numerrtestfails:  None
numnonlinsolvconvfails:  None
       order:  None
    cpu_time:  0.0
   numstepsB:  None
numrhsevalsB:  None
numerrtestfailsB:  None
numnonlinsolvconvfailsB:  None
   cpu_timeB:  0.0
```

The fields `posteq_status` and `posteq_numsteps` in rdata tells us how postequilibration worked:

- the first entry informs us about the status/number of steps in Newton's method (here 0, as Newton's method did not work)
- the second entry tells us, the status/how many integration steps were taken until steady state was reached
- the third entry informs us about the status/number of Newton steps in the second launch, after simulation

The status is encoded as an Integer flag with the following meanings:

- 1: Successful run
- 0: Did not run
- -1: Error: No further specification is given, the error message should give more information.
- -2: Error: The method did not converge to a steady state within the maximum number of steps (Newton's method or simulation).
- -3: Error: The Jacobian of the right hand side is singular (only Newton's method)
- -4: Error: The damping factor in Newton's method was reduced until it met the lower bound without success (Newton's method only)
- -5: Error: The model was simulated past the timepoint `t=1e100` without finding a steady state. Therefore, it is likely that the model has not steady state for the given parameter vector.

Here, only the second entry of `posteq_status` contains a positive integer: The first run of Newton's method failed due to a Jacobian, which oculd not be factorized, but the second run (simulation) contains the entry 1 (success). The third entry is 0, thus Newton's method was not launched for a second time. More information can be found in`posteq_numsteps`: Also here, only the second entry contains a positive integer, which is smaller than the maximum number of steps taken (<1000). Hence, steady state was reached via simulation, which corresponds to the simulated time written to `posteq_time`.

We want to demonstrate a complete failure if inferring the steady state by reducing the number of integration steps to a lower value:

[6]:
```
# reduce maxsteps for integration
solver.setMaxSteps(100)
rdata = amici.runAmiciSimulation(model, solver)
print("Status of postequilibration:", rdata["posteq_status"])
print(
    "Number of steps employed in postequilibration:", rdata["posteq_numsteps"]
)
```

```
Status of postequilibration: [[-3 -2 -3]]
Number of steps employed in postequilibration: [[  0 100   0]]
```

```
[Warning] AMICI:simulation: AMICI simulation failed:
Steady state computation failed. First run of Newton solver failed: RHS could not be␣
↪factorized. Simulation to steady state failed: No convergence was achieved. Second run␣
↪of Newton solver failed: RHS could not be factorized.
Error occured in:
0          0x1060f7913 amici::SteadystateProblem::handleSteadyStateFailure(amici::Solver␣
↪const*, amici::Model*) + 531
1          0x1060f6b3c amici::SteadystateProblem::findSteadyState(amici::Solver*, amici::
↪NewtonSolver*, amici::Model*, int) + 332
2          0x1060f6882 amici::SteadystateProblem::workSteadyStateProblem(amici::Solver*,␣
↪amici::Model*, int) + 322
3          0x1060a4615 amici::AmiciApplication::runAmiciSimulation(amici::Solver&, amici:
↪:ExpData const*, amici::Model&, bool) + 405
4
```

However, the same logic works, if we use the reduced model. For sufficiently many Newton steps, postequilibration is achieved by Newton's method in the first run. In this specific example, the steady state is found within one step.

[7]:
```
# Call postequilibration by setting an infinity timepoint
model_reduced.setTimepoints(np.full(1, np.inf))
```

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```
# set the solver
solver_reduced = model_reduced.getSolver()
solver_reduced.setNewtonMaxSteps(10)
solver_reduced.setMaxSteps(100)
rdata_reduced = amici.runAmiciSimulation(model_reduced, solver_reduced)

print("Status of postequilibration:", rdata_reduced["posteq_status"])
print(
    "Number of steps employed in postequilibration:",
    rdata_reduced["posteq_numsteps"],
)
```

```
Status of postequilibration: [[1 0 0]]
Number of steps employed in postequilibration: [[2 0 0]]
```

Postequilibration with sensitivities

Equilibration is possible with forward and adjoint sensitivity analysis. As for the main simulation part, adjoint sensitivity analysis yields less information than forward sensitivity analysis, since no state sensitivities are computed. However, it has a better scaling behavior towards large model sizes.

Postequilibration with forward sensitivities

If forward sensitivity analysis is used, then state sensitivities at the timepoint `np.inf` will be computed. This can be done in (currently) two different ways:

1. If the Jacobian $\nabla_x f$ of the right hand side f is not (close to) singular, the most efficient approach will be solving the linear system of equations, which defines the steady state sensitivities:

$$0 = \dot{s}^x = (\nabla_x f) s^x + \frac{\partial f}{\partial \theta} \qquad \Rightarrow \qquad (\nabla_x f) s^x = -\frac{\partial f}{\partial \theta}$$

   This approach will always be chosen by AMICI, if the option `model.SteadyStateSensitivityMode` is set to `SteadyStateSensitivityMode.newtonOnly`. Furthermore, it will also be chosen, if the steady state was found by Newton's method, as in this case, the Jacobian is at least not singular (but may still be poorly conditioned). A check for the condition number of the Jacobian is currently missing, but will soon be implemented.

2. If the Jacobian is poorly conditioned or singular, then the only way to obtain a reliable result will be integrating the state variables with state sensitivities until the norm of the right hand side becomes small. This approach will be chosen by AMICI, if the steady state was found by simulation and the option `model.SteadyStateSensitivityMode` is set to `SteadyStateSensitivityMode.simulationFSA`. This approach is numerically more stable, but the computation time for large models may be substantial.

Side remark:

A possible third way may consist in a (relaxed) Richardson iteration type approach, which interprets the entries of the right hand side f as residuals and minimizes the squared residuals $\|f\|^2$ by a Levenberg-Marquart-type algorithm. This approach would also work for poorly conditioned (and even for singular Jacobians if additional constraints are implemented as Lagrange multipliers) while being faster than a long forward simulation.

We want to demonstrate both possibilities to find the steady state sensitivities, as well as the failure of their computation if the Jacobian is singular and the `newtonOnly` setting was used.

[8]:
```
# Call simulation with singular Jacobian and integrateIfNewtonFails mode
model.setTimepoints(np.full(1, np.inf))
model.setSteadyStateSensitivityMode(
    amici.SteadyStateSensitivityMode.integrateIfNewtonFails
)
solver = model.getSolver()
solver.setNewtonMaxSteps(10)
solver.setSensitivityMethod(amici.SensitivityMethod.forward)
solver.setSensitivityOrder(amici.SensitivityOrder.first)
solver.setMaxSteps(10000)
rdata = amici.runAmiciSimulation(model, solver)

print("Status of postequilibration:", rdata["posteq_status"])
print(
    "Number of steps employed in postequilibration:", rdata["posteq_numsteps"]
)
print("Computed state sensitivities:")
print(rdata["sx"][0, :, :])
```

```
Status of postequilibration: [[-3  1  0]]
Number of steps employed in postequilibration: [[   0 1026    0]]
Computed state sensitivities:
[[-1.10000000e-02  0.00000000e+00 -6.70507402e-18 -1.20114408e-11]
 [ 1.00000000e-02  0.00000000e+00 -8.22965063e-19  1.20114329e-11]
 [-1.00000000e-03  0.00000000e+00 -2.00000000e-02 -2.40228711e-11]
 [ 5.50000000e-02  0.00000000e+00  1.00000000e-01  9.99999999e-01]
 [ 0.00000000e+00  0.00000000e+00  0.00000000e+00 -2.00000004e+00]]
```

[9]:
```
# Call simulation with singular Jacobian and newtonOnly mode (will fail)
model.setTimepoints(np.full(1, np.inf))
model.setSteadyStateSensitivityMode(
    amici.SteadyStateSensitivityMode.newtonOnly
)
solver = model.getSolver()
solver.setSensitivityMethod(amici.SensitivityMethod.forward)
solver.setSensitivityOrder(amici.SensitivityOrder.first)
solver.setMaxSteps(10000)
rdata = amici.runAmiciSimulation(model, solver)

print("Status of postequilibration:", rdata["posteq_status"])
print(
    "Number of steps employed in postequilibration:", rdata["posteq_numsteps"]
)
print("Computed state sensitivities:")
print(rdata["sx"][0, :, :])
```

```
Status of postequilibration: [[-2 -1  1]]
Number of steps employed in postequilibration: [[  0 543   0]]
Computed state sensitivities:
[[0. 0. 0. 0.]
 [0. 0. 0. 0.]
 [0. 0. 0. 0.]
 [0. 0. 0. 0.]
 [0. 0. 0. 0.]]
```

```
[Warning] AMICI:simulation: AMICI simulation failed:
Steady state sensitvitiy computation failed due to unsuccessful factorization of RHS␣
↪Jacobian
Error occured in:
0          0x1060f698b amici::SteadystateProblem::workSteadyStateProblem(amici::Solver*,␣
↪amici::Model*, int) + 587
1          0x1060a4615 amici::AmiciApplication::runAmiciSimulation(amici::Solver&, amici:
↪:ExpData const*, amici::Model&, bool) + 405
2          0x1060a4474 amici::runAmiciSimulation(amici::Solver&, amici::ExpData const*,␣
↪amici::Model&, bool) + 36
3          0x106061005 _wrap_runAmiciSimulation(_object*, _object*) + 549
4          0x1021b2309 cfunction_call_varargs + 320
5
```

[10]:
```
# Call postequilibration by setting an infinity timepoint
model_reduced.setTimepoints(np.full(1, np.inf))
model.setSteadyStateSensitivityMode(
    amici.SteadyStateSensitivityMode.newtonOnly
)
solver_reduced = model_reduced.getSolver()
solver_reduced.setNewtonMaxSteps(10)
solver_reduced.setSensitivityMethod(amici.SensitivityMethod.forward)
solver_reduced.setSensitivityOrder(amici.SensitivityOrder.first)
solver_reduced.setMaxSteps(1000)
rdata_reduced = amici.runAmiciSimulation(model_reduced, solver_reduced)

print("Status of postequilibration:", rdata_reduced["posteq_status"])
print(
    "Number of steps employed in postequilibration:",
    rdata_reduced["posteq_numsteps"],
)
print("Computed state sensitivities:")
print(rdata_reduced["sx"][0, :, :])
```

```
Status of postequilibration: [[1 0 0]]
Number of steps employed in postequilibration: [[2 0 0]]
Computed state sensitivities:
[[-1.1e-02  0.0e+00 -0.0e+00 -0.0e+00]
 [ 1.0e-02  0.0e+00 -0.0e+00 -0.0e+00]
 [-1.0e-03  0.0e+00 -2.0e-02 -0.0e+00]
 [ 5.5e-02  0.0e+00  1.0e-01  1.0e+00]
 [-0.0e+00  0.0e+00 -0.0e+00 -2.0e+00]]
```

Postequilibration with adjoint sensitivities

Postequilibration also works with adjoint sensitivities. In this case, it is exploited that the ODE of the adjoint state p will always have the steady state 0, since it's a linear ODE:

$$\frac{d}{dt}p(t) = J(x^*, \theta)^T p(t),$$

where x^* denotes the steady state of the system state. Since the Eigenvalues of the Jacobian are negative and since the Jacobian at steady state is a fixed matrix, this system has a simple algebraic solution:

$$p(t) = e^{tJ(x^*,\theta)^T} p_{\text{end}}.$$

As a consequence, the quadratures in adjoint computation also reduce to a matrix-vector product:

$$Q(x, \theta) = Q(x^*, \theta) = p_{\text{integral}} * \frac{\partial f}{\partial \theta}$$

with

$$p_{\text{integral}} = \int_0^\infty p(s)ds = (J(x^*, \theta)^T)^{-1} p_{\text{end}}.$$

However, this solution is given in terms of a linear system of equations defined by the transposed Jacobian of the right hand side. Hence, if the (transposed) Jacobian is singular, it is not applicable. In this case, standard integration must be carried out.

[11]:
```
# Call adjoint postequilibration by setting an infinity timepoint
# and create an edata object, which is needed for adjoint computation
edata = amici.ExpData(2, 0, 0, np.array([float("inf")]))
edata.setObservedData([1.8] * 2)
edata.fixedParameters = np.array([3.0, 5.0])

model_reduced.setSteadyStateSensitivityMode(
    amici.SteadyStateSensitivityMode.newtonOnly
)
solver_reduced = model_reduced.getSolver()
solver_reduced.setNewtonMaxSteps(10)
solver_reduced.setSensitivityMethod(amici.SensitivityMethod.adjoint)
solver_reduced.setSensitivityOrder(amici.SensitivityOrder.first)
solver_reduced.setMaxSteps(1000)
rdata_reduced = amici.runAmiciSimulation(model_reduced, solver_reduced, edata)

print("Status of postequilibration:", rdata_reduced["posteq_status"])
print(
    "Number of steps employed in postequilibration:",
    rdata_reduced["posteq_numsteps"],
)
print(
    "Number of backward steps employed in postequilibration:",
    rdata_reduced["posteq_numstepsB"],
)
print("Computed gradient:", rdata_reduced["sllh"])
```

```
Status of postequilibration: [[1 0 0]]
Number of steps employed in postequilibration: [[2 0 0]]
Number of backward steps employed in postequilibration: 0.0
Computed gradient: [-1.85900e-02  1.69000e-02 -1.69000e-03 -3.16282e+00  1.60000e+01]
```

If we carry out the same computation with a system that has a singular Jacobian, then `posteq_numstepsB` will not be `0` any more (which indicates that the linear system solve was used to compute backward postequilibration). Now, integration is carried out and hence `posteq_numstepsB > 0`

[12]:
```
# Call adjoint postequilibration with model with singular Jacobian
model.setSteadyStateSensitivityMode(
    amici.SteadyStateSensitivityMode.newtonOnly
)
solver = model.getSolver()
solver.setNewtonMaxSteps(10)
solver.setSensitivityMethod(amici.SensitivityMethod.adjoint)
solver.setSensitivityOrder(amici.SensitivityOrder.first)
rdata = amici.runAmiciSimulation(model, solver, edata)

print("Status of postequilibration:", rdata["posteq_status"])
print(
    "Number of steps employed in postequilibration:", rdata["posteq_numsteps"]
)
print(
    "Number of backward steps employed in postequilibration:",
    rdata["posteq_numstepsB"],
)
print("Computed gradient:", rdata["sllh"])
```

```
Status of postequilibration: [[-3 -1  1]]
Number of steps employed in postequilibration: [[  0 479   0]]
Number of backward steps employed in postequilibration: 3076.0
Computed gradient: [-1.85899987e-02  1.68999988e-02 -1.69000055e-03 -3.16282001e+00
  1.60000000e+01]
```

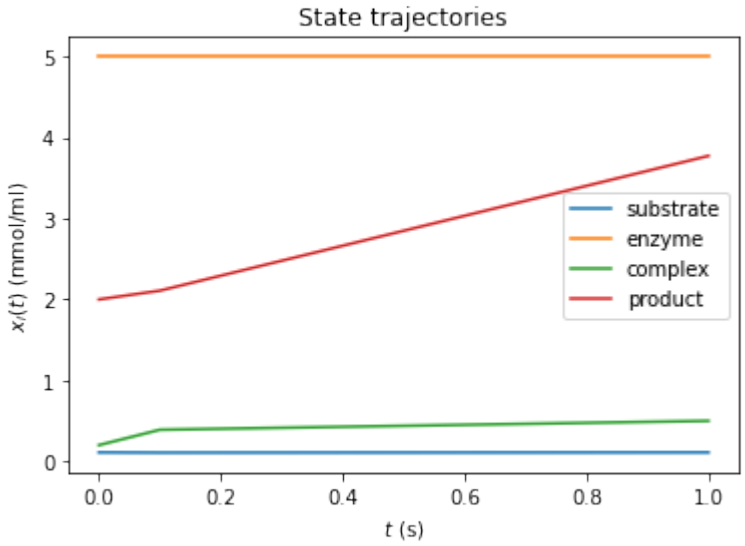
Preequilibrating the model

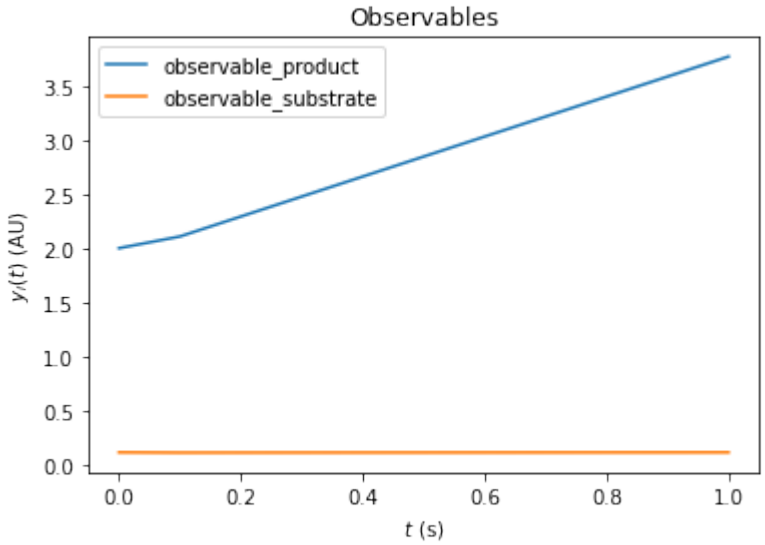
Sometimes, we want to launch a solver run from a steady state which was inferred numerically, i.e., the system was preequilibrated. In order to do this with AMICI, we need to pass an ExpData object, which contains fixed parameter for the actual simulation and for preequilibration of the model.

[13]:
```
# create edata, with 3 timepoints and 2 observables:
edata = amici.ExpData(2, 0, 0, np.array([0.0, 0.1, 1.0]))
edata.setObservedData([1.8] * 6)
edata.fixedParameters = np.array([3.0, 5.0])
edata.fixedParametersPreequilibration = np.array([0.0, 2.0])
edata.reinitializeFixedParameterInitialStates = True
```

[14]:
```
# create the solver object and run the simulation
solver_reduced = model_reduced.getSolver()
solver_reduced.setNewtonMaxSteps(10)
rdata_reduced = amici.runAmiciSimulation(model_reduced, solver_reduced, edata)

amici.plotting.plotStateTrajectories(rdata_reduced, model=model_reduced)
amici.plotting.plotObservableTrajectories(rdata_reduced, model=model_reduced)
```





We can also combine pre- and postequilibration.

[15]:
```
# Change the last timepoint to an infinity timepoint.
edata.setTimepoints(np.array([0.0, 0.1, float("inf")]))

# run the simulation
rdata_reduced = amici.runAmiciSimulation(model_reduced, solver_reduced, edata)
```

Preequilibration with sensitivities

Beyond the need for an ExpData object, the steady state solver logic in preequilibration is the same as in postequilibration, also if sensitivities are requested. The computation will fail for singular Jacobians, if `SteadyStateSensitivityMode` is set to `newtonOnly`, or if not enough steps can be taken. However, if forward simulation with steady state sensitivities is allowed, or if the Jacobian is not singular, it will work.

Prequilibration with forward sensitivities

[16]:
```
# No postquilibration this time.
edata.setTimepoints(np.array([0.0, 0.1, 1.0]))

# create the solver object and run the simulation, singular Jacobian, enforce Newton␣
↪solver for sensitivities
model.setSteadyStateSensitivityMode(
    amici.SteadyStateSensitivityMode.newtonOnly
)
solver = model.getSolver()
solver.setNewtonMaxSteps(10)
solver.setSensitivityMethod(amici.SensitivityMethod.forward)
solver.setSensitivityOrder(amici.SensitivityOrder.first)
rdata = amici.runAmiciSimulation(model, solver, edata)

for key, value in rdata.items():
    if key[0:6] == "preeq_":
        print("%20s: " % key, value)
```

```
          preeq_wrms:  0.5604257578208488
             preeq_t:  19.2252094591474
   preeq_numlinsteps:  None
      preeq_numsteps:  [[  0 417   0]]
     preeq_numstepsB:  0.0
        preeq_status:  [[-3  1  0]]
      preeq_cpu_time:  1.723
     preeq_cpu_timeB:  0.0
```

```
[Warning] AMICI:simulation: AMICI simulation failed:
Steady state sensitvitiy computation failed due to unsuccessful factorization of RHS␣
↪Jacobian
Error occured in:
0          0x1060f698b amici::SteadystateProblem::workSteadyStateProblem(amici::Solver*,␣
↪amici::Model*, int) + 587
1          0x1060a456f amici::AmiciApplication::runAmiciSimulation(amici::Solver&, amici:
↪:ExpData const*, amici::Model&, bool) + 239
2          0x1060a4474 amici::runAmiciSimulation(amici::Solver&, amici::ExpData const*,␣
↪amici::Model&, bool) + 36
3          0x106061005 _wrap_runAmiciSimulation(_object*, _object*) + 549
4          0x1021b2309 cfunction_call_varargs + 320
5
```

[17]:
```
# Singular Jacobian, use simulation
model.setSteadyStateSensitivityMode(
    amici.SteadyStateSensitivityMode.integrateIfNewtonFails
```

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```
)
solver = model.getSolver()
solver.setNewtonMaxSteps(10)
solver.setSensitivityMethod(amici.SensitivityMethod.forward)
solver.setSensitivityOrder(amici.SensitivityOrder.first)
rdata = amici.runAmiciSimulation(model, solver, edata)

for key, value in rdata.items():
    if key[0:6] == "preeq_":
        print("%20s: " % key, value)
```

```
          preeq_wrms:  0.9920376238481097
             preeq_t:  21.270502326483026
   preeq_numlinsteps:  None
      preeq_numsteps:  [[   0 1026    0]]
     preeq_numstepsB:  0.0
        preeq_status:  [[-3  1  0]]
      preeq_cpu_time:  12.439
     preeq_cpu_timeB:  0.0
```

[18]:
```
# Non-singular Jacobian, use Newton solver
solver_reduced = model_reduced.getSolver()
solver_reduced.setNewtonMaxSteps(10)
solver_reduced.setSensitivityMethod(amici.SensitivityMethod.forward)
solver_reduced.setSensitivityOrder(amici.SensitivityOrder.first)
rdata_reduced = amici.runAmiciSimulation(model_reduced, solver_reduced, edata)

for key, value in rdata_reduced.items():
    if key[0:6] == "preeq_":
        print("%20s: " % key, value)
```

```
          preeq_wrms:  0.0
             preeq_t:  nan
   preeq_numlinsteps:  None
      preeq_numsteps:  [[2 0 0]]
     preeq_numstepsB:  0.0
        preeq_status:  [[1 0 0]]
      preeq_cpu_time:  0.036
     preeq_cpu_timeB:  0.0
```

Prequilibration with adjoint sensitivities

When using preequilibration, adjoint sensitivity analysis can be used for simulation. This is a particularly interesting case: Standard adjoint sensitivity analysis requires the initial state sensitivities `sx0` to work, at least if data is given for finite (i.e., not exclusively postequilibration) timepoints: For each parameter, a contribution to the gradient is given by the scalar product of the corresponding state sensitivity vector at timepoint $t = 0$, (column in `sx0`), with the adjoint state ($p(t = 0)$). Hence, the matrix `sx0` is needed. This scalar product "closes the loop" from forward to adjoint simulation.

By default, if adjoint sensitivity analysis is called with preequilibration, the initial state sensitivities are computed in just the same way as if this way done for forward sensitivity analysis. The only difference in the internal logic is that, if the steady state gets inferred via simulation, a separate solver object is used in order to ensure that the steady state simulation does not interfere with the snapshotting of the forward trajectory from the actual time course.

However, also an adjoint version of preequilibration is possible: In this case, the "loop" from forward to adjoint simulation needs no closure: The simulation time is extended by preequilibration: forward from $t = -\infty$ to $t = 0$, and after adjoint simulation also backward from $t = 0$ to $t = -\infty$. Similar to adjoint postequilibration, the steady state of the adjoint state (at $t = -\infty$) is $p = 0$, hence the scalar product (at $t = -\infty$) for the initial state sensitivities of preequilibration with the adjoint state vanishes. Instead, this gradient contribution is covered by additional quadratures $\int_{-\infty}^{0} p(s)ds \cdot \frac{\partial f}{\partial \theta}$. In order to compute these quadratures correctly, the adjoint state from the main adjoint simulation must be passed on to the initial adjoint state of backward preequilibration.

However, as the adjoint state must be passed on from backward computation to preequilibration, it is currently not allowed to alter (reinitialize) states of the model at $t = 0$, unless these states are constant, as otherwise this alteration would lead to a discontinuity in the adjoints state as well and hence to an incorrect gradient.

[19]:
```
# Non-singular Jacobian, use Newton solver and adjoints with initial state sensitivities
solver_reduced = model_reduced.getSolver()
solver_reduced.setNewtonMaxSteps(10)
solver_reduced.setSensitivityMethod(amici.SensitivityMethod.adjoint)
solver_reduced.setSensitivityOrder(amici.SensitivityOrder.first)
rdata_reduced = amici.runAmiciSimulation(model_reduced, solver_reduced, edata)

for key, value in rdata_reduced.items():
    if key[0:6] == "preeq_":
        print("%20s: " % key, value)
print("Gradient:", rdata_reduced["sllh"])
```

```
          preeq_wrms:  0.0
             preeq_t:  nan
   preeq_numlinsteps:  None
      preeq_numsteps:  [[2 0 0]]
     preeq_numstepsB:  0.0
        preeq_status:  [[1 0 0]]
      preeq_cpu_time:  0.039
     preeq_cpu_timeB:  0.0
Gradient: [-0.05528395  0.0461776  -0.03354519 -2.34602219  6.314481  ]
```

[20]:
```
# Non-singular Jacobian, use simulation solver and adjoints with initial state␣
↪sensitivities
solver_reduced = model_reduced.getSolver()
solver_reduced.setNewtonMaxSteps(0)
solver_reduced.setSensitivityMethod(amici.SensitivityMethod.adjoint)
solver_reduced.setSensitivityOrder(amici.SensitivityOrder.first)
rdata_reduced = amici.runAmiciSimulation(model_reduced, solver_reduced, edata)

for key, value in rdata_reduced.items():
    if key[0:6] == "preeq_":
        print("%20s: " % key, value)
print("Gradient:", rdata_reduced["sllh"])
```

```
          preeq_wrms:  0.8470065245264354
             preeq_t:  19.213162474372176
   preeq_numlinsteps:  None
      preeq_numsteps:  [[  0 426   0]]
     preeq_numstepsB:  0.0
        preeq_status:  [[-2  1  0]]
      preeq_cpu_time:  1.753
     preeq_cpu_timeB:  0.0
```

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```
Gradient: [-0.05528395  0.0461776  -0.03354519 -2.34602226  6.3144812 ]
```

[21]:
```
# Non-singular Jacobian, use Newton solver and adjoints with fully adjoint␣
↪preequilibration
solver_reduced = model_reduced.getSolver()
solver_reduced.setNewtonMaxSteps(10)
solver_reduced.setSensitivityMethod(amici.SensitivityMethod.adjoint)
solver_reduced.setSensitivityMethodPreequilibration(
    amici.SensitivityMethod.adjoint
)
solver_reduced.setSensitivityOrder(amici.SensitivityOrder.first)
rdata_reduced = amici.runAmiciSimulation(model_reduced, solver_reduced, edata)

for key, value in rdata_reduced.items():
    if key[0:6] == "preeq_":
        print("%20s: " % key, value)
print("Gradient:", rdata_reduced["sllh"])
```

```
          preeq_wrms:  0.0
             preeq_t:  nan
   preeq_numlinsteps:  None
      preeq_numsteps:  [[2 0 0]]
     preeq_numstepsB:  0.0
        preeq_status:  [[1 0 0]]
      preeq_cpu_time:  0.042
     preeq_cpu_timeB:  0.009
Gradient: [-0.05528395  0.0461776  -0.03354519 -2.34602219  6.314481  ]
```

As for postquilibration, adjoint preequilibration has an analytic solution (via the linear system), which will be preferred. If used for models with singular Jacobian, numerical integration will be carried out, which is indicated by `preeq_numstepsB`.

[22]:
```
# Non-singular Jacobian, use Newton solver and adjoints with fully adjoint␣
↪preequilibration
solver = model.getSolver()
solver.setNewtonMaxSteps(10)
solver.setSensitivityMethod(amici.SensitivityMethod.adjoint)
solver.setSensitivityMethodPreequilibration(amici.SensitivityMethod.adjoint)
solver.setSensitivityOrder(amici.SensitivityOrder.first)
rdata = amici.runAmiciSimulation(model, solver, edata)

for key, value in rdata.items():
    if key[0:6] == "preeq_":
        print("%20s: " % key, value)
print("Gradient:", rdata["sllh"])
```

```
          preeq_wrms:  0.9986067660342685
             preeq_t:  36.94272314329062
   preeq_numlinsteps:  None
      preeq_numsteps:  [[  0 417   0]]
     preeq_numstepsB:  1371.0
        preeq_status:  [[-3  1  0]]
      preeq_cpu_time:  2.488
```

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```
    preeq_cpu_timeB:  5.016
Gradient: [-0.05528395  0.04617759 -0.03354518 -2.34602224  6.3144811 ]
```

Controlling the error tolerances in pre- and postequilibration

When solving ODEs or DAEs, AMICI uses the default logic of CVODES and IDAS to control error tolerances. This means that error weights are computed based on the absolute error tolerances and the product of current state variables of the system and their respective relative error tolerances. If this error combination is then controlled.

The respective tolerances for equilibrating a system with AMICI can be controlled by the user via the getter/setter functions `[get|set][Absolute|Relative]ToleranceSteadyState[Sensi]`:

[23]:
```
# Non-singular Jacobian, use simulation
model_reduced.setSteadyStateSensitivityMode(
    amici.SteadyStateSensitivityMode.integrateIfNewtonFails
)
solver_reduced = model_reduced.getSolver()
solver_reduced.setNewtonMaxSteps(0)
solver_reduced.setSensitivityMethod(amici.SensitivityMethod.forward)
solver_reduced.setSensitivityOrder(amici.SensitivityOrder.first)

# run with lax tolerances
solver_reduced.setRelativeToleranceSteadyState(1e-2)
solver_reduced.setAbsoluteToleranceSteadyState(1e-3)
solver_reduced.setRelativeToleranceSteadyStateSensi(1e-2)
solver_reduced.setAbsoluteToleranceSteadyStateSensi(1e-3)
rdata_reduced_lax = amici.runAmiciSimulation(
    model_reduced, solver_reduced, edata
)

# run with strict tolerances
solver_reduced.setRelativeToleranceSteadyState(1e-12)
solver_reduced.setAbsoluteToleranceSteadyState(1e-16)
solver_reduced.setRelativeToleranceSteadyStateSensi(1e-12)
solver_reduced.setAbsoluteToleranceSteadyStateSensi(1e-16)
rdata_reduced_strict = amici.runAmiciSimulation(
    model_reduced, solver_reduced, edata
)

# compare ODE outputs
print("\nODE solver steps, which were necessary to reach steady state:")
print("lax tolerances: ", rdata_reduced_lax["preeq_numsteps"])
print("strict tolerances: ", rdata_reduced_strict["preeq_numsteps"])

print("\nsimulation time corresponding to steady state:")
print(rdata_reduced_lax["preeq_t"])
print(rdata_reduced_strict["preeq_t"])

print("\ncomputation time to reach steady state:")
print(rdata_reduced_lax["preeq_cpu_time"])
print(rdata_reduced_strict["preeq_cpu_time"])
```

```
ODE solver steps, which were necessary to reach steady state:
lax tolerances:  [[  0 733   0]]
strict tolerances:  [[   0 1031    0]]

simulation time correpsonding to steady state:
6.002011407974004
31.0689293433781

computation time to reach steady state:
7.646
7.837
```

10.2.6 Debugging simulation failures

Objective: Demonstrate common simulation failures and give some hints for interpreting, debugging, and fixing them.

[1]:
```
%matplotlib inline
import os
from contextlib import suppress
from pathlib import Path

import matplotlib.pyplot as plt
import numpy as np

import amici
from amici.petab.petab_import import import_petab_problem
from amici.petab.simulations import simulate_petab, RDATAS, EDATAS
from amici.plotting import plot_state_trajectories, plot_jacobian

try:
    import benchmark_models_petab
except ModuleNotFoundError:
    # install `benchmark_models_petab` if necessary
    %pip install -q -e "git+https://github.com/Benchmarking-Initiative/Benchmark-Models-
↪PEtab.git@master#subdirectory=src/python&egg=benchmark_models_petab"
    try:
        import benchmark_models_petab
    except ModuleNotFoundError:
        print("** Please restart the kernel. **")
```

Overview

In the following, we will simulate models contained in the PEtab Benchmark Collection to demonstrate a number of simulation failures to analyze and fix them. We use the PEtab format, as it makes model import and simulation much easier, but everything illustrated here, also applies to plain SBML or PySB import.

Note that, due to numerical issues, the examples below may not be fully reproducible on every system.

If any simulation failures occur, they will be printed via Python logging.

Programmatically, simulation success can be checked via `ReturnDataView.status`. In case of a successful simulation, and only then, this value corresponds to `amici.AMICI_SUCCESS`. In case of a simulation error, all quantities in `ReturnData/ReturnDataView` will be reported up to the time of failure, the rest will be `NaN`. The likelihood and it's gradient will always be `NaN` in case of failure.

AMICI_TOO_MUCH_WORK - mxstep steps taken before reaching tout

Let's run a simulation:

[2]:
```
petab_problem = benchmark_models_petab.get_problem("Fujita_SciSignal2010")
amici_model = import_petab_problem(
    petab_problem, verbose=False, compile_=None
)

np.random.seed(2991)
problem_parameters = dict(
    zip(
        petab_problem.x_free_ids,
        petab_problem.sample_parameter_startpoints(n_starts=1)[0],
    )
)
res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
)
print(
    "Status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)
assert [
    amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]
] == [
    "AMICI_SUCCESS",
    "AMICI_SUCCESS",
    "AMICI_SUCCESS",
    "AMICI_TOO_MUCH_WORK",
    "AMICI_NOT_RUN",
    "AMICI_NOT_RUN",
]
```

```
2024-03-07 23:10:00.470 - amici.swig_wrappers - DEBUG - [condition_step_03_0][CVODES:
↪CVode:TOO_MUCH_WORK] AMICI ERROR: in module CVODES in function CVode : At t = 3031.8,␣
↪mxstep steps taken before reaching tout.
```

```
2024-03-07 23:10:00.471 - amici.swig_wrappers - ERROR - [condition_step_03_0][FORWARD_
↪FAILURE] AMICI forward simulation failed at t = 3031.8: AMICI failed to integrate the␣
↪forward problem
```

```
Status: ['AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_TOO_MUCH_WORK',
↪'AMICI_NOT_RUN', 'AMICI_NOT_RUN']
```

What happened?

AMICI failed to integrate the forward problem. The problem occurred for only one simulation condition, `condition_step_03_0`. The issue occurred at $t = 3031.8$, where the CVODES reached the maximum number of steps.

How to address?

The number of steps the solver has to take is closely related to the chosen error tolerance. More accurate results, more steps. Therefore, this problem can be solved in two ways:

1. Increasing the maximum number of steps via amici.Solver.setMaxSteps. Note that this will increase the time required for simulation, and that simulation may still fail eventually. Sometimes it may be preferable to not increase this limit but rather fail fast. Also note that increasing the number of allowed steps increase RAM requirements (even if fewer steps are actually taken), so don't set this to ridiculously large values in order to avoid this error.
2. Reducing the number of steps CVODES has to take. This is determined by the required error tolerance. There are various solver error tolerances than can be adjusted. The most relevant ones are those controlled via amici.Solver.setRelativeTolerance() and amici.Solver.setAbsoluteTolerance().

So, let's fix that:

[3]:
```
# let's increase the allowed number of steps by 10x:
print("Increasing allowed number of steps ...")
amici_solver = amici_model.getSolver()
amici_solver.setMaxSteps(10 * amici_solver.getMaxSteps())

res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
    solver=amici_solver,
)

print(
    "Status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)
assert all(rdata.status == amici.AMICI_SUCCESS for rdata in res[RDATAS])
print("Simulations finished successfully.")
print()


# let's relax the relative error tolerance by a factor of 50
print("Relaxing relative error tolerance ...")
amici_solver = amici_model.getSolver()
amici_solver.setRelativeTolerance(50 * amici_solver.getRelativeTolerance())
```

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```
res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
    solver=amici_solver,
)
print(
    "Status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)
assert all(rdata.status == amici.AMICI_SUCCESS for rdata in res[RDATAS])
print("Simulations finished successfully.")
```

```
Increasing allowed number of steps ...
```

```
Status: ['AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_
↪SUCCESS', 'AMICI_SUCCESS']
Simulations finished successfully.

Relaxing relative error tolerance ...
```

```
Status: ['AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_
↪SUCCESS', 'AMICI_SUCCESS']
Simulations finished successfully.
```

Internal t = [...] and h = [...] are such that t + h = t on the next step

Let's run a simulation:

[4]:
```
petab_problem = benchmark_models_petab.get_problem("Crauste_CellSystems2017")
amici_model = import_petab_problem(petab_problem, verbose=False)

np.random.seed(1)
problem_parameters = dict(
    zip(
        petab_problem.x_free_ids,
        petab_problem.sample_parameter_startpoints(n_starts=1)[0],
    )
)
res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
)
print(
    "Status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)
assert [
```

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```
    amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]
] == ["AMICI_TOO_MUCH_WORK"]
```

```
2024-03-07 23:10:00.977 - amici.swig_wrappers - DEBUG - [model1_data1][CVODES:CVode:
↪WARNING] AMICI ERROR: in module CVODES in function CVode : Internal t = 0.330112 and h␣
↪= 2.06577e-17 are such that t + h = t on the next step. The solver will continue␣
↪anyway.
2024-03-07 23:10:00.978 - amici.swig_wrappers - DEBUG - [model1_data1][CVODES:CVode:
↪WARNING] AMICI ERROR: in module CVODES in function CVode : Internal t = 0.330112 and h␣
↪= 2.06577e-17 are such that t + h = t on the next step. The solver will continue␣
↪anyway.
2024-03-07 23:10:00.979 - amici.swig_wrappers - DEBUG - [model1_data1][CVODES:CVode:
↪WARNING] AMICI ERROR: in module CVODES in function CVode : Internal t = 0.330112 and h␣
↪= 2.06577e-17 are such that t + h = t on the next step. The solver will continue␣
↪anyway.
2024-03-07 23:10:00.979 - amici.swig_wrappers - DEBUG - [model1_data1][CVODES:CVode:
↪WARNING] AMICI ERROR: in module CVODES in function CVode : Internal t = 0.330112 and h␣
↪= 2.06577e-17 are such that t + h = t on the next step. The solver will continue␣
↪anyway.
2024-03-07 23:10:00.980 - amici.swig_wrappers - DEBUG - [model1_data1][CVODES:CVode:
↪WARNING] AMICI ERROR: in module CVODES in function CVode : Internal t = 0.330112 and h␣
↪= 2.06577e-17 are such that t + h = t on the next step. The solver will continue␣
↪anyway.
2024-03-07 23:10:00.981 - amici.swig_wrappers - DEBUG - [model1_data1][CVODES:CVode:
↪WARNING] AMICI ERROR: in module CVODES in function CVode : Internal t = 0.330112 and h␣
↪= 2.06577e-17 are such that t + h = t on the next step. The solver will continue␣
↪anyway.
2024-03-07 23:10:00.982 - amici.swig_wrappers - DEBUG - [model1_data1][CVODES:CVode:
↪WARNING] AMICI ERROR: in module CVODES in function CVode : Internal t = 0.330112 and h␣
↪= 2.06577e-17 are such that t + h = t on the next step. The solver will continue␣
↪anyway.
2024-03-07 23:10:00.983 - amici.swig_wrappers - DEBUG - [model1_data1][CVODES:CVode:
↪WARNING] AMICI ERROR: in module CVODES in function CVode : Internal t = 0.330112 and h␣
↪= 2.06577e-17 are such that t + h = t on the next step. The solver will continue␣
↪anyway.
2024-03-07 23:10:00.983 - amici.swig_wrappers - DEBUG - [model1_data1][CVODES:CVode:
↪WARNING] AMICI ERROR: in module CVODES in function CVode : Internal t = 0.330112 and h␣
↪= 2.06577e-17 are such that t + h = t on the next step. The solver will continue␣
↪anyway.
2024-03-07 23:10:00.984 - amici.swig_wrappers - DEBUG - [model1_data1][CVODES:CVode:
↪WARNING] AMICI ERROR: in module CVODES in function CVode : Internal t = 0.330112 and h␣
↪= 2.06577e-17 are such that t + h = t on the next step. The solver will continue␣
↪anyway.
2024-03-07 23:10:00.985 - amici.swig_wrappers - DEBUG - [model1_data1][CVODES:CVode:
↪WARNING] AMICI ERROR: in module CVODES in function CVode : The above warning has been␣
↪issued mxhnil times and will not be issued again for this problem.
```

```
2024-03-07 23:10:00.986 - amici.swig_wrappers - DEBUG - [model1_data1][CVODES:CVode:TOO_
↪MUCH_WORK] AMICI ERROR: in module CVODES in function CVode : At t = 0.330112, mxstep␣
↪steps taken before reaching tout.
2024-03-07 23:10:00.986 - amici.swig_wrappers - ERROR - [model1_data1][FORWARD_FAILURE]␣
↪AMICI forward simulation failed at t = 0.330112: AMICI failed to integrate the forward␣
↪problem
Status: ['AMICI_TOO_MUCH_WORK']
```

What happened?

The forward simulation failed because the AMICI solver exceeded the maximum number of steps. Unlike in the previous case of `mxstep steps taken before reaching tout` (see above), here we got several additional warnings that the current step size h is numerically zero.

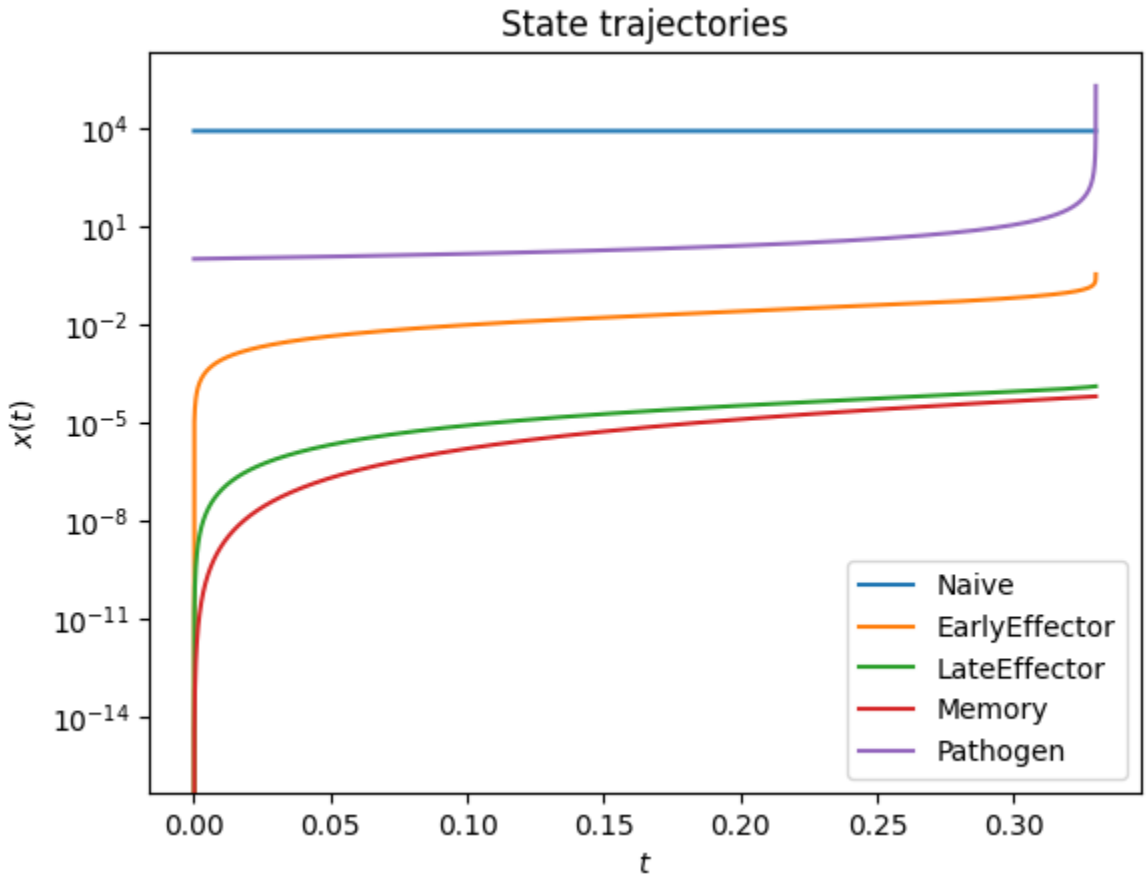
How to address?

The warning `Internal t = [...] and h = [...] are such that t + h = t on the next step` tells us that the solver is not able to move forward. The solver may be able to recover from that, but not always.

Let's look at the state trajectories to see what's going on. Such a tiny step size is usually related to very fast dynamics. We repeat the simulation with additional timepoints before the point of failure:

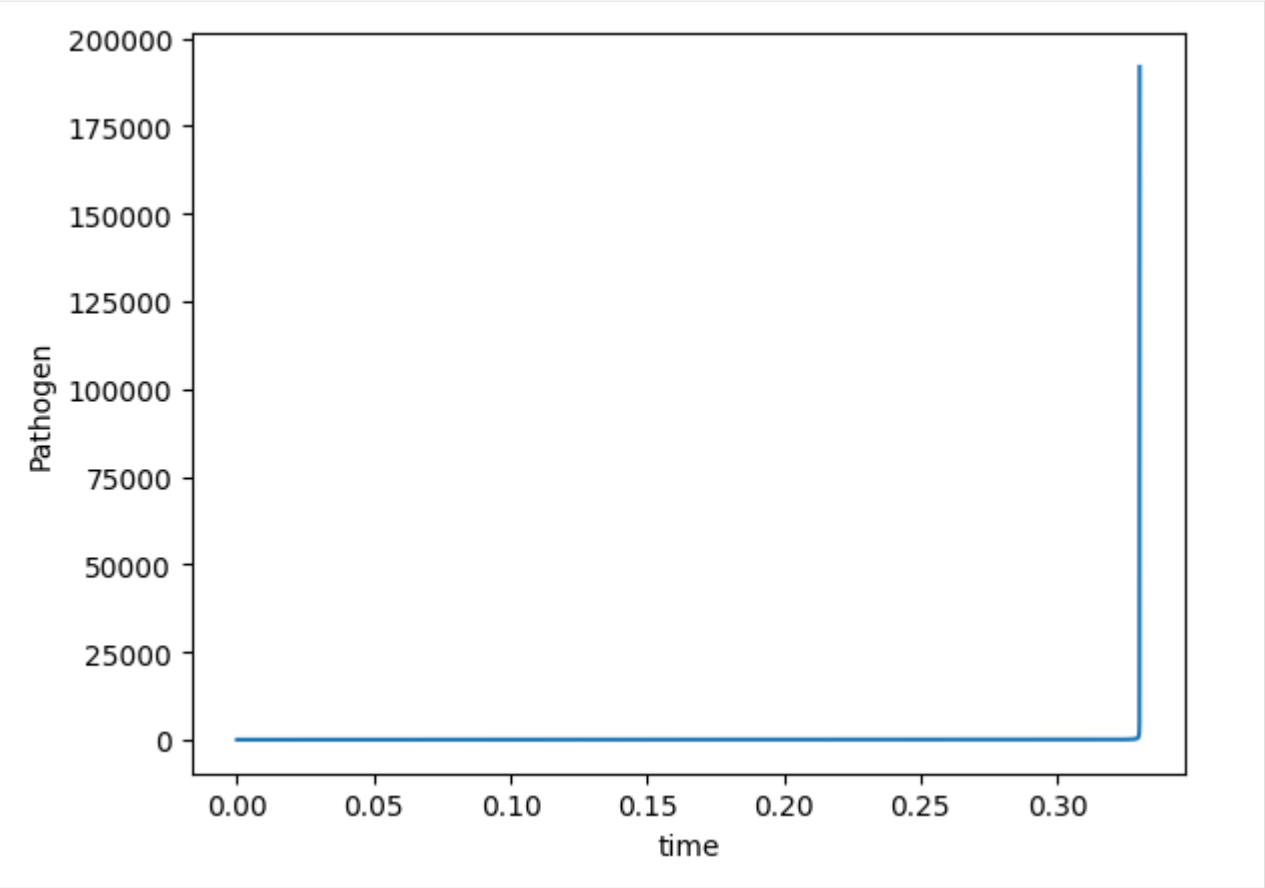
[5]:
```
# Create a copy of this simulation condition
edata = amici.ExpData(res[EDATAS][0])
edata.setTimepoints(np.linspace(0, 0.33011, 5000))
amici_solver = amici_model.getSolver()
rdata = amici.runAmiciSimulation(amici_model, amici_solver, edata)

# Visualize state trajectories
plot_state_trajectories(rdata, model=amici_model)
plt.yscale("log")
```



We can see a steep increase for `Pathogen` just before the error occurs. Let's zoom in:

[6]:
```
plt.plot(rdata.t, rdata.by_id("Pathogen"))
plt.xlabel("time")
plt.ylabel("Pathogen");
```



The solver is unable to handle such a steep increase. There is not much we can do. Increasing the tolerances will let the solver proceed a bit further, but this is usually not enough. Most likely there is a problem in the model or in the choice of parameter values.

the error test failed repeatedly or with |h| = hmin

Let's run a simulation:

[7]:
```
petab_problem = benchmark_models_petab.get_problem("Fujita_SciSignal2010")
amici_model = import_petab_problem(petab_problem, verbose=False)

np.random.seed(4920)
problem_parameters = dict(
    zip(
        petab_problem.x_free_ids,
        petab_problem.sample_parameter_startpoints(n_starts=1)[0],
    )
)
res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
)
```

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```
print(
    "Status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)

assert [
    amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]
] == [
    "AMICI_SUCCESS",
    "AMICI_ERR_FAILURE",
    "AMICI_NOT_RUN",
    "AMICI_NOT_RUN",
    "AMICI_NOT_RUN",
    "AMICI_NOT_RUN",
]
```

```
2024-03-07 23:10:02.103 - amici.swig_wrappers - DEBUG - [condition_step_00_3][CVODES:
↪CVode:ERR_FAILURE] AMICI ERROR: in module CVODES in function CVode : At t = 429.232␣
↪and h = 7.75194e-05, the error test failed repeatedly or with |h| = hmin.
```

```
2024-03-07 23:10:02.104 - amici.swig_wrappers - ERROR - [condition_step_00_3][FORWARD_
↪FAILURE] AMICI forward simulation failed at t = 429.232: AMICI failed to integrate the␣
↪forward problem
```

```
Status: ['AMICI_SUCCESS', 'AMICI_ERR_FAILURE', 'AMICI_NOT_RUN', 'AMICI_NOT_RUN', 'AMICI_
↪NOT_RUN', 'AMICI_NOT_RUN']
```

What happened?

AMICI failed to integrate the forward problem. The problem occurred for only one simulation condition, `condition_step_00_3`. The issue occurred at $t = 429.232$, where the error test failed. This means, the solver is unable to take a step of non-zero size without violating the chosen error tolerances.

How to address?

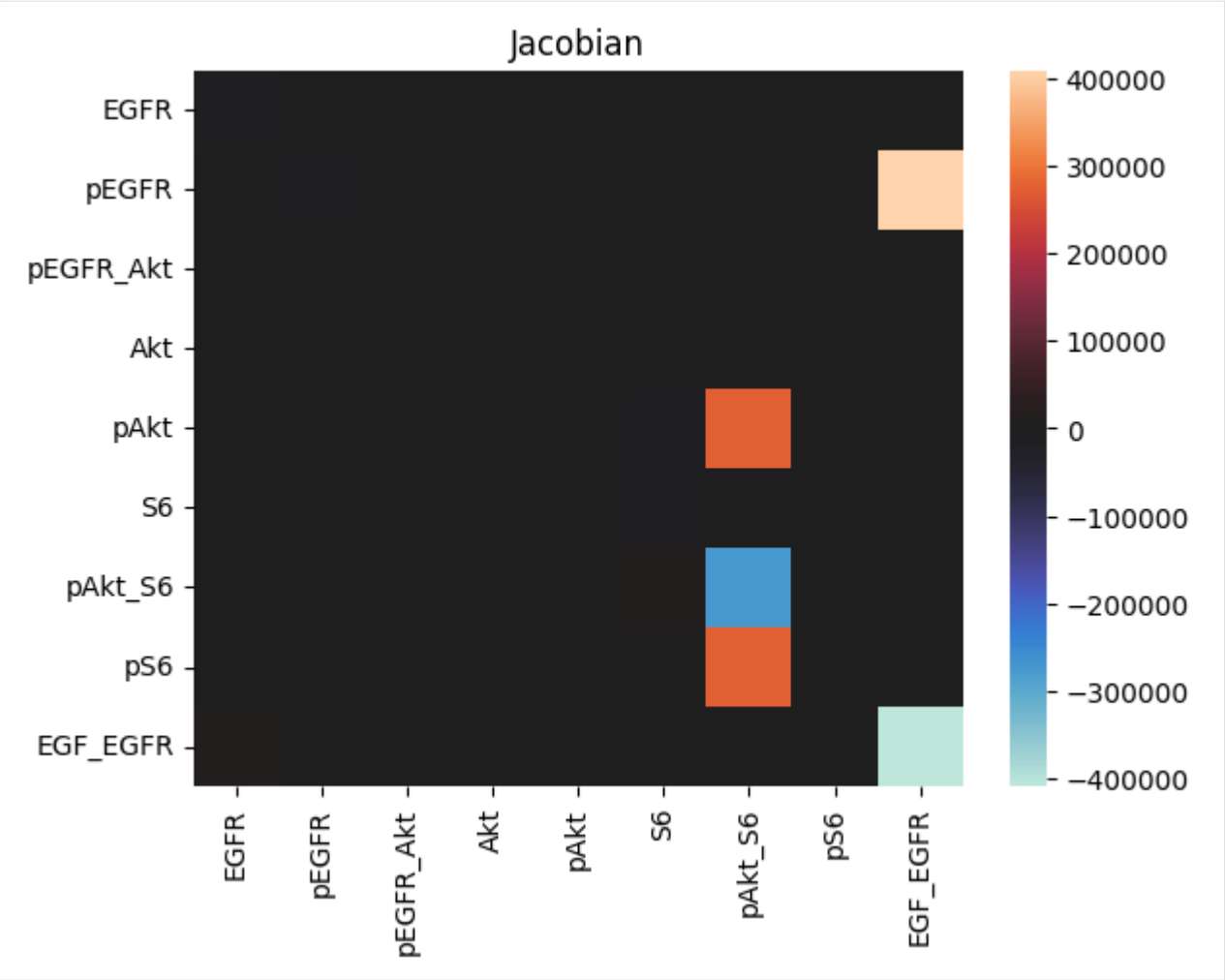
The step size is computed based on the Jacobian. Inspecting `ReturnData.J` shows us that we have rather large values in the Jacobian:

[8]:
```
rdata = res[RDATAS][1]

# Show Jacobian as heatmap
plot_jacobian(rdata)

print(f"largest absolute Jacobian value: {np.max(np.abs(rdata.J)):.3g}")
```

```
largest absolute Jacobian value: 4.09e+05
```



In this case, the default relative error tolerance may be too high and lead too large absolute errors.

Let's retry simulation using stricter tolerances:

[9]:
```
# set stricter relative error tolerance
amici_solver = amici_model.getSolver()
amici_solver.setRelativeTolerance(amici_solver.getRelativeTolerance() / 10)

res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
    solver=amici_solver,
)
print(
    "Status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)
assert all(rdata.status == amici.AMICI_SUCCESS for rdata in res[RDATAS])
print("Simulations finished successfully.")
```

```
Status: ['AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_
↪SUCCESS', 'AMICI_SUCCESS']
Simulations finished successfully.
```

Cvode routine CVode returned a root after reinitialization

Let's run a simulation:

[10]:
```
petab_problem = benchmark_models_petab.get_problem("Weber_BMC2015")
amici_model = import_petab_problem(
    petab_problem, verbose=False, compile_=None
)

np.random.seed(4)
problem_parameters = dict(
    zip(
        petab_problem.x_free_ids,
        petab_problem.sample_parameter_startpoints(n_starts=1)[0],
    )
)
res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
)
print(
    "Status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)
assert [
    amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]
] == [
    "AMICI_ERROR",
    "AMICI_NOT_RUN",
]
```

```
2024-03-07 23:10:02.818 - amici.swig_wrappers - ERROR - [model1_data2+model1_
↪data1][OTHER] AMICI simulation failed: CVODE routine CVode returned a root after␣
↪reinitialization. The initial step-size after the event or Heaviside function is too␣
↪small. To fix this, increase absolute and relative tolerances! failed with error code␣
↪2.
```

```
Status: ['AMICI_ERROR', 'AMICI_NOT_RUN']
```

What happened?

The simulation failed because the initial step-size after an event or heaviside function was too small. The error occurred during simulation of condition `model1_data1` after successful preequilibration (`model1_data2`).

How to address?

The error message already suggests a fix for this situation, so let's try increasing the relative tolerance:

[11]:
```
amici_solver = amici_model.getSolver()
amici_solver.setRelativeTolerance(200 * amici_solver.getRelativeTolerance())

np.random.seed(4)
problem_parameters = dict(
    zip(
        petab_problem.x_free_ids,
        petab_problem.sample_parameter_startpoints(n_starts=1)[0],
    )
)
res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
    solver=amici_solver,
)
print(
    "Status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)
assert all(rdata.status == amici.AMICI_SUCCESS for rdata in res[RDATAS])
```

```
Status: ['AMICI_SUCCESS', 'AMICI_SUCCESS']
```

AMICI encountered a NaN / Inf value for [...]

Let's run a simulation:

[12]:
```
petab_problem = benchmark_models_petab.get_problem("Borghans_BiophysChem1997")
amici_model = import_petab_problem(petab_problem, verbose=False)

np.random.seed(18)
problem_parameters = dict(
    zip(
        petab_problem.x_free_ids,
        petab_problem.sample_parameter_startpoints(n_starts=1)[0],
    )
)
res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
)
print(
    "Status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)
assert [
    amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]
] == ["AMICI_FIRST_RHSFUNC_ERR"]
```

```
2024-03-07 23:10:03.191 - amici.swig_wrappers - WARNING - [model1_data1][AMICI:NaN]␣
↪AMICI encountered a NaN value for xdot[2] (A_state) at t=0.000000
2024-03-07 23:10:03.192 - amici.swig_wrappers - WARNING - [model1_data1][AMICI:NaN]␣
↪AMICI encountered a NaN value for w[6] (flux_v7_v_6) at t=0.000000
2024-03-07 23:10:03.193 - amici.swig_wrappers - DEBUG - [model1_data1][CVODES:CVode:
↪FIRST_RHSFUNC_ERR] AMICI ERROR: in module CVODES in function CVode : The right-hand␣
↪side routine failed at the first call.
2024-03-07 23:10:03.194 - amici.swig_wrappers - ERROR - [model1_data1][FORWARD_FAILURE]␣
↪AMICI forward simulation failed at t = 0: AMICI failed to integrate the forward problem
```

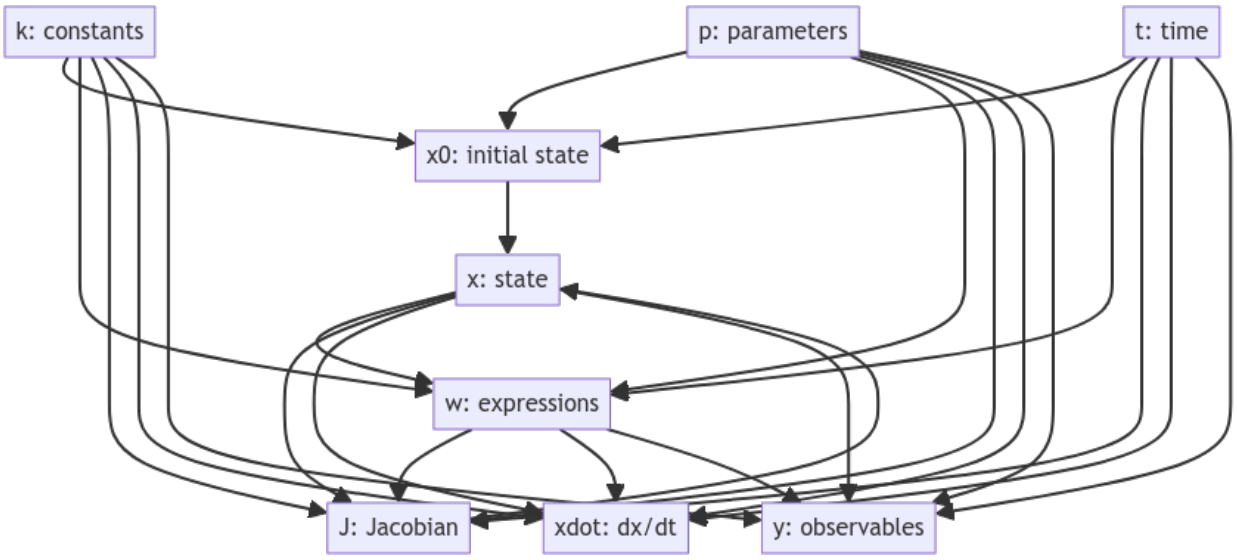
```
Status: ['AMICI_FIRST_RHSFUNC_ERR']
```

What happened?

The forward simulation failed because AMICI encountered a `NaN` value when simulating condition `model1_data1`. Then `NaN`s occurred in $\dot{x}$ and w (model expressions, such as reaction fluxes or assignment rules). Furthermore, the failure occurred at the first call, so at $t = t_0$ (here: $t = 0$).

How to address?

The `NaN` in $\dot{x}$ is most likely a consequence of the one in w. (A subset of) the dependency tree looks something like:



Always look for the most basic (furthest up) model quantities. In cases where non-finite values occur in expressions further down, rerunning the simulation after calling `Model.setAlwaysCheckFinite(True)` may give some further hints on where the issue originates.

The `NaN` in w occurred for `flux_v7_v_6` (see error log), i.e., when computing the reaction flux for reaction `v7_v_6`. As w only depends on (t, p, k, x) and no non-finite values have been reported for those, the issue has to be in the respective flux equation.

Let's look at that expression. This can either be done by inspecting the underlying SBML model (e.g., using COPASI), or by checking the generated model code:

[13]:
```
# model source code location
model_src_dir = Path(amici_model.module.__file__).parents[1]
```

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```
# find the problematic expression in the model source code
!grep flux_v7_v_6 {model_src_dir}/w.cpp
```

```
    flux_v7_v_6 = 1.0*std::pow(A_state, 2)*Vd*std::pow(Z_state, n_par)/((std::pow(A_
↪state, 2) + std::pow(Kp, 2))*(std::pow(Kd, n_par) + std::pow(Z_state, n_par)));  //␣
↪w[6]
```

What could go wrong? We can obtain `NaN` from any of these symbols being `NaN`, or through division by zero.

Let's let's check the denominator first:

$$(A\_state^2 + Kp^2) * (Kd^{n\_par} + Z\_state^{n\_par})$$

`A_state` and `Z_state` are state variables, `Kd`, `K_p`, and `n_par` are parameters.

As the error occurred at $t = t_0$, let's ensure the initial state is non-zero and finite:

[14]:
```
rdata = res[RDATAS][0]
edata = res[EDATAS][0]
# check initial states
x0 = dict(zip(amici_model.getStateIds(), rdata.x0))
print(f"{x0=}")
```

```
x0={'Z_state': 0.6869701913398437, 'Y_state': 0.2977237418558598, 'A_state': 0.
↪1116031306650328}
```

The initial states are fine - the first multiplicand is non-zero, as x_0 was non-zero.

So let's check the parameter values occurring in the second multiplicand:

[15]:
```
# we have to account for the chosen parameter scale
from itertools import starmap

unscaled_parameter = dict(
    zip(
        amici_model.getParameterIds(),
        starmap(
            amici.getUnscaledParameter, zip(edata.parameters, edata.pscale)
        ),
    )
)
print(dict((p, unscaled_parameter[p]) for p in ("Kd", "Kp", "n_par")))
```

```
{'Kd': 0.028491925689008366, 'Kp': 1002.513636749445, 'n_par': 7816.430091706722}
```

Considering that `n_par` occurs as exponent, it's magnitude looks pretty high. This term is very likely causing the problem - let's check:

[16]:
```
print(
    f"{x0['Z_state']**unscaled_parameter['n_par'] + unscaled_parameter['Kd']**unscaled_
↪parameter['n_par']=}"
)
```

```
x0['Z_state']**unscaled_parameter['n_par'] + unscaled_parameter['Kd']**unscaled_
↪parameter['n_par']=0.0
```

Indeed, no way we can fix this for the given model. This was most likely an unrealistic parameter value, originating from a too high upper parameter bound for `n_par`. Therefore, if this error occurs during optimization, a first step could be adapting the respective parameter bounds. In other cases, this may be a result of unfortunate arrangement of model expressions, which can sometimes be solved by passing a suitable simplification function to the model import.

Steady state sensitivity computation failed due to unsuccessful factorization of RHS Jacobian

Let's run a simulation:

[17]:
```
petab_problem = benchmark_models_petab.get_problem("Blasi_CellSystems2016")
with suppress(KeyError):
    del os.environ["AMICI_EXPERIMENTAL_SBML_NONCONST_CLS"]
amici_model = import_petab_problem(
    petab_problem,
    verbose=False,
    compile_=True,
    model_name="Blasi_CellSystems2016_1",
)

amici_solver = amici_model.getSolver()
amici_solver.setSensitivityMethod(amici.SensitivityMethod.forward)
amici_solver.setSensitivityOrder(amici.SensitivityOrder.first)
amici_model.setSteadyStateSensitivityMode(
    amici.SteadyStateSensitivityMode.newtonOnly
)

np.random.seed(2020)
problem_parameters = dict(
    zip(
        petab_problem.x_free_ids,
        petab_problem.sample_parameter_startpoints(n_starts=1)[0],
    )
)
res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
    solver=amici_solver,
)
print(
    "Status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)

# hard to reproduce on GHA
if os.getenv("GITHUB_ACTIONS") is None:
    assert [
        amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]
    ] == ["AMICI_ERROR"]
```

```
Visualization table not available. Skipping.
```

```
2024-03-07 23:10:24.920 - amici.swig_wrappers - ERROR - [control][OTHER] AMICI␣
↪simulation failed: Steady state sensitivity computation failed due to unsuccessful␣
↪factorization of RHS Jacobian
```

```
Status: ['AMICI_ERROR']
```

What happened?

AMICI failed to compute steady-state sensitivities, because it was not able to factorize the Jacobian.

How to address?

This is most likely a result of a singular Jacobian. Let's check the condition number:

[18]:
```
rdata = res[RDATAS][0]
np.linalg.cond(rdata.J)
```

[18]:
```
3.01187419527941e+19
```

Indeed, the condition number shows that the Jacobian is numerically singular. If this happens consistently, it is usually due to conserved quantities in the model.

There are two ways we can address that:

1. Use numerical integration to compute sensitivities, for which a singular Jacobian is not an issue. This is, usually, slower, though.
2. Remove any conserved quantities.

Let's try both approaches:

[19]:
```
# use numerical integration
amici_model.setSteadyStateSensitivityMode(
    amici.SteadyStateSensitivityMode.integrationOnly
)

res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
    solver=amici_solver,
)
print(
    "Status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)
assert all(rdata.status == amici.AMICI_SUCCESS for rdata in res[RDATAS])
```

```
Status: ['AMICI_SUCCESS']
```

[20]:
```
# Remove conserved quantities - this requires re-importing the model

# this is enabled by the `AMICI_EXPERIMENTAL_SBML_NONCONST_CLS` environment variable
os.environ["AMICI_EXPERIMENTAL_SBML_NONCONST_CLS"] = "1"
amici_model = import_petab_problem(
    petab_problem,
    verbose=False,
```

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```
    # we need a different model name if we import the model again
    # we cannot load a model with the same name as an already loaded model
    model_name="Blasi_CellSystems2016_2",
    compile_=True,
)
del os.environ["AMICI_EXPERIMENTAL_SBML_NONCONST_CLS"]

amici_solver = amici_model.getSolver()
amici_solver.setSensitivityMethod(amici.SensitivityMethod.forward)
amici_solver.setSensitivityOrder(amici.SensitivityOrder.first)

res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
    solver=amici_solver,
)
print(
    "Status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)
assert all(rdata.status == amici.AMICI_SUCCESS for rdata in res[RDATAS])
```

```
Visualization table not available. Skipping.
```

```
Status: ['AMICI_SUCCESS']
```

Steady state computation failed

Let's run a simulation:

[21]:
```
petab_problem = benchmark_models_petab.get_problem("Brannmark_JBC2010")
amici_model = import_petab_problem(
    petab_problem,
    verbose=False,
)

amici_solver = amici_model.getSolver()


np.random.seed(1851)
problem_parameters = dict(
    zip(
        petab_problem.x_free_ids,
        petab_problem.sample_parameter_startpoints(n_starts=1)[0],
    )
)
res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
```

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```
    scaled_parameters=True,
    solver=amici_solver,
)

print(
    "Status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)

# hard to reproduce on GHA
if os.getenv("GITHUB_ACTIONS") is None:
    assert [
        amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]
    ] == [
        "AMICI_ERROR",
        "AMICI_NOT_RUN",
        "AMICI_NOT_RUN",
        "AMICI_NOT_RUN",
        "AMICI_NOT_RUN",
        "AMICI_NOT_RUN",
        "AMICI_NOT_RUN",
        "AMICI_NOT_RUN",
    ]
```

```
2024-03-07 23:10:48.498 - amici.swig_wrappers - DEBUG - [Dose_0+Dose_0][CVODES:CVode:ERR_
↪FAILURE] AMICI ERROR: in module CVODES in function CVode : At t = 736.713 and h = 0.
↪000145837, the error test failed repeatedly or with |h| = hmin.
```

```
2024-03-07 23:10:48.498 - amici.swig_wrappers - DEBUG - [Dose_0+Dose_0][OTHER] AMICI␣
↪equilibration failed at t=736.713.
```

```
2024-03-07 23:10:48.499 - amici.swig_wrappers - ERROR - [Dose_0+Dose_0][OTHER] AMICI␣
↪simulation failed: Steady state computation failed. Simulation to steady state failed.
```

```
Status: ['AMICI_ERROR', 'AMICI_NOT_RUN', 'AMICI_NOT_RUN', 'AMICI_NOT_RUN', 'AMICI_NOT_RUN
↪', 'AMICI_NOT_RUN', 'AMICI_NOT_RUN', 'AMICI_NOT_RUN']
```

What happened?

All given experimental conditions require pre-equilibration, i.e., finding a steady state. AMICI first tries to find a steady state using the Newton solver, if that fails, it tries simulating until steady state, if that also fails, it tries the Newton solver from the end of the simulation. In this case, all three failed. Neither Newton's method nor simulation yielded a steady state satisfying the required tolerances.

This can also be seen in `ReturnDataView.preeq_status` (the three statuses corresponds to Newton #1, Simulation, Newton #2):

[22]:
```
rdata = res[RDATAS][0]
list(map(amici.SteadyStateStatus, rdata.preeq_status.flatten()))
```

[22]:
```
[<SteadyStateStatus.not_run: 0>,
 <SteadyStateStatus.failed: -1>,
 <SteadyStateStatus.not_run: 0>]
```

How to address?

There are several ways to address that:

1. Stricter integration tolerances (preferred if affordable - higher accuracy, but generally slower)
2. Looser steady-state tolerances (lower accuracy, generally faster)
3. Increase the number of allowed steps for Newton's method

Let's try all of them:

[23]:
```
# Reduce relative tolerance for integration
amici_solver = amici_model.getSolver()
amici_solver.setRelativeTolerance(
    1 / 100 * amici_solver.getRelativeTolerance()
)

res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
    solver=amici_solver,
)
print(
    "status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)

rdata = res[RDATAS][0]
print(
    f"preeq_status={list(map(amici.SteadyStateStatus, rdata.preeq_status.flatten()))}"
)
print(f"{rdata.preeq_numsteps=}")

# hard to reproduce on GHA
if os.getenv("GITHUB_ACTIONS") is None:
    assert all(rdata.status == amici.AMICI_SUCCESS for rdata in res[RDATAS])
```

```
status: ['AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_
↪SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS']
preeq_status=[<SteadyStateStatus.not_run: 0>, <SteadyStateStatus.success: 1>,
↪<SteadyStateStatus.not_run: 0>]
rdata.preeq_numsteps=array([[   0, 3150,    0]])
```

[24]:
```
# Increase relative steady state tolerance
for log10_relaxation_factor in range(1, 10):
    print(f"Relaxing tolerances by factor {10 ** log10_relaxation_factor}")
    amici_solver = amici_model.getSolver()
    amici_solver.setRelativeToleranceSteadyState(
        amici_solver.getRelativeToleranceSteadyState()
        * 10**log10_relaxation_factor
    )

    res = simulate_petab(
        petab_problem=petab_problem,
        amici_model=amici_model,
        problem_parameters=problem_parameters,
```

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```
        scaled_parameters=True,
        solver=amici_solver,
    )
    if all(rdata.status == amici.AMICI_SUCCESS for rdata in res[RDATAS]):
        print(
            f"-> Succeeded with relative steady state tolerance {amici_solver.
↪getRelativeToleranceSteadyState()}\n"
        )
        break
    else:
        print("-> Failed.\n")

print(
    "status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)

rdata = res[RDATAS][0]
print(
    f"preeq_status={list(map(amici.SteadyStateStatus, rdata.preeq_status.flatten()))}"
)
print(f"{rdata.preeq_numsteps=}")
assert all(rdata.status == amici.AMICI_SUCCESS for rdata in res[RDATAS])
```

```
Relaxing tolerances by factor 10
```

```
2024-03-07 23:10:48.926 - amici.swig_wrappers - DEBUG - [Dose_0+Dose_0][CVODES:CVode:ERR_
↪FAILURE] AMICI ERROR: in module CVODES in function CVode : At t = 736.713 and h = 0.
↪000145837, the error test failed repeatedly or with |h| = hmin.
```

```
2024-03-07 23:10:48.926 - amici.swig_wrappers - DEBUG - [Dose_0+Dose_0][OTHER] AMICI␣
↪equilibration failed at t=736.713.
```

```
2024-03-07 23:10:48.927 - amici.swig_wrappers - ERROR - [Dose_0+Dose_0][OTHER] AMICI␣
↪simulation failed: Steady state computation failed. Simulation to steady state failed.
```

```
-> Failed.

Relaxing tolerances by factor 100
```

```
2024-03-07 23:10:49.108 - amici.swig_wrappers - DEBUG - [Dose_0+Dose_0][CVODES:CVode:ERR_
↪FAILURE] AMICI ERROR: in module CVODES in function CVode : At t = 736.713 and h = 0.
↪000145837, the error test failed repeatedly or with |h| = hmin.
```

```
2024-03-07 23:10:49.108 - amici.swig_wrappers - DEBUG - [Dose_0+Dose_0][OTHER] AMICI␣
↪equilibration failed at t=736.713.
```

```
2024-03-07 23:10:49.109 - amici.swig_wrappers - ERROR - [Dose_0+Dose_0][OTHER] AMICI␣
↪simulation failed: Steady state computation failed. Simulation to steady state failed.
```

```
-> Failed.

Relaxing tolerances by factor 1000
```

```
2024-03-07 23:10:49.288 - amici.swig_wrappers - DEBUG - [Dose_0+Dose_0][CVODES:CVode:ERR_
↪FAILURE] AMICI ERROR: in module CVODES in function CVode : At t = 736.713 and h = 0.
↪000145837, the error test failed repeatedly or with |h| = hmin.
```

```
2024-03-07 23:10:49.288 - amici.swig_wrappers - DEBUG - [Dose_0+Dose_0][OTHER] AMICI␣
↪equilibration failed at t=736.713.
2024-03-07 23:10:49.289 - amici.swig_wrappers - ERROR - [Dose_0+Dose_0][OTHER] AMICI␣
↪simulation failed: Steady state computation failed. Simulation to steady state failed.
-> Failed.

Relaxing tolerances by factor 10000
-> Succeeded with relative steady state tolerance 0.01

status: ['AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_
↪SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS', 'AMICI_SUCCESS']
preeq_status=[<SteadyStateStatus.not_run: 0>, <SteadyStateStatus.success: 1>,
↪<SteadyStateStatus.not_run: 0>]
rdata.preeq_numsteps=array([[  0, 577,   0]])
```

That fixed the error, and took only a quarter of the number steps as the previous run, but at the cost of much lower accuracy.

[25]:
```
# Let's try increasing the number of Newton steps
# (this is 0 by default, so the Newton solver wasn't used before,
#  as can be seen from the 0 in `rdata.preeq_numsteps[0]`)
amici_solver = amici_model.getSolver()
amici_solver.setNewtonMaxSteps(10**4)

res = simulate_petab(
    petab_problem=petab_problem,
    amici_model=amici_model,
    problem_parameters=problem_parameters,
    scaled_parameters=True,
    solver=amici_solver,
)
print(
    "status:",
    [amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]],
)

rdata = res[RDATAS][0]
print(
    f"preeq_status={list(map(amici.SteadyStateStatus, rdata.preeq_status.flatten()))}"
)
print(f"{rdata.preeq_numsteps=}")
# hard to reproduce on GHA
if os.getenv("GITHUB_ACTIONS") is None:
    assert [
        amici.simulation_status_to_str(rdata.status) for rdata in res[RDATAS]
    ] == [
        "AMICI_ERROR",
        "AMICI_NOT_RUN",
        "AMICI_NOT_RUN",
        "AMICI_NOT_RUN",
        "AMICI_NOT_RUN",
```

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```
        "AMICI_NOT_RUN",
        "AMICI_NOT_RUN",
        "AMICI_NOT_RUN",
    ]
```

```
2024-03-07 23:10:49.659 - amici.swig_wrappers - DEBUG - [Dose_0+Dose_0][CVODES:CVode:ERR_
↪FAILURE] AMICI ERROR: in module CVODES in function CVode : At t = 736.713 and h = 0.
↪000145837, the error test failed repeatedly or with |h| = hmin.
```

```
2024-03-07 23:10:49.660 - amici.swig_wrappers - DEBUG - [Dose_0+Dose_0][OTHER] AMICI␣
↪equilibration failed at t=736.713.
```

```
2024-03-07 23:10:49.661 - amici.swig_wrappers - ERROR - [Dose_0+Dose_0][OTHER] AMICI␣
↪simulation failed: Steady state computation failed. First run of Newton solver failed:␣
↪RHS could not be factorized. Simulation to steady state failed. Second run of Newton␣
↪solver failed: RHS could not be factorized.
```

```
status: ['AMICI_ERROR', 'AMICI_NOT_RUN', 'AMICI_NOT_RUN', 'AMICI_NOT_RUN', 'AMICI_NOT_RUN
↪', 'AMICI_NOT_RUN', 'AMICI_NOT_RUN', 'AMICI_NOT_RUN']
preeq_status=[<SteadyStateStatus.failed_factorization: -3>, <SteadyStateStatus.failed: -
↪1>, <SteadyStateStatus.failed_factorization: -3>]
rdata.preeq_numsteps=array([[   0, 1105,    0]])
```

Increasing the maximum number of Newton steps doesn't seem to help here. The Jacobian was numerically singular and its factorization failed. This can be a result of conserved quantities in the model. Section *Steady state sensitivity computation failed due to unsuccessful factorization of RHS Jacobian* shows how to address that.

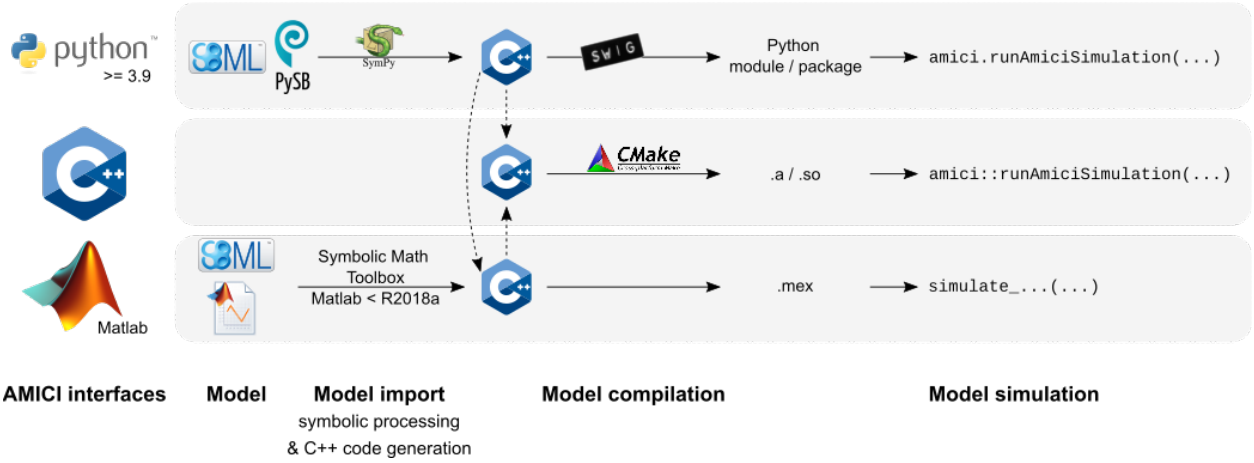
10.2.7 Speeding up model import and simulation - with a focus on large models

Objective: Give some hints to speed up import and simulation of larger models

This notebook gives some hints that may help to speed up import and simulation of (mostly) larger models. While some of these settings may also yield slight performance improvements for smaller models, other settings may make things slower. The impact may be highly model-dependent (number of states, number of parameters, rate expressions) or system-dependent, and it's worthwhile doing some benchmarking.

To simulate models in AMICI, a model specified in a high-level format needs to be imported first, as shown in the following figure. This roughly involves the following steps:

1. Generating the ODEs
2. Computing derivatives
3. Generating C++ code
4. Compiling the generated code
5. Simulating the model



There are various options to speed up individual steps of this process. Generally, faster import comes with slower simulation and vice versa. During parameter estimation, a model is often imported only once, and then millions of simulations are run. Therefore, faster simulation will easily compensate for slower import (one-off cost). In other cases, many models may to have to be imported, but only few simulations will be executed. In this case, faster import may be more relevant.

In the following, we will present various settings that (may) influence import and simulation time. We will follow the order of steps outlined above.

Since many of the following demonstrations take quite some time to compute, this notebook mostly shows pre-generated results.

[1]:
```
from IPython.core.pylabtools import figsize
import matplotlib.pyplot as plt
import pandas as pd

plt.rcParams.update({"font.size": 12})
```

Examples

The demos below make use of the following models contained in the PEtab benchmark collection and other publications:

Model	# parameters	# states
Chen_MSB2009	155	500
Froehlich_CellSystems2018	4231	1396
FröhlichGer2022 (RTKERK__base)	105	2272
hello_pysb	4	3

All data has been generated with AMICI v0.15.0 or v0.16.0 unless stated otherwise.

Model import

Symbolic processing

Parameters as constants

By default, AMICI will generate sensitivity equations with respect to all model parameters. If it is clear upfront, that sensitivities with respect to certain parameters will not be required, their IDs can be passed to amici.sbml_import.SbmlImporter.sbml2amici or amici.pysb_import.pysb2amici via the `constant_parameters` argument to not generate the respective equations. This will reduce CPU time and RAM requirements during import and simulation. The PEtab import will automatically pass all parameters with `petab.ESTIMATE==False` as `constant_parameters` arguments.

See also the following section for the case that no sensitivities are required at all.

Not generating sensitivity code

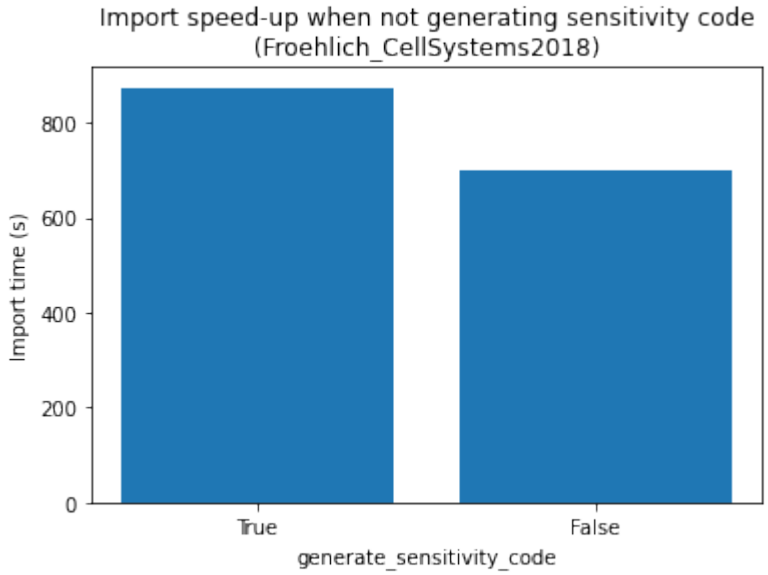
If only forward simulations of a model are required, a modest import speedup can be obtained from not generating sensitivity code. This can be enabled via the `generate_sensitivity_code` argument of amici.sbml_import.SbmlImporter.sbml2amici or amici.pysb_import.pysb2amici.

Example:

```
petab_yaml="https://raw.githubusercontent.com/Benchmarking-Initiative/Benchmark-Models-
↪PEtab/master/Benchmark-Models/Froehlich_CellSystems2018/Froehlich_CellSystems2018.yaml"
/usr/bin/time -v amici_import_petab -y "$petab_yaml" --no-compile
# vs.
/usr/bin/time -v amici_import_petab -y "$petab_yaml" --no-compile --no-sensitivities
```

[2]:
```
figsize(4, 4)
plt.bar(["True", "False"], [873.54, 697.85])
plt.xlabel("generate_sensitivity_code")
plt.ylabel("Import time (s)")
plt.title(
    "Import speed-up when not generating sensitivity code\n(Froehlich_CellSystems2018)"
)
plt.show()

print(f"speedup: {873.54/697.85:.2f}x")
```




```
speedup: 1.25x
```

Extracting common subexpressions

For some models, the size of the generated model code can be significantly reduced by extracting common subexpressions. This can yield substantial reductions of compile times and RAM-requirements. Very large models might not compile without this option. Extracting common subexpressions can be enabled by setting an environment variable `AMICI_EXTRACT_CSE=1` before model import. The downside is, that the generated model code becomes rather unreadable. The increase in import time when enabling this feature is usually <15%, the effect on code size and compile time is highly model dependent. Mostly models with tightly coupled ODEs, as obtained from complex rate laws or spatial discretizations of ODEs, seem to benefit. For models with mass action or similar kinetics, this option seems to not be helpful and rather increases compile time (e.g., for FröhlichGer2022, the compile time doubles).

Benchmark result from here (SBML import, `AMICI_IMPORT_NPROCS=2`, sequential compilation with clang14, `CFLAGS=-O2`):

	default	`AMICI_EXTRACT_CSE=1`
import time	160 min (100%)	164 min (103%)
code size	89 MB (100%)	27 MB (30%)
compile time	169 min (100%)	90 min (53%)
compile RAM	7.49 GB (100%)	1.18 GB (16%)
simulation time (*)	100%	97%

(*) lowest out of 20 identical simulations using ASA

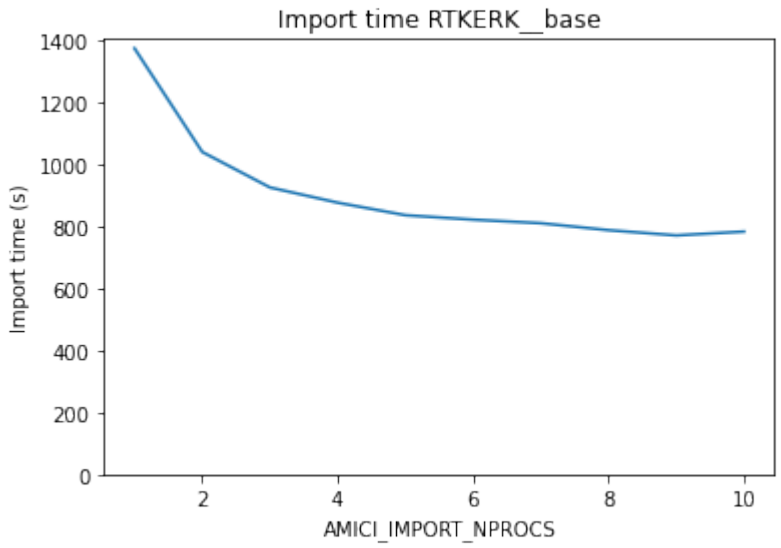
Parallelization

For large models or complex model expressions, symbolic computation of the derivatives can be quite time-consuming. This can be parallelized by setting the environment variable `AMICI_IMPORT_NPROCS` to the number of parallel processes that should be used. The impact strongly depends on the model. Note that setting this value too high may have a negative performance impact (benchmark!).

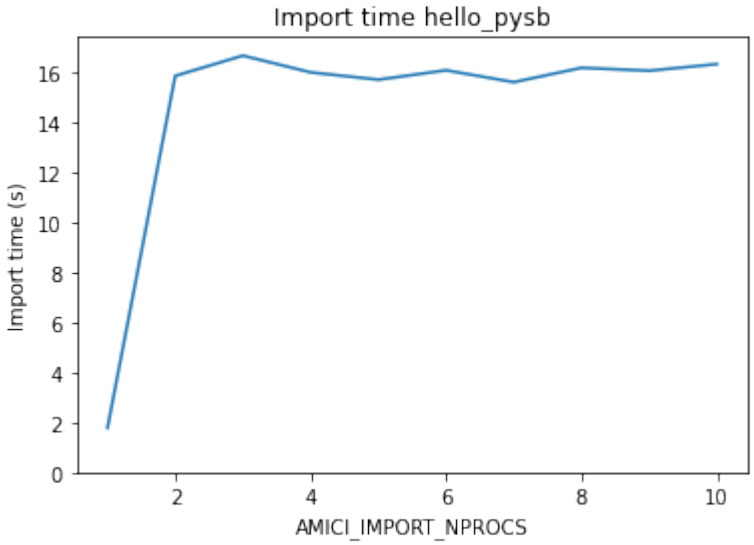
Impact for a large and a tiny model:

[3]:
```
df_import = pd.read_csv("results_import.tsv", sep="\t")
for model_name, df in df_import.groupby("model_name"):
    plt.plot(df.nprocs, df.time)
    plt.title(f"Import time {model_name}")
    plt.xlabel("AMICI_IMPORT_NPROCS")
    plt.ylabel("Import time (s)")
    plt.ylim(ymin=0)
    plt.show()

    import_times = df.sort_values("nprocs")["time"].values
    percent_change = (
        (import_times[0] - min(import_times[1:])) / import_times[0] * 100
    )
    if percent_change > 0:
        print(f"Import time decreased by up to ~{percent_change:.0f}%.")
    else:
        print(f"Import time increased by at least ~{-percent_change:.0f}%.")
```




```
Import time decreased by up to ~44%.
```




```
Import time increased by at least ~774%.
```

(No) simplification of model expressions

By default, AMICI will try to perform some basic simplification of model expressions. For complex model expressions, or for large models, this can become costly. It very much depends on the model expressions, whether the benefits outweigh the cost.

Simplification of model expressions can be disabled by passing `simplify=None` to amici.sbml_import.SbmlImporter.sbml2amici or amici.pysb_import.pysb2amici.

Depending on the given model, different simplification schemes may be cheaper or more beneficial than the default. SymPy's simplification functions are well documented.

Compilation

Choice of compiler

From own experience, `clang` seems to handle larger models, or more specifically, their large source files, better than `g++`, both in terms of memory requirement and compile time. You can use a different compiler by setting the `CC` and `CXX` environment variables to, e.g., `CC=clang`, `CXX=clang`.

[4]:
```
figsize(8, 4)
compilation_time_s = [3022.453, 289.518]
labels = [
    "g++ (Ubuntu 12.2.0-3ubuntu1) 12.2.0",
    "Ubuntu clang version 15.0.2-1",
]
plt.bar(labels, compilation_time_s)
plt.ylim(ymin=0)
plt.title("Choice of compiler - FröhlichGer2022")
plt.xlabel("Compiler")
plt.ylabel("Walltime for compilation (s)")
```

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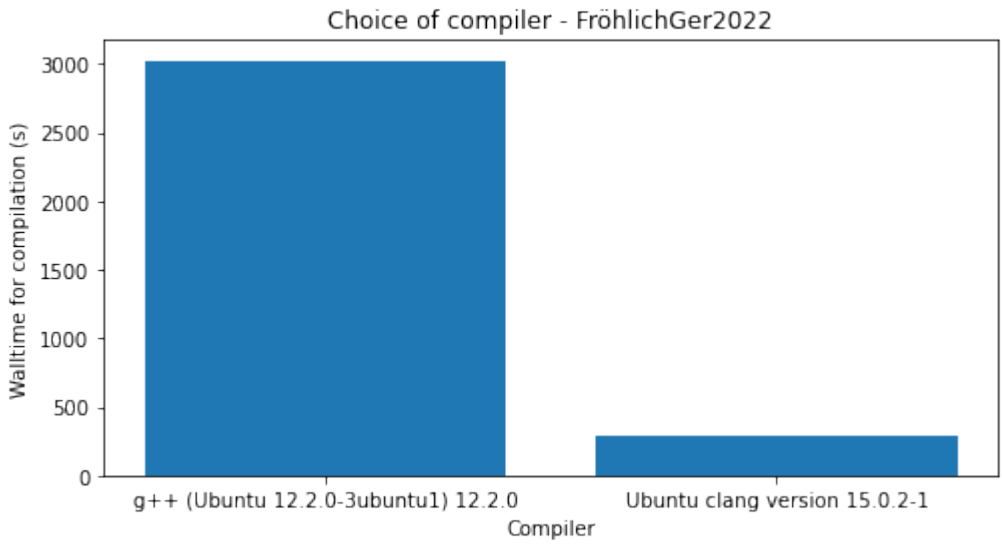
```
plt.show()
print(
    f"Clang was ~{compilation_time_s[0] / compilation_time_s[1]:.0f}x as fast as g++."
)
```




```
Clang was ~10x as fast as g++.
```

Parallel compilation

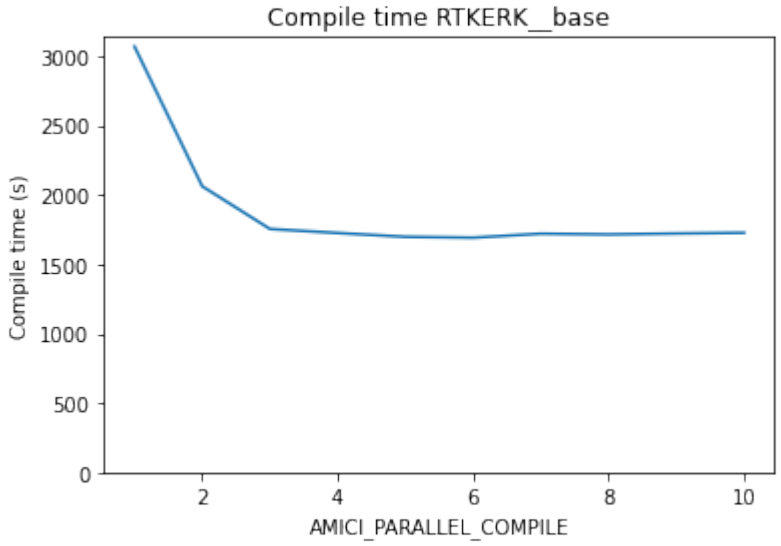
It's possible to compile multiple source files in parallel by specifying the number of parallel processes via the `AMICI_PARALLEL_COMPILE` environment variable. This is also beneficial for small models. Note, however, that for large models, this may require significant amounts of RAM.

Example for a large and tiny model:

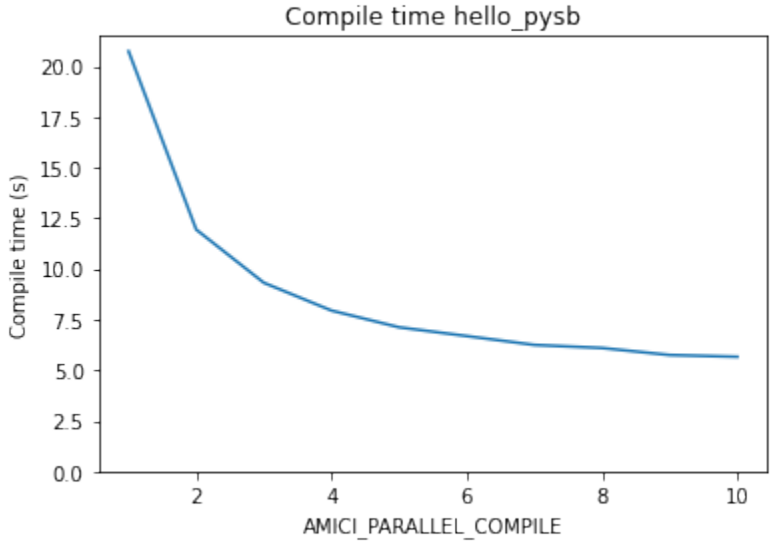
[5]:
```
df_compile = pd.read_csv("results_compile.tsv", sep="\t")
figsize(6, 4)

for model_name, df in df_compile.groupby("model_name"):
    plt.plot(df.nprocs, df.time)
    plt.title(f"Compile time {model_name}")
    plt.xlabel("AMICI_PARALLEL_COMPILE")
    plt.ylabel("Compile time (s)")
    plt.ylim(ymin=0)
    plt.show()

    compilation_time_s = df.sort_values("nprocs")["time"].values
    print(
        "We were able to reduce compile time by up to "
        f"~{(compilation_time_s[0] - min(compilation_time_s[1:])) / compilation_time_
↪s[0] * 100:.0f}%."
    )
```




```
We were able to reduce compile time by up to ~45%.
```




```
We were able to reduce compile time by up to ~73%.
```

Compiler flags

For most compilers, different machine code optimizations can be enabled/disabled by the `-O0`, `-O1`, `-O2`, `-O3` flags, where a higher number enables more optimizations. For faster simulation, `-O3` should be used. However, these optimizations come at the cost of increased compile times. If models grow very large, some optimizations (especially with `g++`, see above) become prohibitively slow. In this case, a lower optimization level may be necessary to be able to compile models at all.

Another potential performance gain can be obtained from using CPU-specific instructions using `-march=native`. The disadvantage is, that the compiled model extension will only run on CPUs supporting the same instruction set. This may be become problematic when attempting to use an AMICI model on a machine other than on which it was compiled (e.g. on heterogeneous compute clusters).

These compiler flags should be set for both, AMICI installation and model compilation.

For AMICI installation, e.g.,

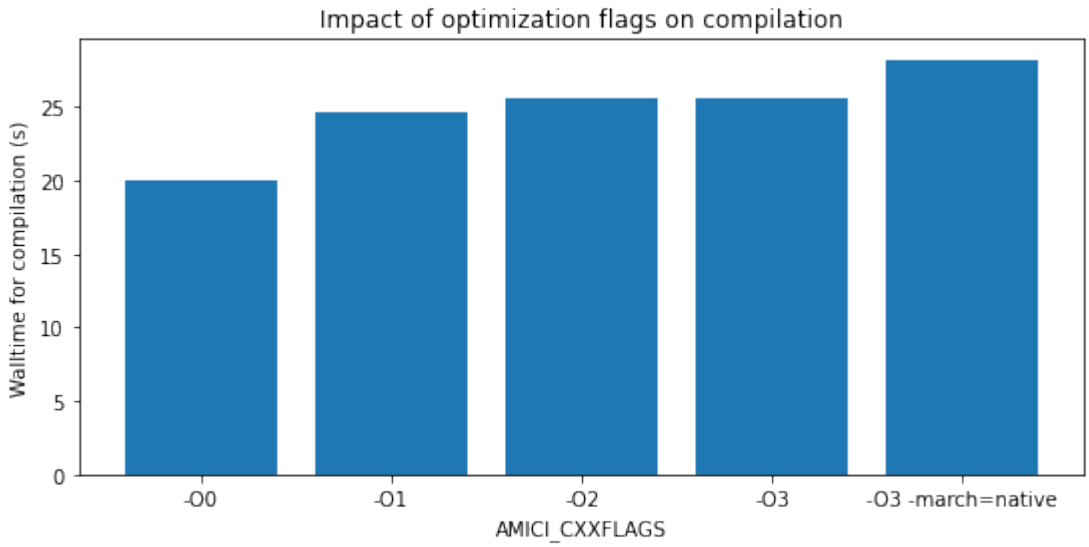
```
CFLAGS="-O3 -march=native" pip install amici
```

For model compilation, flags can be passed via the `AMICI_CXXFLAGS` environment variable.

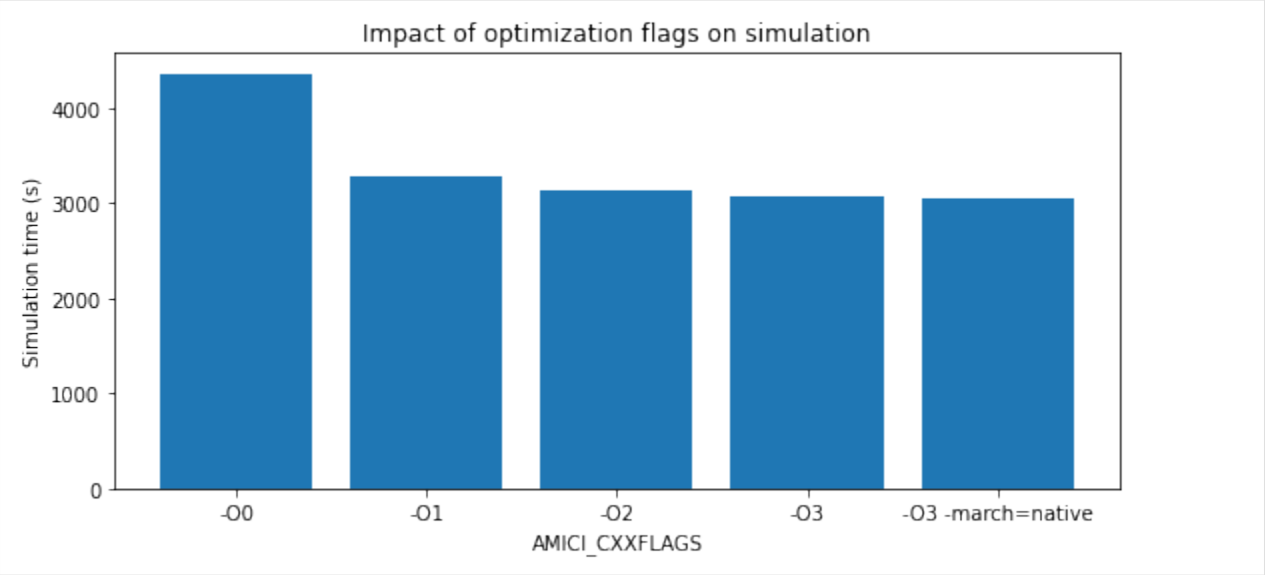
Example:

```
petab_yaml="https://raw.githubusercontent.com/Benchmarking-Initiative/Benchmark-Models-
↪PEtab/master/Benchmark-Models/Chen_MSB2009/Chen_MSB2009.yaml"
amici_import_petab -y "${petab_yaml}" --no-compile
cd Chen_MSB2009-amici0.16.0/
for cflags in "-O0" "-O1" "-O2" "-O3" "-O3 -march=native"
    # this line only builds the model extension, and is normally performed automatically␣
↪during import
    do AMICI_PARALLEL_COMPILE=1 AMICI_CXXFLAGS=${cflags} /usr/bin/time -v python setup.
↪py build_ext --force --build-lib .
done
```

[6]:
```
compilation_time_s = [20.01, 24.62, 25.59, 25.63, 28.21]
labels = ["-O0", "-O1", "-O2", "-O3", "-O3 -march=native"]
figsize(9, 4)
plt.bar(labels, compilation_time_s)
plt.title("Impact of optimization flags on compilation")
plt.xlabel("AMICI_CXXFLAGS")
plt.ylabel("Walltime for compilation (s)");
```



[7]:
```
plt.bar(
    ["-O0", "-O1", "-O2", "-O3", "-O3 -march=native"],
    [4357.768, 3276.873, 3140.092, 3069.855, 3039.262],
)
plt.title("Impact of optimization flags on simulation")
plt.xlabel("AMICI_CXXFLAGS")
plt.ylabel("Simulation time (s)");
```



Using some optimized BLAS

You might have access to some custom BLAS optimized for your hardware which might speed up your simulations somewhat. We are not aware of any systematic evaluation and cannot make any recommendation. You pass the respective compiler and linker flags via the environment variables `BLAS_CFLAGS` and `BLAS_LIBS`, respectively.

Model simulation

A major determinant of simulation time for a given model is the required accuracy and the selected solvers. This has been evaluated, for example, in https://doi.org/10.1038/s41598-021-82196-2 and is not covered further here.

Adjoint *vs.* forward sensitivities

If only the objective function gradient is required, adjoint sensitivity analysis are often preferable over forward sensitivity analysis. As a rule of thumb, adjoint sensitivity analysis seems to outperform forward sensitivity analysis for models with more than 20 parameters:

Sensitivities w.r.t. a subset of parameters

If only sensitivities with respect to a subset of model parameters are of interest to you (see also *Parameters as constants* above), you can speed up the simulation by selecting the relevant parameter indices via amici.Model.setParameterList.

Parallel simulation of multiple conditions

Whenever there are multiple independent simulations to perform, you can use amici.runAmiciSimulations(..., num_threads=...) instead of amici.runAmiciSimulations(...) to run them in parallel. Note that all simulation results have to be kept in memory, which may become problematic for very large numbers of simulations. Parallelization is based on OpenMP and does not come with the issues associated with Python's multiprocessing or multithreading (spawning extra processes or limitations related to the global interpreter lock).

Reporting mode

During model simulation, many quantities are calculated, but not all might be of interest for you. For example, for parameter estimation you might only be interested in the likelihood and gradient. In this case, you can save time and memory using
amici.Solver.setReturnDataReportingMode(amici.RDataReporting.likelihood).

10.2.8 AMICI & JAX

Overview

The purpose of this guide is to showcase how AMICI can be combined with differentiable programming in JAX. We will do so by reimplementing the parameter transformations available in AMICI in JAX and comparing it to the native implementation.

[1]:
```
import jax
import jax.numpy as jnp
```

Preparation

To get started, we will import a model using the petab. To this end, we will use the benchmark collection, which features a variety of different models. For more details about petab import, see the respective notebook petab notebook.

From the benchmark collection, we now import the Böhm model.

[2]:
```
import petab

model_name = "Boehm_JProteomeRes2014"
yaml_file = f"https://raw.githubusercontent.com/Benchmarking-Initiative/Benchmark-Models-
↪PEtab/master/Benchmark-Models/{model_name}/{model_name}.yaml"
petab_problem = petab.Problem.from_yaml(yaml_file)
```

The petab problem includes information about parameter scaling in it's the parameter table. For the boehm model, all estimated parameters (`petab.ESTIMATE` column equal to 1) have a `petab.LOG10` as parameter scaling.

[3]:
```
petab_problem.parameter_df
```

[3]:
```
                              parameterName parameterScale  lowerBound
parameterId
Epo_degradation_BaF3  EPO_{degradation,BaF3}          log10     0.00001  \
```

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```
k_exp_hetero                  k_{exp,hetero}          log10     0.00001
k_exp_homo                      k_{exp,homo}          log10     0.00001
k_imp_hetero                  k_{imp,hetero}          log10     0.00001
k_imp_homo                      k_{imp,homo}          log10     0.00001
k_phos                              k_{phos}          log10     0.00001
ratio                                  ratio            lin    -5.00000
sd_pSTAT5A_rel          \sigma_{pSTAT5A,rel}          log10     0.00001
sd_pSTAT5B_rel          \sigma_{pSTAT5B,rel}          log10     0.00001
sd_rSTAT5A_rel          \sigma_{rSTAT5A,rel}          log10     0.00001
specC17                              specC17            lin    -5.00000

                       upperBound  nominalValue  estimate
parameterId
Epo_degradation_BaF3       100000      0.026983         1
k_exp_hetero               100000      0.000010         1
k_exp_homo                 100000      0.006170         1
k_imp_hetero               100000      0.016368         1
k_imp_homo                 100000  97749.379402         1
k_phos                     100000  15766.507020         1
ratio                           5      0.693000         0
sd_pSTAT5A_rel             100000      3.852612         1
sd_pSTAT5B_rel             100000      6.591478         1
sd_rSTAT5A_rel             100000      3.152713         1
specC17                         5      0.107000         0
```

We now import the petab problem using amici.petab_import.

[4]:
```
from amici.petab.petab_import import import_petab_problem

amici_model = import_petab_problem(
    petab_problem, compile_=True, verbose=False
)
```

JAX implementation

For full jax support, we would have to implement a new primitive, which would require quite a bit of engineering, and in the end wouldn't add much benefit since AMICI can't run on GPUs. Instead, will interface AMICI using the experimental jax module host_callback.

To do so, we define a base function that only takes a single argument (the parameters) and runs simulation using petab via simulate_petab. To enable gradient computation later on, we create a solver object and set the sensitivity order to first order and pass it to `simulate_petab`. Moreover, `simulate_petab` expects a dictionary of parameters, so we create a dictionary using the free parameter ids from the petab problem. As we want to implement parameter transformation in JAX, we disable parameter scaling in petab by passing `scaled_parameters=True`.

[5]:
```
from amici.petab.simulations import simulate_petab
import amici

amici_solver = amici_model.getSolver()
amici_solver.setSensitivityOrder(amici.SensitivityOrder.first)
```

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```
def amici_hcb_base(parameters: jnp.array):
    return simulate_petab(
        petab_problem,
        amici_model,
        problem_parameters=dict(zip(petab_problem.x_free_ids, parameters)),
        solver=amici_solver,
    )
```

Now we can use this base function to create two separate functions that compute the log-likelihood (`llh`) and its gradient (`sllh`) in two individual routines. Note that, as we are using the same base function here, the log-likelihood computation will also run with sensitivities which is not necessary and will add some overhead. This is only out of convenience and should be fixed in an application where efficiency is important.

[6]:
```
def amici_hcb_llh(parameters: jnp.array):
    return amici_hcb_base(parameters)["llh"]


def amici_hcb_sllh(parameters: jnp.array):
    sllh = amici_hcb_base(parameters)["sllh"]
    return jnp.asarray(
        tuple(sllh[par_id] for par_id in petab_problem.x_free_ids)
    )
```

Now we can finally define the JAX function that runs amici simulation using the host callback. We add a `custom_jvp` decorator so that we can define a custom jacobian vector product function in the next step. More details about custom jacobian vector product functions can be found in the JAX documentation

[7]:
```
import jax.experimental.host_callback as hcb
from jax import custom_jvp

import numpy as np


@custom_jvp
def jax_objective(parameters: jnp.array):
    return hcb.call(
        amici_hcb_llh,
        parameters,
        result_shape=jax.ShapeDtypeStruct((), np.float64),
    )
```

Now we define the function that implement the jacobian vector product. This effectively just returns the objective function value (computed using the previously defined `jax_objective`) as well as the inner product of the gradient (computed using a host callback to the previously defined `amici_hcb_sllh`) and the tangents vector. Note that this implementation performs two simulation runs, one for the function value and one for the gradient, which is inefficient and could be avoided by caching solutions.

[8]:
```
@jax_objective.defjvp
def jax_objective_jvp(primals: jnp.array, tangents: jnp.array):
    (parameters,) = primals
    (x_dot,) = tangents
    llh = jax_objective(parameters)
    sllh = hcb.call(
```

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```
        amici_hcb_sllh,
        parameters,
        result_shape=jax.ShapeDtypeStruct(
            (petab_problem.parameter_df.estimate.sum(),), np.float64
        ),
    )
    return llh, sllh.dot(x_dot)
```

As last step, we implement the parameter transformation in jax. This effectively just extracts parameter scales from the petab problem, implements rescaling in jax and then passes the scaled parameters to the previously objective function we previously defined. We add the `value_and_grad` decorator such that the generated jax function returns both function value and function gradient in a tuple. Moreover, we add the `jax.jit` decorator such that the function is just in time compiled upon the first function call.

[9]:
```
from jax import value_and_grad

parameter_scales = petab_problem.parameter_df.loc[
    petab_problem.x_free_ids, petab.PARAMETER_SCALE
].values


@jax.jit
@value_and_grad
def jax_objective_with_parameter_transform(parameters: jnp.array):
    par_scaled = jnp.asarray(
        tuple(
            value
            if scale == petab.LIN
            else jnp.exp(value)
            if scale == petab.LOG
            else jnp.power(10, value)
            for value, scale in zip(parameters, parameter_scales)
        )
    )
    return jax_objective(par_scaled)
```

Testing

We can now run the function to compute the log-likelihood and the gradient.

[10]:
```
parameters = dict(zip(petab_problem.x_free_ids, petab_problem.x_nominal_free))
scaled_parameters = petab_problem.scale_parameters(parameters)
scaled_parameters_np = np.asarray(list(scaled_parameters.values()))
```

[11]:
```
llh_jax, sllh_jax = jax_objective_with_parameter_transform(
    scaled_parameters_np
)
```

As a sanity check, we compare the computed value to native parameter transformation in amici.

[12]:
```
r = simulate_petab(
    petab_problem,
    amici_model,
    solver=amici_solver,
    scaled_parameters=True,
    scaled_gradients=True,
    problem_parameters=scaled_parameters,
)
```

[13]:
```
import pandas as pd

pd.DataFrame(
    dict(
        amici=r["llh"],
        jax=float(llh_jax),
        rel_diff=(r["llh"] - float(llh_jax)) / r["llh"],
    ),
    index=("llh",),
)
```

[13]:
```
          amici      jax      rel_diff
llh -138.221997 -138.222 -2.135248e-08
```

[14]:
```
grad_amici = np.asarray(list(r["sllh"].values()))
grad_jax = np.asarray(sllh_jax)
rel_diff = (grad_amici - grad_jax) / grad_jax
pd.DataFrame(
    index=r["sllh"].keys(),
    data=dict(amici=grad_amici, jax=grad_jax, rel_diff=rel_diff),
)
```

[14]:
```
                         amici       jax      rel_diff
Epo_degradation_BaF3 -0.022045 -0.022034  4.645833e-04
k_exp_hetero         -0.055323 -0.055323  8.646725e-08
k_exp_homo           -0.005789 -0.005801 -2.013520e-03
k_imp_hetero         -0.005414 -0.005403  1.973517e-03
k_imp_homo            0.000045  0.000045  1.119566e-06
k_phos               -0.007907 -0.007794  1.447768e-02
sd_pSTAT5A_rel       -0.010784 -0.010800 -1.469604e-03
sd_pSTAT5B_rel       -0.024037 -0.024037 -8.729860e-06
sd_rSTAT5A_rel       -0.019191 -0.019186  2.829431e-04
```

We see quite some differences in the gradient calculation, with over to 1% error for `k_phos`. The primary reason is that running JAX in default configuration will use float32 precision for the parameters that are passed to AMICI, which uses float64, and the derivative of the parameter transformation. As AMICI simulations that run on the CPU are the most expensive operation, there is barely any tradeoff for using float32 vs. float64 in JAX. Therefore, we configure JAX to use float64 instead and rerun simulations.

[15]:
```
jax.config.update("jax_enable_x64", True)
llh_jax, sllh_jax = jax_objective_with_parameter_transform(
    scaled_parameters_np
)
```

We can now evaluate the results again and see that differences between pure AMICI and AMICI/JAX implementations

have now disappeared.

[16]:
```
pd.DataFrame(
    dict(
        amici=r["llh"],
        jax=float(llh_jax),
        rel_diff=(r["llh"] - float(llh_jax)) / r["llh"],
    ),
    index=("llh",),
)
```

[16]:
```
          amici         jax  rel_diff
llh -138.221997 -138.221997      -0.0
```

[17]:
```
grad_amici = np.asarray(list(r["sllh"].values()))
grad_jax = np.asarray(sllh_jax)
rel_diff = (grad_amici - grad_jax) / grad_jax
pd.DataFrame(
    index=r["sllh"].keys(),
    data=dict(amici=grad_amici, jax=grad_jax, rel_diff=rel_diff),
)
```

[17]:
```
                        amici       jax  rel_diff
Epo_degradation_BaF3 -0.022045 -0.022045      -0.0
k_exp_hetero         -0.055323 -0.055323      -0.0
k_exp_homo           -0.005789 -0.005789      -0.0
k_imp_hetero         -0.005414 -0.005414      -0.0
k_imp_homo            0.000045  0.000045       0.0
k_phos               -0.007907 -0.007907      -0.0
sd_pSTAT5A_rel       -0.010784 -0.010784      -0.0
sd_pSTAT5B_rel       -0.024037 -0.024037      -0.0
sd_rSTAT5A_rel       -0.019191 -0.019191      -0.0
```

10.2.9 AMICI Python example "splines"

This is an example showing how to add spline assignment rules to a pre-existing SBML model.

Utility functions

[1]:
```
import os
import sys
from importlib import import_module
from shutil import rmtree
from tempfile import TemporaryDirectory
from uuid import uuid1

import matplotlib as mpl
import numpy as np
import sympy as sp
from matplotlib import pyplot as plt
```

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```
import amici

# Choose build directory
BUILD_PATH = None  # temporary folder
# BUILD_PATH = 'build' # specified folder for debugging
if BUILD_PATH is not None:
    # Remove previous models
    rmtree(BUILD_PATH, ignore_errors=True)
    os.mkdir(BUILD_PATH)


def simulate(sbml_model, parameters=None, *, model_name=None, **kwargs):
    if model_name is None:
        model_name = "model_" + uuid1().hex
    if BUILD_PATH is None:
        with TemporaryDirectory() as build_dir:
            return _simulate(
                sbml_model,
                parameters,
                build_dir=build_dir,
                model_name=model_name,
                **kwargs
            )
    else:
        build_dir = os.path.join(BUILD_PATH, model_name)
        rmtree(build_dir, ignore_errors=True)
        return _simulate(
            sbml_model,
            parameters,
            build_dir=build_dir,
            model_name=model_name,
            **kwargs
        )


def _simulate(
    sbml_model,
    parameters,
    *,
    build_dir,
    model_name,
    T=1,
    discard_annotations=False,
    plot=True
):
    if parameters is None:
        parameters = {}
    # Build the model module from the SBML file
    sbml_importer = amici.SbmlImporter(
        sbml_model, discard_annotations=discard_annotations
    )
```

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```
    sbml_importer.sbml2amici(model_name, build_dir)
    # Import the model module
    sys.path.insert(0, os.path.abspath(build_dir))
    model_module = import_module(model_name)
    # Setup simulation timepoints and parameters
    model = model_module.getModel()
    for name, value in parameters.items():
        model.setParameterByName(name, value)
    if isinstance(T, (int, float)):
        T = np.linspace(0, T, 100)
    model.setTimepoints([float(t) for t in T])
    solver = model.getSolver()
    solver.setSensitivityOrder(amici.SensitivityOrder.first)
    solver.setSensitivityMethod(amici.SensitivityMethod.forward)
    # Simulate
    rdata = amici.runAmiciSimulation(model, solver)
    # Plot results
    if plot:
        fig, ax = plt.subplots()
        ax.plot(rdata["t"], rdata["x"])
        ax.set_xlabel("time")
        ax.set_ylabel("concentration")
    return model, rdata
```

A simple SBML model

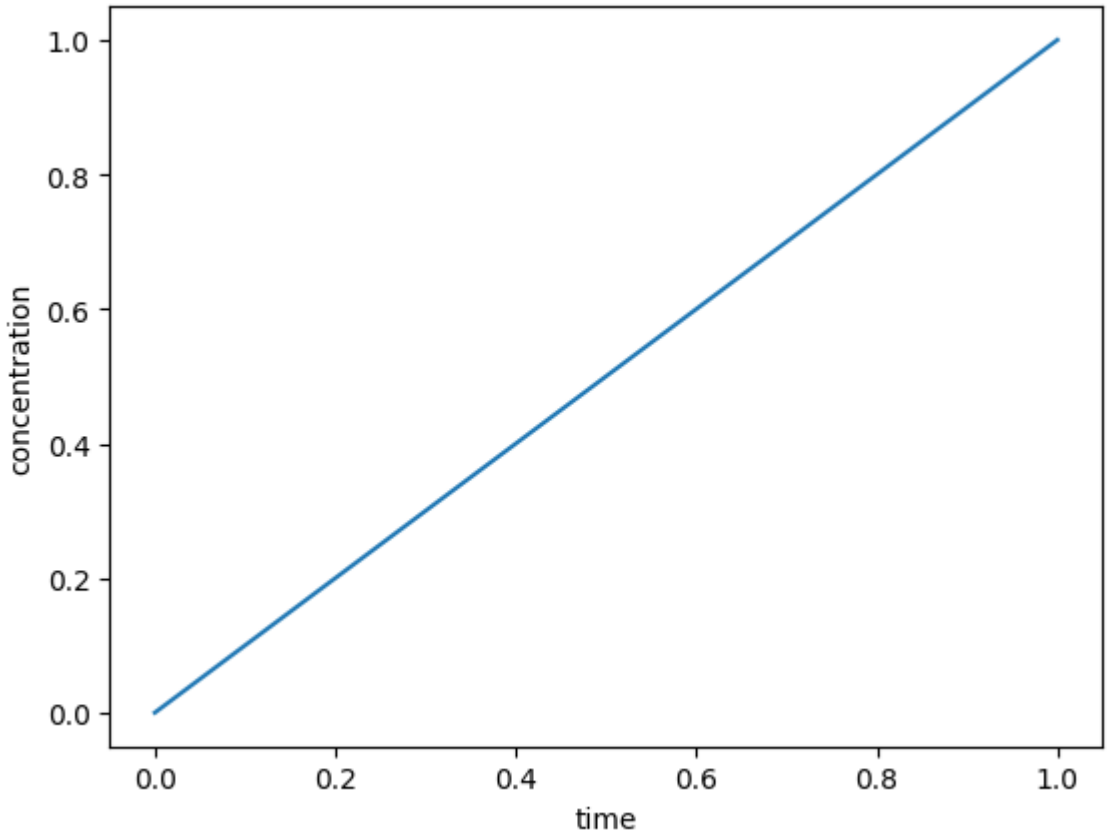
Let us consider the following SBML model:

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level2/version5" level="2" version="5">
  <model id="example_splines">
    <listOfCompartments>
      <compartment id="compartment" size="1"/>
    </listOfCompartments>
    <listOfSpecies>
      <species id="x" compartment="compartment" initialAmount="0"/>
    </listOfSpecies>
    <listOfParameters>
      <parameter id="f" constant="false"/>
    </listOfParameters>
    <listOfRules>
      <rateRule variable="x">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <ci> f </ci>
        </math>
      </rateRule>
    </listOfRules>
  </model>
</sbml>
```

This model corresponds to the simple ODE $\dot{x} = f$ for a species x and a parameter f.

We can easily import and simulate this model in AMICI.

[2]:
```
simulate("example_splines.xml", dict(f=1));
```



Adding a simple spline

Instead of using a constant parameter f, we want to use a smooth time-dependent function $f(t)$ whose value is known only at a finite number of time instants. The value of $f(t)$ outside such grid points needs to be smoothly interpolated. Several methods have been developed for this problem over the years; AMICI at the moment supports only cubic Hermite splines.

We can add a spline function to an existing SBML model with the following code. The resulting time-dependent parameter $f(t)$ will assume values $(1, -0.5, 2)$ at the equally spaced points $(0, 0.5, 1)$ and smoothly vary elsewhere.

AMICI encodes the spline as a SBML assignment rule for the parameter f. Such a rule consists of a piecewise-polynomial formula which can be interpreted in any SBML-compliant software. However, such very complex formulas are computationally inefficient; e.g., in AMICI they lead to very long model creation times. To solve such problem the code below adds AMICI-specific SBML annotations to the assignment rule which can be used by AMICI to recreate the correct interpolant without reading the inefficient piecewise formula.

[3]:
```
# Create a spline object
spline = amici.splines.CubicHermiteSpline(
    sbml_id="f",
    evaluate_at=amici.sbml_utils.amici_time_symbol,  # the spline function is evaluated␣
↪at the current time point
    nodes=amici.splines.UniformGrid(0, 1, number_of_nodes=3),
```

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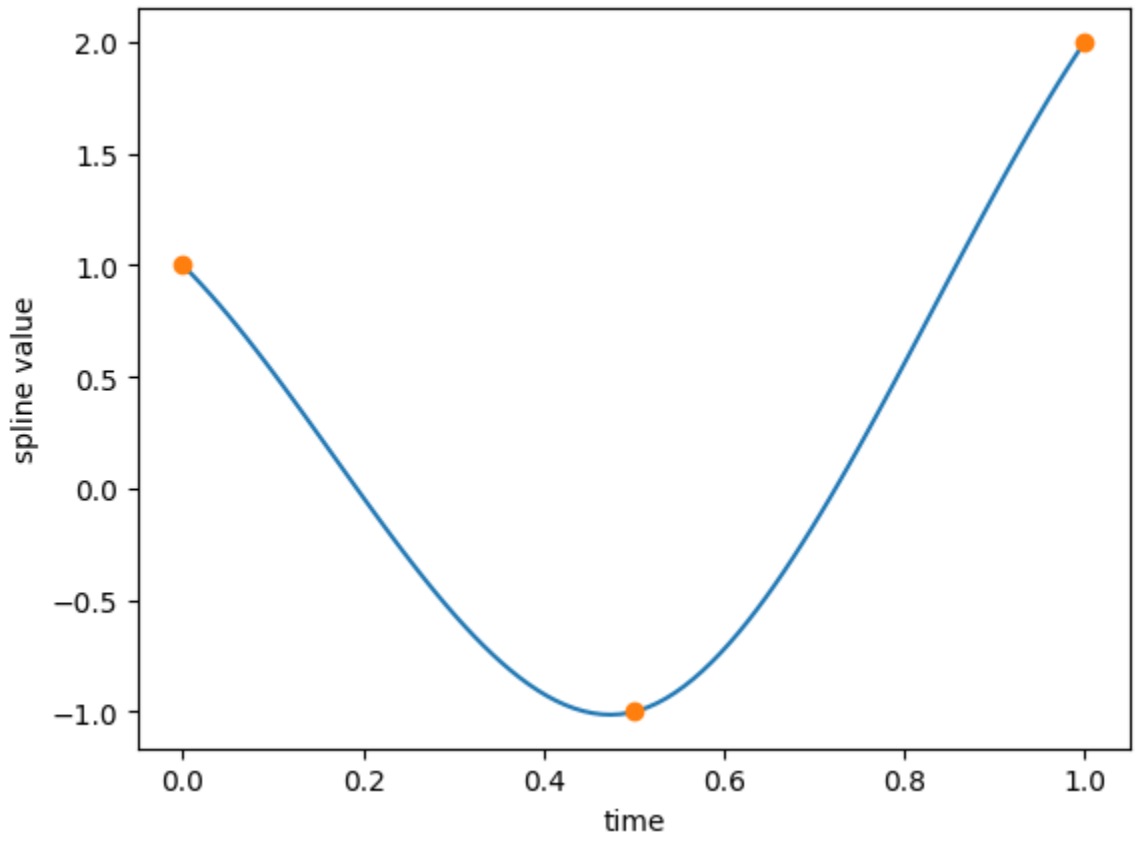
```
    values_at_nodes=[1, -1, 2],
)
```

[4]:
```
# This spline object can be evaluated at any point
# and so can its derivative/integral
print(f"spline value at 0.3 = {spline.evaluate(0.3)}")
print(f"spline derivative at 0.3 = {spline.derivative(0.3)}")
print(f"spline integral between 0 and 1 = {spline.integrate(0.0, 1.0)}")
```

```
spline value at 0.3 = -0.560000000000000
spline derivative at 0.3 = -4.60000000000000
spline integral between 0 and 1 = 0.0416666666666672
```

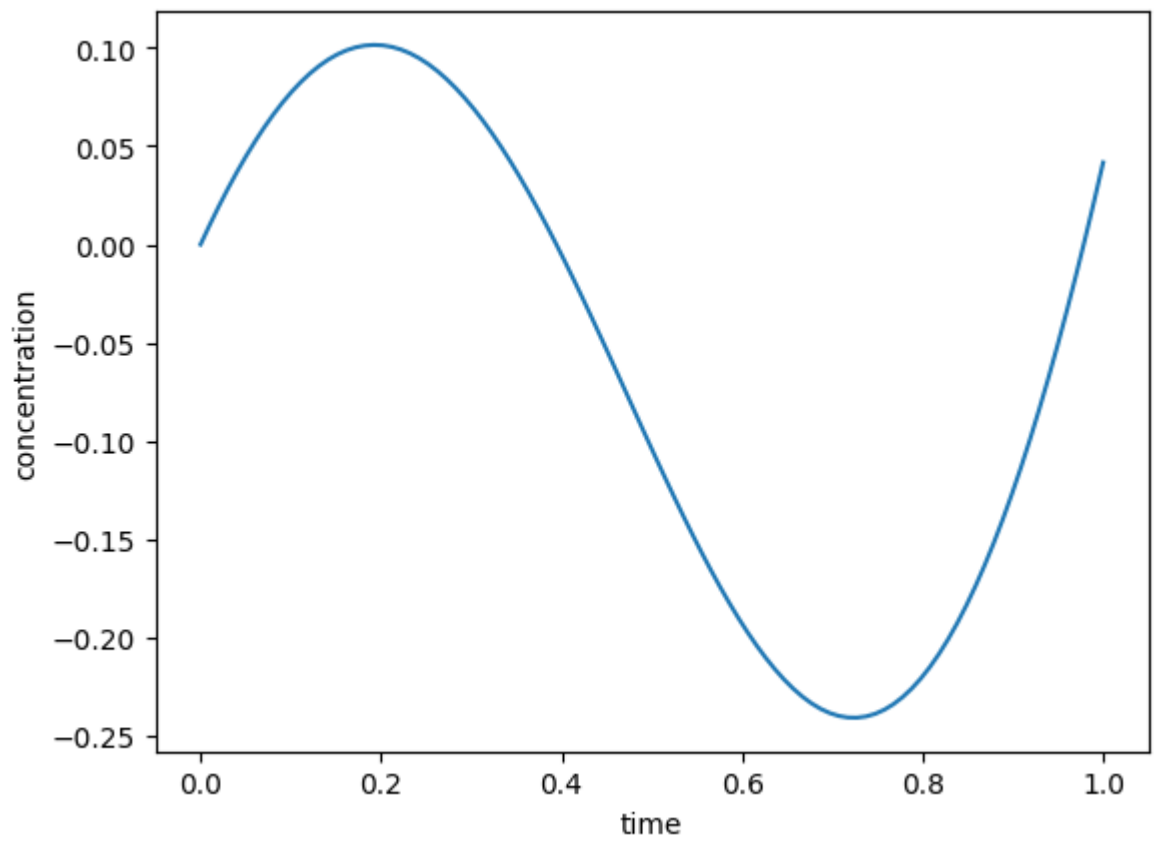
[5]:
```
# Plot the spline
spline.plot(xlabel="time");
```



[6]:
```
# Load SBML model using libsbml
import libsbml

sbml_doc = libsbml.SBMLReader().readSBML("example_splines.xml")
sbml_model = sbml_doc.getModel()
# We can add the spline assignment rule to the SBML model
spline.add_to_sbml_model(sbml_model)
```

[7]:
```
# Finally, we can simulate it in AMICI
model, rdata = simulate(sbml_model);
```



[8]:
```
# Final value should be equal to the integral computed above
assert np.allclose(rdata["x"][-1], float(spline.integrate(0.0, 1.0)))
```

The following is the SBML code for the above model

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level2/version5" level="2" version="5">
  <model id="example_splines">
    <listOfCompartments>
      <compartment id="compartment" size="1"/>
    </listOfCompartments>
    <listOfSpecies>
      <species id="x" compartment="compartment" initialAmount="0"/>
    </listOfSpecies>
    <listOfParameters>
      <parameter id="f" constant="false"/>
    </listOfParameters>
    <listOfRules>
      <rateRule variable="x">
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <ci> f </ci>
        </math>
```

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```
      </rateRule>
      <assignmentRule variable="f">
        <annotation>
          <amici:spline xmlns:amici="https://github.com/AMICI-dev/AMICI" amici:spline_
↪method="cubic_hermite">
            <amici:spline_evaluation_point>
              <math xmlns="http://www.w3.org/1998/Math/MathML">
                <csymbol encoding="text" definitionURL="http://www.sbml.org/sbml/symbols/
↪time"> time </csymbol>
              </math>
            </amici:spline_evaluation_point>
            <amici:spline_uniform_grid>
              <math xmlns="http://www.w3.org/1998/Math/MathML">
                <cn>0</cn>
              </math>
              <math xmlns="http://www.w3.org/1998/Math/MathML">
                <cn>1</cn>
              </math>
              <math xmlns="http://www.w3.org/1998/Math/MathML">
                <apply>
                  <divide/>
                  <cn>1</cn>
                  <cn>2</cn>
                </apply>
              </math>
            </amici:spline_uniform_grid>
            <amici:spline_values>
              <math xmlns="http://www.w3.org/1998/Math/MathML">
                <cn>1</cn>
              </math>
              <math xmlns="http://www.w3.org/1998/Math/MathML">
                <cn>-1</cn>
              </math>
              <math xmlns="http://www.w3.org/1998/Math/MathML">
                <cn>2</cn>
              </math>
            </amici:spline_values>
          </amici:spline>
        </annotation>
        <math xmlns="http://www.w3.org/1998/Math/MathML">
          <piecewise>
            ... piecewise representation of the spline ...
          </piecewise>
        </math>
      </assignmentRule>
    </listOfRules>
  </model>
</sbml>
```

The spline annotation on its own can be accessed by

[9]:
```
print(spline.amici_annotation)
```

```
<amici:spline xmlns:amici="https://github.com/AMICI-dev/AMICI" amici:spline_method=
↪"cubic_hermite">
        <amici:spline_evaluation_point>
                <math xmlns="http://www.w3.org/1998/Math/MathML">
                        <csymbol encoding="text" definitionURL="http://www.sbml.org/sbml/
↪symbols/time"> time </csymbol>
                </math>
        </amici:spline_evaluation_point>
        <amici:spline_uniform_grid>
                <math xmlns="http://www.w3.org/1998/Math/MathML">
                        <cn>0</cn>
                </math>
                <math xmlns="http://www.w3.org/1998/Math/MathML">
                        <cn>1</cn>
                </math>
                <math xmlns="http://www.w3.org/1998/Math/MathML">
                        <apply>
                                <divide/>
                                <cn>1</cn>
                                <cn>2</cn>
                        </apply>
                </math>
        </amici:spline_uniform_grid>
        <amici:spline_values>
                <math xmlns="http://www.w3.org/1998/Math/MathML">
                        <cn>1</cn>
                </math>
                <math xmlns="http://www.w3.org/1998/Math/MathML">
                        <cn>-1</cn>
                </math>
                <math xmlns="http://www.w3.org/1998/Math/MathML">
                        <cn>2</cn>
                </math>
        </amici:spline_values>
</amici:spline>
```

Splines can be parametrized

Instead of constant values, SBML parameters can be used as spline values. These can also be automatically added to the model when adding the assignment rule.

[10]:
```
spline = amici.splines.CubicHermiteSpline(
    sbml_id="f",
    evaluate_at=amici.sbml_utils.amici_time_symbol,
    nodes=amici.splines.UniformGrid(0, 1, number_of_nodes=3),
    values_at_nodes=sp.symbols("f0:3"),
)
```

[11]:
```
sbml_doc = libsbml.SBMLReader().readSBML("example_splines.xml")
sbml_model = sbml_doc.getModel()
spline.add_to_sbml_model(
```

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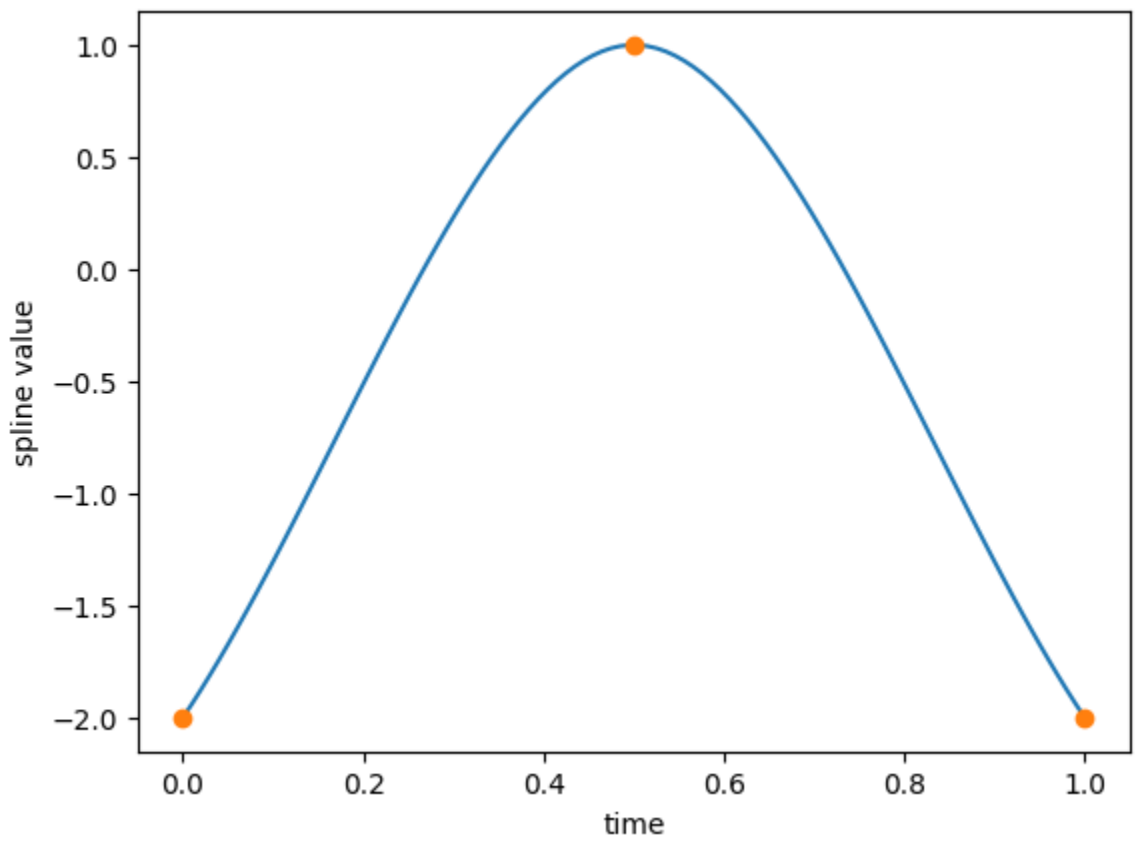
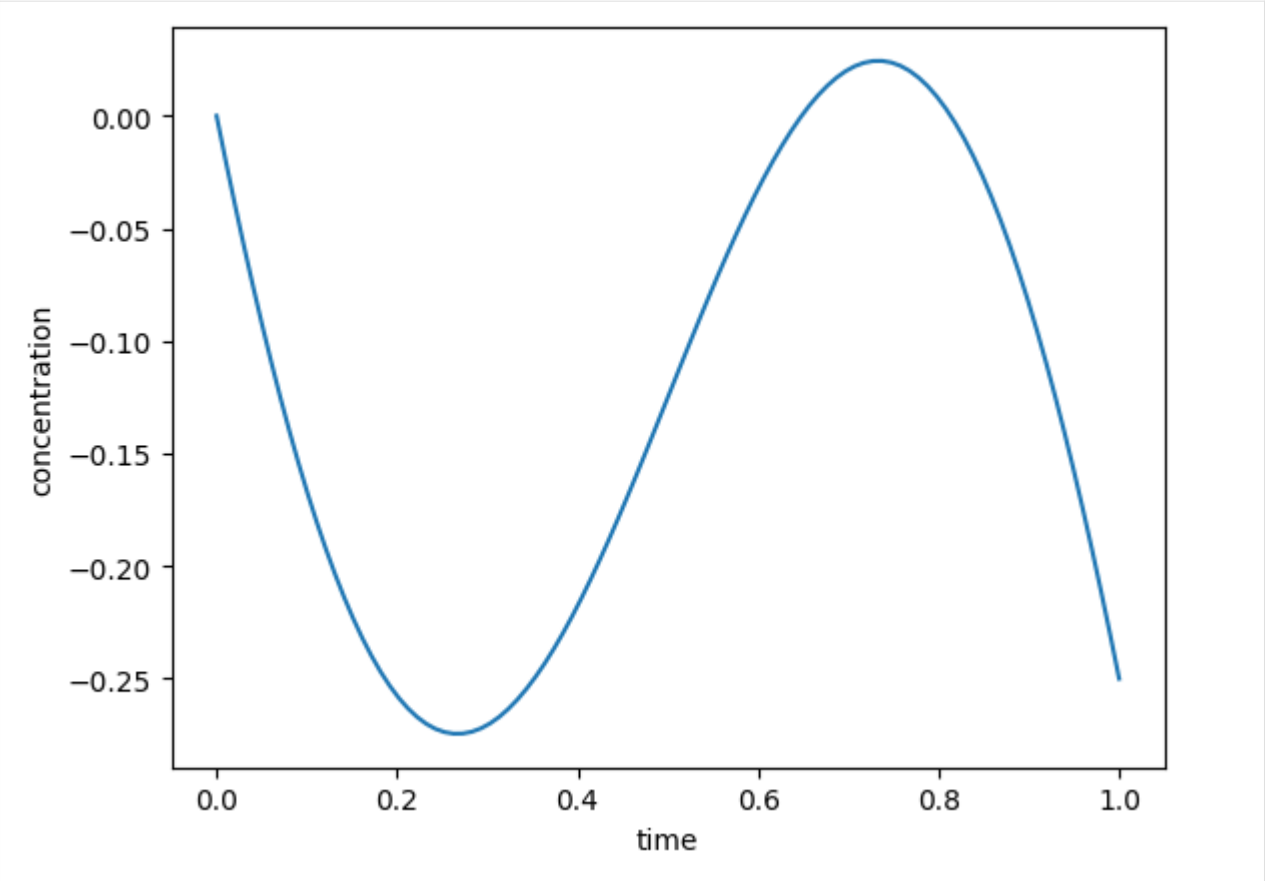
```
    sbml_model,
    auto_add=True,
    y_nominal=[1, -0.5, 2],
)
```

[12]:
```
parameters = dict(f0=-2, f1=1, f2=-2)
```

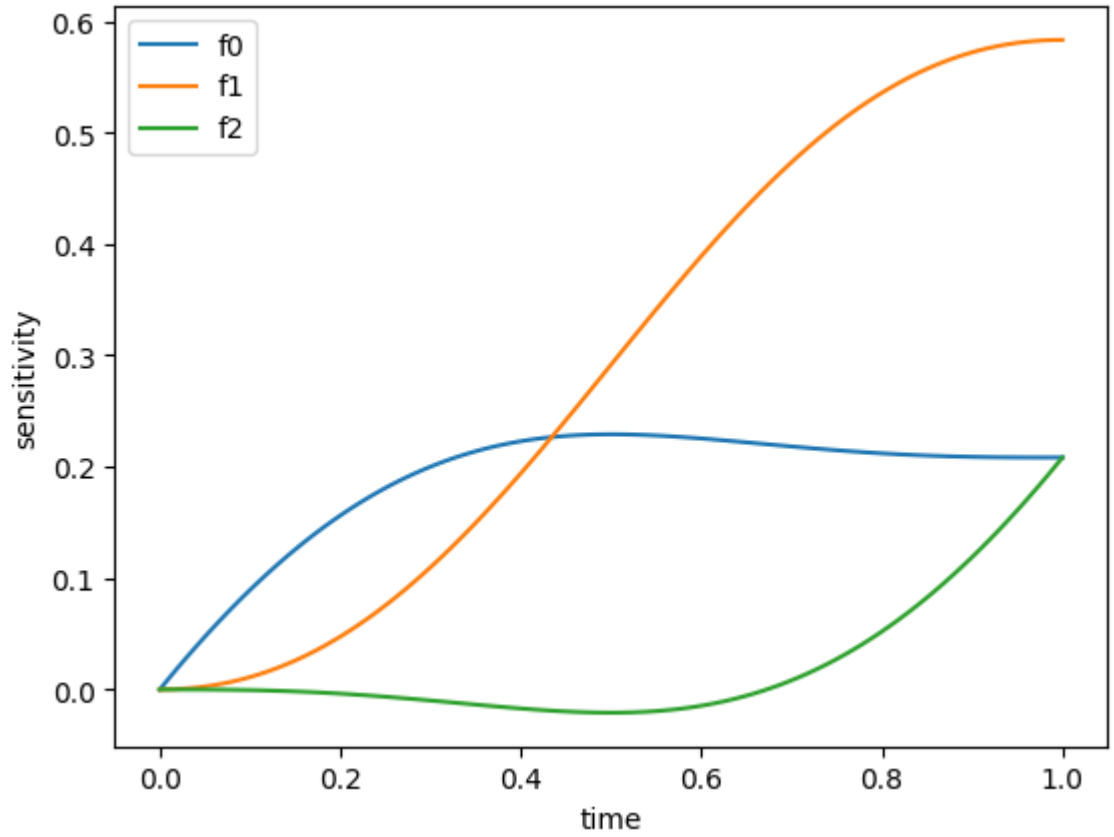
[13]:
```
spline.plot(parameters, xlabel="time");
```



[14]:
```
model, rdata = simulate(sbml_model, parameters)
```



[15]:
```
# Sensitivities with respect to the spline values can be computed
fig, ax = plt.subplots()
ax.plot(rdata["t"], rdata.sx[:, 0], label=model.getParameterNames()[0])
ax.plot(rdata["t"], rdata.sx[:, 1], label=model.getParameterNames()[1])
ax.plot(rdata["t"], rdata.sx[:, 2], label=model.getParameterNames()[2])
ax.set_xlabel("time")
ax.set_ylabel("sensitivity")
ax.legend();
```

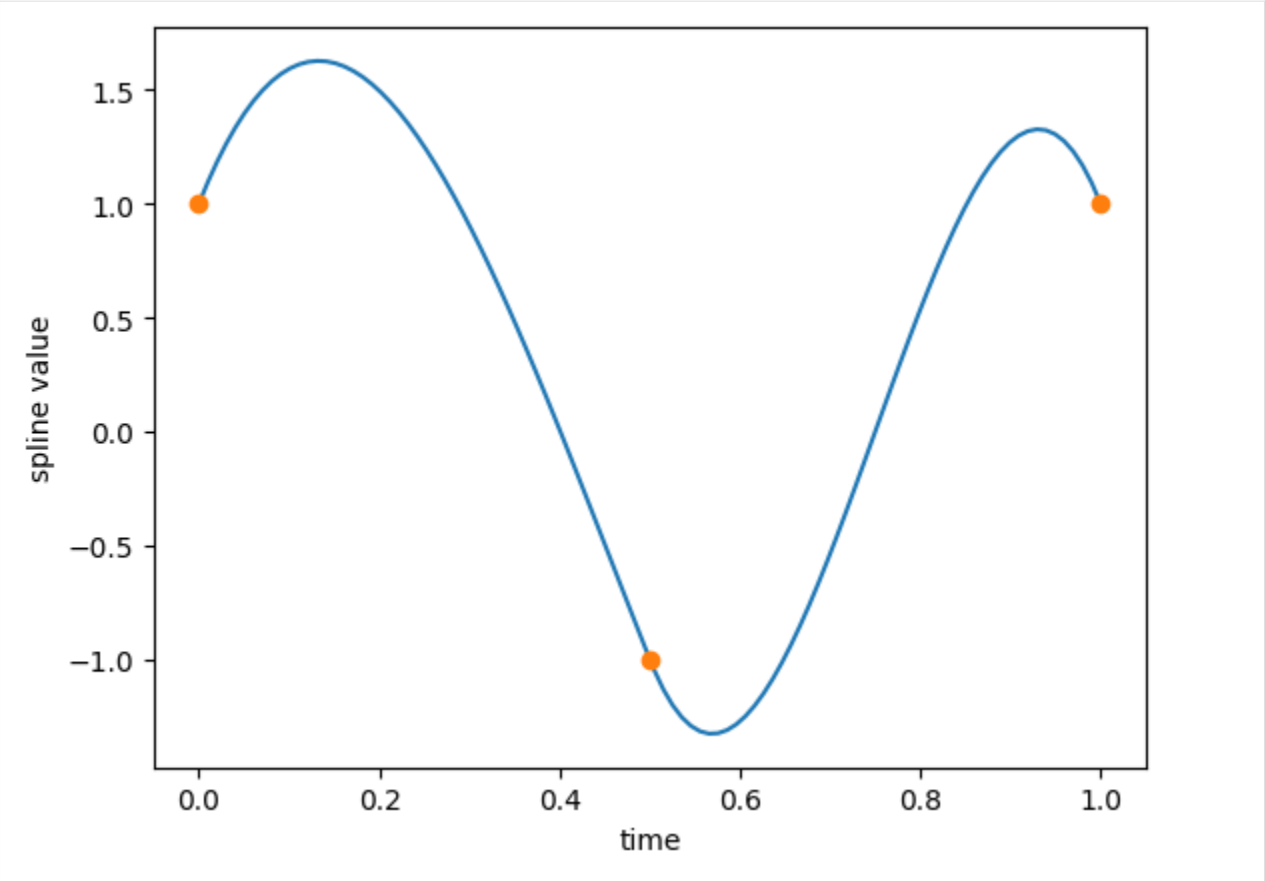


Specifying derivatives, boundary conditions and extrapolation methods

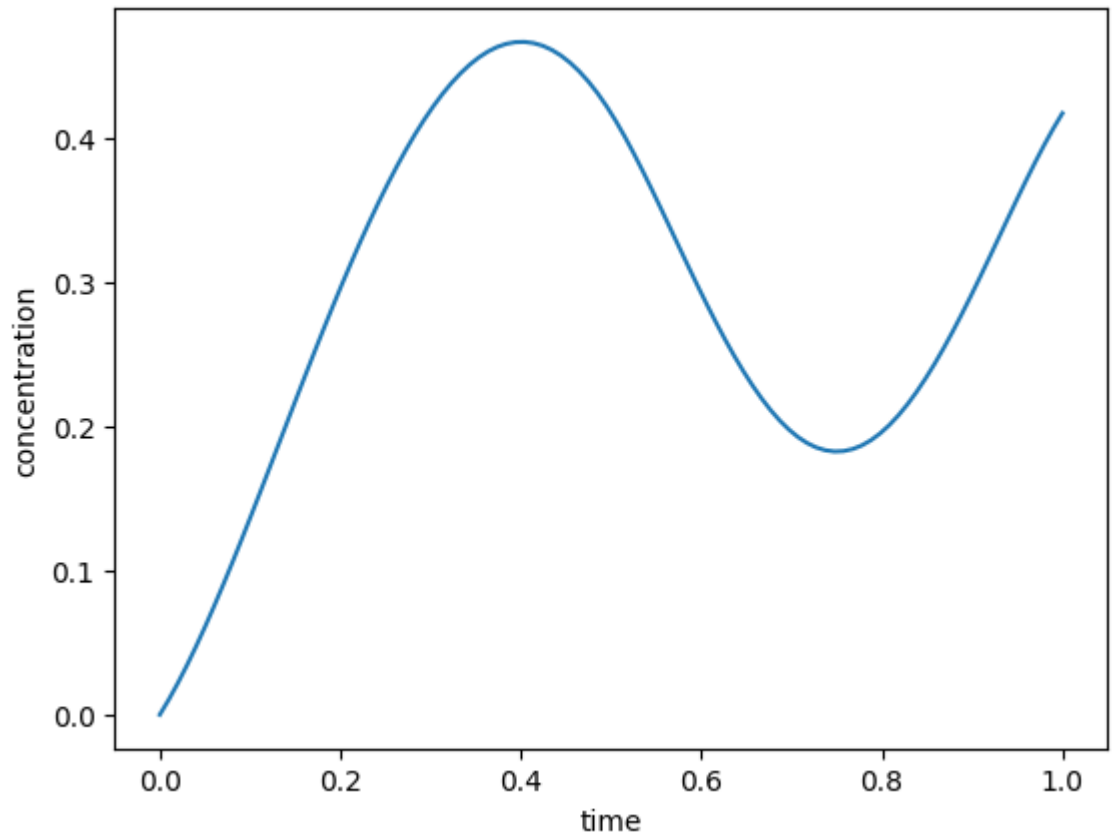
When derivatives are not specified in the `CubicHermiteSpline` constructor, they are computed automatically using finite differences and according to the boundary conditions. If their form is known a priori (e.g., they are known constants or functions of parameters), they can be passed explicitly to the spline constructor.

[16]:
```
# A simple spline for which finite differencing would give a different result
spline = amici.splines.CubicHermiteSpline(
    sbml_id="f",
    evaluate_at=amici.sbml_utils.amici_time_symbol,
    nodes=amici.splines.UniformGrid(0, 1, number_of_nodes=3),
    values_at_nodes=[1.0, -1.0, 1.0],
    derivatives_at_nodes=[10.0, -10.0, -10.0],
)
```

[17]:
```
spline.plot(xlabel="time");
```



[18]:
```
# Simulation
sbml_doc = libsbml.SBMLReader().readSBML("example_splines.xml")
sbml_model = sbml_doc.getModel()
spline.add_to_sbml_model(sbml_model)
simulate(sbml_model, T=1);
```



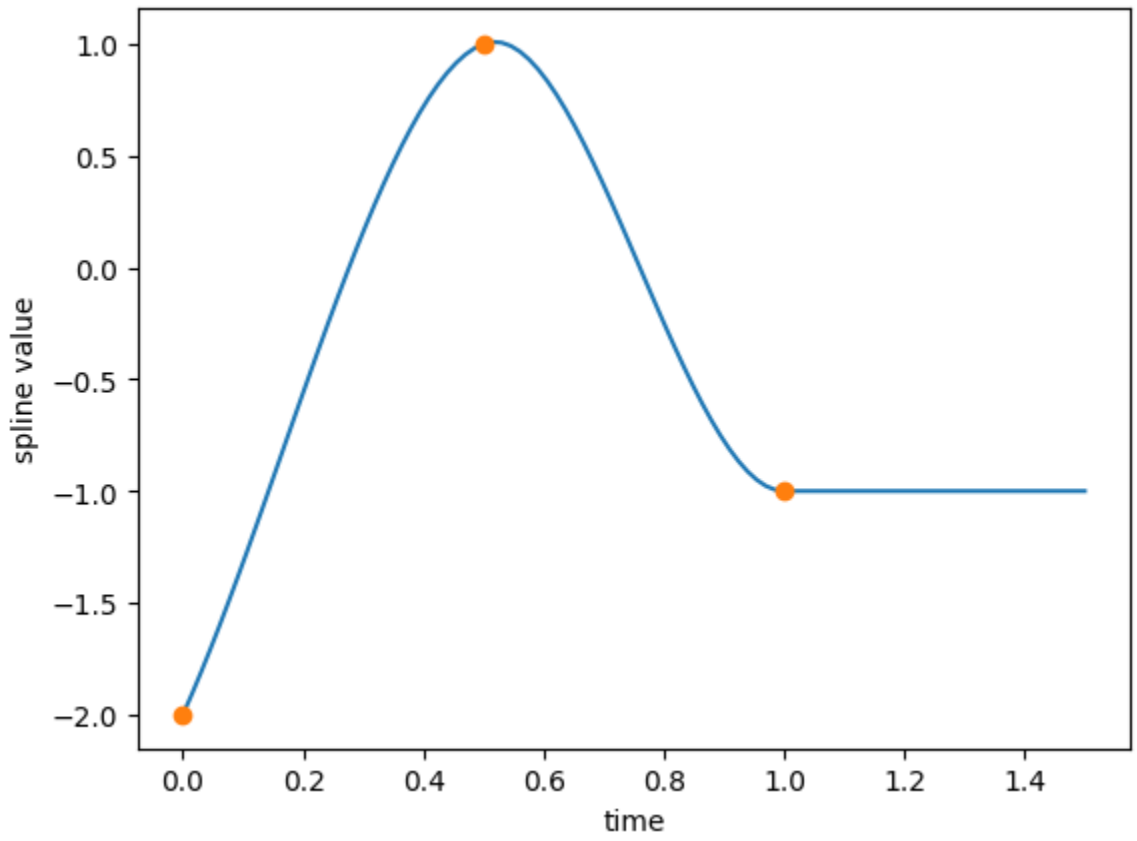
The spline annotation in this case is

```
<amici:spline xmlns:amici="https://github.com/AMICI-dev/AMICI" amici:spline_method=
↪"cubic_hermite">
    <amici:spline_evaluation_point> ... </amici:spline_evaluation_point>
    <amici:spline_uniform_grid> ... </amici:spline_uniform_grid>
    <amici:spline_values> ... </amici:spline_values>
    <amici:spline_derivatives>
        <math xmlns="http://www.w3.org/1998/Math/MathML">
            <cn>10</cn>
        </math>
        <math xmlns="http://www.w3.org/1998/Math/MathML">
            <cn>-10</cn>
        </math>
        <math xmlns="http://www.w3.org/1998/Math/MathML">
            <cn>-10</cn>
        </math>
    </amici:spline_derivatives>
</amici:spline>
```

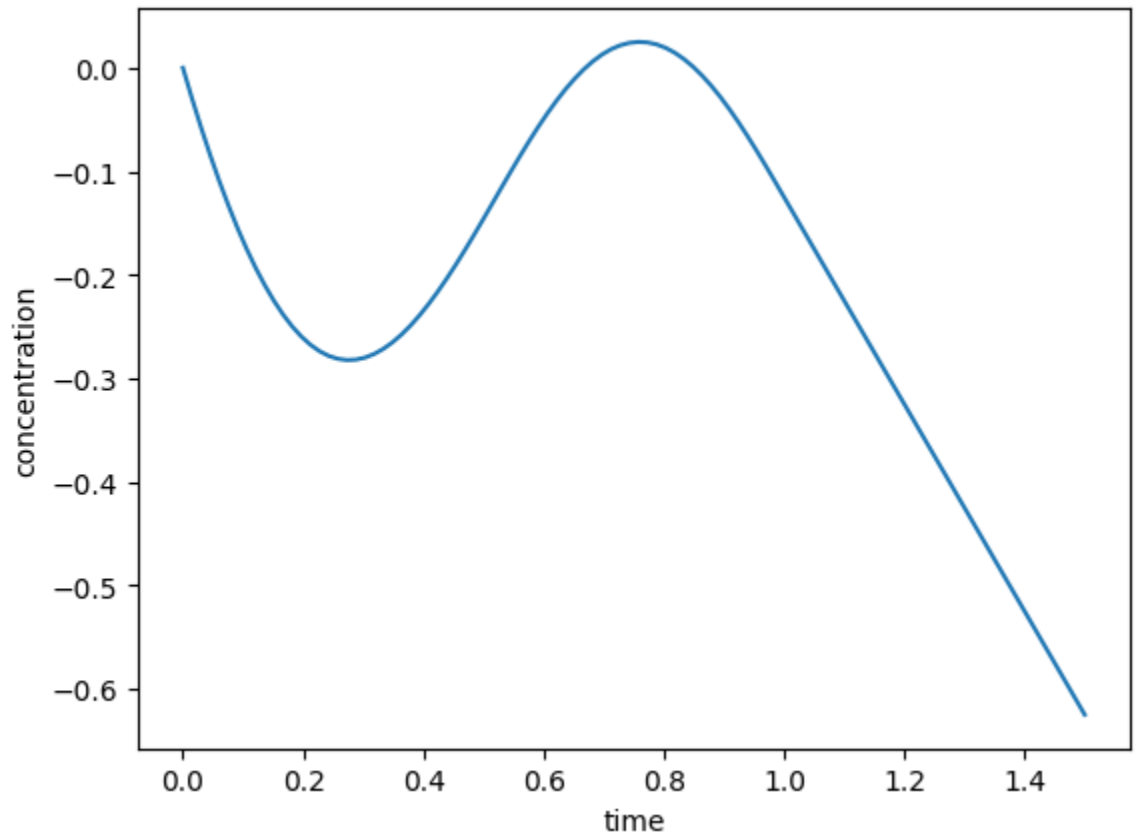
The default boundary conditions depend on the extrapolation method (which defaults to no extrapolation). For example, below we have a spline with constant extrapolation.

[19]:
```
spline = amici.splines.CubicHermiteSpline(
    sbml_id="f",
    evaluate_at=amici.sbml_utils.amici_time_symbol,
    nodes=amici.splines.UniformGrid(0, 1, number_of_nodes=3),
    values_at_nodes=[-2, 1, -1],
    extrapolate=(
        None,
        "constant",
    ),  # no extrapolation required on the left side
)
```

[20]:
```
spline.plot(xlabel="time", xlim=(0, 1.5));
```



[21]:
```
sbml_doc = libsbml.SBMLReader().readSBML("example_splines.xml")
sbml_model = sbml_doc.getModel()
spline.add_to_sbml_model(sbml_model)
simulate(sbml_model, T=1.5);
```



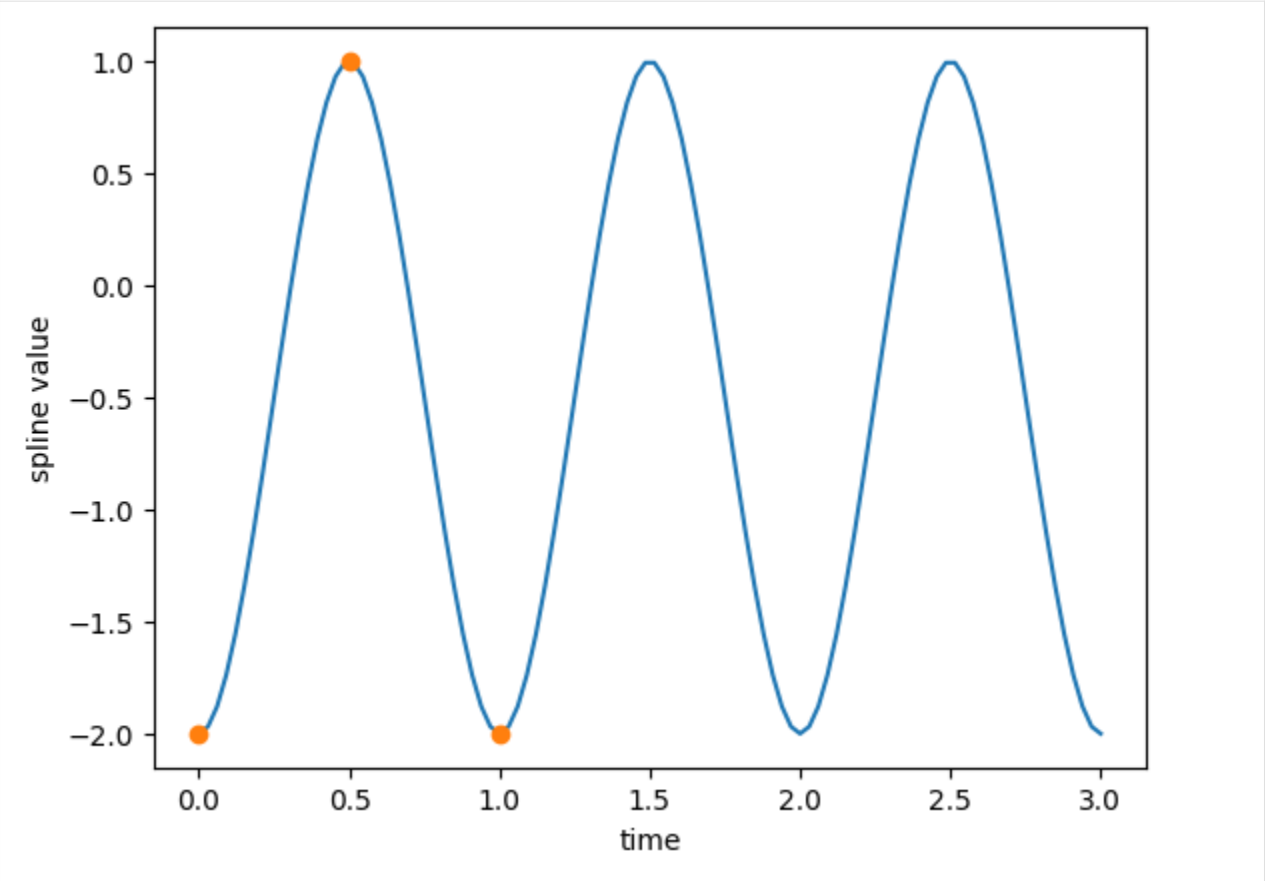
The spline annotation in this case is

```
<amici:spline xmlns:amici="https://github.com/AMICI-dev/AMICI" amici:spline_method=
↪"cubic_hermite" amici:spline_bc="(no_bc, zeroderivative)" amici:spline_extrapolate=
↪"(no_extrapolation, constant)">
    <amici:spline_evaluation_point> ... </amici:spline_evaluation_point>
    <amici:spline_uniform_grid> ... </amici:spline_uniform_grid>
    <amici:spline_values> ... </amici:spline_values>
</amici:spline>
```

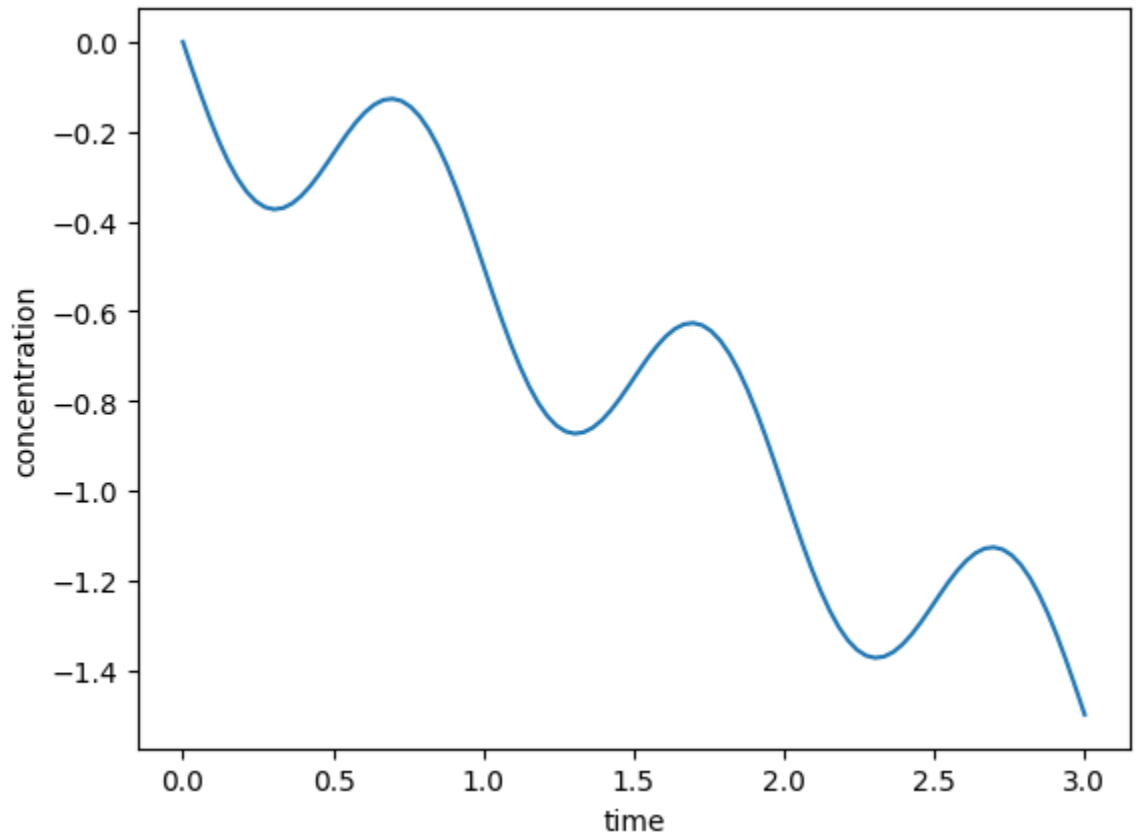
And here we have a periodic spline.

[22]:
```
spline = amici.splines.CubicHermiteSpline(
    sbml_id="f",
    evaluate_at=amici.sbml_utils.amici_time_symbol,
    nodes=amici.splines.UniformGrid(0, 1, number_of_nodes=3),
    values_at_nodes=[-2, 1, -2],  # first and last node must coincide
    extrapolate="periodic",
)
```

[23]:
```
spline.plot(xlabel="time", xlim=(0, 3));
```



[24]:
```
sbml_doc = libsbml.SBMLReader().readSBML("example_splines.xml")
sbml_model = sbml_doc.getModel()
spline.add_to_sbml_model(sbml_model)
simulate(sbml_model, T=3);
```



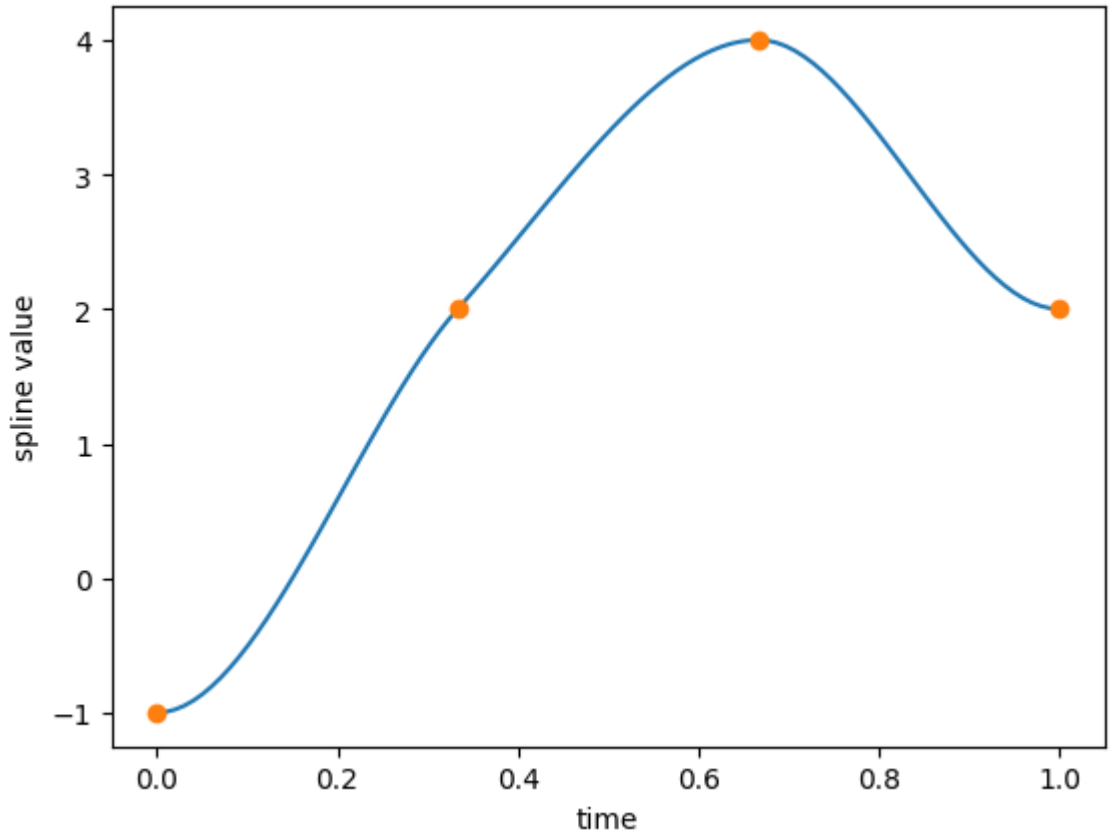
The spline annotation in this case is

```
<amici:spline xmlns:amici="https://github.com/AMICI-dev/AMICI" amici:spline_method=
↪"cubic_hermite" amici:spline_bc="periodic" amici:spline_extrapolate="periodic">
    <amici:spline_evaluation_point> ... </amici:spline_evaluation_point>
    <amici:spline_uniform_grid> ... </amici:spline_uniform_grid>
    <amici:spline_values> ... </amici:spline_values>
</amici:spline>
```

We can modify the spline's boundary conditions, for example requiring that the derivatives is zero.

[25]:
```
spline = amici.splines.CubicHermiteSpline(
    sbml_id="f",
    evaluate_at=amici.sbml_utils.amici_time_symbol,
    nodes=amici.splines.UniformGrid(0, 1, number_of_nodes=4),
    values_at_nodes=[-1, 2, 4, 2],
    bc="zeroderivative",
)
```

[26]:
```
spline.plot(xlabel="time");
```

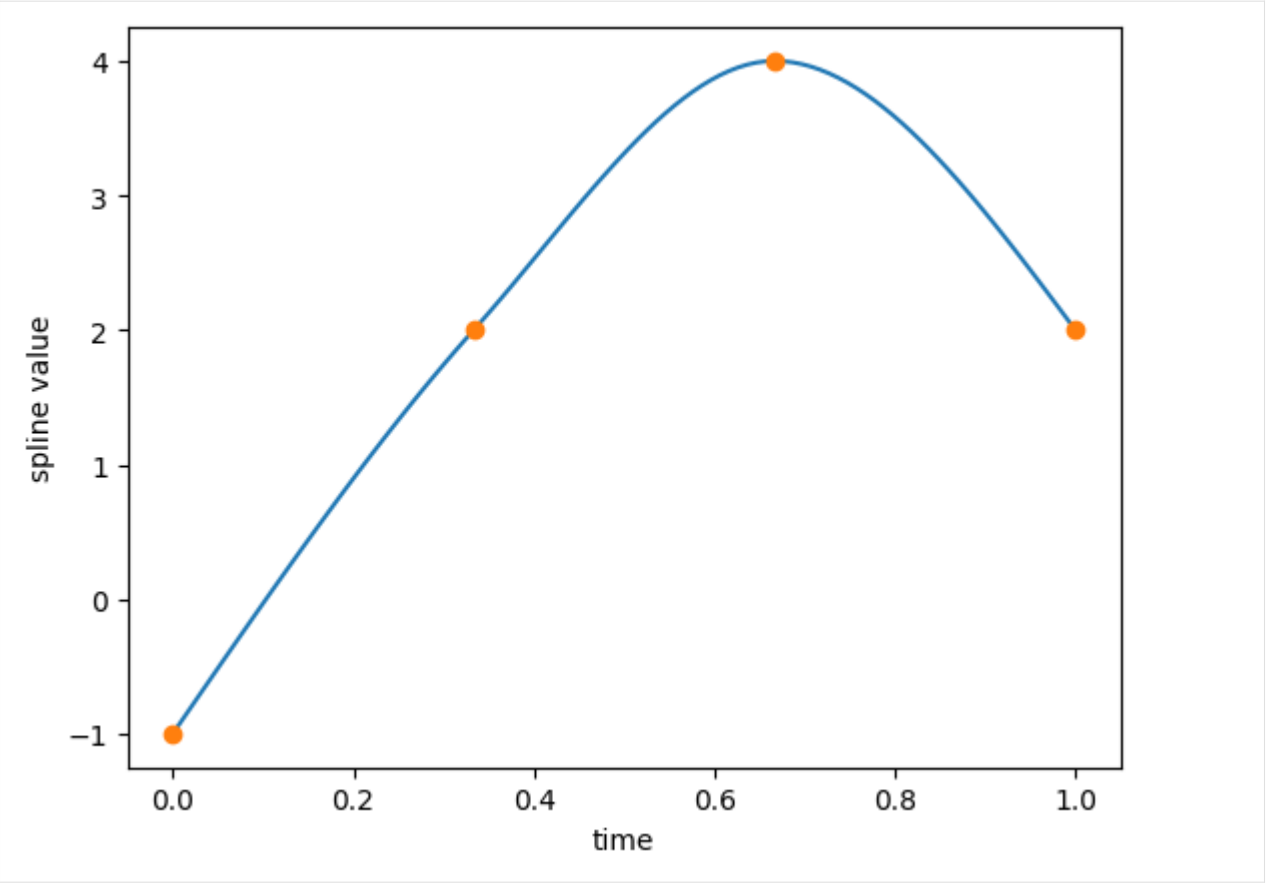



```
<amici:spline xmlns:amici="https://github.com/AMICI-dev/AMICI" amici:spline_method=
↪"cubic_hermite" amici:spline_bc="zeroderivative">
    <amici:spline_evaluation_point> ... </amici:spline_evaluation_point>
    <amici:spline_uniform_grid> ... </amici:spline_uniform_grid>
    <amici:spline_values> ... </amici:spline_values>
</amici:spline>
```

Or we can impose natural boundary conditions.

[27]:
```
spline = amici.splines.CubicHermiteSpline(
    sbml_id="f",
    evaluate_at=amici.sbml_utils.amici_time_symbol,
    nodes=amici.splines.UniformGrid(0, 1, number_of_nodes=4),
    values_at_nodes=[-1, 2, 4, 2],
    bc="natural",
)
```

[28]:
```
spline.plot(xlabel="time");
```

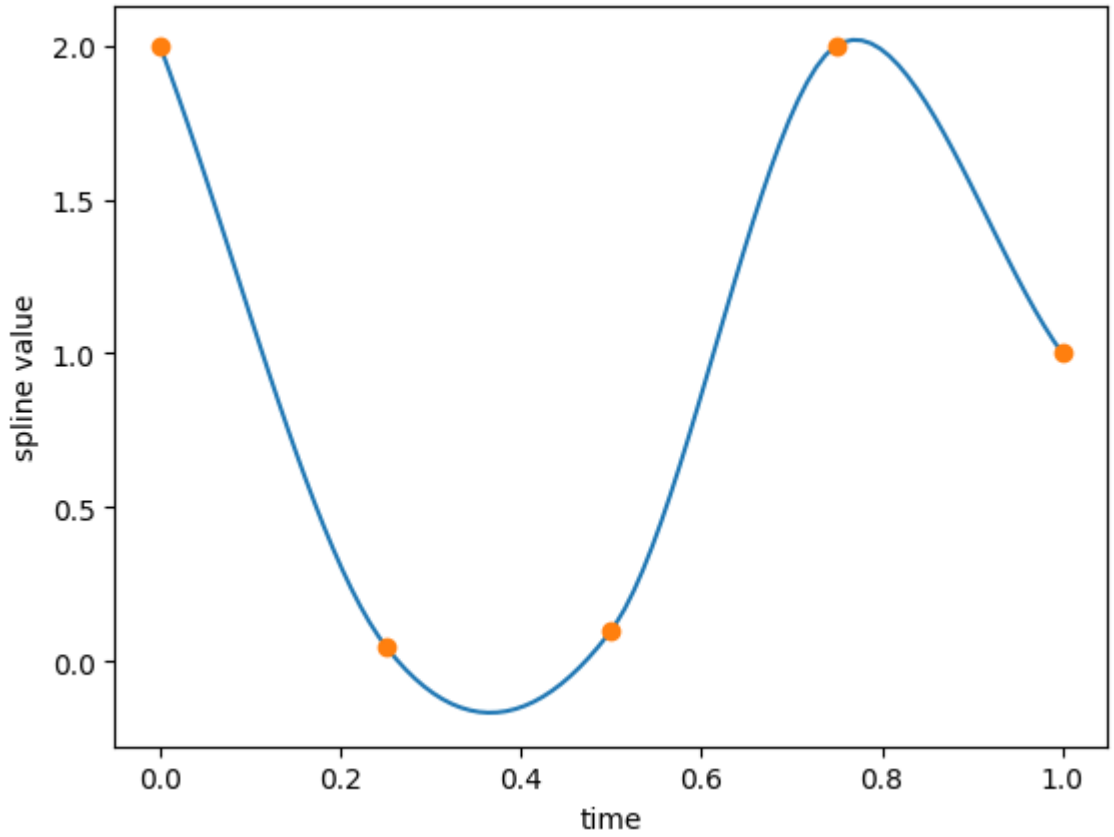



```
<amici:spline xmlns:amici="https://github.com/AMICI-dev/AMICI" amici:spline_method=
↪"cubic_hermite" amici:spline_bc="natural">
    <amici:spline_evaluation_point> ... </amici:spline_evaluation_point>
    <amici:spline_uniform_grid> ... </amici:spline_uniform_grid>
    <amici:spline_values> ... </amici:spline_values>
</amici:spline>
```

Even if all node values are positive, due to under-shooting a cubic Hermite spline can assume negative values. In certain settings (e.g., when the spline represents a chemical reaction rate) this should be avoided. A possible solution is to carry out the interpolation in log-space (the resulting function is no longer a spline, but it is still a smooth interpolant).

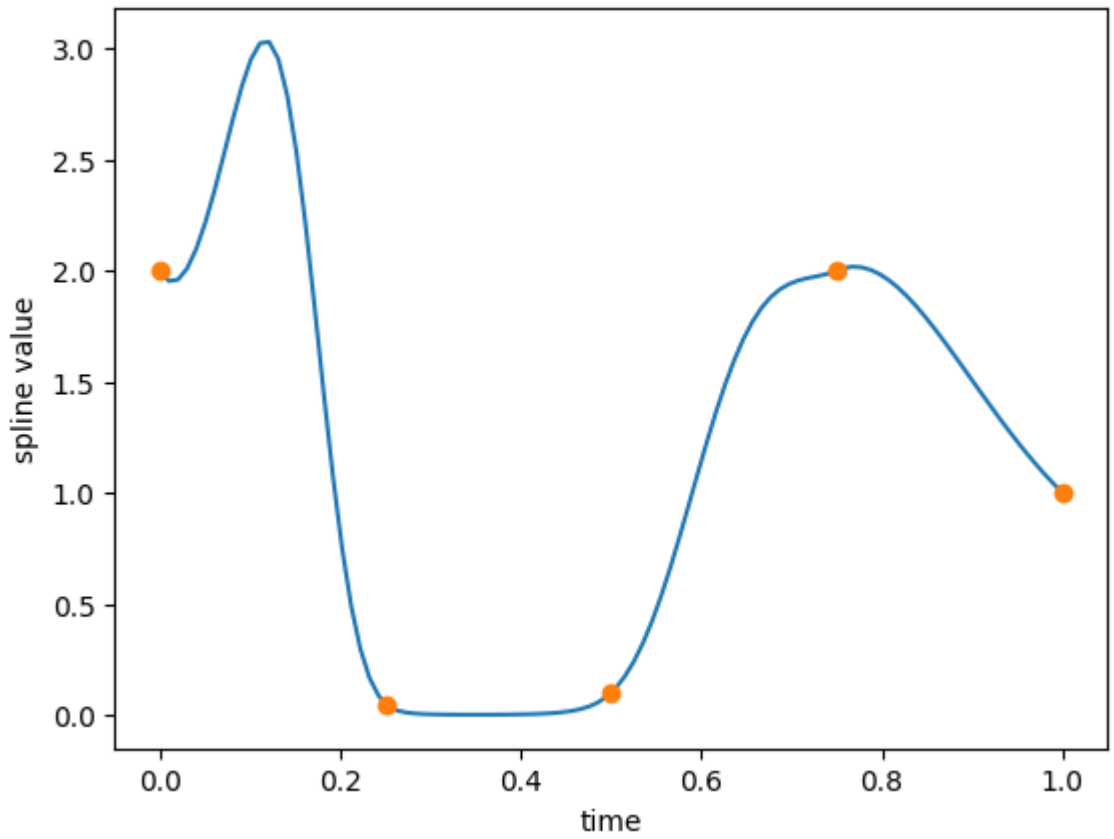
[29]:
```
spline = amici.splines.CubicHermiteSpline(
    sbml_id="f",
    evaluate_at=amici.sbml_utils.amici_time_symbol,
    nodes=amici.splines.UniformGrid(0, 1, number_of_nodes=5),
    values_at_nodes=[2, 0.05, 0.1, 2, 1],
)
```

[30]:
```
# This spline assumes negative values!
spline.plot(xlabel="time");
```



[31]:
```
spline = amici.splines.CubicHermiteSpline(
    sbml_id="f",
    evaluate_at=amici.sbml_utils.amici_time_symbol,
    nodes=amici.splines.UniformGrid(0, 1, number_of_nodes=5),
    values_at_nodes=[2, 0.05, 0.1, 2, 1],
    logarithmic_parametrization=True,
)
```

[33]:
```
# Instead of under-shooting we now have over-shooting,
# but at least the "spline" is always positive
spline.plot(xlabel="time");
```



The spline annotation in this case is

```
<amici:spline xmlns:amici="https://github.com/AMICI-dev/AMICI" amici:spline_method=
↪"cubic_hermite" amici:spline_logarithmic_parametrization="true">
    <amici:spline_evaluation_point> ... </amici:spline_evaluation_point>
    <amici:spline_uniform_grid> ... </amici:spline_uniform_grid>
    <amici:spline_values> ... </amici:spline_values>
</amici:spline>
```

Comparing model import time for the SBML-native piecewise implementation and the AMICI spline implementation

[33]:
```
import pandas as pd
import tempfile
import time
```

[34]:
```
nruns = 6  # number of replicates
num_nodes = [
    5,
    10,
    15,
    20,
    25,
```

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```
    30,
    40,
]  # benchmark model import for these node numbers
amici_only_nodes = [
    50,
    75,
    100,
    125,
    150,
    175,
    200,
    225,
    250,
]  # for these node numbers, only benchmark the annotation-based implementation
```

[35]:
```
# If running as a GitHub action, just do the minimal amount of work required to check␣
↪whether the code is working
if os.getenv("GITHUB_ACTIONS") is not None:
    nruns = 1
    num_nodes = [4]
    amici_only_nodes = [5]
```

[36]:
```
df = None
for n in num_nodes + amici_only_nodes:
    # Create model
    spline = amici.splines.CubicHermiteSpline(
        sbml_id="f",
        evaluate_at=amici.sbml_utils.amici_time_symbol,
        nodes=amici.splines.UniformGrid(0, 1, number_of_nodes=n),
        values_at_nodes=np.random.rand(n),
    )
    sbml_doc = libsbml.SBMLReader().readSBML("example_splines.xml")
    sbml_model = sbml_doc.getModel()
    spline.add_to_sbml_model(sbml_model)
    # Benchmark model creation
    timings_amici = []
    timings_piecewise = []
    for _ in range(nruns):
        with tempfile.TemporaryDirectory() as tmpdir:
            t0 = time.perf_counter_ns()
            amici.SbmlImporter(sbml_model).sbml2amici("benchmark", tmpdir)
            dt = time.perf_counter_ns() - t0
            timings_amici.append(dt / 1e9)
        if n in num_nodes:
            with tempfile.TemporaryDirectory() as tmpdir:
                t0 = time.perf_counter_ns()
                amici.SbmlImporter(
                    sbml_model, discard_annotations=True
                ).sbml2amici("benchmark", tmpdir)
                dt = time.perf_counter_ns() - t0
                timings_piecewise.append(dt / 1e9)
```

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```
    # Append benchmark data to dataframe
    df_amici = pd.DataFrame(
        dict(num_nodes=n, time=timings_amici, use_annotations=True)
    )
    df_piecewise = pd.DataFrame(
        dict(num_nodes=n, time=timings_piecewise, use_annotations=False)
    )
    if df is None:
        df = pd.concat(
            [df_amici, df_piecewise], ignore_index=True, verify_integrity=True
        )
    else:
        df = pd.concat(
            [df, df_amici, df_piecewise],
            ignore_index=True,
            verify_integrity=True,
        )
```

[88]:
```
kwargs = dict(markersize=7.5)
df_avg = df.groupby(["use_annotations", "num_nodes"]).mean().reset_index()
fig, ax = plt.subplots(1, 1, figsize=(6.5, 3.5))
ax.plot(
    df_avg[np.logical_not(df_avg["use_annotations"])]["num_nodes"],
    df_avg[np.logical_not(df_avg["use_annotations"])]["time"],
    ".",
    label="MathML piecewise",
    **kwargs,
)
ax.plot(
    df_avg[df_avg["use_annotations"]]["num_nodes"],
    df_avg[df_avg["use_annotations"]]["time"],
    ".",
    label="AMICI annotations",
    **kwargs,
)
ax.set_ylabel("model import time (s)")
ax.set_xlabel("number of spline nodes")
ax.set_yscale("log")
ax.yaxis.set_major_formatter(
    mpl.ticker.FuncFormatter(lambda x, pos: f"{x:.0f}")
)
ax.xaxis.set_ticks(
    [
        10,
        20,
        30,
        40,
        60,
        70,
        80,
        90,
        110,
```

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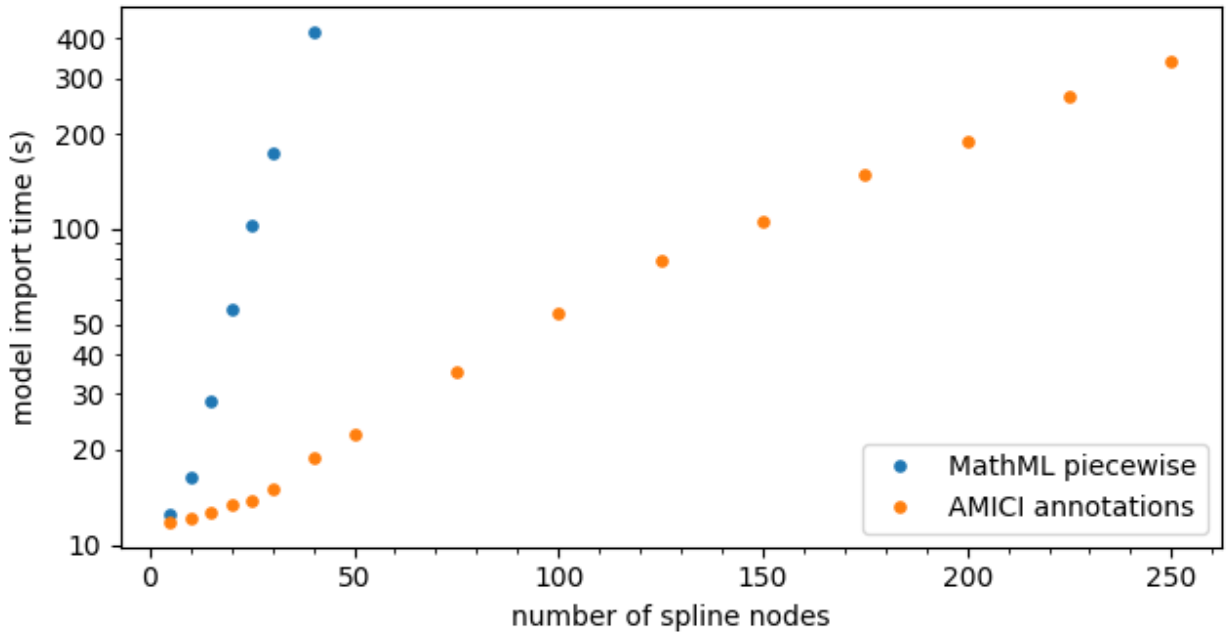
```
        120,
        130,
        140,
        160,
        170,
        180,
        190,
        210,
        220,
        230,
        240,
        260,
    ],
    minor=True,
)
ax.yaxis.set_ticks(
    [20, 30, 40, 50, 60, 70, 80, 90, 200, 300, 400],
    ["20", "30", "40", "50", None, None, None, None, "200", "300", "400"],
    minor=True,
)
ax.legend()
ax.figure.tight_layout()
# ax.figure.savefig('benchmark_import.pdf')
```



10.2.10 Spline implementation of JAK2-STAT5 signaling pathway

In this notebook a practical example of the usage of AMICI spline functionalities is shown. The model under consideration is the JAK2-STAT5 signaling pathway (Swameye et al., 2003), in which the dynamics of the system depend on a measured input function (the quantity `pEpoR` in the model).

Following the approach of (Schelker et al., 2012), a continuous approximation of this input function is estimated together with the other parameters. As in the original paper, we will use a spline with logarithmic parameterization in order to enforce the positivity constraint.

The model of the signaling pathway will be implemented in SBML using AMICI's spline annotations, experimental data integrated using the PEtab format and parameter estimation will be carried out using the pyPESTO library.

[ ]:
```
%pip install pypesto
```

[ ]:
```
%pip install fides
```

[1]:
```
import copy
import logging
import os

import libsbml
import numpy as np
import pandas as pd
import petab
import pypesto.petab
import sympy as sp
from matplotlib import pyplot as plt

import amici
```

[2]:
```
# Number of multi-starts for MAP estimation
n_starts = 150
# n_starts = 0 # when loading results
```

[ ]:
```
# Set default pypesto engine/optimizer
pypesto_optimizer = pypesto.optimize.FidesOptimizer(verbose=logging.WARNING)
pypesto_engine = pypesto.engine.MultiProcessEngine()
```

[4]:
```
# If running as a GitHub action, just do the minimal amount of work required to check␣
↪whether the code is working
if os.getenv("GITHUB_ACTIONS") is not None:
    n_starts = 25
    pypesto_optimizer = pypesto.optimize.FidesOptimizer(
        verbose=logging.WARNING, options=dict(maxiter=10)
    )
    pypesto_engine = pypesto.engine.MultiProcessEngine()
```

[5]:
```
# A dictionary to store different approaches for a final comparison
all_results = {}
```

Spline approximation with few nodes, using finite differences for the derivatives

As a first attempt, we fix a small amount of nodes, create new parameters for the values of the splines at the nodes and let AMICI compute the derivative at the nodes by using finite differences.

Creating the PEtab model

[6]:
```
# Problem name
name = "Swameye_PNAS2003_5nodes_FD"
```

First, we create a spline to represent the input function pEpoR, parametrized by its values at the nodes. Since the value of the input function reaches its steady state by the end of the experiment, we extrapolate constantly after that (useful if we need to simulate the model after the last spline node).

[7]:
```
# Create spline for pEpoR
nodes = [0, 5, 10, 20, 60]
values_at_nodes = [
    sp.Symbol(f"pEpoR_t{str(t).replace('.', '_dot_')}") for t in nodes
]  # new parameter symbols for spline values
spline = amici.splines.CubicHermiteSpline(
    sbml_id="pEpoR",  # matches name of species in SBML model
    evaluate_at=amici.sbml_utils.amici_time_symbol,  # the spline is evaluated at the␣
↪current time
    nodes=nodes,
    values_at_nodes=values_at_nodes,  # values at the nodes (in linear scale)
    extrapolate=(None, "constant"),  # because steady state is reached
    bc="auto",  # automatically determined from extrapolate (bc at right end will be
↪'zero_derivative')
    logarithmic_parametrization=True,
)
```

We can then add the spline to a skeleton SBML model based on the d2d implementation by (Schelker et al., 2012). The skeleton SBML model defines a species pEpoR which interacts with the other species, but has no reactions or rate rules of its own. The code below creates an assignment rule for pEpoR using the spline formula, completing the model. The parameters pEpoR_t* are automatically added to the SBML model too (using nominal values of 0.1 and declaring them to be constant).

[8]:
```
# Add spline formula to SBML model
sbml_doc = libsbml.SBMLReader().readSBML(
    os.path.join("Swameye_PNAS2003", "swameye2003_model.xml")
)
sbml_model = sbml_doc.getModel()
spline.add_to_sbml_model(
    sbml_model, auto_add=True, y_nominal=0.1, y_constant=True
)
```

A skeleton PEtab problem is provided, containing parameter bounds, observable definitions and experimental data. Of particular relevance is the noise model used for the measurements of pEpoR, normal additive noise with standard deviation equal to 0.0274 + 0.1 * pEpoR; this is the same choice used in (Schelker et al., 2012), where it was estimated from experimental replicates.

However, the parameters associated to the spline are to be added too. The code below defines parameter bounds for them according to the PEtab format and then creates a full PEtab problem integrating them together with the edited

SBML file. The condition, measurement and observable PEtab tables do not require additional modification and can be used as they are.

[9]:
```
# Extra parameters associated to the spline
spline_parameters_df = pd.DataFrame(
    dict(
        parameterScale="log",
        lowerBound=0.001,
        upperBound=10,
        nominalValue=0.1,
        estimate=1,
    ),
    index=pd.Series(list(map(str, values_at_nodes)), name="parameterId"),
)
```

[10]:
```
# Create PEtab problem
petab_problem = petab.Problem(
    sbml_model,
    condition_df=petab.conditions.get_condition_df(
        os.path.join("Swameye_PNAS2003", "swameye2003_conditions.tsv")
    ),
    measurement_df=petab.measurements.get_measurement_df(
        os.path.join("Swameye_PNAS2003", "swameye2003_measurements.tsv")
    ),
    parameter_df=petab.core.concat_tables(
        [
            os.path.join("Swameye_PNAS2003", "swameye2003_parameters.tsv"),
            spline_parameters_df,
        ],
        petab.parameters.get_parameter_df,
    ),
    observable_df=petab.observables.get_observable_df(
        os.path.join("Swameye_PNAS2003", "swameye2003_observables.tsv")
    ),
)
```

The resulting PEtab problem can be checked for errors and exported to disk if needed.

[11]:
```
# Check whether PEtab model is valid
assert not petab.lint_problem(petab_problem)
```

[12]:
```
# Save PEtab problem to disk
# import shutil
# shutil.rmtree(name, ignore_errors=True)
# os.mkdir(name)
# petab_problem.to_files_generic(prefix_path=name)
```

Creating the pyPESTO problem

We can now create a pyPESTO problem directly from the PEtab problem. Due to technical limitations in AMICI, currently the PEtab problem has to be "flattened" before it can be simulated from, but such operation is merely syntactical and thus does not change the essence of the model.

[13]:
```
# Problem must be "flattened" to be used with AMICI
petab.core.flatten_timepoint_specific_output_overrides(petab_problem)
```

[14]:
```
# Check whether simulation from the PEtab problem works
# import amici.petab_simulate
# simulator = amici.petab_simulate.PetabSimulator(petab_problem)
# simulator.simulate(noise=False)
```

[15]:
```
# Import PEtab problem into pyPESTO
pypesto_problem = pypesto.petab.PetabImporter(
    petab_problem, model_name=name
).create_problem()

# Increase maximum number of steps for AMICI
pypesto_problem.objective.amici_solver.setMaxSteps(10**5)
```

Maximum Likelihood estimation

Using pyPESTO we can optimize for the parameter vector that maximizes the probability of observing the experimental data (maximum likelihood estimation).

A multistart method with local gradient-based optimization is used and the results of each multistart can be visualized in a waterfall plot.

[16]:
```
# Load existing results if available
if os.path.exists(f"{name}.h5"):
    pypesto_result = pypesto.store.read_result(
        f"{name}.h5", problem=pypesto_problem
    )
else:
    pypesto_result = None
# Overwrite
# pypesto_result = None
```

[ ]:
```
# Parallel multistart optimization with pyPESTO and FIDES
if n_starts > 0:
    if pypesto_result is None:
        new_ids = [str(i) for i in range(n_starts)]
    else:
        last_id = max(int(i) for i in pypesto_result.optimize_result.id)
        new_ids = [str(i) for i in range(last_id + 1, last_id + n_starts + 1)]
    pypesto_result = pypesto.optimize.minimize(
        pypesto_problem,
        n_starts=n_starts,
        ids=new_ids,
```

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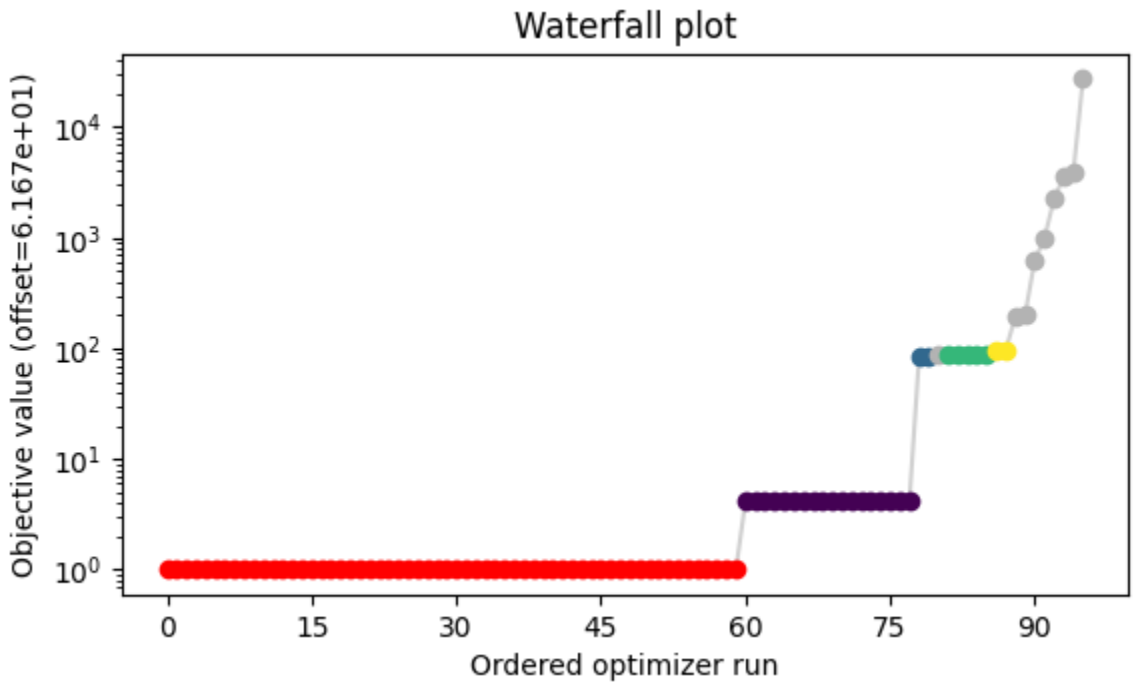
```
        optimizer=pypesto_optimizer,
        engine=pypesto_engine,
        result=pypesto_result,
    )
    pypesto_result.optimize_result.sort()
    if pypesto_result.optimize_result.x[0] is None:
        raise Exception(
            "All multistarts failed (n_starts is probably too small)! If this error␣
↪occurred during CI, just run the workflow again."
        )
```

[18]:
```
# Save results to disk
# pypesto.store.write_result(pypesto_result, f'{name}.h5', overwrite=True)
```

[19]:
```
# Print result table
# pypesto_result.optimize_result.as_dataframe()
```

[20]:
```
# Visualize the results of the multistarts
pypesto.visualize.waterfall(pypesto_result, size=[6.5, 3.5]);
```



Below the maximum likelihood estimates for pEpoR and the other observables are plotted, together with the experimental measurements.

To assess whether the noise model used in the observable is reasonable, we have also plotted 2-sigma error bands for pEpoR.

[21]:
```
# Functions for simulating observables given a parameter vector
def _simulate(x=None, *, problem=None, result=None, N=500, **kwargs):
    if result is None:
```

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```
        result = pypesto_result
    if problem is None:
        problem = pypesto_problem
    if x is None:
        x = result.optimize_result.x[0]
    if N is None:
        objective = problem.objective
    else:
        objective = problem.objective.set_custom_timepoints(
            timepoints_global=np.linspace(0, 60, N)
        )
    if len(x) != len(problem.x_free_indices):
        x = x[problem.x_free_indices]
    simresult = objective(x, return_dict=True, **kwargs)
    return problem, simresult["rdatas"][0]


def simulate_pEpoR(x=None, **kwargs):
    problem, rdata = _simulate(x, **kwargs)
    assert problem.objective.amici_model.getObservableIds()[0].startswith(
        "pEpoR"
    )
    return rdata["t"], rdata["y"][:, 0]


def simulate_pSTAT5(x=None, **kwargs):
    problem, rdata = _simulate(x, **kwargs)
    assert problem.objective.amici_model.getObservableIds()[1].startswith(
        "pSTAT5"
    )
    return rdata["t"], rdata["y"][:, 1]


def simulate_tSTAT5(x=None, **kwargs):
    problem, rdata = _simulate(x, **kwargs)
    assert problem.objective.amici_model.getObservableIds()[-1].startswith(
        "tSTAT5"
    )
    return rdata["t"], rdata["y"][:, -1]


# Experimental data
df_measurements = petab.measurements.get_measurement_df(
    os.path.join("Swameye_PNAS2003", "swameye2003_measurements.tsv")
)
df_pEpoR = df_measurements[
    df_measurements["observableId"].str.startswith("pEpoR")
]
df_pSTAT5 = df_measurements[
    df_measurements["observableId"].str.startswith("pSTAT5")
]
df_tSTAT5 = df_measurements[
```

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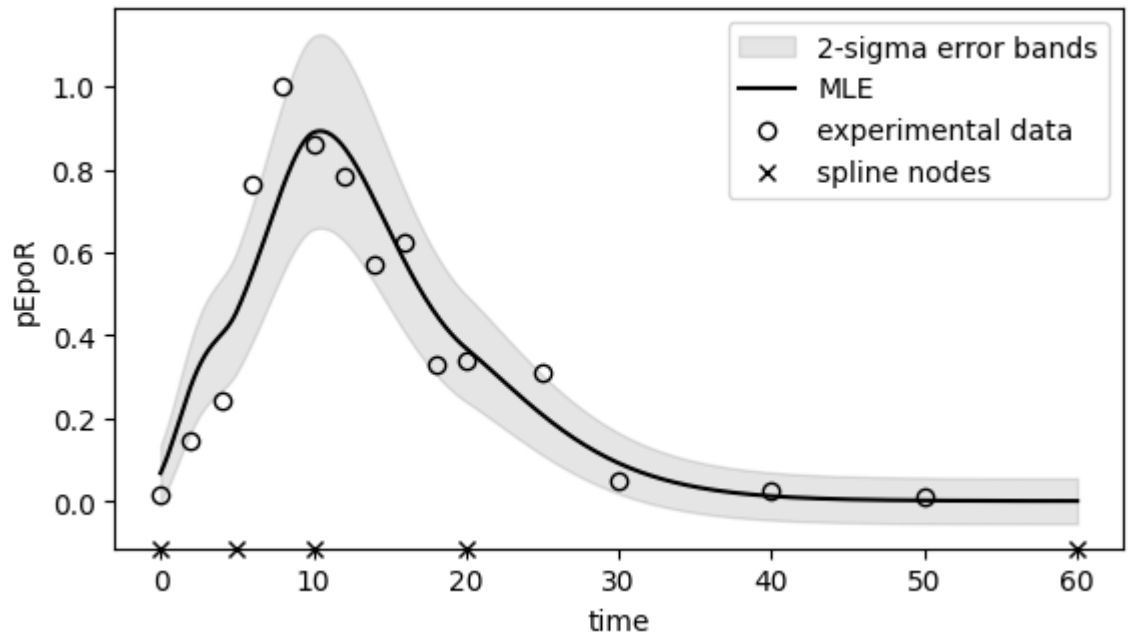
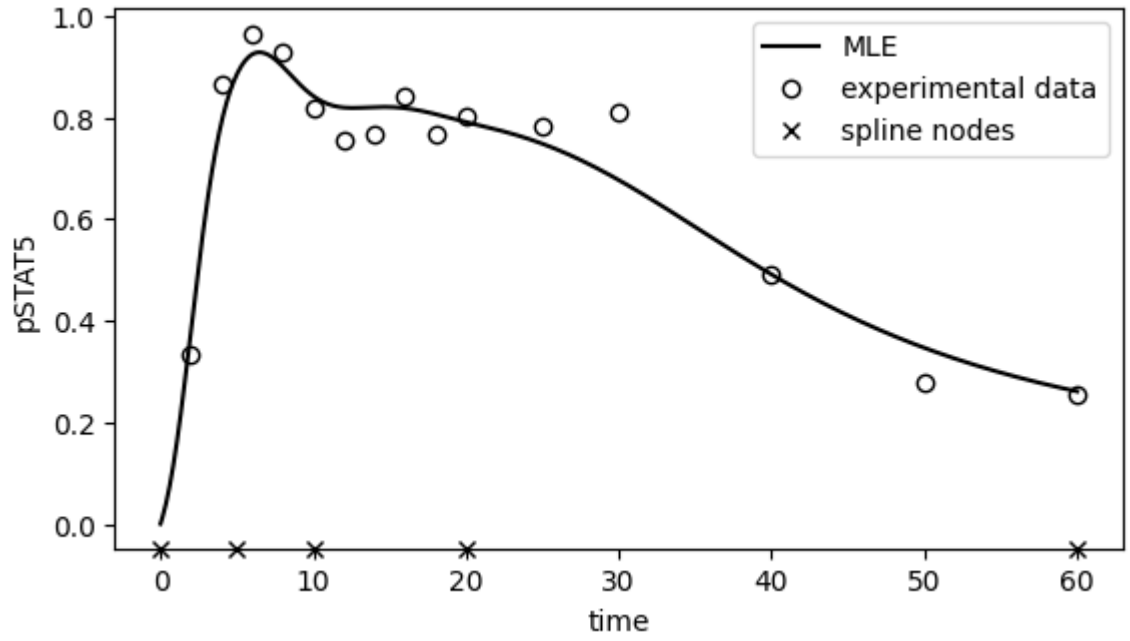
```
    df_measurements["observableId"].str.startswith("tSTAT5")
]
```

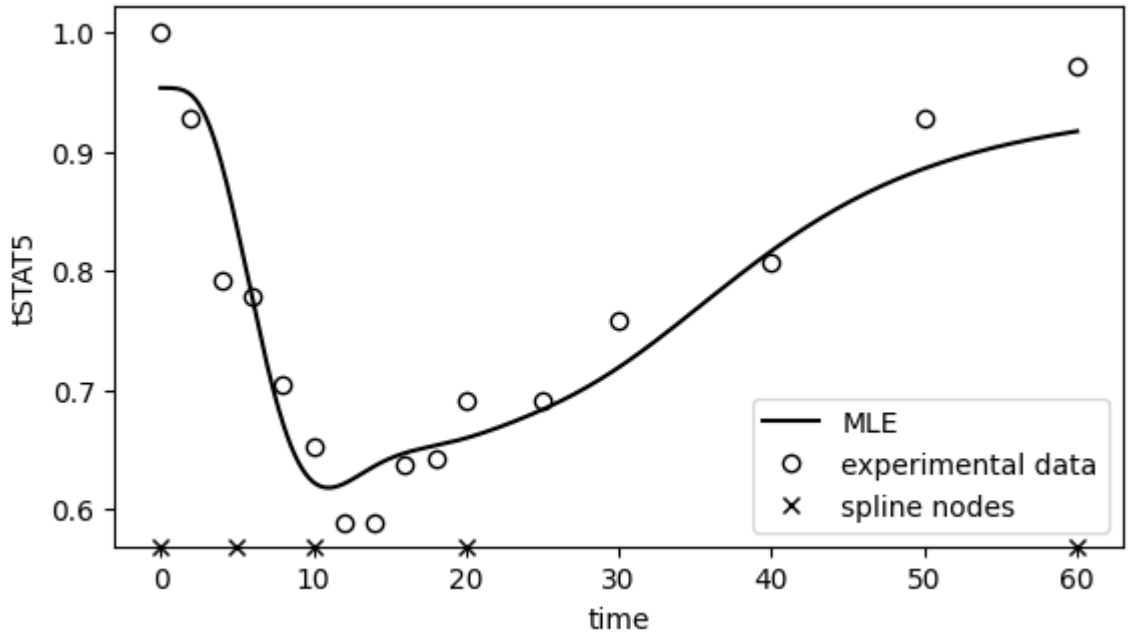
[22]:
```
# Plot ML fit for pEpoR
fig, ax = plt.subplots(figsize=(6.5, 3.5))
t, pEpoR = simulate_pEpoR()
sigma_pEpoR = 0.0274 + 0.1 * pEpoR
ax.fill_between(
    t,
    pEpoR - 2 * sigma_pEpoR,
    pEpoR + 2 * sigma_pEpoR,
    color="black",
    alpha=0.10,
    interpolate=True,
    label="2-sigma error bands",
)
ax.plot(t, pEpoR, color="black", label="MLE")
ax.plot(
    df_pEpoR["time"],
    df_pEpoR["measurement"],
    "o",
    color="black",
    markerfacecolor="none",
    label="experimental data",
)
ylim1 = ax.get_ylim()[0]
ax.plot(
    nodes,
    len(nodes) * [ylim1],
    "x",
    color="black",
    label="spline nodes",
    zorder=10,
    clip_on=False,
)
ax.set_ylim(ylim1, ax.get_ylim()[1])
ax.set_xlabel("time")
ax.set_ylabel("pEpoR")
ax.legend();
```



[23]:
```
# Plot ML fit for pSTAT5
fig, ax = plt.subplots(figsize=(6.5, 3.5))
t, pSTAT5 = simulate_pSTAT5()
ax.plot(t, pSTAT5, color="black", label="MLE")
ax.plot(
    df_pSTAT5["time"],
    df_pSTAT5["measurement"],
    "o",
    color="black",
    markerfacecolor="none",
    label="experimental data",
)
ylim1 = ax.get_ylim()[0]
ax.plot(
    nodes,
    len(nodes) * [ylim1],
    "x",
    color="black",
    label="spline nodes",
    zorder=10,
    clip_on=False,
)
ax.set_ylim(ylim1, ax.get_ylim()[1])
ax.set_xlabel("time")
ax.set_ylabel("pSTAT5")
ax.legend();
```



[24]:
```
# Plot ML fit for tSTAT5
fig, ax = plt.subplots(figsize=(6.5, 3.5))
t, tSTAT5 = simulate_tSTAT5()
ax.plot(t, tSTAT5, color="black", label="MLE")
ax.plot(
    df_tSTAT5["time"],
    df_tSTAT5["measurement"],
    "o",
    color="black",
    markerfacecolor="none",
    label="experimental data",
)
ylim1 = ax.get_ylim()[0]
ax.plot(
    nodes,
    len(nodes) * [ylim1],
    "x",
    color="black",
    label="spline nodes",
    zorder=10,
    clip_on=False,
)
ax.set_ylim(ylim1, ax.get_ylim()[1])
ax.set_xlabel("time")
ax.set_ylabel("tSTAT5")
ax.legend();
```



[25]:
```
# Store results for later
all_results["5 nodes, FD"] = (pypesto_problem, pypesto_result)
```

Spline approximation with many nodes, using finite differences for the derivatives

Five nodes is arguably not enough to represent all plausible input choices. Increasing the number of nodes would give the spline more freedom and it can be done with minimal changes to the example above. However, more degrees of freedom mean more chance of overfitting. Thus, following (Schelker et al., 2012), we will add a regularization term consisting in the squared L2 norm of the spline's curvature, which promotes smoother and less oscillating functions. The value for the regularization strength λ is chosen by comparing the sum of squared normalized residuals with its expected value, which can be computing by assuming it is roughly χ^2-distributed.

Creating the PEtab model

[26]:
```
# Problem name
name = "Swameye_PNAS2003_15nodes_FD"
```

[27]:
```
# Create spline for pEpoR
nodes = [0, 2.5, 5.0, 7.5, 10.0, 12.5, 15.0, 17.5, 20, 25, 30, 35, 40, 50, 60]
values_at_nodes = [
    sp.Symbol(f"pEpoR_t{str(t).replace('.', '_dot_')}") for t in nodes
]
spline = amici.splines.CubicHermiteSpline(
    sbml_id="pEpoR",
    evaluate_at=amici.sbml_utils.amici_time_symbol,
    nodes=nodes,
    values_at_nodes=values_at_nodes,
    extrapolate=(None, "constant"),
```

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```
    bc="auto",
    logarithmic_parametrization=True,
)
```

The regularization term can be easily computed by symbolic manipulation of the spline expression using AMICI and SymPy. Since it is very commonly used, we already provide a function for it in AMICI. Note: we regularize the curvature of the spline, which for positivity-enforcing spline is the logarithm of the function.

In order add the regularization term to the PEtab likelihood, a dummy observable has to be created.

[28]:
```
# Compute L2 norm of the curvature of pEpoR
regularization = spline.squared_L2_norm_of_curvature()
```

[29]:
```
# Add a parameter for regularization strength
reg_parameters_df = pd.DataFrame(
    dict(
        parameterScale="log10",
        lowerBound=1e-6,
        upperBound=1e6,
        nominalValue=1.0,
        estimate=0,
    ),
    index=pd.Series(["regularization_strength"], name="parameterId"),
)
# Encode regularization term as an additional observable
reg_observables_df = pd.DataFrame(
    dict(
        observableFormula=f"sqrt({regularization})".replace("**", "^"),
        observableTransformation="lin",
        noiseFormula="1/sqrt(regularization_strength)",
        noiseDistribution="normal",
    ),
    index=pd.Series(["regularization"], name="observableId"),
)
# and correspoding measurement
reg_measurements_df = pd.DataFrame(
    dict(
        observableId="regularization",
        simulationConditionId="condition1",
        measurement=0,
        time=0,
        observableTransformation="lin",
    ),
    index=pd.Series([0]),
)
```

[30]:
```
# Add spline formula to SBML model
sbml_doc = libsbml.SBMLReader().readSBML(
    os.path.join("Swameye_PNAS2003", "swameye2003_model.xml")
)
sbml_model = sbml_doc.getModel()
spline.add_to_sbml_model(
```

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```
    sbml_model, auto_add=True, y_nominal=0.1, y_constant=True
)
```

[31]:
```
# Extra parameters associated to the spline
spline_parameters_df = pd.DataFrame(
    dict(
        parameterScale="log",
        lowerBound=0.001,
        upperBound=10,
        nominalValue=0.1,
        estimate=1,
    ),
    index=pd.Series(list(map(str, values_at_nodes)), name="parameterId"),
)
```

[32]:
```
# Create PEtab problem
petab_problem = petab.Problem(
    sbml_model,
    condition_df=petab.conditions.get_condition_df(
        os.path.join("Swameye_PNAS2003", "swameye2003_conditions.tsv")
    ),
    measurement_df=petab.core.concat_tables(
        [
            os.path.join("Swameye_PNAS2003", "swameye2003_measurements.tsv"),
            reg_measurements_df,
        ],
        petab.measurements.get_measurement_df,
    ).reset_index(drop=True),
    parameter_df=petab.core.concat_tables(
        [
            os.path.join("Swameye_PNAS2003", "swameye2003_parameters.tsv"),
            spline_parameters_df,
            reg_parameters_df,
        ],
        petab.parameters.get_parameter_df,
    ),
    observable_df=petab.core.concat_tables(
        [
            os.path.join("Swameye_PNAS2003", "swameye2003_observables.tsv"),
            reg_observables_df,
        ],
        petab.observables.get_observable_df,
    ),
)
```

[33]:
```
# Check whether PEtab model is valid
assert not petab.lint_problem(petab_problem)
```

[34]:
```
# Save PEtab problem to disk
# import shutil
# shutil.rmtree(name, ignore_errors=True)
```

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```
# os.mkdir(name)
# petab_problem.to_files_generic(prefix_path=name)
```

Creating the pyPESTO problem

[35]:
```
# Problem must be "flattened" to be used with AMICI
petab.core.flatten_timepoint_specific_output_overrides(petab_problem)
```

[36]:
```
# Check whether simulation from the PEtab problem works
# import amici.petab_simulate
# simulator = amici.petab_simulate.PetabSimulator(petab_problem)
# simulator.simulate(noise=False)
```

[37]:
```
# Import PEtab problem into pyPESTO
pypesto_problem = pypesto.petab.PetabImporter(
    petab_problem, model_name=name
).create_problem()
```

Maximum Likelihood estimation

We will optimize the problem for different values of the regularization strength λ, then compute the sum of squared normalized residuals for each of the resulting parameter vectors. The one for which such a value is nearest to its expected value of 15 (the number of observations from the input function) will be chosen as the final estimate.

[ ]:
```
# Try different regularization strengths
regstrengths = np.asarray([1, 10, 40, 75, 150, 500])
if os.getenv("GITHUB_ACTIONS") is not None:
    regstrengths = np.asarray([75])
regproblems = {}
regresults = {}

for regstrength in regstrengths:
    # Fix parameter in pypesto problem
    name = f"Swameye_PNAS2003_15nodes_FD_reg{regstrength}"
    pypesto_problem.fix_parameters(
        pypesto_problem.x_names.index("regularization_strength"),
        np.log10(
            regstrength
        ),  # parameter is specified as log10 scale in PEtab
    )
    regproblem = copy.deepcopy(pypesto_problem)

    # Load existing results if available
    if os.path.exists(f"{name}.h5"):
        regresult = pypesto.store.read_result(f"{name}.h5", problem=regproblem)
    else:
        regresult = None
    # Overwrite
```

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```
    # regresult = None

    # Parallel multistart optimization with pyPESTO and FIDES
    if n_starts > 0:
        if regresult is None:
            new_ids = [str(i) for i in range(n_starts)]
        else:
            last_id = max(int(i) for i in regresult.optimize_result.id)
            new_ids = [
                str(i) for i in range(last_id + 1, last_id + n_starts + 1)
            ]
        regresult = pypesto.optimize.minimize(
            regproblem,
            n_starts=n_starts,
            ids=new_ids,
            optimizer=pypesto_optimizer,
            engine=pypesto_engine,
            result=regresult,
        )
        regresult.optimize_result.sort()
        if regresult.optimize_result.x[0] is None:
            raise Exception(
                "All multistarts failed (n_starts is probably too small)! If this error␣
↪occurred during CI, just run the workflow again."
            )

    # Save results to disk
    # pypesto.store.write_result(regresult, f'{name}.h5', overwrite=True)

    # Store result
    regproblems[regstrength] = regproblem
    regresults[regstrength] = regresult
```

[39]:
```
# Compute sum of squared normalized residuals
print(f"Target value is {len(df_pEpoR['time'])}")
regstrengths = sorted(regproblems.keys())
stats = []
for regstrength in regstrengths:
    t, pEpoR = simulate_pEpoR(
        N=None,
        problem=regproblems[regstrength],
        result=regresults[regstrength],
    )
    assert np.array_equal(df_pEpoR["time"], t[:-1])
    pEpoR = pEpoR[:-1]
    sigma_pEpoR = 0.0274 + 0.1 * pEpoR
    stat = np.sum(((pEpoR - df_pEpoR["measurement"]) / sigma_pEpoR) ** 2)
    print(f"Regularization strength: {regstrength}. Statistic is {stat}")
    stats.append(stat)
# Select best regularization strength
chosen_regstrength = regstrengths[
    np.abs(np.asarray(stats) - len(df_pEpoR["time"])).argmin()
```

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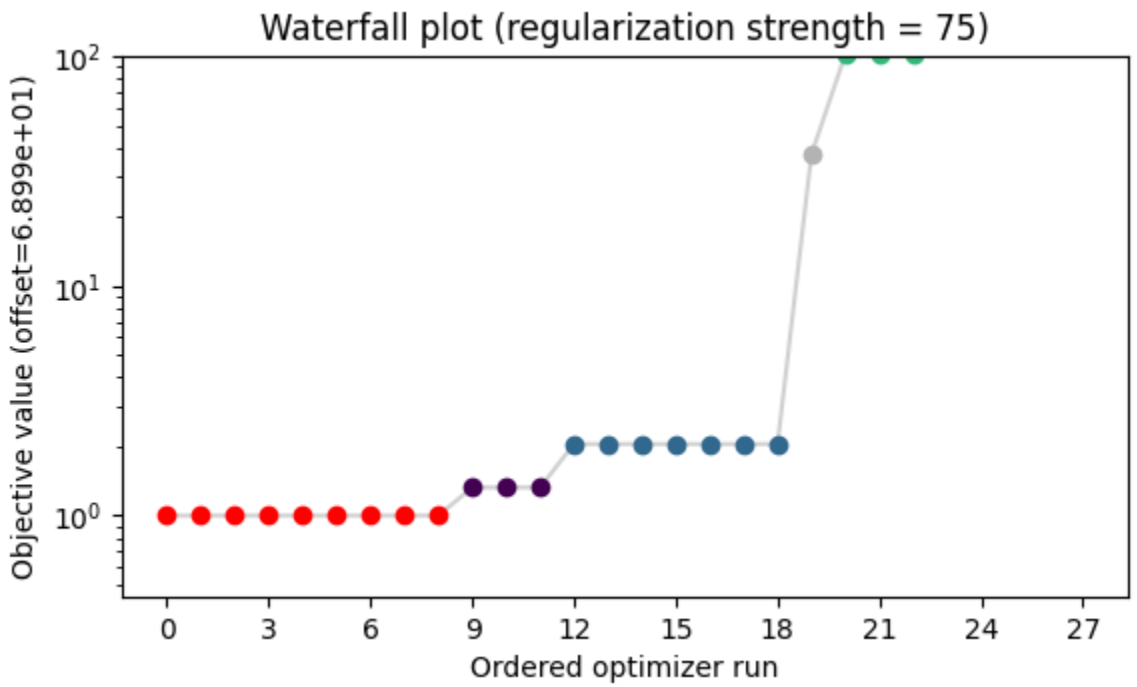
```
]
```

```
Target value is 15
Regularization strength: 1. Statistic is 6.794369874307712
Regularization strength: 10. Statistic is 8.435094498146606
Regularization strength: 40. Statistic is 11.83872830962955
Regularization strength: 75. Statistic is 15.030926511510327
Regularization strength: 150. Statistic is 19.971139477161476
Regularization strength: 500. Statistic is 32.44623424533765
```

[40]:
```
# Visualize the results of the multistarts for a chosen regularization strength
ax = pypesto.visualize.waterfall(
    regresults[chosen_regstrength], size=[6.5, 3.5]
)
ax.set_title(
    f"Waterfall plot (regularization strength = {chosen_regstrength})"
)
ax.set_ylim(ax.get_ylim()[0], 100);
```



[46]:
```
# Plot ML fit for pEpoR (all regularization strengths)
fig, ax = plt.subplots(figsize=(6.5, 3.5))
for regstrength in sorted(regproblems.keys()):
    t, pEpoR = simulate_pEpoR(
        problem=regproblems[regstrength], result=regresults[regstrength]
    )
    if regstrength == chosen_regstrength:
        kwargs = dict(
            color="black",
            label=f"$\\mathbf{{\\lambda = {regstrength}}}$",
```

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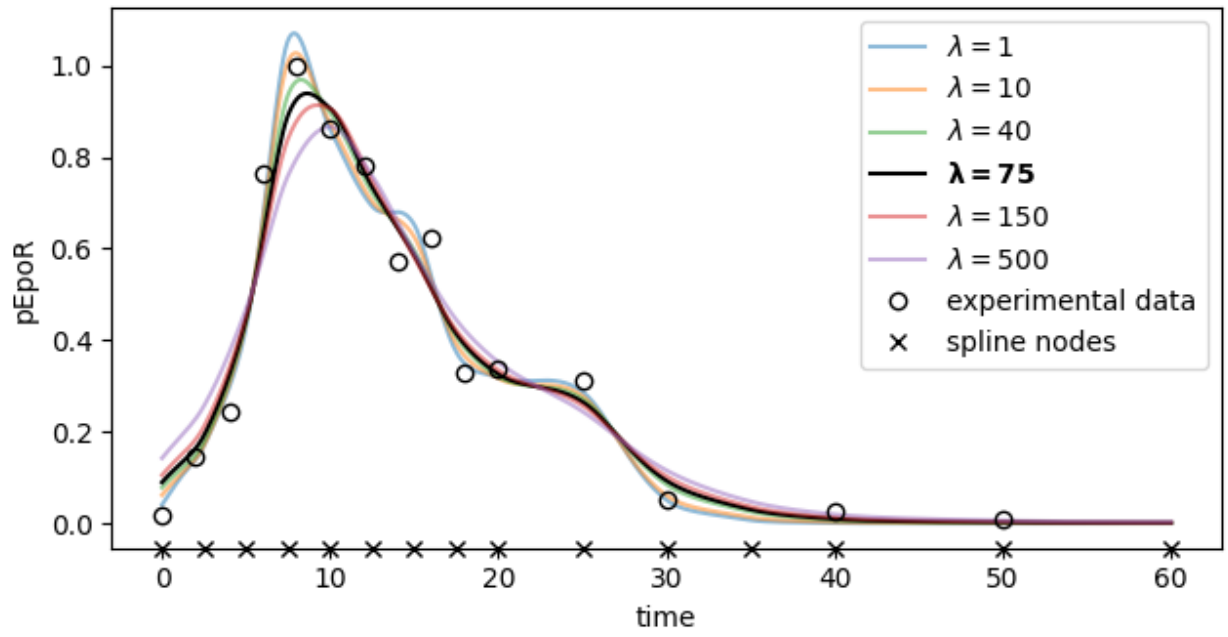
```
            zorder=2,
        )
    else:
        kwargs = dict(label=f"$\\lambda = {regstrength}$", alpha=0.5)
    ax.plot(t, pEpoR, **kwargs)
ax.plot(
    df_pEpoR["time"],
    df_pEpoR["measurement"],
    "o",
    color="black",
    markerfacecolor="none",
    label="experimental data",
)
ylim1 = ax.get_ylim()[0]
ax.plot(
    nodes,
    len(nodes) * [ylim1],
    "x",
    color="black",
    label="spline nodes",
    zorder=10,
    clip_on=False,
)
ax.set_ylim(ylim1, ax.get_ylim()[1])
ax.set_xlabel("time")
ax.set_ylabel("pEpoR")
ax.set_xlim(-3.0, 63.0)
ax.set_ylim(-0.0529905202238870 4, 1.126290214024833)
ax.legend()
ax.figure.tight_layout()
# ax.set_ylabel("input function")
# print(f"xlim = {ax.get_xlim()}, ylim = {ax.get_ylim()}")
# ax.figure.savefig('fit_15nodes_lambdas.pdf')
```



[47]:
```
# Plot ML fit for pSTAT5 (all regularization strengths)
fig, ax = plt.subplots(figsize=(6.5, 3.5))
for regstrength in sorted(regproblems.keys()):
    t, pSTAT5 = simulate_pSTAT5(
        problem=regproblems[regstrength], result=regresults[regstrength]
    )
    if regstrength == chosen_regstrength:
        kwargs = dict(
            color="black",
            label=f"$\\mathbf{{\\lambda = {regstrength}}}$",
            zorder=2,
        )
    else:
        kwargs = dict(label=f"$\\lambda = {regstrength}$", alpha=0.5)
    ax.plot(t, pSTAT5, **kwargs)
ax.plot(
    df_pSTAT5["time"],
    df_pSTAT5["measurement"],
    "o",
    color="black",
    markerfacecolor="none",
    label="experimental data",
)
ylim1 = ax.get_ylim()[0]
ax.plot(
    nodes,
    len(nodes) * [ylim1],
    "x",
    color="black",
    label="spline nodes",
```

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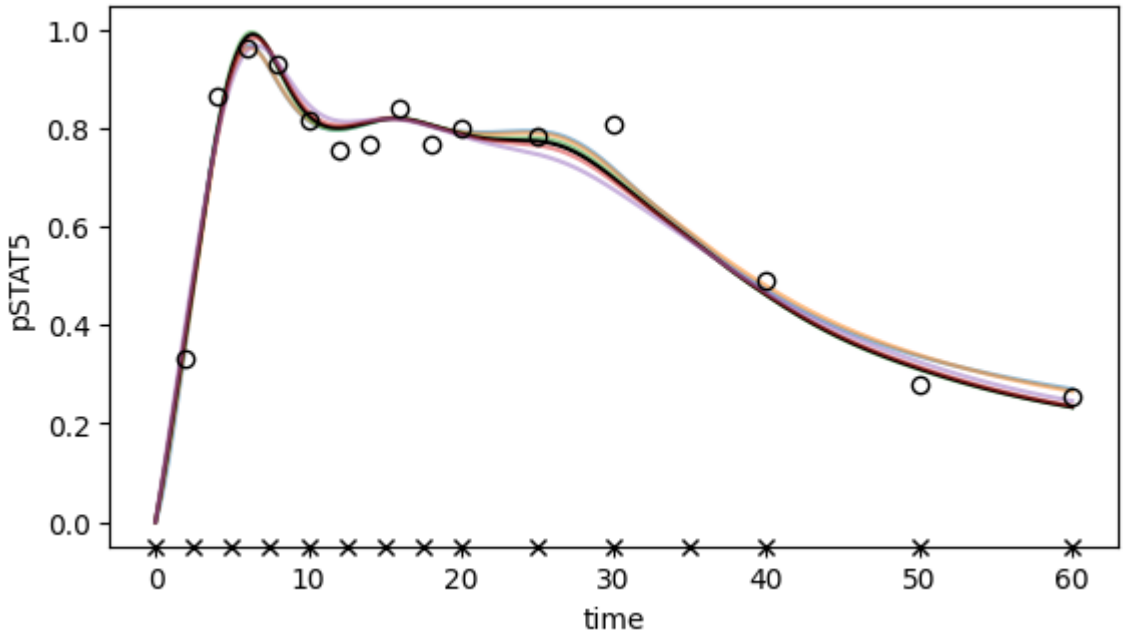
```
    zorder=10,
    clip_on=False,
)
ax.set_ylim(ylim1, ax.get_ylim()[1])
ax.set_xlabel("time")
ax.set_ylabel("pSTAT5");
# ax.legend();
```



[48]:
```
# Plot ML fit for tSTAT5 (all regularization strengths)
fig, ax = plt.subplots(figsize=(6.5, 3.5))
for regstrength in sorted(regproblems.keys()):
    t, tSTAT5 = simulate_tSTAT5(
        problem=regproblems[regstrength], result=regresults[regstrength]
    )
    if regstrength == chosen_regstrength:
        kwargs = dict(
            color="black",
            label=f"$\\mathbf{{\\lambda = {regstrength}}}$",
            zorder=2,
        )
    else:
        kwargs = dict(label=f"$\\lambda = {regstrength}$", alpha=0.5)
    ax.plot(t, tSTAT5, **kwargs)
ax.plot(
    df_tSTAT5["time"],
    df_tSTAT5["measurement"],
    "o",
    color="black",
    markerfacecolor="none",
    label="experimental data",
```

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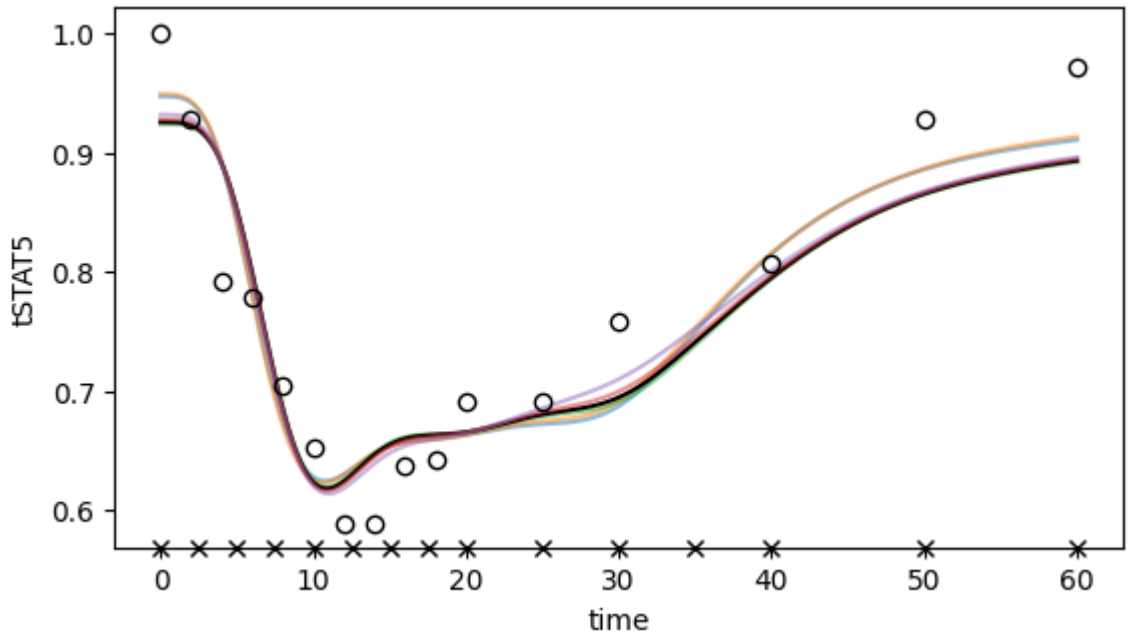
```
)
ylim1 = ax.get_ylim()[0]
ax.plot(
    nodes,
    len(nodes) * [ylim1],
    "x",
    color="black",
    label="spline nodes",
    zorder=10,
    clip_on=False,
)
ax.set_ylim(ylim1, ax.get_ylim()[1])
ax.set_xlabel("time")
ax.set_ylabel("tSTAT5");
# ax.legend();
```



[49]:
```
# Plot ML fit for pEpoR (single regularization strength with noise model)
fig, ax = plt.subplots(figsize=(6.5, 3.5))
t, pEpoR = simulate_pEpoR(
    problem=regproblems[chosen_regstrength],
    result=regresults[chosen_regstrength],
)
sigma_pEpoR = 0.0274 + 0.1 * pEpoR
ax.fill_between(
    t,
    pEpoR - 2 * sigma_pEpoR,
    pEpoR + 2 * sigma_pEpoR,
    color="black",
    alpha=0.10,
    interpolate=True,
```

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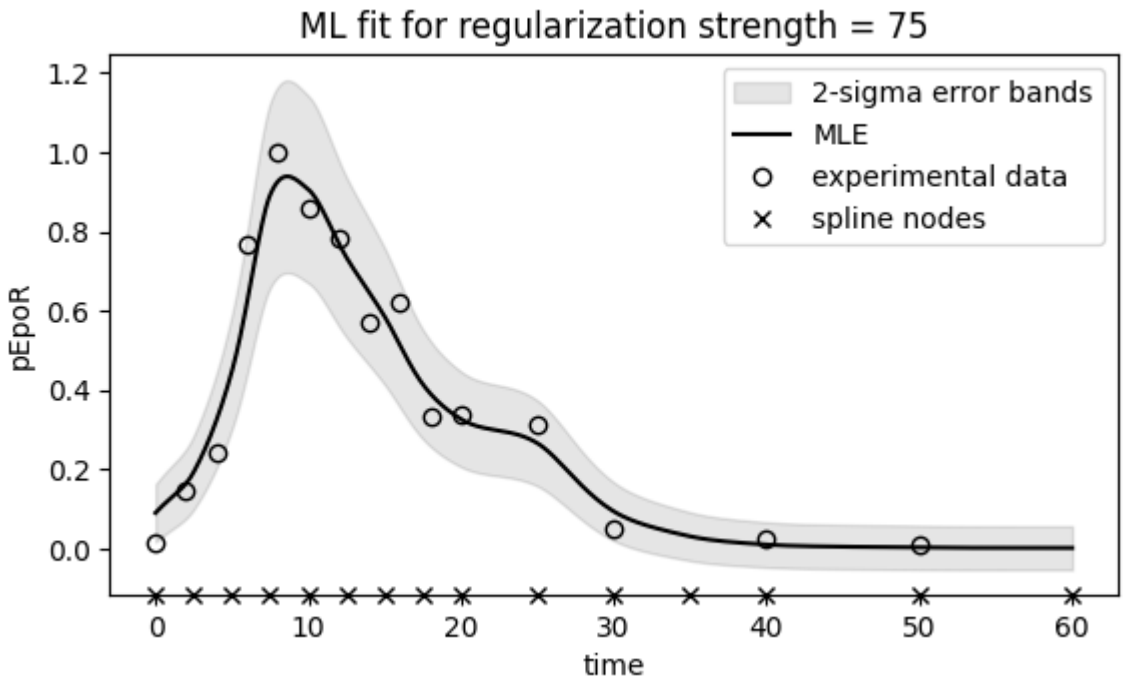
```
    label="2-sigma error bands",
)
ax.plot(t, pEpoR, color="black", label="MLE")
ax.plot(
    df_pEpoR["time"],
    df_pEpoR["measurement"],
    "o",
    color="black",
    markerfacecolor="none",
    label="experimental data",
)
ylim1 = ax.get_ylim()[0]
ax.plot(
    nodes,
    len(nodes) * [ylim1],
    "x",
    color="black",
    label="spline nodes",
    zorder=10,
    clip_on=False,
)
ax.set_ylim(ylim1, ax.get_ylim()[1])
ax.set_xlabel("time")
ax.set_ylabel("pEpoR")
ax.set_title(f"ML fit for regularization strength = {chosen_regstrength}")
ax.legend();
```



[50]:
```
# Store results for later
all_results["15 nodes, FD"] = (
```

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```
    regproblems[chosen_regstrength],
    regresults[chosen_regstrength],
)
```

Spline approximation with few nodes, optimizing derivatives explicitly

An alternative way to achieve higher expressivity, while not increasing the number of nodes, is to optimize the derivatives of the spline at the nodes instead of computing them by finite differencing. The risk of overfitting is still present, so we will include regularization as in the above example.

Creating the PEtab model

[51]:
```
# Problem name
name = "Swameye_PNAS2003_5nodes"
```

We now need to create additional parameters for the spline derivatives too.

[52]:
```
# Create spline for pEpoR
nodes = [0, 5, 10, 20, 60]
values_at_nodes = [
    sp.Symbol(f"pEpoR_t{str(t).replace('.', '_dot_')}") for t in nodes
]
derivatives_at_nodes = [
    sp.Symbol(f"derivative_pEpoR_t{str(t).replace('.', '_dot_')}")
    for t in nodes[:-1]
]
spline = amici.splines.CubicHermiteSpline(
    sbml_id="pEpoR",
    evaluate_at=amici.sbml_utils.amici_time_symbol,
    nodes=nodes,
    values_at_nodes=values_at_nodes,
    derivatives_at_nodes=derivatives_at_nodes
    + [0],  # last value is zero because steady state is reached
    extrapolate=(None, "constant"),
    bc="auto",
    logarithmic_parametrization=True,
)
```

[53]:
```
# Compute L2 norm of the curvature of pEpoR
regularization = spline.squared_L2_norm_of_curvature()
```

[54]:
```
# Add a parameter for regularization strength
reg_parameters_df = pd.DataFrame(
    dict(
        parameterScale="log10",
        lowerBound=1e-6,
        upperBound=1e6,
        nominalValue=1.0,
        estimate=0,
```

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```
    ),
    index=pd.Series(["regularization_strength"], name="parameterId"),
)
# Encode regularization term as an additional observable
reg_observables_df = pd.DataFrame(
    dict(
        observableFormula=f"sqrt({regularization})".replace("**", "^"),
        observableTransformation="lin",
        noiseFormula="1/sqrt(regularization_strength)",
        noiseDistribution="normal",
    ),
    index=pd.Series(["regularization"], name="observableId"),
)
# and correspoding measurement
reg_measurements_df = pd.DataFrame(
    dict(
        observableId="regularization",
        simulationConditionId="condition1",
        measurement=0,
        time=0,
        observableTransformation="lin",
    ),
    index=pd.Series([0]),
)
```

[55]:
```
# Add spline formula to SBML model
sbml_doc = libsbml.SBMLReader().readSBML(
    os.path.join("Swameye_PNAS2003", "swameye2003_model.xml")
)
sbml_model = sbml_doc.getModel()
spline.add_to_sbml_model(
    sbml_model, auto_add=True, y_nominal=0.1, y_constant=True
)
```

[56]:
```
# Derivative parameters must be added separately
for p in derivatives_at_nodes:
    amici.sbml_utils.add_parameter(sbml_model, p, value=0.0, constant=True)
```

[57]:
```
# Extra parameters associated to the spline
spline_parameters_df1 = pd.DataFrame(
    dict(
        parameterScale="log",
        lowerBound=0.001,
        upperBound=10,
        nominalValue=0.1,
        estimate=1,
    ),
    index=pd.Series(list(map(str, values_at_nodes)), name="parameterId"),
)
spline_parameters_df2 = pd.DataFrame(
    dict(
```

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```
        parameterScale="lin",
        lowerBound=-0.666,
        upperBound=0.666,
        nominalValue=0.0,
        estimate=1,
    ),
    index=pd.Series(list(map(str, derivatives_at_nodes)), name="parameterId"),
)
```

[58]:
```
# Create PEtab problem
petab_problem = petab.Problem(
    sbml_model,
    condition_df=petab.conditions.get_condition_df(
        os.path.join("Swameye_PNAS2003", "swameye2003_conditions.tsv")
    ),
    measurement_df=petab.core.concat_tables(
        [
            os.path.join("Swameye_PNAS2003", "swameye2003_measurements.tsv"),
            reg_measurements_df,
        ],
        petab.measurements.get_measurement_df,
    ).reset_index(drop=True),
    parameter_df=petab.core.concat_tables(
        [
            os.path.join("Swameye_PNAS2003", "swameye2003_parameters.tsv"),
            spline_parameters_df1,
            spline_parameters_df2,
            reg_parameters_df,
        ],
        petab.parameters.get_parameter_df,
    ),
    observable_df=petab.core.concat_tables(
        [
            os.path.join("Swameye_PNAS2003", "swameye2003_observables.tsv"),
            reg_observables_df,
        ],
        petab.observables.get_observable_df,
    ),
)
```

[59]:
```
# Check whether PEtab model is valid
assert not petab.lint_problem(petab_problem)
```

[60]:
```
# Save PEtab problem to disk
# import shutil
# shutil.rmtree(name, ignore_errors=True)
# os.mkdir(name)
# petab_problem.to_files_generic(prefix_path=name)
```

Creating the pyPESTO problem

[61]:
```
# Problem must be "flattened" to be used with AMICI
petab.core.flatten_timepoint_specific_output_overrides(petab_problem)
```

[62]:
```
# Check whether simulation from the PEtab problem works
# import amici.petab_simulate
# simulator = amici.petab_simulate.PetabSimulator(petab_problem)
# simulator.simulate(noise=False)
```

[63]:
```
# Import PEtab problem into pyPESTO
pypesto_problem = pypesto.petab.PetabImporter(
    petab_problem, model_name=name
).create_problem()
```

Maximum Likelihood estimation

[ ]:
```
# Try different regularization strengths
regstrengths = np.asarray([1, 175, 500, 1000])
if os.getenv("GITHUB_ACTIONS") is not None:
    regstrengths = np.asarray([175])
regproblems = {}
regresults = {}

for regstrength in regstrengths:
    # Fix parameter in pypesto problem
    name = f"Swameye_PNAS2003_5nodes_reg{regstrength}"
    pypesto_problem.fix_parameters(
        pypesto_problem.x_names.index("regularization_strength"),
        np.log10(
            regstrength
        ),  # parameter is specified as log10 scale in PEtab
    )
    regproblem = copy.deepcopy(pypesto_problem)

    # Load existing results if available
    if os.path.exists(f"{name}.h5"):
        regresult = pypesto.store.read_result(f"{name}.h5", problem=regproblem)
    else:
        regresult = None
    # Overwrite
    # regresult = None

    # Parallel multistart optimization with pyPESTO and FIDES
    if n_starts > 0:
        if regresult is None:
            new_ids = [str(i) for i in range(n_starts)]
        else:
            last_id = max(int(i) for i in regresult.optimize_result.id)
            new_ids = [
```

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```
                str(i) for i in range(last_id + 1, last_id + n_starts + 1)
            ]
        regresult = pypesto.optimize.minimize(
            regproblem,
            n_starts=n_starts,
            ids=new_ids,
            optimizer=pypesto_optimizer,
            engine=pypesto_engine,
            result=regresult,
        )
        regresult.optimize_result.sort()
        if regresult.optimize_result.x[0] is None:
            raise Exception(
                "All multistarts failed (n_starts is probably too small)! If this error␣
↪occurred during CI, just run the workflow again."
            )

    # Save results to disk
    # pypesto.store.write_result(regresult, f'{name}.h5', overwrite=True)

    # Store result
    regproblems[regstrength] = regproblem
    regresults[regstrength] = regresult
```

[65]:
```
# Compute sum of squared normalized residuals
print(f"Target value is {len(df_pEpoR['time'])}")
regstrengths = sorted(regproblems.keys())
stats = []
for regstrength in regstrengths:
    t, pEpoR = simulate_pEpoR(
        N=None,
        problem=regproblems[regstrength],
        result=regresults[regstrength],
    )
    assert np.array_equal(df_pEpoR["time"], t[:-1])
    pEpoR = pEpoR[:-1]
    sigma_pEpoR = 0.0274 + 0.1 * pEpoR
    stat = np.sum(((pEpoR - df_pEpoR["measurement"]) / sigma_pEpoR) ** 2)
    print(f"Regularization strength: {regstrength}. Statistic is {stat}")
    stats.append(stat)
# Select best regularization strength
chosen_regstrength = regstrengths[
    np.abs(np.asarray(stats) - len(df_pEpoR["time"])).argmin()
]
```

```
Target value is 15
Regularization strength: 1. Statistic is 9.638207938045252
Regularization strength: 175. Statistic is 15.115255701660317
Regularization strength: 500. Statistic is 19.156287450444093
Regularization strength: 1000. Statistic is 25.09224919998158
```

[66]:
```
# Visualize the results of the multistarts for a chosen regularization strength
```

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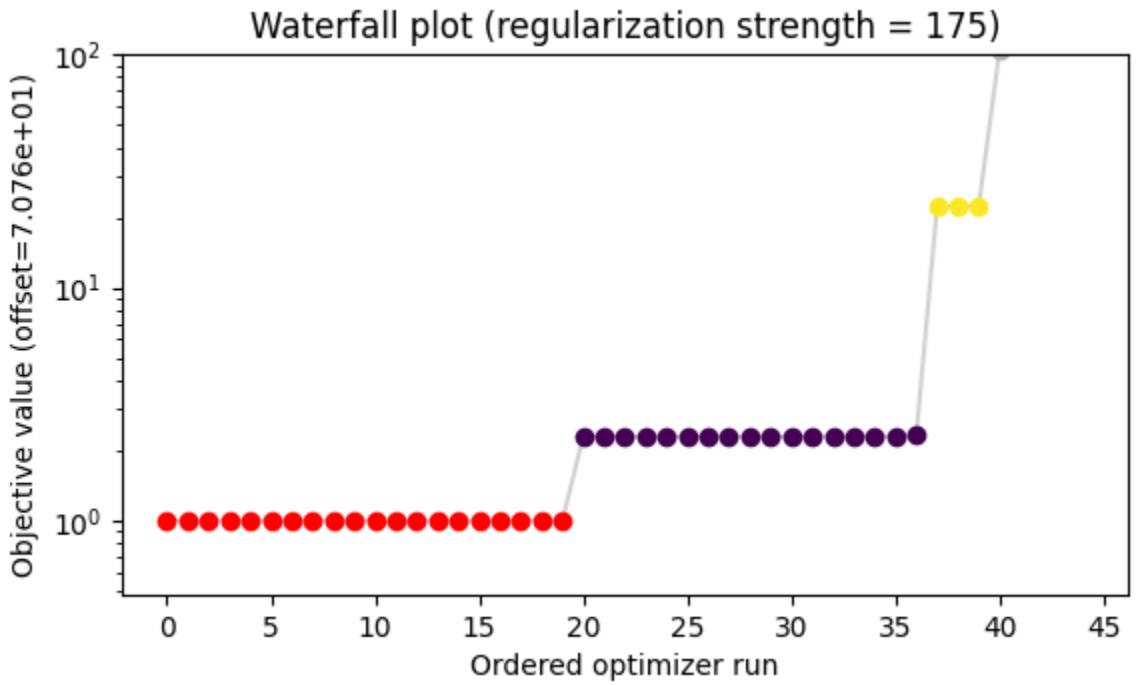
```
ax = pypesto.visualize.waterfall(
    regresults[chosen_regstrength], size=[6.5, 3.5]
)
ax.set_title(
    f"Waterfall plot (regularization strength = {chosen_regstrength})"
)
ax.set_ylim(ax.get_ylim()[0], 100);
```



[76]:
```
# Plot ML fit for pEpoR (all regularization strengths)
fig, ax = plt.subplots(figsize=(6.5, 3.5))
for regstrength in sorted(regproblems.keys()):
    t, pEpoR = simulate_pEpoR(
        problem=regproblems[regstrength], result=regresults[regstrength]
    )
    if regstrength == chosen_regstrength:
        kwargs = dict(
            color="black",
            label=f"$\\mathbf{{\\lambda = {regstrength}}}$",
            zorder=2,
        )
    else:
        kwargs = dict(label=f"$\\lambda = {regstrength}$", alpha=0.5)
    ax.plot(t, pEpoR, **kwargs)
ax.plot(
    df_pEpoR["time"],
    df_pEpoR["measurement"],
    "o",
    color="black",
    markerfacecolor="none",
```

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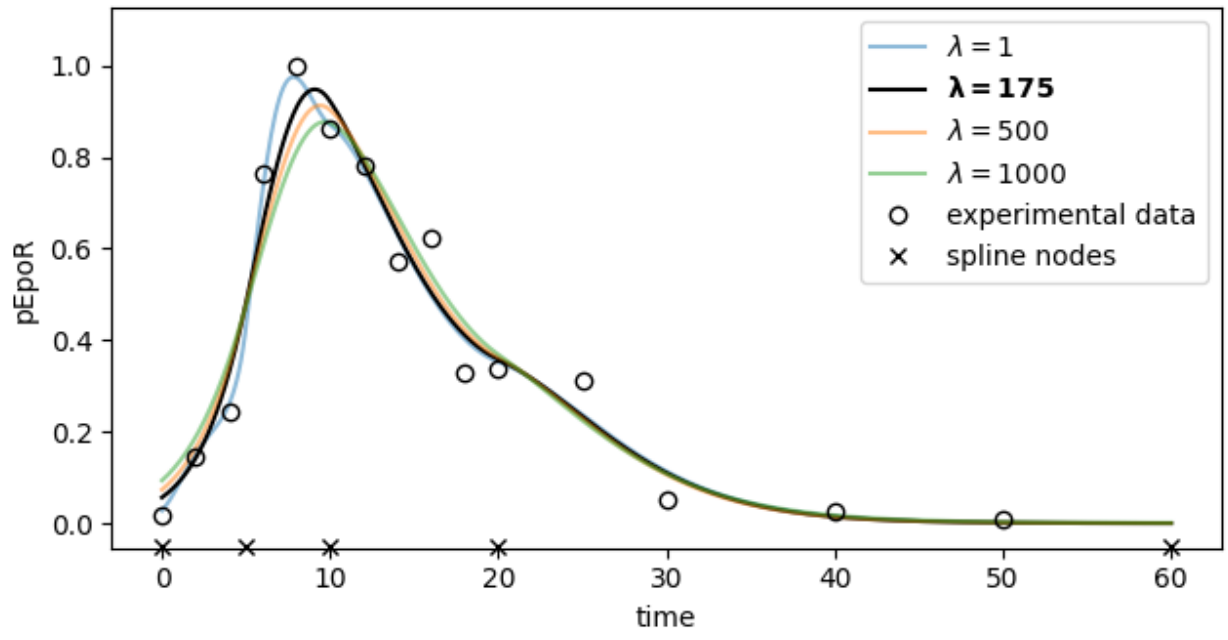
```
    label="experimental data",
)
ylim1 = ax.get_ylim()[0]
ax.plot(
    nodes,
    len(nodes) * [ylim1],
    "x",
    color="black",
    label="spline nodes",
    zorder=10,
    clip_on=False,
)
ax.set_ylim(ylim1, ax.get_ylim()[1])
ax.set_xlabel("time")
ax.set_ylabel("pEpoR")
ax.set_xlim(-3.0, 63.0)
ax.set_ylim(-0.0529905202238870 4, 1.126290214024833)
ax.legend()
ax.figure.tight_layout()
# ax.set_ylabel("input function")
# ax.figure.savefig('fit_5nodes_lambdas.pdf')
```



[68]:
```
# Plot ML fit for pSTAT5 (all regularization strengths)
fig, ax = plt.subplots(figsize=(6.5, 3.5))
for regstrength in sorted(regproblems.keys()):
    t, pSTAT5 = simulate_pSTAT5(
        problem=regproblems[regstrength], result=regresults[regstrength]
    )
    if regstrength == chosen_regstrength:
        kwargs = dict(
```

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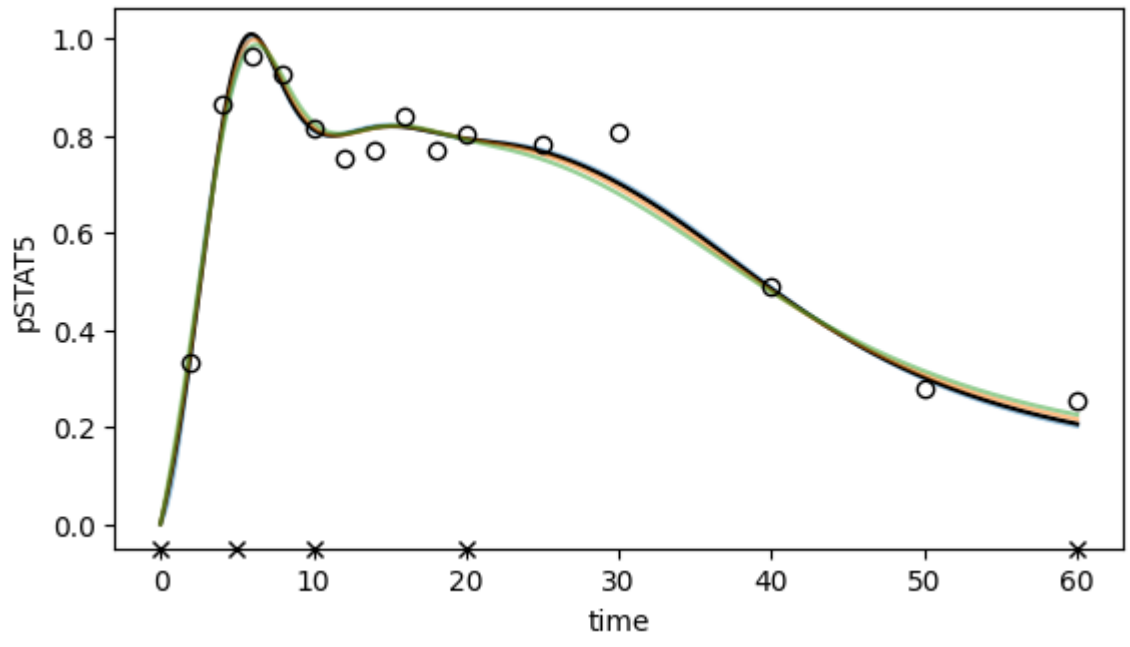
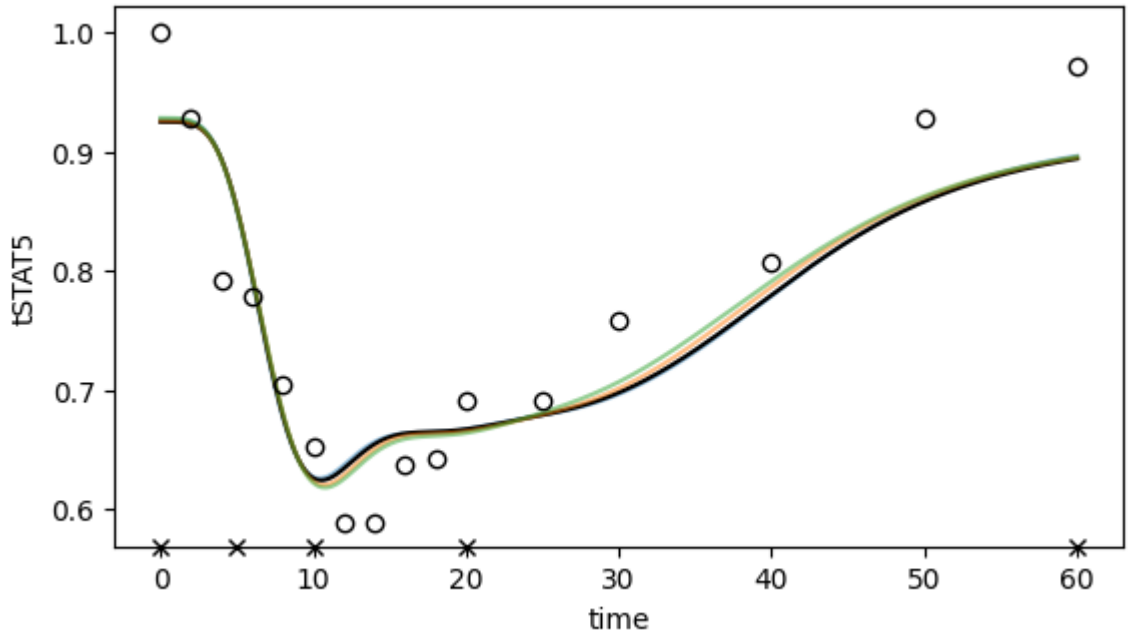
```
            color="black",
            label=f"$\\mathbf{{\\lambda = {regstrength}}}$",
            zorder=2,
        )
    else:
        kwargs = dict(label=f"$\\lambda = {regstrength}$", alpha=0.5)
    ax.plot(t, pSTAT5, **kwargs)
ax.plot(
    df_pSTAT5["time"],
    df_pSTAT5["measurement"],
    "o",
    color="black",
    markerfacecolor="none",
    label="experimental data",
)
ylim1 = ax.get_ylim()[0]
ax.plot(
    nodes,
    len(nodes) * [ylim1],
    "x",
    color="black",
    label="spline nodes",
    zorder=10,
    clip_on=False,
)
ax.set_ylim(ylim1, ax.get_ylim()[1])
ax.set_xlabel("time")
ax.set_ylabel("pSTAT5");
# ax.legend();
```



[69]:
```
# Plot ML fit for tSTAT5 (all regularization strengths)
fig, ax = plt.subplots(figsize=(6.5, 3.5))
for regstrength in sorted(regproblems.keys()):
    t, tSTAT5 = simulate_tSTAT5(
        problem=regproblems[regstrength], result=regresults[regstrength]
    )
    if regstrength == chosen_regstrength:
        kwargs = dict(
            color="black",
            label=f"$\\mathbf{{\\lambda = {regstrength}}}$",
            zorder=2,
        )
    else:
        kwargs = dict(label=f"$\\lambda = {regstrength}$", alpha=0.5)
    ax.plot(t, tSTAT5, **kwargs)
ax.plot(
    df_tSTAT5["time"],
    df_tSTAT5["measurement"],
    "o",
    color="black",
    markerfacecolor="none",
    label="experimental data",
)
ylim1 = ax.get_ylim()[0]
ax.plot(
    nodes,
    len(nodes) * [ylim1],
    "x",
    color="black",
    label="spline nodes",
    zorder=10,
    clip_on=False,
)
ax.set_ylim(ylim1, ax.get_ylim()[1])
ax.set_xlabel("time")
ax.set_ylabel("tSTAT5");
# ax.legend();
```



[70]:
```
# Plot ML fit for pEpoR (single regularization strength with noise model)
fig, ax = plt.subplots(figsize=(6.5, 3.5))
t, pEpoR = simulate_pEpoR(
    problem=regproblems[chosen_regstrength],
    result=regresults[chosen_regstrength],
)
sigma_pEpoR = 0.0274 + 0.1 * pEpoR
ax.fill_between(
    t,
    pEpoR - 2 * sigma_pEpoR,
    pEpoR + 2 * sigma_pEpoR,
    color="black",
    alpha=0.10,
    interpolate=True,
    label="2-sigma error bands",
)
ax.plot(t, pEpoR, color="black", label="MLE")
ax.plot(
    df_pEpoR["time"],
    df_pEpoR["measurement"],
    "o",
    color="black",
    markerfacecolor="none",
    label="experimental data",
)
ylim1 = ax.get_ylim()[0]
ax.plot(
    nodes,
    len(nodes) * [ylim1],
    "x",
```

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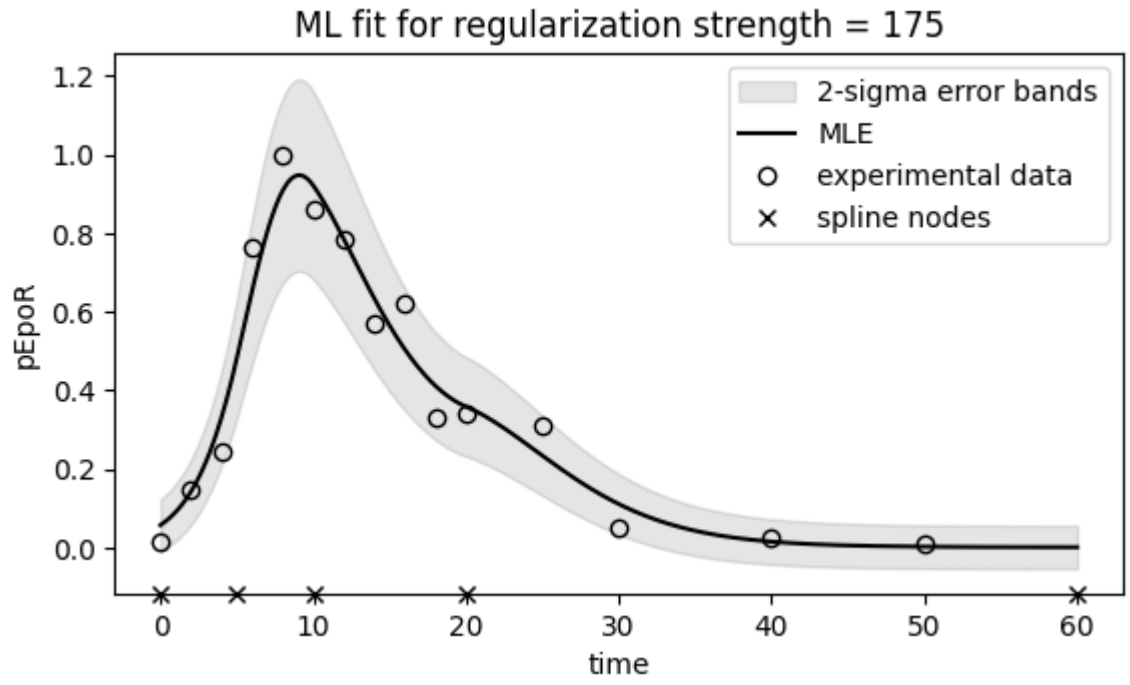
```
    color="black",
    label="spline nodes",
    zorder=10,
    clip_on=False,
)
ax.set_ylim(ylim1, ax.get_ylim()[1])
ax.set_xlabel("time")
ax.set_ylabel("pEpoR")
ax.set_title(f"ML fit for regularization strength = {chosen_regstrength}")
ax.legend();
```



[71]:
```
# Store results for later
all_results["5 nodes"] = (
    regproblems[chosen_regstrength],
    regresults[chosen_regstrength],
)
```

Comparing the three approaches

[72]:
```
# Plot ML fit for pEpoR
fig, ax = plt.subplots(figsize=(6.5, 3.5))
for label, (problem, result) in all_results.items():
    t, pEpoR = simulate_pEpoR(problem=problem, result=result)
    ax.plot(t, pEpoR, label=label)
ax.plot(
    df_pEpoR["time"],
    df_pEpoR["measurement"],
```

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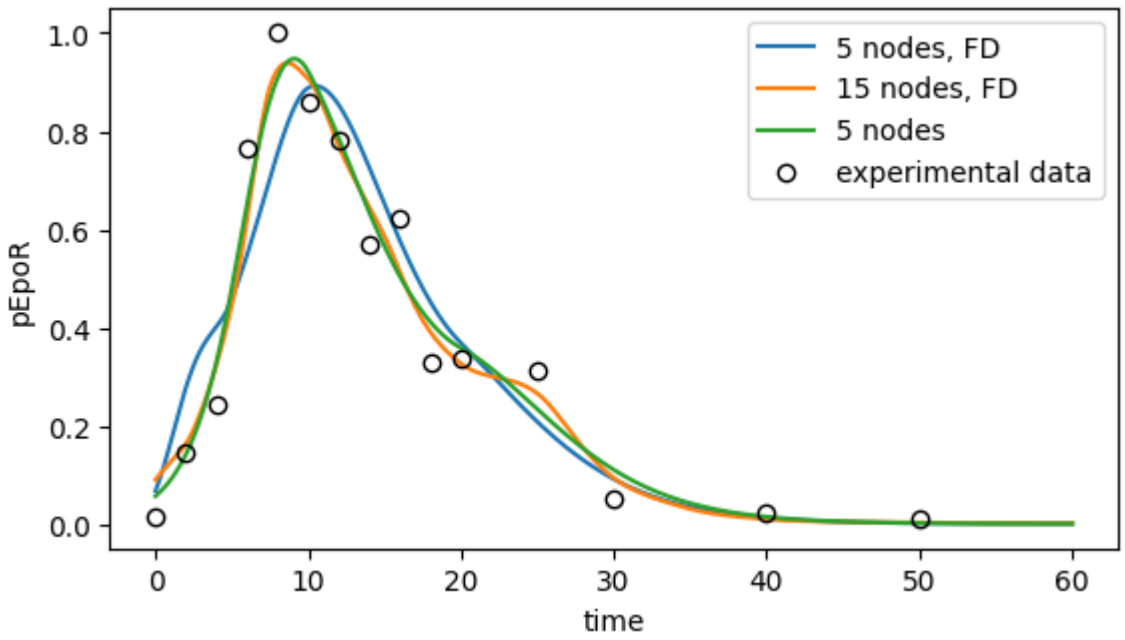
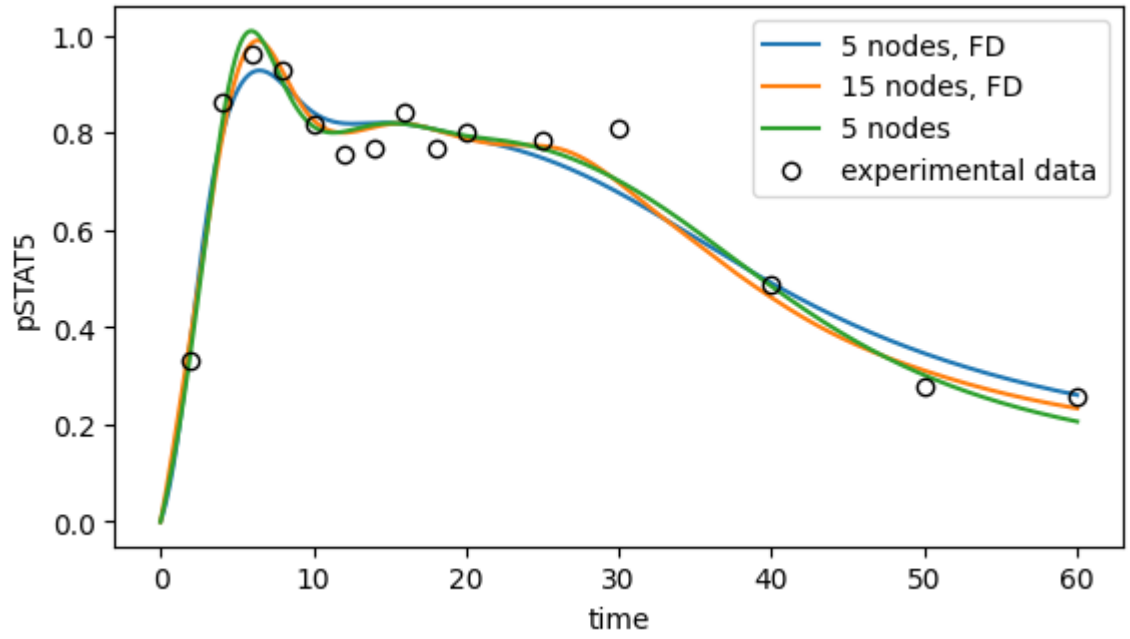
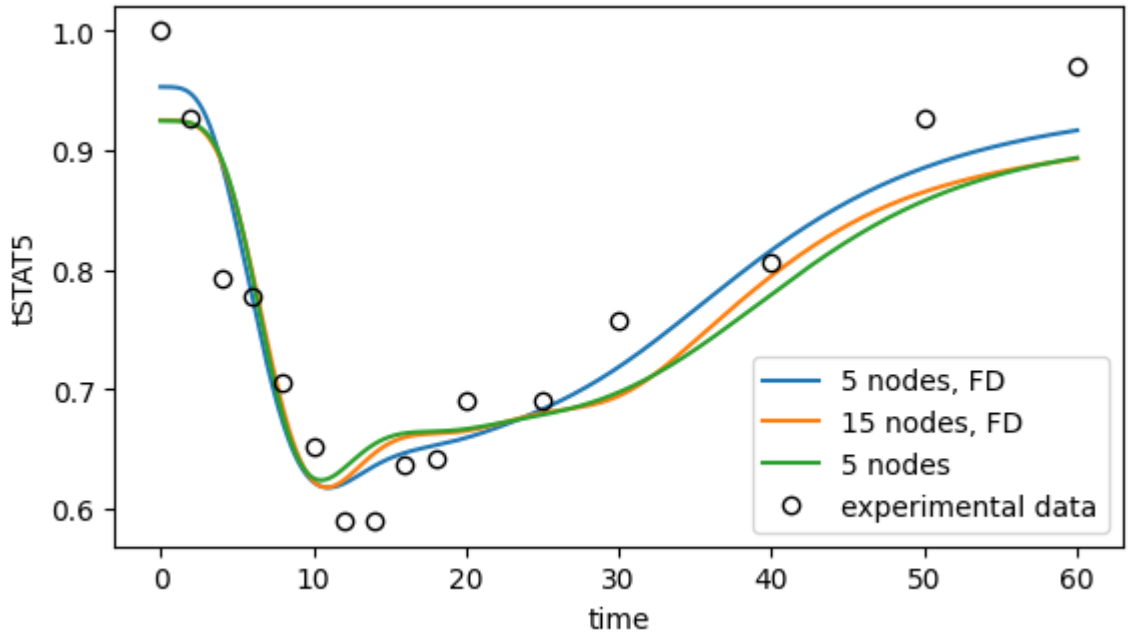
```
    "o",
    color="black",
    markerfacecolor="none",
    label="experimental data",
)
ax.set_xlabel("time")
ax.set_ylabel("pEpoR")
ax.legend();
```



[73]:
```
# Plot ML fit for pSTAT5
fig, ax = plt.subplots(figsize=(6.5, 3.5))
for label, (problem, result) in all_results.items():
    t, pSTAT5 = simulate_pSTAT5(problem=problem, result=result)
    ax.plot(t, pSTAT5, label=label)
ax.plot(
    df_pSTAT5["time"],
    df_pSTAT5["measurement"],
    "o",
    color="black",
    markerfacecolor="none",
    label="experimental data",
)
ax.set_xlabel("time")
ax.set_ylabel("pSTAT5")
ax.legend();
```



[74]:
```
# Plot ML fit for tSTAT5
fig, ax = plt.subplots(figsize=(6.5, 3.5))
for label, (problem, result) in all_results.items():
    t, tSTAT5 = simulate_tSTAT5(problem=problem, result=result)
    ax.plot(t, tSTAT5, label=label)
ax.plot(
    df_tSTAT5["time"],
    df_tSTAT5["measurement"],
    "o",
    color="black",
    markerfacecolor="none",
    label="experimental data",
)
ax.set_xlabel("time")
ax.set_ylabel("tSTAT5")
ax.legend();
```



[75]:
```
# Compare parameter values
for label, (problem, result) in all_results.items():
    print(f"\n### {label}")
    x = result.optimize_result.x[0]
    if len(x) == len(problem.x_free_indices):
        names = problem.x_names[problem.x_free_indices]
    else:
        names = problem.x_names
    for name, value in zip(names, x):
        print(f"{name} = {value}")
```

```
### 5 nodes, FD
k1 = -0.012344171128634264
k2 = -1.11975626735931
k3 = 5.999999816644789
k4 = 0.22576351403212522
scale_tSTAT5 = -0.020792663448966672
scale_pSTAT5 = 0.1422550065768319
sigma_pEpoR_abs = -1.562249437179612
sigma_pEpoR_rel = -1.0
pEpoR_t0 = -2.6870875267006804
pEpoR_t5 = -0.7797622417853871
pEpoR_t10 = -0.11820562755751975
pEpoR_t20 = -0.9974218537437654
pEpoR_t60 = -6.90775527898212

### 15 nodes, FD
k1 = 0.1543170078851364
k2 = -1.0042579083153138
k3 = -0.17925294344845363
```

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```
k4 = 0.31486258696137254
scale_tSTAT5 = -0.03364700359730668
scale_pSTAT5 = 0.11013784140762342
sigma_pEpoR_abs = -1.562249437179612
sigma_pEpoR_rel = -1.0
pEpoR_t0 = -2.40456191981547
pEpoR_t2_dot_5 = -1.6438670641678346
pEpoR_t5_dot_0 = -0.80437214623219
pEpoR_t7_dot_5 = -0.1144993579909219
pEpoR_t10_dot_0 = -0.09849380649928209
pEpoR_t12_dot_5 = -0.30861764847405077
pEpoR_t15_dot_0 = -0.535565172217061
pEpoR_t17_dot_5 = -0.8808659628360864
pEpoR_t20 = -1.1184724117332843
pEpoR_t25 = -1.3245209689075161
pEpoR_t30 = -2.3651756746835053
pEpoR_t35 = -3.4734027477458524
pEpoR_t40 = -4.578132101040909
pEpoR_t50 = -5.7968417139258435
pEpoR_t60 = -6.268875988124801
regularization_strength = 1.8750612633917

### 5 nodes
k1 = 0.2486924371230916
k2 = -0.9010429810987043
k3 = -0.3408591074551208
k4 = 0.3594353532480489
scale_tSTAT5 = -0.03395751814386045
scale_pSTAT5 = 0.1008121903144357
sigma_pEpoR_abs = -1.562249437179612
sigma_pEpoR_rel = -1.0
pEpoR_t0 = -2.8601663957890175
pEpoR_t5 = -0.7275787612811422
pEpoR_t10 = -0.08172482568007049
pEpoR_t20 = -1.02532663950965
pEpoR_t60 = -6.907755278982137
derivative_pEpoR_t0 = 0.026587630472163528
derivative_pEpoR_t5 = 0.17154606724507934
derivative_pEpoR_t10 = -0.05503215878900286
derivative_pEpoR_t20 = -0.016352876798592663
regularization_strength = 2.2430380486862944
```

Bibliography

Schelker, M. et al. (2012). "Comprehensive estimation of input signals and dynamics in biochemical reaction networks". In: Bioinformatics 28.18, pp. i529–i534. doi: 10.1093/bioinformatics/bts393.

Swameye, I. et al. (2003). "Identification of nucleocytoplasmic cycling as a remote sensor in cellular signaling by databased modeling". In: Proceedings of the National Academy of Sciences 100.3, pp. 1028–1033. doi: 10.1073/pnas.0237333100.

10.3 Using AMICI's Python interface

In the following we will give a detailed overview how to specify models in Python and how to call the generated simulation files.

10.3.1 Model definition

This document provides an overview of different interfaces to import models in AMICI. Further examples are available in the AMICI repository in the python/examples directory.

SBML import

AMICI can import *SBML* models via the *amici.sbml_import.SbmlImporter()* class.

Status of SBML support in Python-AMICI

Python-AMICI currently **passes 1247 out of the 1821 (~68%) test cases** from the semantic SBML Test Suite (current status).

The following SBML test suite tags are currently supported (i.e., at least one test case with the respective test passes; tag descriptions):

Component tags:

- AlgebraicRule
- AssignmentRule
- comp
- Compartment
- CSymbolAvogadro
- CSymbolRateOf
- CSymbolTime
- Deletion
- EventNoDelay
- ExternalModelDefinition
- FunctionDefinition
- InitialAssignment
- ModelDefinition

- Parameter
- Port
- RateRule
- Reaction
- ReplacedBy
- ReplacedElement
- SBaseRef
- Species
- Submodel

Test tags:

- 0D-Compartment
- Amount
- AssignedConstantStoichiometry
- AssignedVariableStoichiometry
- BoolNumericSwap
- BoundaryCondition
- comp
- Concentration
- ConstantSpecies
- ConversionFactor
- ConversionFactors
- DefaultValue
- EventT0Firing
- ExtentConversionFactor
- HasOnlySubstanceUnits
- InitialValueReassigned
- L3v2MathML
- LocalParameters
- MultiCompartment
- NoMathML
- NonConstantCompartment
- NonConstantParameter
- NonUnityCompartment
- NonUnityStoichiometry
- ReversibleReaction
- SpeciesReferenceInMath

- SubmodelOutput
- TimeConversionFactor
- UncommonMathML
- VolumeConcentrationRates

Additional support may be added in the future. However, the following features are unlikely to be supported:

- *factorial()*, *ceil()*, *floor()*, due to incompatibility with symbolic sensitivity computations
- *delay()* due to missing *SUNDIALS* solver support
- events with delays, events with non-persistent triggers

Tutorials

A basic tutorial on how to import and simulate SBML models is available in the *Getting Started notebook*, while a more detailed example including customized import and sensitivity computation is available in the *Example Steadystate notebook*.

PySB import

AMICI can import *PySB* models via `amici.pysb_import.pysb2amici()`.

BNGL import

AMICI can import *BNGL* models via `amici.bngl_import.bngl2amici()`.

PEtab import

AMICI can import *PEtab*-based model definitions and run simulations for the specified simulations conditions. For usage, see *python/examples/example_petab/petab.ipynb*.

Importing plain ODEs

The AMICI Python interface does not currently support direct import of ODEs. However, it is straightforward to encode them as RateRules in an SBML model. The most convenient options to do that are maybe Antimony and yaml2sbml.

An example using Antimony to specify the Lotka-Volterra equations is shown below:

```
ant_model = """

model lotka_volterra
    # see https://en.wikipedia.org/wiki/Lotka%E2%80%93Volterra_equations

    # initial conditions
    prey_density = 10;
    predator_density = 10;

    # parameters
    prey_growth_rate = 1.1;
    predator_effect_on_prey = 0.4;
```

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```
    predator_death_rate = 0.4;
    prey_effect_on_predator = 0.1;

    # dx/dt
    prey_density' = prey_growth_rate * prey_density - predator_effect_on_prey * prey_
↪density * predator_density;
    predator_density' = prey_effect_on_predator * prey_density * predator_density -␣
↪predator_death_rate * predator_density;
end
"""
module_name = "test_antimony_example_lv"
from amici.antimony_import import antimony2amici
antimony2amici(
    ant_model,
    model_name=module_name,
    output_dir=module_name,
)
model_module = amici.import_model_module(
    module_name=module_name, module_path=outdir
)
amici_model = model_module.getModel()
amici_model.setTimepoints(np.linspace(0, 100, 200))
amici_solver = amici_model.getSolver()
rdata = amici.runAmiciSimulation(amici_model, amici_solver)

from amici.plotting import plot_state_trajectories
plot_state_trajectories(rdata, model=amici_model)
```

The yaml2sbml package creates SBML models from a YAML-based specification of an ODE model. Various examples are provided. Besides the SBML model, yaml2sbml can also create PEtab files.

SED-ML import

We also plan to implement support for the Simulation Experiment Description Markup Language (SED-ML).

10.3.2 Environment variables affecting model import

In addition to the environment variables listed *here*, the following environment variables control various behaviours during model import and compilation:

Table 1: Environment variables affecting model import

Variable	Purpose	Example
AMICI_EXTRACT_CSE	Extract common subexpressions. May significantly reduce file size and compile time for large models, but makes the generated code less readable. Disabled by default.	AMICI_EXTRACT_CSE=1
AMICI_IMPORT_NPROCS	Number of processes to be used for model import. Defaults to 1. Speeds up import of large models. Will slow down import of small models, benchmarking recommended.	AMICI_IMPORT_NPROCS=4
AMICI_EXPERIMENTAL_SBI	Compute conservation laws for non-constant species. SBML-import only. See *amici.sbml_import.SbmlImporter.sbml2amici()*.	

10.3.3 Miscellaneous

OpenMP support for parallelized simulation for multiple experimental conditions

AMICI can be built with OpenMP support, which allows to parallelize model simulations for multiple experimental conditions.

On Linux and OSX this is enabled by default. This can be verified using:

```
import amici
amici.compiledWithOpenMP()
```

If not already enabled by default, you can enable OpenMP support by setting the environment variables `AMICI_CXXFLAGS` and `AMICI_LDFLAGS` to the correct OpenMP flags of your compiler and linker, respectively. This has to be done for both AMICI package installation *and* model compilation. When using `gcc` on Linux, this would be:

```
# on your shell:
AMICI_CXXFLAGS=-fopenmp AMICI_LDFLAGS=-fopenmp pip3 install amici
```

```
# in python, before model compilation:
import os
os.environ['AMICI_CXXFLAGS'] = '-fopenmp'
os.environ['AMICI_LDFLAGS'] = '-fopenmp'
```

10.4 FAQ

Q: I am trying to install the AMICI Python package, but installation fails with something like

```
amici/src/cblas.cpp:16:13: fatal error: cblas.h: No such file or directory
#include <cblas.h>
         ^~~~~~~~~
compilation terminated.
error: command 'x86_64-linux-gnu-gcc' failed with exit status 1
```

A: You will have to install a CBLAS-compatible BLAS library and/or set `BLAS_CFLAGS` as described in the *installation guide*.

Q: Importing my model fails with something like `ImportError: _someModelName.cpython-37m-x86_64-linux-gnu.so: undefined symbol: omp_get_thread_num`.

A: You probably installed the AMICI package with OpenMP support, but did not have the relevant compiler/linker flags set when importing/building the model. See *here*.

10.5 AMICI Python API

Modules

amici	AMICI
amici.amici	Core C++ bindings
amici.sbml_import	SBML Import This module provides all necessary functionality to import a model specified in the Systems Biology Markup Language (SBML).
amici.pysb_import	PySB Import This module provides all necessary functionality to import a model specified in the pysb.core.Model format.
amici.bngl_import	BNGL Import This module provides all necessary functionality to import a model specified in the BNGL format.
amici.petab	PEtab import related code.
amici.petab.conditions	PEtab conditions to AMICI ExpDatas.
amici.petab.import_helpers	General helper functions for PEtab import.
amici.petab.parameter_mapping	
amici.petab.petab_import	PEtab Import Import a model in the petab (https://github.com/PEtab-dev/PEtab) format into AMICI.
amici.petab.pysb_import	PySB-PEtab Import Import a model in the PySB-adapted petab (https://github.com/PEtab-dev/PEtab) format into AMICI.
amici.petab.sbml_import	
amici.petab.simulations	Functionality related to simulation of PEtab problems.
amici.petab.simulator	PEtab Simulator Functionality related to the use of AMICI for simulation with petab.Simulator.
amici.petab_import	PEtab Import Import a model in the petab (https://github.com/PEtab-dev/PEtab) format into AMICI.
amici.petab_import_pysb	PEtab import for PySB models
amici.petab_objective	Evaluate a PEtab objective function.
amici.petab_simulate	Simulate a PEtab problem
amici.import_utils	Miscellaneous functions related to model import, independent of any specific model format

continues on next page

Table 2 – continued from previous page

amici.de_export	C++ Export This module provides all necessary functionality to specify a differential equation model and generate executable C++ simulation code. The user generally won't have to directly call any function from this module as this will be done by amici.pysb_import.pysb2amici(), amici.sbml_import.SbmlImporter.sbml2amici() and amici.petab_import.import_model().
amici.de_model	Symbolic differential equation model.
amici.de_model_components	Objects for AMICI's internal differential equation model representation
amici.plotting	Plotting Plotting related functions
amici.pandas	Pandas Wrappers This module contains convenience wrappers that allow for easy interconversion between C++ objects from amici.amici and pandas DataFrames
amici.logging	Logging This module provides custom logging functionality for other amici modules
amici.gradient_check	Finite Difference Check This module provides functions to automatically check correctness of amici computed sensitivities using finite difference approximations
amici.parameter_mapping	Parameter mapping between AMICI and PEtab.
amici.conserved_quantities_demartino	
amici.conserved_quantities_rref	Find conserved quantities deterministically
amici.numpy	C++ object views This module provides views on C++ objects for efficient access.
amici.sbml_utils	SBML Utilities This module provides helper functions for working with SBML.
amici.splines	Splines This module provides helper functions for reading/writing splines with AMICI annotations from/to SBML files and for adding such splines to the AMICI C++ code.

10.5.1 amici

AMICI

The AMICI Python module provides functionality for importing SBML or PySB models and turning them into C++ Python extensions.

Module Attributes

amici_path	absolute root path of the amici repository or Python package
amiciSwigPath	absolute path of the amici swig directory
amiciSrcPath	absolute path of the amici source directory
amiciModulePath	absolute root path of the amici module
hdf5_enabled	boolean indicating if amici was compiled with hdf5 support

Functions

import_model_module(module_name, module_path)	Import Python module of an AMICI model

Classes

ModelModule(*args, **kwargs)	Type of AMICI-generated model modules.
add_path(path)	Context manager for temporarily changing PYTHONPATH

Exceptions

AmiciVersionError	Error thrown if an AMICI model is loaded that is incompatible with the installed AMICI base package

exception amici.**AmiciVersionError**

Error thrown if an AMICI model is loaded that is incompatible with the installed AMICI base package

class amici.**ModelModule**(**args*, ***kwargs*)

Type of AMICI-generated model modules.

To enable static type checking.

__init__(**args*, ***kwargs*)

getModel()

Create a model instance.

Return type
amici.amici.Model

get_model()

Create a model instance.

Return type
amici.amici.Model

class amici.**add_path**(*path*)

Context manager for temporarily changing PYTHONPATH

__init__(*path*)

amici.**amiciModulePath = '/home/docs/checkouts/readthedocs.org/user_builds/amici/checkouts/v0.23.0/python/sdist/amici'**

absolute root path of the amici module

amici.**amiciSrcPath = '/home/docs/checkouts/readthedocs.org/user_builds/amici/checkouts/v0.23.0/python/sdist/amici/src'**

absolute path of the amici source directory

amici.**amiciSwigPath = '/home/docs/checkouts/readthedocs.org/user_builds/amici/checkouts/v0.23.0/python/sdist/amici/swig'**

absolute path of the amici swig directory

amici.**amici_path = '/home/docs/checkouts/readthedocs.org/user_builds/amici/checkouts/v0.23.0/python/sdist/amici'**

absolute root path of the amici repository or Python package

amici.**hdf5_enabled: bool = False**

boolean indicating if amici was compiled with hdf5 support

amici.**import_model_module**(*module_name*, *module_path*)

Import Python module of an AMICI model

Parameters

- **module_name** (str) – Name of the python package of the model
- **module_path** (typing.Union[pathlib.Path, str]) – Absolute or relative path of the package directory

Return type
amici.ModelModule

Returns
The model module

10.5.2 amici.amici

Core C++ bindings

This module encompasses the complete public C++ API of AMICI, which was exposed via swig. All functions listed here are directly accessible in the main amici package, i.e., *amici.amici.ExpData* is available as `amici.ExpData`. Usage of functions and classes from the base `amici` package is generally recommended as they often include convenience wrappers that avoid common pitfalls when accessing C++ types from python and implement some nonstandard type conversions.

Module Attributes

SensitivityOrder_none	Don't compute sensitivities.
SensitivityOrder_first	First-order sensitivities.
SensitivityOrder_second	Second-order sensitivities.
SensitivityMethod_none	Don't compute sensitivities.
SensitivityMethod_forward	Forward sensitivity analysis.
SensitivityMethod_adjoint	Adjoint sensitivity analysis.
NonlinearSolverIteration_fixedpoint	deprecated

Functions

compiledWithOpenMP()	AMICI extension was compiled with OpenMP?
enum(prefix)	
getScaledParameter(unscaledParameter, scaling)	Apply parameter scaling according to *scaling*
getUnscaledParameter(scaledParameter, scaling)	Remove parameter scaling according to *scaling*
parameterScalingFromIntVector(intVec)	Swig-Generated class, which, in contrast to other Vector classes, does not allow for simple interoperability with common Python types, but must be created using *amici.amici.parameterScalingFromIntVector()*
runAmiciSimulation(solver, edata, model[, ...])	Core integration routine.
runAmiciSimulations(solver, edatas, model, ...)	Same as runAmiciSimulation, but for multiple ExpData instances.
scaleParameters(bufferUnscaled, pscale, ...)	Apply parameter scaling according to *scaling*
simulation_status_to_str(status)	Get the string representation of the given simulation status code (see ReturnData::status).
unscaleParameters(bufferScaled, pscale, ...)	Remove parameter scaling according to the parameter scaling in pscale

Classes

BoolVector(*args)	Swig-Generated class templating common python types including `Iterable` [`bool`] and `numpy.array` [`bool`] to facilitate interfacing with C++ bindings.
Constraint(value[, names, module, qualname, ...])	
CpuTimer()	Tracks elapsed CPU time using std::clock.
DoubleVector(*args)	Swig-Generated class templating common python types including `Iterable` [`float`] and `numpy.array` [`float`] to facilitate interfacing with C++ bindings.
ExpData(*args)	ExpData carries all information about experimental or condition-specific data.
ExpDataPtr(*args)	Swig-Generated class that implements smart pointers to ExpData as objects.

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Table 3 – continued from previous page

ExpDataPtrVector(*args)	Swig-Generated class templating common python types including `Iterable` [*amici.amici.ExpData*] and `numpy.array` [*amici.amici.ExpData*] to facilitate interfacing with C++ bindings.
FixedParameterContext(value[, names, ...])	
IntVector(*args)	Swig-Generated class templating common python types including `Iterable` [`int`] and `numpy.array` [`int`] to facilitate interfacing with C++ bindings.
InternalSensitivityMethod(value[, names, ...])	
InterpolationType(value[, names, module, ...])	
LinearMultistepMethod(value[, names, ...])	
LinearSolver(value[, names, module, ...])	
LogItem(*args)	A log item.
LogItemVector(*args)	
Model(*args, **kwargs)	The Model class represents an AMICI ODE/DAE model.
ModelDimensions(*args)	Container for model dimensions.
ModelPtr(*args)	Swig-Generated class that implements smart pointers to Model as objects.
NewtonDampingFactorMode(value[, names, ...])	
NonlinearSolverIteration(value[, names, ...])	
ObservableScaling(value[, names, module, ...])	
ParameterScaling(value[, names, module, ...])	
ParameterScalingVector(*args)	
RDataReporting(value[, names, module, ...])	
ReturnData(*args)	Stores all data to be returned by *amici.amici.runAmiciSimulation()*.
ReturnDataPtr(*args)	Swig-Generated class that implements smart pointers to ReturnData as objects.
SecondOrderMode(value[, names, module, ...])	
SensitivityMethod(value[, names, module, ...])	
SensitivityOrder(value[, names, module, ...])	
SimulationParameters(*args)	Container for various simulation parameters.
Solver(*args, **kwargs)	The Solver class provides a generic interface to CVODES and IDAS solvers, individual realizations are realized in the CVodeSolver and the IDASolver class.

continues on next page

Table 3 – continued from previous page

SolverPtr(*args)	Swig-Generated class that implements smart pointers to Solver as objects.
SteadyStateComputationMode(value[, names, ...])	
SteadyStateSensitivityMode(value[, names, ...])	
SteadyStateStatus(value[, names, module, ...])	
SteadyStateStatusVector(*args)	
StringDoubleMap(*args)	Swig-Generated class templating `Dict` [`str`, `float`] to facilitate interfacing with C++ bindings.
StringVector(*args)	Swig-Generated class templating common python types including `Iterable` [`str`] and `numpy.array` [`str`] to facilitate interfacing with C++ bindings.

class amici.amici.**BoolVector**(**args*)

Swig-Generated class templating common python types including `Iterable` [`bool`] and `numpy.array` [`bool`] to facilitate interfacing with C++ bindings.

class amici.amici.**Constraint**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

negative = -2

non_negative = 1

non_positive = -1

none = 0

positive = 2

class amici.amici.**CpuTimer**

Tracks elapsed CPU time using std::clock.

__init__()

Constructor

elapsed_milliseconds() → float

Get elapsed CPU time in milliseconds since initialization or last reset

Return type
float

Returns
CPU time in milliseconds

elapsed_seconds() → float

Get elapsed CPU time in seconds since initialization or last reset

Return type
float

Returns
CPU time in seconds

`reset()`

Reset the timer

`uses_thread_clock = False`

Whether the timer uses a thread clock (i.e. provides proper, thread-specific CPU time).

`class amici.amici.DoubleVector(*args)`

Swig-Generated class templating common python types including `Iterable [float]` and `numpy.array [float]` to facilitate interfacing with C++ bindings.

`class amici.amici.ExpData(*args)`

ExpData carries all information about experimental or condition-specific data.

`__init__(*args)`

Overload 1:

Default constructor.

Overload 2:

Copy constructor.

Overload 3:

Constructor that only initializes dimensions.

Parameters

- **nytrue** (*int*) – Number of observables
- **nztrue** (*int*) – Number of event outputs
- **nmaxevent** (*int*) – Maximal number of events to track

Overload 4:

constructor that initializes timepoints from vectors

Parameters

- **nytrue** (*int*) – Number of observables
- **nztrue** (*int*) – Number of event outputs
- **nmaxevent** (*int*) – Maximal number of events to track
- **ts** (DoubleVector) – Timepoints (dimension: nt)

Overload 5:

constructor that initializes timepoints and fixed parameters from vectors

Parameters

- **nytrue** (*int*) – Number of observables
- **nztrue** (*int*) – Number of event outputs
- **nmaxevent** (*int*) – Maximal number of events to track
- **ts** (DoubleVector) – Timepoints (dimension: nt)
- **fixedParameters** (DoubleVector) – Model constants (dimension: nk)

Overload 6:

constructor that initializes timepoints and data from vectors

Parameters

- **nytrue** (*int*) – Number of observables
- **nztrue** (*int*) – Number of event outputs
- **nmaxevent** (*int*) – Maximal number of events to track
- **ts** (DoubleVector) – Timepoints (dimension: nt)
- **observedData** (DoubleVector) – observed data (dimension: nt x nytrue, row-major)
- **observedDataStdDev** (DoubleVector) – standard deviation of observed data (dimension: nt x nytrue, row-major)
- **observedEvents** (DoubleVector) – observed events (dimension: nmaxevents x nztrue, row-major)
- **observedEventsStdDev** (DoubleVector) – standard deviation of observed events/roots (dimension: nmaxevents x nztrue, row-major)

Overload 7:

constructor that initializes with Model

Parameters

model (*Model*) – pointer to model specification object

Overload 8:

constructor that initializes with returnData, adds noise according to specified sigmas

Parameters

- **rdata** (*ReturnData*) – return data pointer with stored simulation results
- **sigma_y** (*float*) – scalar standard deviations for all observables
- **sigma_z** (*float*) – scalar standard deviations for all event observables

Overload 9:

constructor that initializes with returnData, adds noise according to specified sigmas

Parameters

- **rdata** (*ReturnData*) – return data pointer with stored simulation results
- **sigma_y** (DoubleVector) – vector of standard deviations for observables (dimension: nytrue or nt x nytrue, row-major)
- **sigma_z** (DoubleVector) – vector of standard deviations for event observables (dimension: nztrue or nmaxevent x nztrue, row-major)

clear_observations()

Set all observations and their standard deviations to NaN.

Useful, e.g., after calling ExpData::setTimepoints.

property fixedParameters

Model constants

Vector of size Model::nk() or empty

property fixedParametersPreequilibration

Model constants for pre-equilibration

Vector of size Model::nk() or empty.

property fixedParametersPresimulation

Model constants for pre-simulation

Vector of size Model::nk() or empty.

getObservedData() → tuple[float]

Get all measurements.

Return type
DoubleVector

Returns
observed data (dimension: nt x nytrue, row-major)

getObservedDataPtr(*it: int*) → amici::realtype const *

Get measurements for a given timepoint index.

Parameters
it (int) – timepoint index

Return type
float

Returns
pointer to observed data at index (dimension: nytrue)

`getObservedDataStdDev()` → tuple[float]

Get measurement standard deviations.

Return type
DoubleVector

Returns
standard deviation of observed data

`getObservedDataStdDevPtr`(*it: int*) → amici::realtype const *

Get pointer to measurement standard deviations.

Parameters
it (int) – timepoint index

Return type
float

Returns
pointer to standard deviation of observed data at index

`getObservedEvents()` → tuple[float]

Get observed event data.

Return type
DoubleVector

Returns
observed event data

`getObservedEventsPtr`(*ie: int*) → amici::realtype const *

Get pointer to observed data at ie-th occurrence.

Parameters
ie (int) – event occurrence

Return type
float

Returns
pointer to observed event data at ie-th occurrence

`getObservedEventsStdDev()` → tuple[float]

Get standard deviation of observed event data.

Return type
DoubleVector

Returns
standard deviation of observed event data

`getObservedEventsStdDevPtr`(*ie: int*) → amici::realtype const *

Get pointer to standard deviation of observed event data at ie-th occurrence.

Parameters
ie (int) – event occurrence

Return type
float

Returns
pointer to standard deviation of observed event data at ie-th occurrence

`getTimepoint`(*it: int*) → float

Get timepoint for the given index

Parameters
it (int) – timepoint index

Return type
float

Returns
timepoint timepoint at index

`getTimepoints`() → tuple[float]

Get output timepoints.

Return type
DoubleVector

Returns
ExpData::ts

`property id`

Arbitrary (not necessarily unique) identifier.

`isSetObservedData`(*it: int*, *iy: int*) → bool

Whether there is a measurement for the given time- and observable- index.

Parameters

- **it** (int) – time index
- **iy** (int) – observable index

Return type
boolean

Returns
boolean specifying if data was set

`isSetObservedDataStdDev`(*it: int*, *iy: int*) → bool

Whether standard deviation for a measurement at specified timepoint- and observable index has been set.

Parameters

- **it** (int) – time index
- **iy** (int) – observable index

Return type
boolean

Returns
boolean specifying if standard deviation of data was set

`isSetObservedEvents`(*ie: int*, *iz: int*) → bool

Check whether event data at specified indices has been set.

Parameters

- **ie** (int) – event index
- **iz** (int) – event observable index

Return type
boolean

Returns
boolean specifying if data was set

isSetObservedEventsStdDev(*ie: int*, *iz: int*) → bool

Check whether standard deviation of event data at specified indices has been set.

Parameters

- **ie** (int) – event index
- **iz** (int) – event observable index

Return type
boolean

Returns
boolean specifying if standard deviation of event data was set

nmaxevent() → int

maximal number of events to track

Return type
int

Returns
maximal number of events to track

nt() → int

number of timepoints

Return type
int

Returns
number of timepoints

nytrue() → int

number of observables of the non-augmented model

Return type
int

Returns
number of observables of the non-augmented model

nztrue() → int

number of event observables of the non-augmented model

Return type
int

Returns
number of event observables of the non-augmented model

property parameters

Model parameters

Vector of size Model::np() or empty with parameter scaled according to SimulationParameter::pscale.

property plist

Parameter indices w.r.t. which to compute sensitivities

property pscale

Parameter scales

Vector of parameter scale of size Model::np(), indicating how/if each parameter is to be scaled.

property reinitialization_state_idxs_presim

Indices of states to be reinitialized based on provided presimulation constants / fixed parameters.

property reinitialization_state_idxs_sim

Indices of states to be reinitialized based on provided constants / fixed parameters.

reinitializeAllFixedParameterDependentInitialStates(*nx_rdata: int*)

Set reinitialization of all states based on model constants for all simulation phases.

Convenience function to populate *reinitialization_state_idxs_presim* and *reinitialization_state_idxs_sim*

Parameters
nx_rdata (int) – Number of states (Model::nx_rdata)

reinitializeAllFixedParameterDependentInitialStatesForPresimulation(*nx_rdata: int*)

Set reinitialization of all states based on model constants for presimulation (only meaningful if preequilibration is performed).

Convenience function to populate *reinitialization_state_idxs_presim* and *reinitialization_state_idxs_sim*

Parameters
nx_rdata (int) – Number of states (Model::nx_rdata)

reinitializeAllFixedParameterDependentInitialStatesForSimulation(*nx_rdata: int*)

Set reinitialization of all states based on model constants for the 'main' simulation (only meaningful if presimulation or preequilibration is performed).

Convenience function to populate *reinitialization_state_idxs_presim* and *reinitialization_state_idxs_sim*

Parameters
nx_rdata (int) – Number of states (Model::nx_rdata)

property reinitializeFixedParameterInitialStates

Flag indicating whether reinitialization of states depending on fixed parameters is activated

setObservedData(**args*)

Overload 1:

Set all measurements.

Parameters
observedData (DoubleVector) – observed data (dimension: nt x nytrue, row-major)

Overload 2:

Set measurements for a given observable index

Parameters

- **observedData** (DoubleVector) – observed data (dimension: nt)
- **iy** (*int*) – observed data index

setObservedDataStdDev(**args*)

Overload 1:

Set standard deviations for measurements.

Parameters
observedDataStdDev (DoubleVector) – standard deviation of observed data (dimension: nt x nytrue, row-major)

Overload 2:

Set identical standard deviation for all measurements.

Parameters
stdDev (*float*) – standard deviation (dimension: scalar)

Overload 3:

Set standard deviations of observed data for a specific observable index.

Parameters

- **observedDataStdDev** (DoubleVector) – standard deviation of observed data (dimension: nt)
- **iy** (*int*) – observed data index

Overload 4:

Set all standard deviation for a given observable index to the input value.

Parameters

- **stdDev** (*float*) – standard deviation (dimension: scalar)
- **iy** (*int*) – observed data index

setObservedEvents(**args*)

Overload 1:

Set observed event data.

Parameters
observedEvents (DoubleVector) – observed data (dimension: nmaxevent x nztrue, row-major)

Overload 2:

Set observed event data for specific event observable.

Parameters

- **observedEvents** (DoubleVector) – observed data (dimension: nmaxevent)
- **iz** (*int*) – observed event data index

setObservedEventsStdDev(**args*)

Overload 1:

Set standard deviation of observed event data.

Parameters
observedEventsStdDev (DoubleVector) – standard deviation of observed event data

Overload 2:

Set standard deviation of observed event data.

Parameters
stdDev (*float*) – standard deviation (dimension: scalar)

Overload 3:

Set standard deviation of observed data for a specific observable.

Parameters

- **observedEventsStdDev** (DoubleVector) – standard deviation of observed data (dimension: nmaxevent)
- **iz** (*int*) – observed data index

Overload 4:

Set all standard deviations of a specific event-observable.

Parameters

- **stdDev** (*float*) – standard deviation (dimension: scalar)
- **iz** (*int*) – observed data index

setTimepoints(*ts: Sequence[float]*)

Set output timepoints.

If the number of timepoint increases, this will grow the observation/sigma matrices and fill new entries with NaN. If the number of timepoints decreases, this will shrink the observation/sigma matrices.

Note that the mapping from timepoints to measurements will not be preserved. E.g., say there are measurements at t = 2, and this function is called with [1, 2], then the old measurements will belong to t = 1.

Parameters
ts (typing.Sequence[float]) – timepoints

property sx0

Initial state sensitivities

Dimensions: Model::nx() * Model::nplist(), Model::nx() * ExpData::plist.size(), if ExpData::plist is not empty, or empty

property t_presim

Duration of pre-simulation.

If this is > 0, presimulation will be performed from (model->t0 - t_presim) to model->t0 using the fixedParameters in fixedParametersPresimulation

property ts_

Timepoints for which model state/outputs/... are requested

Vector of timepoints.

property tstart_

Starting time of the simulation.

Output timepoints are absolute timepoints, independent of t_{start}. For output timepoints $t < t_{start}$, the initial state will be returned.

property x0

Initial state

Vector of size Model::nx() or empty

class amici.amici.**ExpDataPtr**(**args*)

Swig-Generated class that implements smart pointers to ExpData as objects.

property fixedParameters

Model constants

Vector of size Model::nk() or empty

property fixedParametersPreequilibration

Model constants for pre-equilibration

Vector of size Model::nk() or empty.

property fixedParametersPresimulation

Model constants for pre-simulation

Vector of size Model::nk() or empty.

property id

Arbitrary (not necessarily unique) identifier.

property parameters

Model parameters

Vector of size Model::np() or empty with parameter scaled according to SimulationParameter::pscale.

property plist

Parameter indices w.r.t. which to compute sensitivities

property pscale

Parameter scales

Vector of parameter scale of size Model::np(), indicating how/if each parameter is to be scaled.

property reinitialization_state_idxs_presim

Indices of states to be reinitialized based on provided presimulation constants / fixed parameters.

property reinitialization_state_idxs_sim

Indices of states to be reinitialized based on provided constants / fixed parameters.

property reinitializeFixedParameterInitialStates

Flag indicating whether reinitialization of states depending on fixed parameters is activated

property sx0

Initial state sensitivities

Dimensions: Model::nx() * Model::nplist(), Model::nx() * ExpData::plist.size(), if ExpData::plist is not empty, or empty

property t_presim

Duration of pre-simulation.

If this is > 0, presimulation will be performed from (model->t0 - t_presim) to model->t0 using the fixedParameters in fixedParametersPresimulation

property ts_

Timepoints for which model state/outputs/... are requested

Vector of timepoints.

property tstart_

Starting time of the simulation.

Output timepoints are absolute timepoints, independent of t_{start}. For output timepoints $t < t_{start}$, the initial state will be returned.

property x0

Initial state

Vector of size Model::nx() or empty

class amici.amici.**ExpDataPtrVector**(**args*)

Swig-Generated class templating common python types including `Iterable` [*amici.amici.ExpData*] and `numpy.array` [*amici.amici.ExpData*] to facilitate interfacing with C++ bindings.

class amici.amici.**FixedParameterContext**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

preequilibration = 1

presimulation = 2

simulation = 0

class amici.amici.**IntVector**(**args*)

Swig-Generated class templating common python types including `Iterable` [`int`] and `numpy.array` [`int`] to facilitate interfacing with C++ bindings.

class amici.amici.**InternalSensitivityMethod**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

simultaneous = 1

staggered = 2

staggered1 = 3

class amici.amici.**InterpolationType**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

hermite = 1

polynomial = 2

class amici.amici.**LinearMultistepMethod**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

BDF = 2

__init__(**args*, ***kwds*)

adams = 1

class amici.amici.**LinearSolver**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

KLU = 9

LAPACKBand = 4

LAPACKDense = 3

SPBCG = 7

SPGMR = 6

SPTFQMR = 8

SuperLUMT = 10

__init__(**args*, ***kwds*)

band = 2

dense = 1

diag = 5

class amici.amici.**LogItem**(**args*)

A log item.

__init__(**args*)

Overload 1:

Default ctor.

Overload 2:

Construct a LogItem

Parameters

- **severity** (*int*) –
- **identifier** (*str*) –
- **message** (*str*) –

property identifier

Short identifier for the logged event

property message

A more detailed and readable message

property severity

Severity level

class amici.amici.**LogItemVector**(**args*)

class amici.amici.**Model**(**args*, ***kwargs*)

The Model class represents an AMICI ODE/DAE model.

The model can compute various model related quantities based on symbolically generated code.

__init__(**args*, ***kwargs*)

Overload 1:

Default ctor

Overload 2:

Constructor with model dimensions

Parameters

- **nx_rdata** (*int*) – Number of state variables
- **nxtrue_rdata** (*int*) – Number of state variables of the non-augmented model
- **nx_solver** (*int*) – Number of state variables with conservation laws applied
- **nxtrue_solver** (*int*) – Number of state variables of the non-augmented model with conservation laws applied
- **nx_solver_reinit** (*int*) – Number of state variables with conservation laws subject to reinitialization
- **np** (*int*) – Number of parameters
- **nk** (*int*) – Number of constants
- **ny** (*int*) – Number of observables
- **nytrue** (*int*) – Number of observables of the non-augmented model
- **nz** (*int*) – Number of event observables
- **nztrue** (*int*) – Number of event observables of the non-augmented model
- **ne** (*int*) – Number of events
- **ne_solver** (*int*) – Number of events that require root-finding
- **nspl** (*int*) – Number of splines
- **nJ** (*int*) – Number of objective functions
- **nw** (*int*) – Number of repeating elements
- **ndwdx** (*int*) – Number of nonzero elements in the x derivative of the repeating elements
- **ndwdp** (*int*) – Number of nonzero elements in the p derivative of the repeating elements
- **ndwdw** (*int*) – Number of nonzero elements in the w derivative of the repeating elements
- **ndxdotdw** (*int*) – Number of nonzero elements in the w derivative of $xdot$
- **ndJydy** (*IntVector*) – Number of nonzero elements in the y derivative of dJy (shape *nytrue*)
- **ndxrdatadxsolver** (*int*) – Number of nonzero elements in the x derivative of x_rdata
- **ndxrdatadtcl** (*int*) – Number of nonzero elements in the tcl derivative of x_rdata
- **ndtotal_cldx_rdata** (*int*) – Number of nonzero elements in the x_rdata derivative of $total_cl$
- **nnz** (*int*) – Number of nonzero elements in Jacobian
- **ubw** (*int*) – Upper matrix bandwidth in the Jacobian
- **lbw** (*int*) – Lower matrix bandwidth in the Jacobian

clone() → *Model*

Clone this instance.

Return type
Model

Returns
The clone

fdsigmaydy(*dsigmaydy: Iterable[float], t: float const, p: Iterable[float], k: Iterable[float], y: Iterable[float]*)

Model-specific implementation of fsigmay

Parameters

- **dsigmaydy** (typing.Iterable[float]) – partial derivative of standard deviation of measurements w.r.t. model outputs
- **t** (float) – current time
- **p** (typing.Iterable[float]) – parameter vector
- **k** (typing.Iterable[float]) – constant vector
- **y** (typing.Iterable[float]) – model output at timepoint t

fdspline_slopesdp(*dspline_slopesdp: Iterable[float], p: Iterable[float], k: Iterable[float], ip: int const*)

Model-specific implementation the parametric derivatives of slopevalues at spline nodes

Parameters

- **dspline_slopesdp** (typing.Iterable[float]) – vector to which derivatives will be written
- **p** (typing.Iterable[float]) – parameter vector
- **k** (typing.Iterable[float]) – constants vector
- **ip** (int) – Sensitivity index

fdspline_valuesdp(*dspline_valuesdp: Iterable[float], p: Iterable[float], k: Iterable[float], ip: int const*)

Model-specific implementation the parametric derivatives of spline node values

Parameters

- **dspline_valuesdp** (typing.Iterable[float]) – vector to which derivatives will be written
- **p** (typing.Iterable[float]) – parameter vector
- **k** (typing.Iterable[float]) – constants vector
- **ip** (int) – Sensitivity index

fdtotal_cldp(*dtotal_cldp: Iterable[float], x_rdata: Iterable[float], p: Iterable[float], k: Iterable[float], ip: int const*)

Compute dtotal_cl / dp

Parameters

- **dtotal_cldp** (typing.Iterable[float]) – dtotal_cl / dp
- **x_rdata** (typing.Iterable[float]) – State variables with conservation laws applied
- **p** (typing.Iterable[float]) – parameter vector
- **k** (typing.Iterable[float]) – constant vector
- **ip** (int) – Sensitivity index

fdtotal_cldx_rdata(*dtotal_cldx_rdata: Iterable[float], x_rdata: Iterable[float], p: Iterable[float], k: Iterable[float], tcl: Iterable[float]*)

Compute dtotal_cl / dx_rdata

Parameters

- **dtotal_cldx_rdata** (typing.Iterable[float]) – dtotal_cl / dx_rdata

- **x_rdata** (typing.Iterable[float]) – State variables with conservation laws applied
- **p** (typing.Iterable[float]) – parameter vector
- **k** (typing.Iterable[float]) – constant vector
- **tcl** (typing.Iterable[float]) – Total abundances for conservation laws

fdx_rdatadp(*dx_rdatadp: Iterable[float], x: Iterable[float], tcl: Iterable[float], p: Iterable[float], k: Iterable[float], ip: int const*)

Compute dx_rdata / dp

Parameters

- **dx_rdatadp** (typing.Iterable[float]) – dx_rdata / dp
- **p** (typing.Iterable[float]) – parameter vector
- **k** (typing.Iterable[float]) – constant vector
- **x** (typing.Iterable[float]) – State variables with conservation laws applied
- **tcl** (typing.Iterable[float]) – Total abundances for conservation laws
- **ip** (int) – Sensitivity index

fdx_rdatadtcl(*dx_rdatadtcl: Iterable[float], x: Iterable[float], tcl: Iterable[float], p: Iterable[float], k: Iterable[float]*)

Compute dx_rdata / dtcl

Parameters

- **dx_rdatadtcl** (typing.Iterable[float]) – dx_rdata / dtcl
- **p** (typing.Iterable[float]) – parameter vector
- **k** (typing.Iterable[float]) – constant vector
- **x** (typing.Iterable[float]) – State variables with conservation laws applied
- **tcl** (typing.Iterable[float]) – Total abundances for conservation laws

fdx_rdatadx_solver(*dx_rdatadx_solver: Iterable[float], x: Iterable[float], tcl: Iterable[float], p: Iterable[float], k: Iterable[float]*)

Compute dx_rdata / dx_solver

Parameters

- **dx_rdatadx_solver** (typing.Iterable[float]) – dx_rdata / dx_solver
- **p** (typing.Iterable[float]) – parameter vector
- **k** (typing.Iterable[float]) – constant vector
- **x** (typing.Iterable[float]) – State variables with conservation laws applied
- **tcl** (typing.Iterable[float]) – Total abundances for conservation laws

getAddSigmaResiduals() → bool

Checks whether residuals should be added to account for parameter dependent sigma.

Return type
boolean

Returns
sigma_res

getAlwaysCheckFinite() → bool

Get setting of whether the result of every call to *Model::f** should be checked for finiteness.

Return type
boolean

Returns
that

getAmiciCommit() → str

Returns the AMICI commit that was used to generate the model

Return type
str

Returns
AMICI commit string

getAmiciVersion() → str

Returns the AMICI version that was used to generate the model

Return type
str

Returns
AMICI version string

getExpressionIds() → tuple[str]

Get IDs of the expression.

Return type
StringVector

Returns
Expression IDs

getExpressionNames() → tuple[str]

Get names of the expressions.

Return type
StringVector

Returns
Expression names

getFixedParameterById(*par_id: str*) → float

Get value of fixed parameter with the specified ID.

Parameters
par_id (str) – Parameter ID

Return type
float

Returns
Parameter value

getFixedParameterByName(*par_name: str*) → float

Get value of fixed parameter with the specified name.

If multiple parameters have the same name, the first parameter with matching name is returned.

Parameters
par_name (str) – Parameter name

Return type
float

Returns
Parameter value

getFixedParameterIds() → tuple[str]

Get IDs of the fixed model parameters.

Return type
StringVector

Returns
Fixed parameter IDs

getFixedParameterNames() → tuple[str]

Get names of the fixed model parameters.

Return type
StringVector

Returns
Fixed parameter names

getFixedParameters() → tuple[float]

Get values of fixed parameters.

Return type
DoubleVector

Returns
Vector of fixed parameters with same ordering as in Model::getFixedParameterIds

getInitialStateSensitivities() → tuple[float]

Get the initial states sensitivities.

Return type
DoubleVector

Returns
vector of initial state sensitivities

getInitialStates() → tuple[float]

Get the initial states.

Return type
DoubleVector

Returns
Initial state vector

getMinimumSigmaResiduals() → float

Gets the specified estimated lower boundary for sigma_y.

Return type
float

Returns
lower boundary

getName() → str

Get the model name.

Return type
str

Returns
Model name

getObservableIds() → tuple[str]

Get IDs of the observables.

Return type
StringVector

Returns
Observable IDs

getObservableNames() → tuple[str]

Get names of the observables.

Return type
StringVector

Returns
Observable names

getObservableScaling(*iy: int*) → *ObservableScaling*

Get scaling type for observable

Parameters
iy (int) – observable index

Return type
int

Returns
scaling type

getParameterById(*par_id: str*) → float

Get value of first model parameter with the specified ID.

Parameters
par_id (str) – Parameter ID

Return type
float

Returns
Parameter value

getParameterByName(*par_name: str*) → float

Get value of first model parameter with the specified name.

Parameters
par_name (str) – Parameter name

Return type
float

Returns
Parameter value

getParameterIds() → tuple[str]

Get IDs of the model parameters.

Return type
StringVector

Returns
Parameter IDs

getParameterList() → tuple[int]

Get the list of parameters for which sensitivities are computed.

Return type
IntVector

Returns
List of parameter indices

getParameterNames() → tuple[str]

Get names of the model parameters.

Return type
StringVector

Returns
The parameter names

getParameterScale() → *ParameterScalingVector*

Get parameter scale for each parameter.

Return type
ParameterScalingVector

Returns
Vector of parameter scales

getParameters() → tuple[float]

Get parameter vector.

Return type
DoubleVector

Returns
The user-set parameters (see also *Model::getUnscaledParameters*)

getReinitializationStateIdxs() → tuple[int]

Return indices of states to be reinitialized based on provided constants / fixed parameters

Return type
IntVector

Returns
Those indices.

getReinitializeFixedParameterInitialStates() → bool

Get whether initial states depending on fixedParameters are to be reinitialized after preequilibration and presimulation.

Return type
boolean

Returns
flag *true* / *false*

`getSolver()` → *Solver*

Retrieves the solver object

Return type
Solver

Returns
The Solver instance

`getStateIds()` → tuple[str]

Get IDs of the model states.

Return type
StringVector

Returns
State IDs

`getStateIdsSolver()` → tuple[str]

Get IDs of the solver states.

Return type
StringVector

Returns
State IDs

`getStateIsNonNegative()` → tuple[bool]

Get flags indicating whether states should be treated as non-negative.

Return type
BoolVector

Returns
Vector of flags

`getStateNames()` → tuple[str]

Get names of the model states.

Return type
StringVector

Returns
State names

`getStateNamesSolver()` → tuple[str]

Get names of the solver states.

Return type
StringVector

Returns
State names

`getSteadyStateComputationMode()` → amici::SteadyStateComputationMode

Gets the mode how steady state is computed in the steadystate simulation.

Return type
int

Returns
Mode

`getSteadyStateSensitivityMode()` → *SteadyStateSensitivityMode*

Gets the mode how sensitivities are computed in the steadystate simulation.

Return type
SteadyStateSensitivityMode

Returns
Mode

`getTimepoint(it: int)` → float

Get simulation timepoint for time index *it*.

Parameters
it (int) – Time index

Return type
float

Returns
Timepoint

`getTimepoints()` → tuple[float]

Get the timepoint vector.

Return type
DoubleVector

Returns
Timepoint vector

`getUnscaledParameters()` → tuple[float]

Get parameters with transformation according to parameter scale applied.

Return type
DoubleVector

Returns
Unscaled parameters

`get_trigger_timepoints()` → tuple[float]

Get trigger times for events that don't require root-finding.

Return type
DoubleVector

Returns
List of unique trigger points for events that don't require root-finding (i.e. that trigger at predetermined timepoints), in ascending order.

`hasCustomInitialStateSensitivities()` → bool

Return whether custom initial state sensitivities have been set.

Return type
boolean

Returns
true if has custom initial state sensitivities, otherwise *false*.

`hasCustomInitialStates()` → bool

Return whether custom initial states have been set.

Return type
boolean

Returns
true if has custom initial states, otherwise *false*

`hasExpressionIds()` → bool

Report whether the model has expression IDs set.

Return type
boolean

Returns
Boolean indicating whether expression ids were set. Also returns *true* if the number of corresponding variables is just zero.

`hasExpressionNames()` → bool

Report whether the model has expression names set.

Return type
boolean

Returns
Boolean indicating whether expression names were set. Also returns *true* if the number of corresponding variables is just zero.

`hasFixedParameterIds()` → bool

Report whether the model has fixed parameter IDs set.

Return type
boolean

Returns
Boolean indicating whether fixed parameter IDs were set. Also returns *true* if the number of corresponding variables is just zero.

`hasFixedParameterNames()` → bool

Report whether the model has fixed parameter names set.

Return type
boolean

Returns
Boolean indicating whether fixed parameter names were set. Also returns *true* if the number of corresponding variables is just zero.

`hasObservableIds()` → bool

Report whether the model has observable IDs set.

Return type
boolean

Returns
Boolean indicating whether observable ids were set. Also returns *true* if the number of corresponding variables is just zero.

`hasObservableNames()` → bool

Report whether the model has observable names set.

Return type
boolean

Returns
Boolean indicating whether observable names were set. Also returns *true* if the number of corresponding variables is just zero.

`hasParameterIds()` → bool

Report whether the model has parameter IDs set.

Return type
boolean

Returns
Boolean indicating whether parameter IDs were set. Also returns *true* if the number of corresponding variables is just zero.

`hasParameterNames()` → bool

Report whether the model has parameter names set.

Return type
boolean

Returns
Boolean indicating whether parameter names were set. Also returns *true* if the number of corresponding variables is just zero.

`hasQuadraticLLH()` → bool

Checks whether the defined noise model is gaussian, i.e., the nllh is quadratic

Return type
boolean

Returns
boolean flag

`hasStateIds()` → bool

Report whether the model has state IDs set.

Return type
boolean

Returns
Boolean indicating whether state IDs were set. Also returns *true* if the number of corresponding variables is just zero.

`hasStateNames()` → bool

Report whether the model has state names set.

Return type
boolean

Returns
Boolean indicating whether state names were set. Also returns *true* if the number of corresponding variables is just zero.

`property idlist`

Flag array for DAE equations

initializeSplineSensitivities()

Initialization of spline sensitivity functions

initializeSplines()

Initialization of spline functions

isFixedParameterStateReinitializationAllowed() → bool

Function indicating whether reinitialization of states depending on fixed parameters is permissible

Return type
boolean

Returns
flag indicating whether reinitialization of states depending on fixed parameters is permissible

k() → double const *

Get fixed parameters.

Return type
float

Returns
Pointer to constants array

property lbw

Lower bandwidth of the Jacobian

property logger

Logger

property nJ

Dimension of the augmented objective function for 2nd order ASA

nMaxEvent() → int

Get maximum number of events that may occur for each type.

Return type
int

Returns
Maximum number of events that may occur for each type

ncl() → int

Get number of conservation laws.

Return type
int

Returns
Number of conservation laws (i.e., difference between *nx_rdata* and *nx_solver*).

property ndJydy

Number of nonzero elements in the y derivative of dJy (dimension *nytrue*)

property ndtotal_cldx_rdata

Number of nonzero elements in the $x_r data$ derivative of $total_c l$

property ndwdp

Number of nonzero elements in the *p* derivative of the repeating elements

property ndwdw

Number of nonzero elements in the w derivative of the repeating elements

property ndwdx

Number of nonzero elements in the x derivative of the repeating elements

property ndxdotdw

Number of nonzero elements in the w derivative of $xdot$

property ndxrdatadtcl

Number of nonzero elements in the tcl derivative of x_rdata

property ndxrdatadxsolver

Number of nonzero elements in the x derivative of x_rdata

property ne

Number of events

property ne_solver

Number of events that require root-finding

nk() → int

Get number of constants

Return type
int

Returns
Length of constant vector

property nnz

Number of nonzero entries in Jacobian

np() → int

Get total number of model parameters.

Return type
int

Returns
Length of parameter vector

nplist() → int

Get number of parameters wrt to which sensitivities are computed.

Return type
int

Returns
Length of sensitivity index vector

property nspl

Number of spline functions in the model

nt() → int

Get number of timepoints.

Return type
int

Returns
Number of timepoints

property nw

Number of common expressions

property nx_rdata

Number of states

nx_reinit() → int

Get number of solver states subject to reinitialization.

Return type
int

Returns
Model member *nx_solver_reinit*

property nx_solver

Number of states with conservation laws applied

property nx_solver_reinit

Number of solver states subject to reinitialization

property nxtrue_rdata

Number of states in the unaugmented system

property nxtrue_solver

Number of states in the unaugmented system with conservation laws applied

property ny

Number of observables

property nytrue

Number of observables in the unaugmented system

property nz

Number of event outputs

property nztrue

Number of event outputs in the unaugmented system

property o2mode

Flag indicating whether for *amici::Solver::sensi_ == amici::SensitivityOrder::second* directional or full second order derivative will be computed

plist(*pos: int***)** → int

Get entry in parameter list by index.

Parameters
pos (int) – Index in sensitivity parameter list

Return type
int

Returns
Index in parameter list

property pythonGenerated

Flag indicating Matlab- or Python-based model generation

requireSensitivitiesForAllParameters()

Require computation of sensitivities for all parameters p [0..np[in natural order.

NOTE: Resets initial state sensitivities.

setAddSigmaResiduals(*sigma_res: bool*)

Specifies whether residuals should be added to account for parameter dependent sigma.

If set to true, additional residuals of the form $\sqrt{\log(\sigma) + C}$ will be added. This enables least-squares optimization for variables with Gaussian noise assumption and parameter dependent standard deviation sigma. The constant C can be set via *setMinimumSigmaResiduals()*.

Parameters
sigma_res (bool) – if true, additional residuals are added

setAllStatesNonNegative()

Set flags indicating that all states should be treated as non-negative.

setAlwaysCheckFinite(*alwaysCheck: bool*)

Set whether the result of every call to *Model::f** should be checked for finiteness.

Parameters
alwaysCheck (bool) –

setFixedParameterById(*par_id: str*, *value: float*)

Set value of first fixed parameter with the specified ID.

Parameters

- **par_id** (str) – Fixed parameter id
- **value** (float) – Fixed parameter value

setFixedParameterByName(*par_name: str*, *value: float*)

Set value of first fixed parameter with the specified name.

Parameters

- **par_name** (str) – Fixed parameter ID
- **value** (float) – Fixed parameter value

setFixedParameters(*k: Sequence[float]*)

Set values for constants.

Parameters
k (typing.Sequence[float]) – Vector of fixed parameters

setFixedParametersByIdRegex(*par_id_regex: str*, *value: float*) → int

Set values of all fixed parameters with the ID matching the specified regex.

Parameters

- **par_id_regex** (str) – Fixed parameter name regex
- **value** (float) – Fixed parameter value

Return type
int

Returns
Number of fixed parameter IDs that matched the regex

setFixedParametersByNameRegex(*par_name_regex: str*, *value: float*) → int

Set value of all fixed parameters with name matching the specified regex.

Parameters

- **par_name_regex** (str) – Fixed parameter name regex
- **value** (float) – Fixed parameter value

Return type
int

Returns
Number of fixed parameter names that matched the regex

setInitialStateSensitivities(*sx0: Sequence[float]*)

Set the initial state sensitivities.

Parameters
sx0 (typing.Sequence[float]) – vector of initial state sensitivities with chainrule applied. This could be a slice of ReturnData::sx or ReturnData::sx0

setInitialStates(*x0: Sequence[float]*)

Set the initial states.

Parameters
x0 (typing.Sequence[float]) – Initial state vector

setMinimumSigmaResiduals(*min_sigma: float*)

Sets the estimated lower boundary for sigma_y. When *setAddSigmaResiduals()* is activated, this lower boundary must ensure that log(sigma) + min_sigma > 0.

Parameters
min_sigma (float) – lower boundary

setNMaxEvent(*nmaxevent: int*)

Set maximum number of events that may occur for each type.

Parameters
nmaxevent (int) – Maximum number of events that may occur for each type

setParameterById(**args*)

Overload 1:

Set model parameters according to the parameter IDs and mapped values.

Parameters

- **p** (StringDoubleMap) – Map of parameters IDs and values
- **ignoreErrors** (*boolean, optional*) – Ignore errors such as parameter IDs in p which are not model parameters

Overload 2:

Set value of first model parameter with the specified ID.

Parameters

- **par_id** (*str*) – Parameter ID
- **value** (*float*) – Parameter value

setParameterByName(**args*)

Overload 1:

Set value of first model parameter with the specified name.

Parameters

- **par_name** (*str*) – Parameter name
- **value** (*float*) – Parameter value

Overload 2:

Set model parameters according to the parameter name and mapped values.

Parameters

- **p** (StringDoubleMap) – Map of parameters names and values
- **ignoreErrors** (*boolean, optional*) – Ignore errors such as parameter names in p which are not model parameters

Overload 3:

Set model parameters according to the parameter name and mapped values.

Parameters

- **p** (StringDoubleMap) – Map of parameters names and values
- **ignoreErrors** – Ignore errors such as parameter names in p which are not model parameters

setParameterList(*plist: Sequence[int]*)

Set the list of parameters for which sensitivities are to be computed.

NOTE: Resets initial state sensitivities.

Parameters
plist (typing.Sequence[int]) – List of parameter indices

setParameterScale(**args*)

setParameters(*p: Sequence[float]*)

Set the parameter vector.

Parameters
p (typing.Sequence[float]) – Vector of parameters

setParametersByIdRegex(*par_id_regex: str*, *value: float*) → int

Set all values of model parameters with IDs matching the specified regular expression.

Parameters

- **par_id_regex** (str) – Parameter ID regex
- **value** (float) – Parameter value

Return type
int

Returns
Number of parameter IDs that matched the regex

setParametersByNameRegex(*par_name_regex: str*, *value: float*) → int

Set all values of all model parameters with names matching the specified regex.

Parameters

- **par_name_regex** (str) – Parameter name regex
- **value** (float) – Parameter value

Return type
int

Returns
Number of fixed parameter names that matched the regex

setReinitializationStateIdxs(*idxs: Sequence[int]*)

Set indices of states to be reinitialized based on provided constants / fixed parameters

Parameters
idxs (typing.Sequence[int]) – Array of state indices

setReinitializeFixedParameterInitialStates(*flag: bool*)

Set whether initial states depending on fixed parameters are to be reinitialized after preequilibration and presimulation.

Parameters
flag (bool) – Fixed parameters reinitialized?

setStateIsNonNegative(*stateIsNonNegative: Sequence[bool]*)

Set flags indicating whether states should be treated as non-negative.

Parameters
stateIsNonNegative (typing.Sequence[bool]) – Vector of flags

setSteadyStateComputationMode(*mode:* SteadyStateComputationMode)

Set the mode how steady state is computed in the steadystate simulation.

Parameters
mode (*amici.amici.SteadyStateComputationMode*) – Steadystate computation mode

setSteadyStateSensitivityMode(*mode:* SteadyStateSensitivityMode)

Set the mode how sensitivities are computed in the steadystate simulation.

Parameters
mode (*amici.amici.SteadyStateSensitivityMode*) – Steadystate sensitivity mode

setT0(*t0: float*)

Set simulation start time.

Output timepoints are absolute timepoints, independent of t_0. For output timepoints $t < t_0$, the initial state will be returned.

Parameters
t0 (float) – Simulation start time

setTimepoints(*ts: Sequence[float]*)

Set the timepoint vector.

Parameters
ts (typing.Sequence[float]) – New timepoint vector

setUnscaledInitialStateSensitivities(*sx0: Sequence[float]*)

Set the initial state sensitivities.

Parameters
sx0 (typing.Sequence[float]) – Vector of initial state sensitivities without chainrule applied. This could be the readin from a *model.sx0data* saved to HDF5.

property state_independent_events_

Map of trigger timepoints to event indices for events that don't require root-finding.

t0() → float

Get simulation start time.

Return type
float

Returns
Simulation start time

property ubw

Upper bandwidth of the Jacobian

class amici.amici.**ModelDimensions**(**args*)

Container for model dimensions.

Holds number of states, observables, etc.

__init__(**args*)

Overload 1:
Default ctor

Overload 2:

Constructor with model dimensions

Parameters

- **nx_rdata** (*int*) – Number of state variables
- **nxtrue_rdata** (*int*) – Number of state variables of the non-augmented model
- **nx_solver** (*int*) – Number of state variables with conservation laws applied

- **nxtrue_solver** (*int*) – Number of state variables of the non-augmented model with conservation laws applied
- **nx_solver_reinit** (*int*) – Number of state variables with conservation laws subject to reinitialization
- **np** (*int*) – Number of parameters
- **nk** (*int*) – Number of constants
- **ny** (*int*) – Number of observables
- **nytrue** (*int*) – Number of observables of the non-augmented model
- **nz** (*int*) – Number of event observables
- **nztrue** (*int*) – Number of event observables of the non-augmented model
- **ne** (*int*) – Number of events
- **ne_solver** (*int*) – Number of events that require root-finding
- **nspl** (*int*) – Number of splines
- **nJ** (*int*) – Number of objective functions
- **nw** (*int*) – Number of repeating elements
- **ndwdx** (*int*) – Number of nonzero elements in the *x* derivative of the repeating elements
- **ndwdp** (*int*) – Number of nonzero elements in the *p* derivative of the repeating elements
- **ndwdw** (*int*) – Number of nonzero elements in the *w* derivative of the repeating elements
- **ndxdotdw** (*int*) – Number of nonzero elements in the w derivative of $xdot$
- **ndJydy** (IntVector) – Number of nonzero elements in the y derivative of dJy (shape *nytrue*)
- **ndxrdatadxsolver** (*int*) – Number of nonzero elements in the x derivative of x_rdata
- **ndxrdatadtcl** (*int*) – Number of nonzero elements in the tcl derivative of x_rdata
- **ndtotal_cldx_rdata** (*int*) – Number of nonzero elements in the x_rdata derivative of $total_cl$
- **nnz** (*int*) – Number of nonzero elements in Jacobian
- **ubw** (*int*) – Upper matrix bandwidth in the Jacobian
- **lbw** (*int*) – Lower matrix bandwidth in the Jacobian

property lbw

Lower bandwidth of the Jacobian

property nJ

Dimension of the augmented objective function for 2nd order ASA

property ndJydy

Number of nonzero elements in the y derivative of dJy (dimension *nytrue*)

property ndtotal_cldx_rdata

Number of nonzero elements in the x_rdata derivative of $total_cl$

property ndwdp

Number of nonzero elements in the *p* derivative of the repeating elements

property ndwdw

Number of nonzero elements in the w derivative of the repeating elements

property ndwdx

Number of nonzero elements in the x derivative of the repeating elements

property ndxdotdw

Number of nonzero elements in the w derivative of $xdot$

property ndxrdatadtcl

Number of nonzero elements in the tcl derivative of x_rdata

property ndxrdatadxsolver

Number of nonzero elements in the x derivative of x_rdata

property ne

Number of events

property ne_solver

Number of events that require root-finding

property nk

Number of constants

property nnz

Number of nonzero entries in Jacobian

property np

Number of parameters

property nspl

Number of spline functions in the model

property nw

Number of common expressions

property nx_rdata

Number of states

property nx_solver

Number of states with conservation laws applied

property nx_solver_reinit

Number of solver states subject to reinitialization

property nxtrue_rdata

Number of states in the unaugmented system

property nxtrue_solver

Number of states in the unaugmented system with conservation laws applied

property ny

Number of observables

property nytrue

Number of observables in the unaugmented system

property nz

Number of event outputs

property nztrue

Number of event outputs in the unaugmented system

property ubw

Upper bandwidth of the Jacobian

class amici.amici.**ModelPtr**(**args*)

Swig-Generated class that implements smart pointers to Model as objects.

property idlist

Flag array for DAE equations

property lbw

Lower bandwidth of the Jacobian

property logger

Logger

property nJ

Dimension of the augmented objective function for 2nd order ASA

property ndJydy

Number of nonzero elements in the y derivative of dJy (dimension *nytrue*)

property ndtotal_cldx_rdata

Number of nonzero elements in the x_rdata derivative of $total_cl$

property ndwdp

Number of nonzero elements in the *p* derivative of the repeating elements

property ndwdw

Number of nonzero elements in the *w* derivative of the repeating elements

property ndwdx

Number of nonzero elements in the *x* derivative of the repeating elements

property ndxdotdw

Number of nonzero elements in the w derivative of $xdot$

property ndxrdatadtcl

Number of nonzero elements in the tcl derivative of x_rdata

property ndxrdatadxsolver

Number of nonzero elements in the x derivative of x_rdata

property ne

Number of events

property ne_solver

Number of events that require root-finding

property nnz

Number of nonzero entries in Jacobian

property nspl

Number of spline functions in the model

property nw

Number of common expressions

property nx_rdata

Number of states

property nx_solver

Number of states with conservation laws applied

property nx_solver_reinit

Number of solver states subject to reinitialization

property nxtrue_rdata

Number of states in the unaugmented system

property nxtrue_solver

Number of states in the unaugmented system with conservation laws applied

property ny

Number of observables

property nytrue

Number of observables in the unaugmented system

property nz

Number of event outputs

property nztrue

Number of event outputs in the unaugmented system

property o2mode

Flag indicating whether for *amici::Solver::sensi_ == amici::SensitivityOrder::second* directional or full second order derivative will be computed

property pythonGenerated

Flag indicating Matlab- or Python-based model generation

property state_independent_events_

Map of trigger timepoints to event indices for events that don't require root-finding.

property ubw

Upper bandwidth of the Jacobian

class amici.amici.**NewtonDampingFactorMode**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

off = 0

on = 1

class amici.amici.**NonlinearSolverIteration**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

fixedpoint = 1

functional = 1

newton = 2

amici.amici.**NonlinearSolverIteration_fixedpoint = 1**

deprecated

class amici.amici.**ObservableScaling**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

lin = 0

log = 1

log10 = 2

class amici.amici.**ParameterScaling**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

ln = 1

log10 = 2

none = 0

class amici.amici.**ParameterScalingVector**(**args*)

class amici.amici.**RDataReporting**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

full = 0

likelihood = 2

residuals = 1

class amici.amici.**ReturnData**(**args*)

Stores all data to be returned by *amici.amici.runAmiciSimulation()*.

NOTE: multi-dimensional arrays are stored in row-major order (C-style)

property FIM

fisher information matrix (shape *nplist* x *nplist*, row-major)

property J

Jacobian of differential equation right hand side (shape *nx* x *nx*, row-major) evaluated at *t_last*.

__init__(**args*)

Overload 1:

Default constructor

Overload 2:

Constructor

Parameters

- **ts** (DoubleVector) – see amici::SimulationParameters::ts
- **model_dimensions** (*ModelDimensions*) – Model dimensions
- **nplist** (*int*) – see amici::ModelDimensions::nplist
- **nmaxevent** (*int*) – see amici::ModelDimensions::nmaxevent
- **nt** (*int*) – see amici::ModelDimensions::nt
- **newton_maxsteps** (*int*) – see amici::Solver::newton_maxsteps
- **pscale** (ParameterScalingVector) – see amici::SimulationParameters::pscale
- **o2mode** (*int*) – see amici::SimulationParameters::o2mode
- **sensi** (SensitivityOrder) – see amici::Solver::sensi
- **sensi_meth** (SensitivityMethod) – see amici::Solver::sensi_meth
- **rdrm** (RDataReporting) – see amici::Solver::rdata_reporting
- **quadratic_llh** (*boolean*) – whether model defines a quadratic nllh and computing res, sres and FIM makes sense
- **sigma_res** (*boolean*) – indicates whether additional residuals are to be added for each sigma
- **sigma_offset** (*float*) – offset to ensure real-valuedness of sigma residuals

Overload 3:

constructor that uses information from model and solver to appropriately initialize fields

Parameters

- **solver** (*Solver*) – solver instance
- **model** (*Model*) – model instance

property chi2

χ^2 value

property cpu_time

computation time of forward solve [ms]

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property cpu_timeB

computation time of backward solve [ms]

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property cpu_time_total

total CPU time from entering runAmiciSimulation until exiting [ms]

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property id

Arbitrary (not necessarily unique) identifier.

property lbw

Lower bandwidth of the Jacobian

property llh

log-likelihood value

property messages

log messages

property nJ

Dimension of the augmented objective function for 2nd order ASA

property ndJydy

Number of nonzero elements in the y derivative of dJy (dimension *nytrue*)

property ndtotal_cldx_rdata

Number of nonzero elements in the $x_r data$ derivative of $total_c l$

property ndwdp

Number of nonzero elements in the *p* derivative of the repeating elements

property ndwdw

Number of nonzero elements in the *w* derivative of the repeating elements

property ndwdx

Number of nonzero elements in the *x* derivative of the repeating elements

property ndxdotdw

Number of nonzero elements in the w derivative of $xdot$

property ndxrdatadtcl

Number of nonzero elements in the tcl derivative of $x_r data$

property ndxrdatadxsolver

Number of nonzero elements in the x derivative of $x_r data$

property ne

Number of events

property ne_solver

Number of events that require root-finding

property newton_maxsteps

maximal number of newton iterations for steady state calculation

property nk

Number of constants

property nmaxevent

maximal number of occurring events (for every event type)

property nnz

Number of nonzero entries in Jacobian

property np

Number of parameters

property nplist

number of parameter for which sensitivities were requested

property nspl

Number of spline functions in the model

property nt

number of considered timepoints

property numerrtestfails

number of error test failures forward problem (shape *nt*)

property numerrtestfailsB

number of error test failures backward problem (shape *nt*)

property numnonlinsolvconvfails

number of linear solver convergence failures forward problem (shape *nt*)

property numnonlinsolvconvfailsB

number of linear solver convergence failures backward problem (shape *nt*)

property numrhsevals

number of right hand side evaluations forward problem (shape *nt*)

property numrhsevalsB

number of right hand side evaluations backward problem (shape *nt*)

property numsteps

number of integration steps forward problem (shape *nt*)

property numstepsB

number of integration steps backward problem (shape *nt*)

property nw

Number of common expressions

property nx

number of states (alias *nx_rdata*, kept for backward compatibility)

property nx_rdata

Number of states

property nx_solver

Number of states with conservation laws applied

property nx_solver_reinit

Number of solver states subject to reinitialization

property nxtrue

number of states in the unaugmented system (alias nxtrue_rdata, kept for backward compatibility)

property nxtrue_rdata

Number of states in the unaugmented system

property nxtrue_solver

Number of states in the unaugmented system with conservation laws applied

property ny

Number of observables

property nytrue

Number of observables in the unaugmented system

property nz

Number of event outputs

property nztrue

Number of event outputs in the unaugmented system

property o2mode

flag indicating whether second-order sensitivities were requested

property order

employed order forward problem (shape *nt*)

property posteq_cpu_time

computation time of the steady state solver [ms] (postequilibration)

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property posteq_cpu_timeB

computation time of the steady state solver of the backward problem [ms] (postequilibration)

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property posteq_numsteps

number of Newton steps for steady state problem (preequilibration) [newton, simulation, newton] (shape *3*) (postequilibration)

property posteq_numstepsB

number of simulation steps for adjoint steady state problem (postequilibration) [== 0 if analytical solution worked, > 0 otherwise]

property posteq_status

flags indicating success of steady state solver (postequilibration)

property posteq_t

time when steadystate was reached via simulation (postequilibration)

property posteq_wrms

weighted root-mean-square of the rhs when steadystate was reached (postequilibration)

property preeq_cpu_time

computation time of the steady state solver [ms] (preequilibration)

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property preeq_cpu_timeB

computation time of the steady state solver of the backward problem [ms] (preequilibration)

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property preeq_numsteps

number of Newton steps for steady state problem (preequilibration) [newton, simulation, newton] (length = 3)

property preeq_numstepsB

number of simulation steps for adjoint steady state problem (preequilibration) [== 0 if analytical solution worked, > 0 otherwise]

property preeq_status

flags indicating success of steady state solver (preequilibration)

property preeq_t

time when steadystate was reached via simulation (preequilibration)

property preeq_wrms

weighted root-mean-square of the rhs when steadystate was reached (preequilibration)

property pscale

scaling of parameterization

property rdata_reporting

reporting mode

property res

observable (shape *nt*ny*, row-major)

property rz

event trigger output (shape *nmaxevent* x *nz*, row-major)

property s2llh

second-order parameter derivative of log-likelihood (shape *nJ-1* x *nplist*, row-major)

property s2rz

second-order parameter derivative of event trigger output (shape *nmaxevent* x *nztrue* x *nplist* x *nplist*, row-major)

property sensi

sensitivity order

property sensi_meth

sensitivity method

property sigma_res

boolean indicating whether residuals for standard deviations have been added

property sigmay

observable standard deviation (shape *nt* x *ny*, row-major)

property sigmaz

event output sigma standard deviation (shape *nmaxevent* x *nz*, row-major)

property sllh

parameter derivative of log-likelihood (shape *nplist*)

property sres

parameter derivative of residual (shape *nt*ny* x *nplist*, row-major)

property srz

parameter derivative of event trigger output (shape *nmaxevent* x *nplist* x *nz*, row-major)

property ssigmay

parameter derivative of observable standard deviation (shape *nt* x *nplist* x *ny*, row-major)

property ssigmaz

parameter derivative of event output standard deviation (shape *nmaxevent* x *nplist* x *nz*, row-major)

property status

Simulation status code.

One of:

- AMICI_SUCCESS, indicating successful simulation
- AMICI_MAX_TIME_EXCEEDED, indicating that the simulation did not finish within the allowed time (see Solver.{set,get}MaxTime)
- AMICI_ERROR, indicating that some error occurred during simulation (a more detailed error message will have been printed).
- AMICI_NOT_RUN, if no simulation was started

property sx

parameter derivative of state (shape *nt* x *nplist* x *nx*, row-major)

property sx0

initial sensitivities (shape *nplist* x *nx*, row-major)

property sx_ss

preequilibration sensitivities (shape *nplist* x *nx*, row-major)

property sy

parameter derivative of observable (shape *nt* x *nplist* x *ny*, row-major)

property sz

parameter derivative of event output (shape *nmaxevent* x *nplist* x *nz*, row-major)

property t_last

The final internal time of the solver.

property ts

timepoints (shape *nt*)

property ubw

Upper bandwidth of the Jacobian

property w

w data from the model (recurring terms in xdot, for imported SBML models from python, this contains the flux vector) (shape *nt* x *nw*, row major)

property x

state (shape *nt* x *nx*, row-major)

property x0

initial state (shape *nx*)

property x_ss

preequilibration steady state (shape *nx*)

property xdot

time derivative (shape *nx*) evaluated at *t_last*.

property y

observable (shape *nt* x *ny*, row-major)

property z

event output (shape *nmaxevent* x *nz*, row-major)

class amici.amici.**ReturnDataPtr**(**args*)

Swig-Generated class that implements smart pointers to ReturnData as objects.

property FIM

fisher information matrix (shape *nplist* x *nplist*, row-major)

property J

Jacobian of differential equation right hand side (shape *nx* x *nx*, row-major) evaluated at *t_last*.

property chi2

χ^2 value

property cpu_time

computation time of forward solve [ms]

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property cpu_timeB

computation time of backward solve [ms]

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property cpu_time_total

total CPU time from entering runAmiciSimulation until exiting [ms]

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property id

Arbitrary (not necessarily unique) identifier.

property lbw

Lower bandwidth of the Jacobian

property llh

log-likelihood value

property messages

log messages

property nJ

Dimension of the augmented objective function for 2nd order ASA

property ndJydy

Number of nonzero elements in the y derivative of dJy (dimension *nytrue*)

property ndtotal_cldx_rdata

Number of nonzero elements in the $x_r data$ derivative of $total_c l$

property ndwdp

Number of nonzero elements in the *p* derivative of the repeating elements

property ndwdw

Number of nonzero elements in the *w* derivative of the repeating elements

property ndwdx

Number of nonzero elements in the *x* derivative of the repeating elements

property ndxdotdw

Number of nonzero elements in the w derivative of $xdot$

property ndxrdatadtcl

Number of nonzero elements in the tcl derivative of $x_r data$

property ndxrdatadxsolver

Number of nonzero elements in the x derivative of $x_r data$

property ne

Number of events

property ne_solver

Number of events that require root-finding

property newton_maxsteps

maximal number of newton iterations for steady state calculation

property nk

Number of constants

property nmaxevent

maximal number of occurring events (for every event type)

property nnz

Number of nonzero entries in Jacobian

property np

Number of parameters

property nplist

number of parameter for which sensitivities were requested

property nspl

Number of spline functions in the model

property nt

number of considered timepoints

property numerrtestfails

number of error test failures forward problem (shape *nt*)

property numerrtestfailsB

number of error test failures backward problem (shape *nt*)

property numnonlinsolvconvfails

number of linear solver convergence failures forward problem (shape *nt*)

property numnonlinsolvconvfailsB

number of linear solver convergence failures backward problem (shape *nt*)

property numrhsevals

number of right hand side evaluations forward problem (shape *nt*)

property numrhsevalsB

number of right hand side evaluations backward problem (shape *nt*)

property numsteps

number of integration steps forward problem (shape *nt*)

property numstepsB

number of integration steps backward problem (shape *nt*)

property nw

Number of common expressions

property nx

number of states (alias *nx_rdata*, kept for backward compatibility)

property nx_rdata

Number of states

property nx_solver

Number of states with conservation laws applied

property nx_solver_reinit

Number of solver states subject to reinitialization

property nxtrue

number of states in the unaugmented system (alias nxtrue_rdata, kept for backward compatibility)

property nxtrue_rdata

Number of states in the unaugmented system

property nxtrue_solver

Number of states in the unaugmented system with conservation laws applied

property ny

Number of observables

property nytrue

Number of observables in the unaugmented system

property nz

Number of event outputs

property nztrue

Number of event outputs in the unaugmented system

property o2mode

flag indicating whether second-order sensitivities were requested

property order

employed order forward problem (shape *nt*)

property posteq_cpu_time

computation time of the steady state solver [ms] (postequilibration)

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property posteq_cpu_timeB

computation time of the steady state solver of the backward problem [ms] (postequilibration)

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property posteq_numsteps

number of Newton steps for steady state problem (preequilibration) [newton, simulation, newton] (shape *3*) (postequilibration)

property posteq_numstepsB

number of simulation steps for adjoint steady state problem (postequilibration) [== 0 if analytical solution worked, > 0 otherwise]

property posteq_status

flags indicating success of steady state solver (postequilibration)

property posteq_t

time when steadystate was reached via simulation (postequilibration)

property posteq_wrms

weighted root-mean-square of the rhs when steadystate was reached (postequilibration)

property preeq_cpu_time

computation time of the steady state solver [ms] (preequilibration)

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property preeq_cpu_timeB

computation time of the steady state solver of the backward problem [ms] (preequilibration)

> **Warning:** If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

property preeq_numsteps

number of Newton steps for steady state problem (preequilibration) [newton, simulation, newton] (length = 3)

property preeq_numstepsB

number of simulation steps for adjoint steady state problem (preequilibration) [== 0 if analytical solution worked, > 0 otherwise]

property preeq_status

flags indicating success of steady state solver (preequilibration)

property preeq_t

time when steadystate was reached via simulation (preequilibration)

property preeq_wrms

weighted root-mean-square of the rhs when steadystate was reached (preequilibration)

property pscale

scaling of parameterization

property rdata_reporting

reporting mode

property res

observable (shape *nt*ny*, row-major)

property rz

event trigger output (shape *nmaxevent* x *nz*, row-major)

property s2llh

second-order parameter derivative of log-likelihood (shape *nJ-1* x *nplist*, row-major)

property s2rz

second-order parameter derivative of event trigger output (shape *nmaxevent* x *nztrue* x *nplist* x *nplist*, row-major)

property sensi

sensitivity order

property sensi_meth

sensitivity method

property sigma_res

boolean indicating whether residuals for standard deviations have been added

property sigmay

observable standard deviation (shape *nt* x *ny*, row-major)

property sigmaz

event output sigma standard deviation (shape *nmaxevent* x *nz*, row-major)

property sllh

parameter derivative of log-likelihood (shape *nplist*)

property sres

parameter derivative of residual (shape *nt*ny* x *nplist*, row-major)

property srz

parameter derivative of event trigger output (shape *nmaxevent* x *nplist* x *nz*, row-major)

property ssigmay

parameter derivative of observable standard deviation (shape *nt* x *nplist* x *ny*, row-major)

property ssigmaz

parameter derivative of event output standard deviation (shape *nmaxevent* x *nplist* x *nz*, row-major)

property status

Simulation status code.

One of:

- AMICI_SUCCESS, indicating successful simulation
- AMICI_MAX_TIME_EXCEEDED, indicating that the simulation did not finish within the allowed time (see Solver.{set,get}MaxTime)
- AMICI_ERROR, indicating that some error occurred during simulation (a more detailed error message will have been printed).
- AMICI_NOT_RUN, if no simulation was started

property sx

parameter derivative of state (shape *nt* x *nplist* x *nx*, row-major)

property sx0

initial sensitivities (shape *nplist* x *nx*, row-major)

property sx_ss

preequilibration sensitivities (shape *nplist* x *nx*, row-major)

property sy

parameter derivative of observable (shape *nt* x *nplist* x *ny*, row-major)

property sz

parameter derivative of event output (shape *nmaxevent* x *nplist* x *nz*, row-major)

property t_last

The final internal time of the solver.

property ts

timepoints (shape *nt*)

property ubw

Upper bandwidth of the Jacobian

property w

w data from the model (recurring terms in xdot, for imported SBML models from python, this contains the flux vector) (shape *nt* x *nw*, row major)

property x

state (shape *nt* x *nx*, row-major)

property x0

initial state (shape *nx*)

property x_ss

preequilibration steady state (shape *nx*)

property xdot

time derivative (shape *nx*) evaluated at *t_last*.

property y

observable (shape *nt* x *ny*, row-major)

property z

event output (shape *nmaxevent* x *nz*, row-major)

class amici.amici.**SecondOrderMode**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

directional = 2

full = 1

none = 0

class amici.amici.**SensitivityMethod**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

adjoint = 2

forward = 1

none = 0

amici.amici.**SensitivityMethod_adjoint = 2**

Adjoint sensitivity analysis.

amici.amici.**SensitivityMethod_forward = 1**

Forward sensitivity analysis.

amici.amici.**SensitivityMethod_none = 0**

Don't compute sensitivities.

class amici.amici.**SensitivityOrder**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

first = 1

none = 0

second = 2

amici.amici.**SensitivityOrder_first = 1**

First-order sensitivities.

amici.amici.**SensitivityOrder_none = 0**

Don't compute sensitivities.

amici.amici.**SensitivityOrder_second = 2**

Second-order sensitivities.

class amici.amici.**SimulationParameters**(**args*)

Container for various simulation parameters.

__init__(**args*)

Overload 1:

Constructor

Parameters

timepoints (DoubleVector) – Timepoints for which simulation results are requested

Overload 2:

Constructor

Parameters

- **fixedParameters** (DoubleVector) – Model constants
- **parameters** (DoubleVector) – Model parameters

property fixedParameters

Model constants

Vector of size Model::nk() or empty

property fixedParametersPreequilibration

Model constants for pre-equilibration

Vector of size Model::nk() or empty.

property fixedParametersPresimulation

Model constants for pre-simulation

Vector of size Model::nk() or empty.

property parameters

Model parameters

Vector of size Model::np() or empty with parameter scaled according to SimulationParameter::pscale.

property plist

Parameter indices w.r.t. which to compute sensitivities

property pscale

Parameter scales

Vector of parameter scale of size Model::np(), indicating how/if each parameter is to be scaled.

property reinitialization_state_idxs_presim

Indices of states to be reinitialized based on provided presimulation constants / fixed parameters.

property reinitialization_state_idxs_sim

Indices of states to be reinitialized based on provided constants / fixed parameters.

reinitializeAllFixedParameterDependentInitialStates(*nx_rdata: int*)

Set reinitialization of all states based on model constants for all simulation phases.

Convenience function to populate *reinitialization_state_idxs_presim* and *reinitialization_state_idxs_sim*

Parameters
nx_rdata (int) – Number of states (Model::nx_rdata)

reinitializeAllFixedParameterDependentInitialStatesForPresimulation(*nx_rdata: int*)

Set reinitialization of all states based on model constants for presimulation (only meaningful if preequilibration is performed).

Convenience function to populate *reinitialization_state_idxs_presim* and *reinitialization_state_idxs_sim*

Parameters
nx_rdata (int) – Number of states (Model::nx_rdata)

reinitializeAllFixedParameterDependentInitialStatesForSimulation(*nx_rdata: int*)

Set reinitialization of all states based on model constants for the 'main' simulation (only meaningful if presimulation or preequilibration is performed).

Convenience function to populate *reinitialization_state_idxs_presim* and *reinitialization_state_idxs_sim*

Parameters
nx_rdata (int) – Number of states (Model::nx_rdata)

property reinitializeFixedParameterInitialStates

Flag indicating whether reinitialization of states depending on fixed parameters is activated

property sx0

Initial state sensitivities

Dimensions: Model::nx() * Model::nplist(), Model::nx() * ExpData::plist.size(), if ExpData::plist is not empty, or empty

property t_presim

Duration of pre-simulation.

If this is > 0, presimulation will be performed from (model->t0 - t_presim) to model->t0 using the fixedParameters in fixedParametersPresimulation

property ts_

Timepoints for which model state/outputs/... are requested

Vector of timepoints.

property tstart_

Starting time of the simulation.

Output timepoints are absolute timepoints, independent of t_{start}. For output timepoints $t < t_{start}$, the initial state will be returned.

property x0

Initial state

Vector of size Model::nx() or empty

class amici.amici.**Solver**(**args*, ***kwargs*)

The Solver class provides a generic interface to CVODES and IDAS solvers, individual realizations are realized in the CVodeSolver and the IDASolver class. All transient private/protected members (CVODES/IDAS memory, interface variables and status flags) are specified as mutable and not included in serialization or equality checks. No solver setting parameter should be marked mutable.

NOTE: Any changes in data members here must be propagated to copy ctor, equality operator, serialization functions in serialization.h, and amici::hdf5::(read/write)SolverSettings(From/To)HDF5 in hdf5.cpp.

__init__(**args*, ***kwargs*)

clone() → *Solver*

Clone this instance

Return type
Solver

Returns
The clone

computingASA() → bool

check if ASA is being computed

Return type
boolean

Returns
flag

computingFSA() → bool

check if FSA is being computed

Return type
boolean

Returns
flag

getAbsoluteTolerance() → float

Get the absolute tolerances for the forward problem

Same tolerance is used for the backward problem if not specified differently via setAbsoluteToleranceASA.

Return type
float

Returns
absolute tolerances

getAbsoluteToleranceB() → float

Returns the absolute tolerances for the backward problem for adjoint sensitivity analysis

Return type
float

Returns
absolute tolerances

getAbsoluteToleranceFSA() → float

Returns the absolute tolerances for the forward sensitivity problem

Return type
float

Returns
absolute tolerances

getAbsoluteToleranceQuadratures() → float

returns the absolute tolerance for the quadrature problem

Return type
float

Returns
absolute tolerance

getAbsoluteToleranceSteadyState() → float

returns the absolute tolerance for the steady state problem

Return type
float

Returns
absolute tolerance

getAbsoluteToleranceSteadyStateSensi() → float

returns the absolute tolerance for the sensitivities of the steady state problem

Return type
float

Returns
absolute tolerance

`getConstraints()` → tuple[float]

Get constraints on the model state.

Return type
DoubleVector

Returns
constraints

`getInternalSensitivityMethod()` → *InternalSensitivityMethod*

returns the internal sensitivity method

Return type
InternalSensitivityMethod

Returns
internal sensitivity method

`getInterpolationType()` → *InterpolationType*

Return type
InterpolationType

Returns

`getLinearMultistepMethod()` → *LinearMultistepMethod*

returns the linear system multistep method

Return type
LinearMultistepMethod

Returns
linear system multistep method

`getLinearSolver()` → *LinearSolver*

Return type
LinearSolver

Returns

`getMaxConvFails()` → int

Get the maximum number of nonlinear solver convergence failures permitted per step.

Return type
int

Returns
maximum number of nonlinear solver convergence

`getMaxNonlinIters()` → int

Get the maximum number of nonlinear solver iterations permitted per step.

Return type
int

Returns
maximum number of nonlinear solver iterations

getMaxStepSize() → float

Get the maximum step size

Return type
float

Returns
maximum step size

getMaxSteps() → int

returns the maximum number of solver steps for the forward problem

Return type
int

Returns
maximum number of solver steps

getMaxStepsBackwardProblem() → int

returns the maximum number of solver steps for the backward problem

Return type
int

Returns
maximum number of solver steps

getMaxTime() → float

Returns the maximum time allowed for integration

Return type
float

Returns
Time in seconds

getNewtonDampingFactorLowerBound() → float

Get a lower bound of the damping factor used in the Newton solver

Return type
float

Returns

getNewtonDampingFactorMode() → *NewtonDampingFactorMode*

Get a state of the damping factor used in the Newton solver

Return type
NewtonDampingFactorMode

Returns

getNewtonMaxSteps() → int

Get maximum number of allowed Newton steps for steady state computation

Return type
int

Returns

`getNewtonStepSteadyStateCheck()` → bool

Returns how convergence checks for steadystate computation are performed. If activated, convergence checks are limited to every 25 steps in the simulation solver to limit performance impact.

Return type
boolean

Returns
boolean flag indicating newton step (true) or the right hand side (false)

`getNonlinearSolverIteration()` → *NonlinearSolverIteration*

returns the nonlinear system solution method

Return type
NonlinearSolverIteration

Returns

`getRelativeTolerance()` → float

Get the relative tolerances for the forward problem

Same tolerance is used for the backward problem if not specified differently via setRelativeToleranceASA.

Return type
float

Returns
relative tolerances

`getRelativeToleranceB()` → float

Returns the relative tolerances for the adjoint sensitivity problem

Return type
float

Returns
relative tolerances

`getRelativeToleranceFSA()` → float

Returns the relative tolerances for the forward sensitivity problem

Return type
float

Returns
relative tolerances

`getRelativeToleranceQuadratures()` → float

Returns the relative tolerance for the quadrature problem

Return type
float

Returns
relative tolerance

`getRelativeToleranceSteadyState()` → float

returns the relative tolerance for the steady state problem

Return type
float

Returns
relative tolerance

`getRelativeToleranceSteadyStateSensi()` → float

returns the relative tolerance for the sensitivities of the steady state problem

Return type
float

Returns
relative tolerance

`getReturnDataReportingMode()` → *RDataReporting*

returns the ReturnData reporting mode

Return type
RDataReporting

Returns
ReturnData reporting mode

`getSensiSteadyStateCheck()` → bool

Returns how convergence checks for steadystate computation are performed.

Return type
boolean

Returns
boolean flag indicating state and sensitivity equations (true) or only state variables (false).

`getSensitivityMethod()` → *SensitivityMethod*

Return current sensitivity method

Return type
SensitivityMethod

Returns
method enum

`getSensitivityMethodPreequilibration()` → *SensitivityMethod*

Return current sensitivity method during preequilibration

Return type
SensitivityMethod

Returns
method enum

`getSensitivityOrder()` → *SensitivityOrder*

Get sensitivity order

Return type
SensitivityOrder

Returns
sensitivity order

`getStabilityLimitFlag()` → bool

returns stability limit detection mode

Return type
boolean

Returns
stldet can be false (deactivated) or true (activated)

`getStateOrdering()` → int

Gets KLU / SuperLUMT state ordering mode

Return type
int

Returns
State-ordering as integer according to SUNLinSolKLU::StateOrdering or SUNLinSolSuperLUMT::StateOrdering (which differ).

`getSteadyStateSensiToleranceFactor()` → float

returns the steady state sensitivity simulation tolerance factor.

Steady state sensitivity simulation tolerances are the product of the sensitivity simulation tolerances and this factor, unless manually set with *set(Absolute/Relative)ToleranceSteadyStateSensi()*.

Return type
float

Returns
steady state simulation tolerance factor

`getSteadyStateToleranceFactor()` → float

returns the steady state simulation tolerance factor.

Steady state simulation tolerances are the product of the simulation tolerances and this factor, unless manually set with *set(Absolute/Relative)ToleranceSteadyState()*.

Return type
float

Returns
steady state simulation tolerance factor

`property logger`

`nplist()` → int

number of parameters with which the solver was initialized

Return type
int

Returns
sx.getLength()

`nquad()` → int

number of quadratures with which the solver was initialized

Return type
int

Returns
xQB.getLength()

`nx()` → int

number of states with which the solver was initialized

Return type
int

Returns
x.getLength()

setAbsoluteTolerance(*atol: float*)

Sets the absolute tolerances for the forward problem

Same tolerance is used for the backward problem if not specified differently via setAbsoluteToleranceASA.

Parameters
atol (float) – absolute tolerance (non-negative number)

setAbsoluteToleranceB(*atol: float*)

Sets the absolute tolerances for the backward problem for adjoint sensitivity analysis

Parameters
atol (float) – absolute tolerance (non-negative number)

setAbsoluteToleranceFSA(*atol: float*)

Sets the absolute tolerances for the forward sensitivity problem

Parameters
atol (float) – absolute tolerance (non-negative number)

setAbsoluteToleranceQuadratures(*atol: float*)

sets the absolute tolerance for the quadrature problem

Parameters
atol (float) – absolute tolerance (non-negative number)

setAbsoluteToleranceSteadyState(*atol: float*)

sets the absolute tolerance for the steady state problem

Parameters
atol (float) – absolute tolerance (non-negative number)

setAbsoluteToleranceSteadyStateSensi(*atol: float*)

sets the absolute tolerance for the sensitivities of the steady state problem

Parameters
atol (float) – absolute tolerance (non-negative number)

setConstraints(*constraints: Sequence[float]*)

Set constraints on the model state.

See https://sundials.readthedocs.io/en/latest/cvode/Usage/index.html#c.CVodeSetConstraints.

Parameters
constraints (typing.Sequence[float]) –

setInternalSensitivityMethod(*ism:* InternalSensitivityMethod)

sets the internal sensitivity method

Parameters
ism (*amici.amici.InternalSensitivityMethod*) – internal sensitivity method

setInterpolationType(*interpType:* InterpolationType)

sets the interpolation of the forward solution that is used for the backwards problem

Parameters
interpType (*amici.amici.InterpolationType*) – interpolation type

setLinearMultistepMethod(*lmm:* LinearMultistepMethod)

sets the linear system multistep method

Parameters
lmm (*amici.amici.LinearMultistepMethod*) – linear system multistep method

setLinearSolver(*linsol:* LinearSolver)

Parameters
linsol (*amici.amici.LinearSolver*) –

setMaxConvFails(*max_conv_fails: int*)

Set the maximum number of nonlinear solver convergence failures permitted per step.

Parameters
max_conv_fails (int) – maximum number of nonlinear solver convergence

setMaxNonlinIters(*max_nonlin_iters: int*)

Set the maximum number of nonlinear solver iterations permitted per step.

Parameters
max_nonlin_iters (int) – maximum number of nonlinear solver iterations

setMaxStepSize(*max_step_size: float*)

Set the maximum step size

Parameters
max_step_size (float) – maximum step size. *0.0* means no limit.

setMaxSteps(*maxsteps: int*)

sets the maximum number of solver steps for the forward problem

Parameters
maxsteps (int) – maximum number of solver steps (positive number)

setMaxStepsBackwardProblem(*maxsteps: int*)

sets the maximum number of solver steps for the backward problem

Parameters
maxsteps (int) – maximum number of solver steps (non-negative number)

Notes: default behaviour (100 times the value for the forward problem) can be restored by passing maxsteps=0

setMaxTime(*maxtime: float*)

Set the maximum CPU time allowed for integration

Parameters
maxtime (float) – Time in seconds. Zero means infinite time.

setNewtonDampingFactorLowerBound(*dampingFactorLowerBound: float*)

Set a lower bound of the damping factor in the Newton solver

Parameters
dampingFactorLowerBound (float) –

setNewtonDampingFactorMode(*dampingFactorMode:* NewtonDampingFactorMode)

Turn on/off a damping factor in the Newton method

Parameters
dampingFactorMode (*amici.amici.NewtonDampingFactorMode*) –

setNewtonMaxSteps(*newton_maxsteps: int*)

Set maximum number of allowed Newton steps for steady state computation

Parameters
newton_maxsteps (int) –

setNewtonStepSteadyStateCheck(*flag: bool*)

Sets how convergence checks for steadystate computation are performed.

Parameters
flag (bool) – boolean flag to pick newton step (true) or the right hand side (false, default)

setNonlinearSolverIteration(*iter:* NonlinearSolverIteration)

sets the nonlinear system solution method

Parameters
iter (*amici.amici.NonlinearSolverIteration*) – nonlinear system solution method

setRelativeTolerance(*rtol: float*)

Sets the relative tolerances for the forward problem

Same tolerance is used for the backward problem if not specified differently via setRelativeToleranceASA.

Parameters
rtol (float) – relative tolerance (non-negative number)

setRelativeToleranceB(*rtol: float*)

Sets the relative tolerances for the adjoint sensitivity problem

Parameters
rtol (float) – relative tolerance (non-negative number)

setRelativeToleranceFSA(*rtol: float*)

Sets the relative tolerances for the forward sensitivity problem

Parameters
rtol (float) – relative tolerance (non-negative number)

setRelativeToleranceQuadratures(*rtol: float*)

sets the relative tolerance for the quadrature problem

Parameters
rtol (float) – relative tolerance (non-negative number)

setRelativeToleranceSteadyState(*rtol: float*)

sets the relative tolerance for the steady state problem

Parameters
rtol (float) – relative tolerance (non-negative number)

setRelativeToleranceSteadyStateSensi(*rtol: float*)

sets the relative tolerance for the sensitivities of the steady state problem

Parameters
rtol (float) – relative tolerance (non-negative number)

setReturnDataReportingMode(*rdrm:* RDataReporting)

sets the ReturnData reporting mode

Parameters
rdrm (*amici.amici.RDataReporting*) – ReturnData reporting mode

setSensiSteadyStateCheck(*flag: bool*)

Sets for which variables convergence checks for steadystate computation are performed.

Parameters
flag (bool) – boolean flag to pick state and sensitivity equations (true, default) or only state variables (false).

setSensitivityMethod(*sensi_meth:* SensitivityMethod)

Set sensitivity method

Parameters
sensi_meth (*amici.amici.SensitivityMethod*) –

setSensitivityMethodPreequilibration(*sensi_meth_preeq:* SensitivityMethod)

Set sensitivity method for preequilibration

Parameters
sensi_meth_preeq (*amici.amici.SensitivityMethod*) –

setSensitivityOrder(*sensi:* SensitivityOrder)

Set the sensitivity order

Parameters
sensi (*amici.amici.SensitivityOrder*) – sensitivity order

setStabilityLimitFlag(*stldet: bool*)

set stability limit detection mode

Parameters
stldet (bool) – can be false (deactivated) or true (activated)

setStateOrdering(*ordering: int*)

Sets KLU / SuperLUMT state ordering mode

This only applies when linsol is set to LinearSolver::KLU or LinearSolver::SuperLUMT. Mind the difference between SUNLinSolKLU::StateOrdering and SUNLinSolSuperLUMT::StateOrdering.

Parameters
ordering (int) – state ordering

setSteadyStateSensiToleranceFactor(*factor: float*)

set the steady state sensitivity simulation tolerance factor.

Steady state sensitivity simulation tolerances are the product of the sensitivity simulation tolerances and this factor, unless manually set with *set(Absolute/Relative)ToleranceSteadyStateSensi()*.

Parameters
factor (float) – tolerance factor (non-negative number)

setSteadyStateToleranceFactor(*factor: float*)

set the steady state simulation tolerance factor.

Steady state simulation tolerances are the product of the simulation tolerances and this factor, unless manually set with *set(Absolute/Relative)ToleranceSteadyState()*.

Parameters
factor (float) – tolerance factor (non-negative number)

class amici.amici.**SolverPtr**(**args*)

Swig-Generated class that implements smart pointers to Solver as objects.

property logger

class amici.amici.SteadyStateComputationMode(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

integrateIfNewtonFails = 2

integrationOnly = 1

newtonOnly = 0

class amici.amici.SteadyStateSensitivityMode(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

integrateIfNewtonFails = 2

integrationOnly = 1

newtonOnly = 0

class amici.amici.SteadyStateStatus(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

__init__(**args*, ***kwds*)

failed = -1

failed_convergence = -2

failed_damping = -4

failed_factorization = -3

failed_too_long_simulation = -5

not_run = 0

success = 1

class amici.amici.SteadyStateStatusVector(**args*)

class amici.amici.StringDoubleMap(**args*)

Swig-Generated class templating `Dict` [`str`, `float`] to facilitate interfacing with C++ bindings.

class amici.amici.StringVector(**args*)

Swig-Generated class templating common python types including `Iterable` [`str`] and `numpy.array` [`str`] to facilitate interfacing with C++ bindings.

amici.amici.compiledWithOpenMP() → bool

AMICI extension was compiled with OpenMP?

Return type
`bool`

amici.amici.**getScaledParameter**(*unscaledParameter: float*, *scaling:* ParameterScaling) → float

Apply parameter scaling according to *scaling*

Parameters

- **unscaledParameter** (float) –
- **scaling** (*amici.amici.ParameterScaling*) – parameter scaling

Return type
float

Returns
Scaled parameter

amici.amici.**getUnscaledParameter**(*scaledParameter: float*, *scaling:* ParameterScaling) → float

Remove parameter scaling according to *scaling*

Parameters

- **scaledParameter** (float) – scaled parameter
- **scaling** (*amici.amici.ParameterScaling*) – parameter scaling

Return type
float

Returns
Unscaled parameter

amici.amici.**parameterScalingFromIntVector**(*intVec: Sequence[int]*) → tuple[*ParameterScaling*]

Swig-Generated class, which, in contrast to other Vector classes, does not allow for simple interoperability with common Python types, but must be created using *amici.amici.parameterScalingFromIntVector()*

Return type
tuple[*amici.amici.ParameterScaling*]

amici.amici.**runAmiciSimulation**(*solver:* Solver, *edata:* ExpData, *model:* Model, *rethrow: bool = False*) → *ReturnData*

Core integration routine. Initializes the solver and runs the forward and backward problem.

Parameters

- **solver** (*amici.amici.Solver*) – Solver instance
- **edata** (*amici.amici.ExpData*) – pointer to experimental data object
- **model** (*amici.amici.Model*) – model specification object
- **rethrow** (bool) – rethrow integration exceptions?

Return type
ReturnData

Returns
rdata pointer to return data object

amici.amici.**runAmiciSimulations**(*solver:* Solver, *edatas:* ExpDataPtrVector, *model:* Model, *failfast: bool*, *num_threads: int*) → tuple[*ReturnData*]

Same as runAmiciSimulation, but for multiple ExpData instances. When compiled with OpenMP support, this function runs multi-threaded.

Parameters

- **solver** (*amici.amici.Solver*) – Solver instance

- **edatas** (*amici.amici.ExpDataPtrVector*) – experimental data objects
- **model** (*amici.amici.Model*) – model specification object
- **failfast** (bool) – flag to allow early termination
- **num_threads** (int) – number of threads for parallel execution

Return type
Iterable[*ReturnData*]

Returns
vector of pointers to return data objects

amici.amici.**scaleParameters**(*bufferUnscaled: Iterable[float]*, *pscale: Iterable[*ParameterScaling*]*, *bufferScaled: Iterable[float]*)

Apply parameter scaling according to *scaling*

Parameters

- **bufferUnscaled** (typing.Iterable[float]) –
- **pscale** (typing.Iterable[*amici.amici.ParameterScaling*]) – parameter scaling
- **bufferScaled** (typing.Iterable[float]) – destination

amici.amici.**simulation_status_to_str**(*status: int*) → str

Get the string representation of the given simulation status code (see ReturnData::status).

Parameters
status (int) – Status code

Return type
str

Returns
Name of the variable representing this status code.

amici.amici.**unscaleParameters**(*bufferScaled: Iterable[float]*, *pscale: Iterable[*ParameterScaling*]*, *bufferUnscaled: Iterable[float]*)

Remove parameter scaling according to the parameter scaling in pscale

All vectors must be of same length.

Parameters

- **bufferScaled** (typing.Iterable[float]) – scaled parameters
- **pscale** (typing.Iterable[*amici.amici.ParameterScaling*]) – parameter scaling
- **bufferUnscaled** (typing.Iterable[float]) – unscaled parameters are written to the array

10.5.3 amici.sbml_import

SBML Import

This module provides all necessary functionality to import a model specified in the Systems Biology Markup Language (SBML).

Functions

assignmentRules2observables(sbml_model[, ...])	Turn assignment rules into observables.
get_species_initial(species)	Extract the initial concentration from a given species
replace_logx(math_str)	Replace logX(.) by log(., X) since sympy cannot parse the former

Classes

SbmlImporter(sbml_source[, ...])	Class to generate AMICI C++ files for a model provided in the Systems Biology Markup Language (SBML).

class amici.sbml_import.**SbmlImporter**(*sbml_source*, *show_sbml_warnings=False*, *from_file=True*, *discard_annotations=False*)

Class to generate AMICI C++ files for a model provided in the Systems Biology Markup Language (SBML).

Variables

- **show_sbml_warnings** – indicates whether libSBML warnings should be displayed
- **symbols** – dict carrying symbolic definitions
- **sbml_reader** – The libSBML sbml reader

  Warning: Not storing this may result in a segfault.

- **sbml_doc** – document carrying the sbml definition

  Warning: Not storing this may result in a segfault.

- **sbml** – SBML model to import
- **compartments** – dict of compartment ids and compartment volumes
- **stoichiometric_matrix** – stoichiometric matrix of the model
- **flux_vector** – reaction kinetic laws
- **flux_ids** – identifiers for elements of flux_vector
- **_local_symbols** – model symbols for sympy to consider during sympification see *locals`argument in `sympy.sympify*

- **species_assignment_rules** – Assignment rules for species. Key is symbolic identifier and value is assignment value
- **compartment_assignment_rules** – Assignment rules for compartments. Key is symbolic identifier and value is assignment value
- **parameter_assignment_rules** – assignment rules for parameters, these parameters are not permissible for sensitivity analysis
- **initial_assignments** – initial assignments for parameters, these parameters are not permissible for sensitivity analysis
- **sbml_parser_settings** – sets behaviour of SBML Formula parsing

__init__(*sbml_source*, *show_sbml_warnings=False*, *from_file=True*, *discard_annotations=False*)

Create a new Model instance.

Parameters

- **sbml_source** (typing.Union[str, pathlib.Path, libsbml.Model]) – Either a path to SBML file where the model is specified, or a model string as created by sbml.sbmlWriter( ).writeSBMLToString() or an instance of *libsbml.Model*.
- **show_sbml_warnings** (bool) – Indicates whether libSBML warnings should be displayed.
- **from_file** (bool) – Whether *sbml_source* is a file name (True, default), or an SBML string
- **discard_annotations** (bool) – discard information contained in AMICI SBML annotations (debug).

add_d_dt(*d_dt*, *variable*, *variable0*, *name*)

Creates or modifies species, to implement rate rules for compartments and species, respectively.

Parameters

- **d_dt** (sympy.core.expr.Expr) – The rate rule (or, right-hand side of an ODE).
- **variable** (sympy.core.symbol.Symbol) – The subject of the rate rule.
- **variable0** (typing.Union[float, sympy.core.expr.Expr]) – The initial value of the variable.
- **name** (str) – Species name, only applicable if this function generates a new species

Return type
None

add_local_symbol(*key*, *value*)

Add local symbols with some sanity checking for duplication which would indicate redefinition of internals, which SBML permits, but we don't.

Parameters

- **key** (str) – local symbol key
- **value** (sympy.core.expr.Expr) – local symbol value

check_event_support()

Check possible events in the model, as AMICI does currently not support :rtype: None

- delays in events
- priorities of events

- events fired at initial time

Furthermore, event triggers are optional (e.g., if an event is fired at initial time, no trigger function is necessary). In this case, warn that this event will have no effect.

check_support()

Check whether all required SBML features are supported. Also ensures that the SBML contains at least one reaction, or rate rule, or assignment rule, to produce change in the system over time.

Return type
None

is_assignment_rule_target(*element*)

Checks if an element has a valid assignment rule in the specified model.

Parameters
element (libsbml.SBase) – SBML variable

Return type
bool

Returns
boolean indicating truth of function name

is_rate_rule_target(*element*)

Checks if an element has a valid assignment rule in the specified model.

Parameters
element (libsbml.SBase) – SBML variable

Return type
bool

Returns
boolean indicating truth of function name

sbml2amici(*model_name*, *output_dir=None*, *observables=None*, *event_observables=None*, *constant_parameters=None*, *sigmas=None*, *event_sigmas=None*, *noise_distributions=None*, *event_noise_distributions=None*, *verbose=40*, *assume_pow_positivity=False*, *compiler=None*, *allow_reinit_fixpar_initcond=True*, *compile=True*, *compute_conservation_laws=True*, *simplify=<function _default_simplify>*, *cache_simplify=False*, *log_as_log10=True*, *generate_sensitivity_code=True*, *hardcode_symbols=None*)

Generate and compile AMICI C++ files for the model provided to the constructor.

The resulting model can be imported as a regular Python module (if *compile=True*), or used from Matlab or C++ as described in the documentation of the respective AMICI interface.

Note that this generates model ODEs for changes in concentrations, not amounts unless the *hasOnlySubstanceUnits* attribute has been defined for a particular species.

Sensitivity analysis for local parameters is enabled by creating global parameters `_{reactionId}_{localParameterName}`.

Parameters

- **model_name** (str) – Name of the generated model package. Note that in a given Python session, only one model with a given name can be loaded at a time. The generated Python extensions cannot be unloaded. Therefore, make sure to choose a unique name for each model.
- **output_dir** (typing.Union[str, pathlib.Path]) – Directory where the generated model package will be stored.

- **observables** (dict[str, dict[str, str]]) – Observables to be added to the model: `dictionary( observableId:{'name':observableName (optional), 'formula':formulaString)})`.
- **event_observables** (dict[str, dict[str, str]]) – Event observables to be added to the model: `dictionary( eventObservableId:{'name':eventObservableName (optional), 'event':eventId, 'formula':formulaString)})`
- **constant_parameters** (collections.abc.Iterable[str]) – list of SBML Ids identifying constant parameters
- **sigmas** (dict[str, typing.Union[str, float]]) – dictionary(observableId: sigma value or (existing) parameter name)
- **event_sigmas** (dict[str, typing.Union[str, float]]) – dictionary(eventObservableId: sigma value or (existing) parameter name)
- **noise_distributions** (dict[str, typing.Union[str, typing.Callable]]) – dictionary(observableId: noise type). If nothing is passed for some observable id, a normal model is assumed as default. Either pass a noise type identifier, or a callable generating a custom noise string. For noise identifiers, see *amici.import_utils.noise_distribution_to_cost_function()*.
- **event_noise_distributions** (dict[str, typing.Union[str, typing.Callable]]) – dictionary(eventObservableId: noise type). If nothing is passed for some observable id, a normal model is assumed as default. Either pass a noise type identifier, or a callable generating a custom noise string. For noise identifiers, see *amici.import_utils.noise_distribution_to_cost_function()*.
- **verbose** (typing.Union[int, bool]) – verbosity level for logging, `True`/`False` default to `logging.Error`/`logging.DEBUG`
- **assume_pow_positivity** (bool) – if set to `True`, a special pow function is used to avoid problems with state variables that may become negative due to numerical errors
- **compiler** (str) – Absolute path to the compiler executable to be used to build the Python extension, e.g. `/usr/bin/clang`.
- **allow_reinit_fixpar_initcond** (bool) – see `amici.de_export.ODEExporter`
- **compile** (bool) – If `True`, compile the generated Python package, if `False`, just generate code.
- **compute_conservation_laws** (bool) – if set to `True`, conservation laws are automatically computed and applied such that the state-jacobian of the ODE right-hand-side has full rank. This option should be set to `True` when using the Newton algorithm to compute steadystate sensitivities. Conservation laws for constant species are enabled by default. Support for conservation laws for non-constant species is experimental and may be enabled by setting an environment variable `AMICI_EXPERIMENTAL_SBML_NONCONST_CLS` to either `demartino` to use the algorithm proposed by De Martino et al. (2014) https://doi.org/10.1371/journal.pone.0100750, or to any other value to use the deterministic algorithm implemented in `conserved_moieties2.py`. In some cases, the `demartino` may run for a very long time. This has been observed for example in the case of stoichiometric coefficients with many significant digits.
- **simplify** (typing.Optional[typing.Callable]) – see `amici.ODEModel._simplify`
- **cache_simplify** (bool) – see `amici.ODEModel.__init__()`

- **log_as_log10** (bool) – If True, log in the SBML model will be parsed as log10 (default), if False, log will be parsed as natural logarithm ln.
- **generate_sensitivity_code** (bool) – If False, the code required for sensitivity computation will not be generated.
- **hardcode_symbols** (collections.abc.Sequence[str]) – List of SBML entity IDs that are to be hardcoded in the generated model. Their values cannot be changed anymore after model import. Currently only parameters that are not targets of rules or initial assignments are supported.

Return type
None

amici.sbml_import.**assignmentRules2observables**(*sbml_model*, *filter_function=<function <lambda>>*)

Turn assignment rules into observables.

Parameters

- **sbml_model** (libsbml.Model) – Model to operate on
- **filter_function** (typing.Callable) – Callback function taking assignment variable as input and returning True/False to indicate if the respective rule should be turned into an observable.

Returns
A dictionary(observableId:{ 'name': observableName, 'formula': formulaString })

amici.sbml_import.**get_species_initial**(*species*)

Extract the initial concentration from a given species

Parameters
species (libsbml.Species) – species index

Return type
sympy.core.expr.Expr

Returns
initial species concentration

amici.sbml_import.**replace_logx**(*math_str*)

Replace logX(.) by log(., X) since sympy cannot parse the former

Parameters
math_str (typing.Union[str, float, None]) – string for sympification

Return type
typing.Union[str, float, None]

Returns
sympifiable string

10.5.4 amici.pysb_import

PySB Import

This module provides all necessary functionality to import a model specified in the `pysb.core.Model` format.

Functions

extract_monomers(complex_patterns)	Constructs a list of monomer names contained in complex patterns.
has_fixed_parameter_ic(specie, pysb_model, ...)	Wrapper to interface `de_export.DEModel.state_has_fixed_parameter_initial_condition()` from a pysb specie/model arguments
ode_model_from_pysb_importer(model[, ...])	Creates an `amici.DEModel` instance from a `pysb.Model` instance.
pysb2amici(model[, output_dir, observables, ...])	Generate AMICI C++ files for the provided model.
pysb_model_from_path(pysb_model_file)	Load a pysb model module and return the `pysb.Model` instance

amici.pysb_import.**extract_monomers**(*complex_patterns*)

Constructs a list of monomer names contained in complex patterns. Multiplicity of names corresponds to the stoichiometry in the complex.

Parameters
complex_patterns (typing.Union[pysb.core.ComplexPattern, list[pysb.core.ComplexPattern]]) – (list of) complex pattern(s)

Return type
list[str]

Returns
list of monomer names

amici.pysb_import.**has_fixed_parameter_ic**(*specie*, *pysb_model*, *ode_model*)

Wrapper to interface `de_export.DEModel.state_has_fixed_parameter_initial_condition()` from a pysb specie/model arguments

Parameters

- **specie** (pysb.core.ComplexPattern) – pysb species
- **pysb_model** (pysb.core.Model) – pysb model
- **ode_model** (*amici.de_model.DEModel*) – ODE model

Return type
bool

Returns
`False` if the species does not have an initial condition at all. Otherwise the return value of `de_export.DEModel.state_has_fixed_parameter_initial_condition()`

amici.pysb_import.**ode_model_from_pysb_importer**(*model*, *constant_parameters=None*, *observables=None*, *sigmas=None*, *noise_distributions=None*, *compute_conservation_laws=True*, *simplify=<function powsimp>*, *cache_simplify=False*, *verbose=False*)

Creates an amici.DEModel instance from a pysb.Model instance.

Parameters

- **model** (pysb.core.Model) – see *amici.pysb_import.pysb2amici()*
- **constant_parameters** (list[str]) – see *amici.pysb_import.pysb2amici()*
- **observables** (list[str]) – see *amici.pysb_import.pysb2amici()*
- **sigmas** (dict[str, str]) – dict with names of observable Expressions as keys and names of sigma Expressions as value sigma
- **noise_distributions** (typing.Optional[dict[str, typing.Union[str, typing.Callable]]]) – see *amici.pysb_import.pysb2amici()*
- **compute_conservation_laws** (bool) – see *amici.pysb_import.pysb2amici()*
- **simplify** (typing.Callable) – see amici.DEModel._simplify
- **cache_simplify** (bool) – see amici.DEModel.__init__() Note that there are possible issues with PySB models: https://github.com/AMICI-dev/AMICI/pull/1672
- **verbose** (typing.Union[int, bool]) – verbosity level for logging, True/False default to logging.DEBUG/logging.ERROR

Return type
amici.de_model.DEModel

Returns
New DEModel instance according to pysbModel

amici.pysb_import.**pysb2amici**(*model*, *output_dir=None*, *observables=None*, *constant_parameters=None*, *sigmas=None*, *noise_distributions=None*, *verbose=False*, *assume_pow_positivity=False*, *compiler=None*, *compute_conservation_laws=True*, *compile=True*, *simplify=<function _default_simplify>*, *cache_simplify=False*, *generate_sensitivity_code=True*, *model_name=None*)

Generate AMICI C++ files for the provided model.

Warning: PySB models with Compartments

When importing a PySB model with pysb.Compartments, BioNetGen scales reaction fluxes with the compartment size. Instead of using the respective symbols, the compartment size Parameter or Expression is evaluated when generating equations. This may lead to unexpected results if the compartment size parameter is changed for AMICI simulations.

Parameters

- **model** (pysb.core.Model) – pysb model, pysb.Model.name will determine the name of the generated module
- **output_dir** (typing.Union[pathlib.Path, str, None]) – see amici.de_export.ODEExporter.set_paths()
- **observables** (list[str]) – list of pysb.core.Expression or pysb.core.Observable names in the provided model that should be mapped to observables
- **sigmas** (dict[str, str]) – dict of pysb.core.Expression names that should be mapped to sigmas

- **noise_distributions** (typing.Optional[dict[str, typing.Union[str, typing.Callable]]]) – dict with names of observable Expressions as keys and a noise type identifier, or a callable generating a custom noise formula string (see *amici.import_utils.noise_distribution_to_cost_function()*). If nothing is passed for some observable id, a normal model is assumed as default.
- **constant_parameters** (list[str]) – list of pysb.core.Parameter names that should be mapped as fixed parameters
- **verbose** (typing.Union[int, bool]) – verbosity level for logging, True/False default to logging.DEBUG/logging.ERROR
- **assume_pow_positivity** (bool) – if set to True, a special pow function is used to avoid problems with state variables that may become negative due to numerical errors
- **compiler** (str) – Absolute path to the compiler executable to be used to build the Python extension, e.g. /usr/bin/clang.
- **compute_conservation_laws** (bool) – if set to True, conservation laws are automatically computed and applied such that the state-jacobian of the ODE right-hand-side has full rank. This option should be set to True when using the Newton algorithm to compute steadystates
- **compile** (bool) – If True, build the python module for the generated model. If false, just generate the source code.
- **simplify** (typing.Callable) – see amici.DEModel._simplify
- **cache_simplify** (bool) – see amici.DEModel.__init__() Note that there are possible issues with PySB models: https://github.com/AMICI-dev/AMICI/pull/1672
- **generate_sensitivity_code** (bool) – if set to False, code for sensitivity computation will not be generated
- **model_name** (typing.Optional[str]) – Name for the generated model module. If None, pysb.Model.name will be used.

amici.pysb_import.**pysb_model_from_path**(*pysb_model_file*)

Load a pysb model module and return the pysb.Model instance

Parameters
pysb_model_file (typing.Union[str, pathlib.Path]) – Full or relative path to the PySB model module

Return type
pysb.core.Model

Returns
The pysb Model instance

10.5.5 amici.bngl_import

BNGL Import

This module provides all necessary functionality to import a model specified in the *BNGL* format.

Functions

bngl2amici(bngl_model, *args, **kwargs)	Generate AMICI C++ files for the provided model.

amici.bngl_import.**bngl2amici**(*bngl_model*, **args*, ***kwargs*)

Generate AMICI C++ files for the provided model.

Parameters

- **bngl_model** (str) – bngl model file, model name will determine the name of the generated module
- **args** – see *amici.pysb_import.pysb2amici()* for additional arguments
- **kwargs** – see *amici.pysb_import.pysb2amici()* for additional arguments

Return type
None

10.5.6 amici.petab

PEtab import related code.

amici.petab.**import_petab_problem**(*petab_problem*, *model_output_dir=None*, *model_name=None*, *compile_=None*, *non_estimated_parameters_as_constants=True*, ***kwargs*)

Create an AMICI model for a PEtab problem.

Parameters

- **petab_problem** (petab.problem.Problem) – A petab problem containing all relevant information on the model.
- **model_output_dir** (typing.Union[str, pathlib.Path, None]) – Directory to write the model code to. It will be created if it doesn't exist. Defaults to current directory.
- **model_name** (str) – Name of the generated model module. Defaults to the ID of the model or the model file name without the extension.
- **compile** – If True, the model will be compiled. If False, the model will not be compiled. If None, the model will be compiled if it cannot be imported.
- **non_estimated_parameters_as_constants** – Whether parameters marked as non-estimated in PEtab should be considered constant in AMICI. Setting this to True will reduce model size and simulation times. If sensitivities with respect to those parameters are required, this should be set to False.
- **kwargs** – Additional keyword arguments to be passed to *amici.sbml_import.SbmlImporter.sbml2amici()* or *amici.pysb_import.pysb2amici()*, depending on the model type.

Return type
amici.amici.Model

Returns
The imported model.

amici.petab.**rdatas_to_measurement_df**(*rdatas*, *model*, *measurement_df*)

Create a measurement dataframe in the PEtab format from the passed `rdatas` and own information.

Parameters

- **rdatas** (collections.abc.Sequence[*amici.amici.ReturnData*]) – A sequence of rdatas with the ordering of `petab.get_simulation_conditions()`.
- **model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model used to generate `rdatas`.
- **measurement_df** (pandas.core.frame.DataFrame) – PEtab measurement table used to generate `rdatas`.

Return type
pandas.core.frame.DataFrame

Returns
A dataframe built from the rdatas in the format of `measurement_df`.

amici.petab.**rdatas_to_simulation_df**(*rdatas*, *model*, *measurement_df*)

Create a PEtab simulation dataframe from *amici.amici.ReturnData* s.

See *rdatas_to_measurement_df()* for details, only that model outputs will appear in column `simulation` instead of `measurement`.

Return type
pandas.core.frame.DataFrame

amici.petab.**simulate_petab**(*petab_problem*, *amici_model*, *solver=None*, *problem_parameters=None*, *simulation_conditions=None*, *edatas=None*, *parameter_mapping=None*, *scaled_parameters=False*, *log_level=30*, *num_threads=1*, *failfast=True*, *scaled_gradients=False*)

Simulate PEtab model.

Note: Regardless of *scaled_parameters*, unscaled sensitivities are returned, unless *scaled_gradients=True*.

Parameters

- **petab_problem** (petab.problem.Problem) – PEtab problem to work on.
- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI Model assumed to be compatible with `petab_problem`.
- **solver** (typing.Optional[*amici.amici.Solver*]) – An AMICI solver. Will use default options if None.
- **problem_parameters** (typing.Optional[dict[str, float]]) – Run simulation with these parameters. If `None`, PEtab `nominalValues` will be used. To be provided as dict, mapping PEtab problem parameters to SBML IDs.
- **simulation_conditions** (typing.Union[pandas.core.frame.DataFrame, dict]) – Result of `petab.get_simulation_conditions()`. Can be provided to save time if this has be obtained before. Not required if `edatas` and `parameter_mapping` are provided.
- **edatas** (list[typing.Union[amici.swig_wrappers.ExpData, *amici.amici.ExpDataPtr*]]) – Experimental data. Parameters are inserted in-place for simulation.

- **parameter_mapping** (*amici.petab.parameter_mapping.ParameterMapping*) – Optional precomputed PEtab parameter mapping for efficiency, as generated by `create_parameter_mapping()` with `scaled_parameters=True`.
- **scaled_parameters** (typing.Optional[bool]) – If `True`, `problem_parameters` are assumed to be on the scale provided in the PEtab parameter table and will be unscaled. If `False`, they are assumed to be in linear scale. If *parameter_mapping* is provided, this must match the value of *scaled_parameters* used to generate the mapping.
- **log_level** (int) – Log level, see *amici.logging* module.
- **num_threads** (int) – Number of threads to use for simulating multiple conditions (only used if compiled with OpenMP).
- **failfast** (bool) – Returns as soon as an integration failure is encountered, skipping any remaining simulations.
- **scaled_gradients** (bool) – Whether to compute gradients on parameter scale (`True`) or not (`False`).

Return type
dict[str, typing.Any]

Returns

Dictionary of

- cost function value (`LLH`),
- list of *amici.amici.ReturnData* (`RDATAS`),
- list of *amici.amici.ExpData* (`EDATAS`),

corresponding to the different simulation conditions. For ordering of simulation conditions, see `petab.Problem.get_simulation_conditions_from_measurement_df()`.

10.5.7 amici.petab.conditions

PEtab conditions to AMICI ExpDatas.

Functions

create_edata_for_condition(condition, ...)	Get *amici.amici.ExpData* for the given PEtab condition.
create_edatas(amici_model, petab_problem[, ...])	Create list of *amici.amici.ExpData* objects for PEtab problem.
create_parameterized_edatas(amici_model, ...)	Create list of :class:amici.ExpData objects with parameters filled in.
fill_in_parameters(edatas, ...)	Fill fixed and dynamic parameters into the edatas (in-place).
fill_in_parameters_for_condition(edata, ...)	Fill fixed and dynamic parameters into the edata for condition (in-place).

amici.petab.conditions.**create_edata_for_condition**(*condition*, *measurement_df*, *amici_model*, *petab_problem*, *observable_ids*)

Get *amici.amici.ExpData* for the given PEtab condition.

Sets timepoints, observed data and sigmas.

Parameters

- **condition** (typing.Union[dict, pandas.core.series.Series]) – pandas.DataFrame row with `preequilibrationConditionId` and `simulationConditionId`.
- **measurement_df** (pandas.core.frame.DataFrame) – pandas.DataFrame with measurements for the given condition.
- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model
- **petab_problem** (petab.problem.Problem) – Underlying PEtab problem
- **observable_ids** (list[str]) – List of observable IDs

Return type
`amici.swig_wrappers.ExpData`

Returns
ExpData instance.

amici.petab.conditions.**create_edatas**(*amici_model*, *petab_problem*, *simulation_conditions=None*)

Create list of *amici.amici.ExpData* objects for PEtab problem.

Parameters

- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model.
- **petab_problem** (petab.problem.Problem) – Underlying PEtab problem.
- **simulation_conditions** (typing.Union[pandas.core.frame.DataFrame, dict]) – Result of `petab.get_simulation_conditions()`. Can be provided to save time if this has be obtained before.

Return type
list[`amici.swig_wrappers.ExpData`]

Returns
List with one *amici.amici.ExpData* per simulation condition, with filled in timepoints and data.

amici.petab.conditions.**create_parameterized_edatas**(*amici_model*, *petab_problem*, *problem_parameters*, *scaled_parameters=False*, *parameter_mapping=None*, *simulation_conditions=None*)

Create list of :class:amici.ExpData objects with parameters filled in.

Parameters

- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI Model assumed to be compatible with `petab_problem`.
- **petab_problem** (petab.problem.Problem) – PEtab problem to work on.
- **problem_parameters** (dict[str, numbers.Number]) – Run simulation with these parameters. If `None`, PEtab `nominalValues` will be used. To be provided as dict, mapping PEtab problem parameters to SBML IDs.

- **scaled_parameters** (bool) – If True, problem_parameters are assumed to be on the scale provided in the PEtab parameter table and will be unscaled. If False, they are assumed to be in linear scale.
- **parameter_mapping** (*amici.petab.parameter_mapping.ParameterMapping*) – Optional precomputed PEtab parameter mapping for efficiency, as generated by create_parameter_mapping().
- **simulation_conditions** (typing.Union[pandas.core.frame.DataFrame, dict]) – Result of petab.get_simulation_conditions(). Can be provided to save time if this has been obtained before.

Return type
list[amici.swig_wrappers.ExpData]

Returns
List with one *amici.amici.ExpData* per simulation condition, with filled in timepoints, data and parameters.

amici.petab.conditions.**fill_in_parameters**(*edatas*, *problem_parameters*, *scaled_parameters*, *parameter_mapping*, *amici_model*)

Fill fixed and dynamic parameters into the edatas (in-place).

Parameters

- **edatas** (list[amici.swig_wrappers.ExpData]) – List of experimental datas *amici.amici.ExpData* with everything except parameters filled.
- **problem_parameters** (dict[str, numbers.Number]) – Problem parameters as parameterId=>value dict. Only parameters included here will be set. Remaining parameters will be used as currently set in *amici_model*.
- **scaled_parameters** (bool) – If True, problem_parameters are assumed to be on the scale provided in the parameter mapping. If False, they are assumed to be in linear scale.
- **parameter_mapping** (*amici.petab.parameter_mapping.ParameterMapping*) – Parameter mapping for all conditions.
- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model.

Return type
None

amici.petab.conditions.**fill_in_parameters_for_condition**(*edata*, *problem_parameters*, *scaled_parameters*, *parameter_mapping*, *amici_model*)

Fill fixed and dynamic parameters into the edata for condition (in-place).

Parameters

- **edata** (amici.swig_wrappers.ExpData) – Experimental data object to fill parameters into.
- **problem_parameters** (dict[str, numbers.Number]) – Problem parameters as parameterId=>value dict. Only parameters included here will be set. Remaining parameters will be used as already set in *amici_model* and *edata*.
- **scaled_parameters** (bool) – If True, problem_parameters are assumed to be on the scale provided in the parameter mapping. If False, they are assumed to be in linear scale.

- **parameter_mapping** (*amici.petab.parameter_mapping.ParameterMappingForCondition*) – Parameter mapping for current condition.
- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model

Return type
None

10.5.8 amici.petab.import_helpers

General helper functions for PEtab import.

Functions for PEtab import that are independent of the model format.

Functions

check_model(amici_model, petab_problem)	Check that the model is consistent with the PEtab problem.
get_fixed_parameters(petab_problem[, ...])	Determine, set and return fixed model parameters.
get_observation_model(observable_df)	Get observables, sigmas, and noise distributions from PEtab observation table in a format suitable for *amici.sbml_import.SbmlImporter.sbml2amici()*.
petab_noise_distributions_to_amici(observable_	Map from the petab to the amici format of noise distribution identifiers.
petab_scale_to_amici_scale(scale_str)	Convert PEtab parameter scaling string to AMICI scaling integer

amici.petab.import_helpers.**check_model**(*amici_model*, *petab_problem*)

Check that the model is consistent with the PEtab problem.

Return type
None

amici.petab.import_helpers.**get_fixed_parameters**(*petab_problem*, *non_estimated_parameters_as_constants=True*)

Determine, set and return fixed model parameters.

Non-estimated parameters and parameters specified in the condition table are turned into constants (unless they are overridden). Only global SBML parameters are considered. Local parameters are ignored.

Parameters

- **petab_problem** (petab.problem.Problem) – The PEtab problem instance
- **non_estimated_parameters_as_constants** – Whether parameters marked as non-estimated in PEtab should be considered constant in AMICI. Setting this to True will reduce model size and simulation times. If sensitivities with respect to those parameters are required, this should be set to False.

Return type
list[str]

Returns
list of IDs of parameters which are to be considered constant.

amici.petab.import_helpers.**get_observation_model**(*observable_df*)

Get observables, sigmas, and noise distributions from PEtab observation table in a format suitable for *amici.sbml_import.SbmlImporter.sbml2amici()*.

Parameters
observable_df (pandas.core.frame.DataFrame) – PEtab observables table

Return type
tuple[dict[str, dict[str, str]], dict[str, str], dict[str, typing.Union[str, float]]]

Returns
Tuple of dicts with observables, noise distributions, and sigmas.

amici.petab.import_helpers.**petab_noise_distributions_to_amici**(*observable_df*)

Map from the petab to the amici format of noise distribution identifiers.

Parameters
observable_df (pandas.core.frame.DataFrame) – PEtab observable table

Return type
dict[str, str]

Returns
dictionary of observable_id => AMICI noise-distributions

amici.petab.import_helpers.**petab_scale_to_amici_scale**(*scale_str*)

Convert PEtab parameter scaling string to AMICI scaling integer

Return type
int

10.5.9 amici.petab.parameter_mapping

Functions

amici_to_petab_scale(amici_scale)	Convert amici scale id to petab scale id.
create_parameter_mapping(petab_problem, ...)	Generate AMICI specific parameter mapping.
create_parameter_mapping_for_condition(...)	Generate AMICI specific parameter mapping for condition.
petab_to_amici_scale(petab_scale)	Convert petab scale id to amici scale id.
scale_parameter(value, petab_scale)	Bring parameter from linear scale to target scale.
scale_parameters_dict(value_dict, ...)	Bring parameters from linear scale to target scale.
unscale_parameter(value, petab_scale)	Bring parameter from scale to linear scale.
unscale_parameters_dict(value_dict, ...)	Bring parameters from target scale to linear scale.

Classes

ParameterMapping([parameter_mappings])	Parameter mapping for multiple conditions.
ParameterMappingForCondition([map_sim_var, ...])	Parameter mapping for condition.

class amici.petab.parameter_mapping.**ParameterMapping**(*parameter_mappings=None*)

Parameter mapping for multiple conditions.

This can be used like a list of *ParameterMappingForCondition*s.

Parameters

parameter_mappings (list[*amici.petab.parameter_mapping.ParameterMappingForCondition*]) – List of parameter mappings for specific conditions.

__init__(*parameter_mappings=None*)

append(*parameter_mapping_for_condition*)

Append a condition specific parameter mapping.

count(*value*) → integer -- return number of occurrences of value

property free_symbols: set[str]

Get IDs of all (symbolic) parameters present in this mapping

index(*value*[, *start*[, *stop*]]) → integer -- return first index of value.

Raises ValueError if the value is not present.

Supporting start and stop arguments is optional, but recommended.

class amici.petab.parameter_mapping.**ParameterMappingForCondition**(*map_sim_var=None*, *scale_map_sim_var=None*, *map_preeq_fix=None*, *scale_map_preeq_fix=None*, *map_sim_fix=None*, *scale_map_sim_fix=None*)

Parameter mapping for condition.

Contains mappings for free parameters, fixed parameters, and fixed preequilibration parameters, both for parameters and scales.

In the scale mappings, for each simulation parameter the scale on which the value is passed (and potentially gradients are to be returned) is given. In the parameter mappings, for each simulation parameter a corresponding optimization parameter (or a numeric value) is given.

If a mapping is not passed, the parameter mappings are assumed to be empty, and if a scale mapping is not passed, all scales are set to linear.

Parameters

- **map_sim_var** (dict[str, typing.Union[numbers.Number, str]]) – Mapping for free simulation parameters.
- **scale_map_sim_var** (dict[str, str]) – Scales for free simulation parameters.
- **map_preeq_fix** (dict[str, typing.Union[numbers.Number, str]]) – Mapping for fixed preequilibration parameters.
- **scale_map_preeq_fix** (dict[str, str]) – Scales for fixed preequilibration parameters.

- **map_sim_fix** (dict[str, typing.Union[numbers.Number, str]]) – Mapping for fixed simulation parameters.
- **scale_map_sim_fix** (dict[str, str]) – Scales for fixed simulation parameters.

__init__(*map_sim_var=None*, *scale_map_sim_var=None*, *map_preeq_fix=None*, *scale_map_preeq_fix=None*, *map_sim_fix=None*, *scale_map_sim_fix=None*)

property free_symbols: set[str]

Get IDs of all (symbolic) parameters present in this mapping

amici.petab.parameter_mapping.**amici_to_petab_scale**(*amici_scale*)

Convert amici scale id to petab scale id.

Return type
str

amici.petab.parameter_mapping.**create_parameter_mapping**(*petab_problem*, *simulation_conditions*, *scaled_parameters*, *amici_model*, ***parameter_mapping_kwargs*)

Generate AMICI specific parameter mapping.

Parameters

- **petab_problem** (petab.problem.Problem) – PEtab problem
- **simulation_conditions** (pandas.core.frame.DataFrame | list[dict]) – Result of petab.get_simulation_conditions(). Can be provided to save time if this has been obtained before.
- **scaled_parameters** (bool) – If True, problem_parameters are assumed to be on the scale provided in the PEtab parameter table and will be unscaled. If False, they are assumed to be in linear scale.
- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model.
- **parameter_mapping_kwargs** – Optional keyword arguments passed to petab.get_optimization_to_simulation_parameter_mapping(). To allow changing fixed PEtab problem parameters (estimate=0), use fill_fixed_parameters=False.

Return type
amici.petab.parameter_mapping.ParameterMapping

Returns
List of the parameter mappings.

amici.petab.parameter_mapping.**create_parameter_mapping_for_condition**(*parameter_mapping_for_condition*, *condition*, *petab_problem*, *amici_model*)

Generate AMICI specific parameter mapping for condition.

Parameters

- **parameter_mapping_for_condition** (typing.Tuple[typing.Dict[str, typing.Union[str, numbers.Number]], typing.Dict[str, typing.Union[str, numbers.Number]], typing.Dict[str, str], typing.Dict[str, str]]) – Preliminary parameter mapping for condition.
- **condition** (pandas.core.series.Series | dict) – pandas.DataFrame row with preequilibrationConditionId and simulationConditionId.

- **petab_problem** (petab.problem.Problem) – Underlying PEtab problem.
- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model.

Return type
amici.petab.parameter_mapping.ParameterMappingForCondition

Returns
The parameter and parameter scale mappings, for fixed preequilibration, fixed simulation, and variable simulation parameters, and then the respective scalings.

amici.petab.parameter_mapping.**petab_to_amici_scale**(*petab_scale*)

Convert petab scale id to amici scale id.

Return type
int

amici.petab.parameter_mapping.**scale_parameter**(*value*, *petab_scale*)

Bring parameter from linear scale to target scale.

Parameters

- **value** (numbers.Number) – Value to scale
- **petab_scale** (str) – Target scale of value

Return type
numbers.Number

Returns
value on target scale

amici.petab.parameter_mapping.**scale_parameters_dict**(*value_dict*, *petab_scale_dict*)

Bring parameters from linear scale to target scale.

Bring values in value_dict from linear scale to the scale provided in petab_scale_dict (in-place). Both arguments are expected to have the same length and matching keys.

Parameters

- **value_dict** (dict[typing.Any, numbers.Number]) – Values to scale
- **petab_scale_dict** (dict[typing.Any, str]) – Target scales of values

Return type
None

amici.petab.parameter_mapping.**unscale_parameter**(*value*, *petab_scale*)

Bring parameter from scale to linear scale.

Parameters

- **value** (numbers.Number) – Value to scale
- **petab_scale** (str) – Target scale of value

Return type
numbers.Number

Returns
value on linear scale

amici.petab.parameter_mapping.**unscale_parameters_dict**(*value_dict*, *petab_scale_dict*)

Bring parameters from target scale to linear scale.

Bring values in `value_dict` from linear scale to the scale provided in `petab_scale_dict` (in-place). Both arguments are expected to have the same length and matching keys.

Parameters

- **value_dict** (dict[typing.Any, numbers.Number]) – Values to scale
- **petab_scale_dict** (dict[typing.Any, str]) – Target scales of `values`

Return type
None

10.5.10 amici.petab.petab_import

PEtab Import

Import a model in the petab (https://github.com/PEtab-dev/PEtab) format into AMICI.

Functions

import_petab_problem(petab_problem[, ...])	Create an AMICI model for a PEtab problem.

amici.petab.petab_import.**import_petab_problem**(*petab_problem*, *model_output_dir=None*, *model_name=None*, *compile_=None*, *non_estimated_parameters_as_constants=True*, ***kwargs*)

Create an AMICI model for a PEtab problem.

Parameters

- **petab_problem** (petab.problem.Problem) – A petab problem containing all relevant information on the model.
- **model_output_dir** (typing.Union[str, pathlib.Path, None]) – Directory to write the model code to. It will be created if it doesn't exist. Defaults to current directory.
- **model_name** (str) – Name of the generated model module. Defaults to the ID of the model or the model file name without the extension.
- **compile** – If `True`, the model will be compiled. If `False`, the model will not be compiled. If `None`, the model will be compiled if it cannot be imported.
- **non_estimated_parameters_as_constants** – Whether parameters marked as non-estimated in PEtab should be considered constant in AMICI. Setting this to `True` will reduce model size and simulation times. If sensitivities with respect to those parameters are required, this should be set to `False`.
- **kwargs** – Additional keyword arguments to be passed to *amici.sbml_import.SbmlImporter.sbml2amici()* or *amici.pysb_import.pysb2amici()*, depending on the model type.

Return type
amici.amici.Model

Returns
The imported model.

10.5.11 amici.petab.pysb_import

PySB-PEtab Import

Import a model in the PySB-adapted `petab` (https://github.com/PEtab-dev/PEtab) format into AMICI.

Functions

import_model_pysb(petab_problem[, ...])	Create AMICI model from PySB-PEtab problem

amici.petab.pysb_import.**import_model_pysb**(*petab_problem*, *model_output_dir=None*, *verbose=True*, *model_name=None*, ***kwargs*)

Create AMICI model from PySB-PEtab problem

Parameters

- **petab_problem** (`petab.problem.Problem`) – PySB PEtab problem
- **model_output_dir** (`typing.Union`[`pathlib.Path`, `str`, `None`]) – Directory to write the model code to. Will be created if doesn't exist. Defaults to current directory.
- **verbose** (`typing.Union`[`bool`, `int`, `None`]) – Print/log extra information.
- **model_name** (`typing.Optional`[`str`]) – Name of the generated model module
- **kwargs** – Additional keyword arguments to be passed to *amici.pysb_import.pysb2amici()*.

Return type
`None`

10.5.12 amici.petab.sbml_import

Functions

import_model_sbml([sbml_model, ...])	Create AMICI model from PEtab problem
show_model_info(sbml_model)	Log some model quantities
species_to_parameters(species_ids, sbml_model)	Turn a SBML species into parameters and replace species references inside the model instance.

amici.petab.sbml_import.**import_model_sbml**(*sbml_model=None*, *condition_table=None*, *observable_table=None*, *measurement_table=None*, *petab_problem=None*, *model_name=None*, *model_output_dir=None*, *verbose=True*, *allow_reinit_fixpar_initcond=True*, *validate=True*, *non_estimated_parameters_as_constants=True*, *output_parameter_defaults=None*, *discard_sbml_annotations=False*, ***kwargs*)

Create AMICI model from PEtab problem

Parameters

- **sbml_model** (typing.Union[str, pathlib.Path, libsbml.Model]) – PEtab SBML model or SBML file name. Deprecated, pass petab_problem instead.
- **condition_table** (typing.Union[str, pathlib.Path, pandas.core.frame.DataFrame, None]) – PEtab condition table. If provided, parameters from there will be turned into AMICI constant parameters (i.e. parameters w.r.t. which no sensitivities will be computed). Deprecated, pass petab_problem instead.
- **observable_table** (typing.Union[str, pathlib.Path, pandas.core.frame.DataFrame, None]) – PEtab observable table. Deprecated, pass petab_problem instead.
- **measurement_table** (typing.Union[str, pathlib.Path, pandas.core.frame.DataFrame, None]) – PEtab measurement table. Deprecated, pass petab_problem instead.
- **petab_problem** (petab.problem.Problem) – PEtab problem.
- **model_name** (typing.Optional[str]) – Name of the generated model. If model file name was provided, this defaults to the file name without extension, otherwise the SBML model ID will be used.
- **model_output_dir** (typing.Union[pathlib.Path, str, None]) – Directory to write the model code to. Will be created if doesn't exist. Defaults to current directory.
- **verbose** (typing.Union[bool, int, None]) – Print/log extra information.
- **allow_reinit_fixpar_initcond** (bool) – See amici.de_export.ODEExporter. Must be enabled if initial states are to be reset after preequilibration.
- **validate** (bool) – Whether to validate the PEtab problem
- **non_estimated_parameters_as_constants** – Whether parameters marked as non-estimated in PEtab should be considered constant in AMICI. Setting this to True will reduce model size and simulation times. If sensitivities with respect to those parameters are required, this should be set to False.
- **output_parameter_defaults** (typing.Optional[dict[str, float]]) – Optional default parameter values for output parameters introduced in the PEtab observables table, in particular for placeholder parameters. dictionary mapping parameter IDs to default values.
- **discard_sbml_annotations** (bool) – Discard information contained in AMICI SBML annotations (debug).
- **kwargs** – Additional keyword arguments to be passed to *amici.sbml_import.SbmlImporter.sbml2amici()*.

Return type

amici.sbml_import.SbmlImporter

Returns

The created *amici.sbml_import.SbmlImporter* instance.

amici.petab.sbml_import.**show_model_info**(*sbml_model*)

Log some model quantities

amici.petab.sbml_import.**species_to_parameters**(*species_ids*, *sbml_model*)

Turn a SBML species into parameters and replace species references inside the model instance.

Parameters

- **species_ids** (list[str]) – list of SBML species ID to convert to parameters with the same ID as the replaced species.
- **sbml_model** (libsbml.Model) – SBML model to modify

Return type
list[str]

Returns
list of IDs of species which have been converted to parameters

10.5.13 amici.petab.simulations

Functionality related to simulation of PEtab problems.

Functionality related to running simulations or evaluating the objective function as defined by a PEtab problem.

Functions

aggregate_sllh(amici_model, rdatas, ...[, ...])	Aggregate likelihood gradient for all conditions, according to PEtab parameter mapping.
rdatas_to_measurement_df(rdatas, model, ...)	Create a measurement dataframe in the PEtab format from the passed rdatas and own information.
rdatas_to_simulation_df(rdatas, model, ...)	Create a PEtab simulation dataframe from *amici.amici.ReturnData* s.
rescale_sensitivity(sensitivity, ...)	Rescale a sensitivity between parameter scales.
simulate_petab(petab_problem, amici_model[, ...])	Simulate PEtab model.

amici.petab.simulations.**simulate_petab**(*petab_problem*, *amici_model*, *solver=None*, *problem_parameters=None*, *simulation_conditions=None*, *edatas=None*, *parameter_mapping=None*, *scaled_parameters=False*, *log_level=30*, *num_threads=1*, *failfast=True*, *scaled_gradients=False*)

Simulate PEtab model.

Note: Regardless of *scaled_parameters*, unscaled sensitivities are returned, unless *scaled_gradients=True*.

Parameters

- **petab_problem** (petab.problem.Problem) – PEtab problem to work on.
- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI Model assumed to be compatible with petab_problem.
- **solver** (typing.Optional[*amici.amici.Solver*]) – An AMICI solver. Will use default options if None.
- **problem_parameters** (typing.Optional[dict[str, float]]) – Run simulation with these parameters. If None, PEtab nominalValues will be used. To be provided as dict, mapping PEtab problem parameters to SBML IDs.

- **simulation_conditions** (typing.Union[pandas.core.frame.DataFrame, dict]) – Result of petab.get_simulation_conditions(). Can be provided to save time if this has be obtained before. Not required if edatas and parameter_mapping are provided.
- **edatas** (list[typing.Union[amici.swig_wrappers.ExpData, *amici.amici.ExpDataPtr*]]) – Experimental data. Parameters are inserted in-place for simulation.
- **parameter_mapping** (*amici.petab.parameter_mapping.ParameterMapping*) – Optional precomputed PEtab parameter mapping for efficiency, as generated by create_parameter_mapping() with scaled_parameters=True.
- **scaled_parameters** (typing.Optional[bool]) – If True, problem_parameters are assumed to be on the scale provided in the PEtab parameter table and will be unscaled. If False, they are assumed to be in linear scale. If *parameter_mapping* is provided, this must match the value of *scaled_parameters* used to generate the mapping.
- **log_level** (int) – Log level, see *amici.logging* module.
- **num_threads** (int) – Number of threads to use for simulating multiple conditions (only used if compiled with OpenMP).
- **failfast** (bool) – Returns as soon as an integration failure is encountered, skipping any remaining simulations.
- **scaled_gradients** (bool) – Whether to compute gradients on parameter scale (True) or not (False).

Return type
dict[str, typing.Any]

Returns

Dictionary of

- cost function value (LLH),
- list of *amici.amici.ReturnData* (RDATAS),
- list of *amici.amici.ExpData* (EDATAS),

corresponding to the different simulation conditions. For ordering of simulation conditions, see petab.Problem.get_simulation_conditions_from_measurement_df().

10.5.14 amici.petab.simulator

PEtab Simulator

Functionality related to the use of AMICI for simulation with petab.Simulator.

Use cases:

- generate data for use with PEtab's plotting methods
- generate synthetic data

Classes

PetabSimulator(*args[, amici_model])	Implementation of the PEtab *Simulator* class that uses AMICI.

class amici.petab.simulator.**PetabSimulator**(**args*, *amici_model=None*, ***kwargs*)

Implementation of the PEtab *Simulator* class that uses AMICI.

__init__(**args*, *amici_model=None*, ***kwargs*)

Initialize the simulator.

Initialize the simulator with sufficient information to perform a simulation. If no working directory is specified, a temporary one is created.

Parameters

- **petab_problem** – A PEtab problem.
- **working_dir** – All simulator-specific output files will be saved here. This directory and its contents may be modified and deleted, and should be considered ephemeral.

add_noise(*simulation_df*, *noise_scaling_factor=1*, ***kwargs*)

Add noise to simulated data.

Parameters

- **simulation_df** (pandas.core.frame.DataFrame) – A PEtab measurements table that contains simulated data.
- **noise_scaling_factor** (float) – A multiplier of the scale of the noise distribution.
- ****kwargs** – Additional keyword arguments are passed to `sample_noise()`.

Return type
pandas.core.frame.DataFrame

Returns
Simulated data with noise, as a PEtab measurements table.

remove_working_dir(*force=False*, ***kwargs*)

Remove the simulator working directory, and all files within.

See the `petab.simulate.Simulator.__init__()` method arguments.

Parameters

- **force** (bool) – If `True`, the working directory is removed regardless of whether it is a temporary directory.
- ****kwargs** – Additional keyword arguments are passed to `shutil.rmtree()`.

Return type
None

simulate(*noise=False*, *noise_scaling_factor=1*, *as_measurement=False*, ***kwargs*)

Simulate a PEtab problem, optionally with noise.

Parameters

- **noise** (bool) – If True, noise is added to simulated data.
- **noise_scaling_factor** (float) – A multiplier of the scale of the noise distribution.

- **as_measurement** (bool) – Whether the data column is named petab.C.MEASUREMENT (*True*) or petab.C.SIMULATION (*False*).
- ****kwargs** – Additional keyword arguments are passed to petab.simulate.Simulator.simulate_without_noise().

Return type
pandas.core.frame.DataFrame

Returns
Simulated data, as a PEtab measurements table.

simulate_without_noise(***kwargs*)

See petab.simulate.Simulator.simulate() docstring.

Additional keyword arguments can be supplied to specify arguments for the AMICI PEtab import, simulate, and export methods. See the docstrings for the respective methods for argument options: - *amici.petab_import.import_petab_problem()*, and - *amici.petab_objective.simulate_petab()*.

Note that some arguments are expected to have already been specified in the Simulator constructor (including the PEtab problem).

Return type
pandas.core.frame.DataFrame

10.5.15 amici.petab_import

PEtab Import

Import a model in the petab (https://github.com/PEtab-dev/PEtab) format into AMICI.

Deprecated since version 0.21.0: Use *amici.petab* instead.

amici.petab_import.**check_model**(*amici_model*, *petab_problem*)

Check that the model is consistent with the PEtab problem.

Return type
None

amici.petab_import.**get_fixed_parameters**(*petab_problem*, *non_estimated_parameters_as_constants=True*)

Determine, set and return fixed model parameters.

Non-estimated parameters and parameters specified in the condition table are turned into constants (unless they are overridden). Only global SBML parameters are considered. Local parameters are ignored.

Parameters

- **petab_problem** (petab.problem.Problem) – The PEtab problem instance
- **non_estimated_parameters_as_constants** – Whether parameters marked as non-estimated in PEtab should be considered constant in AMICI. Setting this to True will reduce model size and simulation times. If sensitivities with respect to those parameters are required, this should be set to False.

Return type
list[str]

Returns
list of IDs of parameters which are to be considered constant.

amici.petab_import.**get_observation_model**(*observable_df*)

Get observables, sigmas, and noise distributions from PEtab observation table in a format suitable for *amici.sbml_import.SbmlImporter.sbml2amici()*.

Parameters
observable_df (pandas.core.frame.DataFrame) – PEtab observables table

Return type
tuple[dict[str, dict[str, str]], dict[str, str], dict[str, typing.Union[str, float]]]

Returns
Tuple of dicts with observables, noise distributions, and sigmas.

amici.petab_import.**import_model**(*sbml_model=None*, *condition_table=None*, *observable_table=None*, *measurement_table=None*, *petab_problem=None*, *model_name=None*, *model_output_dir=None*, *verbose=True*, *allow_reinit_fixpar_initcond=True*, *validate=True*, *non_estimated_parameters_as_constants=True*, *output_parameter_defaults=None*, *discard_sbml_annotations=False*, ***kwargs*)

Create AMICI model from PEtab problem

Parameters

- **sbml_model** (typing.Union[str, pathlib.Path, libsbml.Model]) – PEtab SBML model or SBML file name. Deprecated, pass `petab_problem` instead.
- **condition_table** (typing.Union[str, pathlib.Path, pandas.core.frame.DataFrame, None]) – PEtab condition table. If provided, parameters from there will be turned into AMICI constant parameters (i.e. parameters w.r.t. which no sensitivities will be computed). Deprecated, pass `petab_problem` instead.
- **observable_table** (typing.Union[str, pathlib.Path, pandas.core.frame.DataFrame, None]) – PEtab observable table. Deprecated, pass `petab_problem` instead.
- **measurement_table** (typing.Union[str, pathlib.Path, pandas.core.frame.DataFrame, None]) – PEtab measurement table. Deprecated, pass `petab_problem` instead.
- **petab_problem** (petab.problem.Problem) – PEtab problem.
- **model_name** (typing.Optional[str]) – Name of the generated model. If model file name was provided, this defaults to the file name without extension, otherwise the SBML model ID will be used.
- **model_output_dir** (typing.Union[pathlib.Path, str, None]) – Directory to write the model code to. Will be created if doesn't exist. Defaults to current directory.
- **verbose** (typing.Union[bool, int, None]) – Print/log extra information.
- **allow_reinit_fixpar_initcond** (bool) – See `amici.de_export.ODEExporter`. Must be enabled if initial states are to be reset after preequilibration.
- **validate** (bool) – Whether to validate the PEtab problem
- **non_estimated_parameters_as_constants** – Whether parameters marked as non-estimated in PEtab should be considered constant in AMICI. Setting this to `True` will reduce model size and simulation times. If sensitivities with respect to those parameters are required, this should be set to `False`.

- **output_parameter_defaults** (typing.Optional[dict[str, float]]) – Optional default parameter values for output parameters introduced in the PEtab observables table, in particular for placeholder parameters. dictionary mapping parameter IDs to default values.
- **discard_sbml_annotations** (bool) – Discard information contained in AMICI SBML annotations (debug).
- **kwargs** – Additional keyword arguments to be passed to *amici.sbml_import.SbmlImporter.sbml2amici()*.

Return type
amici.sbml_import.SbmlImporter

Returns
The created *amici.sbml_import.SbmlImporter* instance.

amici.petab_import.**import_model_sbml**(*sbml_model=None*, *condition_table=None*, *observable_table=None*, *measurement_table=None*, *petab_problem=None*, *model_name=None*, *model_output_dir=None*, *verbose=True*, *allow_reinit_fixpar_initcond=True*, *validate=True*, *non_estimated_parameters_as_constants=True*, *output_parameter_defaults=None*, *discard_sbml_annotations=False*, ***kwargs*)

Create AMICI model from PEtab problem

Parameters

- **sbml_model** (typing.Union[str, pathlib.Path, libsbml.Model]) – PEtab SBML model or SBML file name. Deprecated, pass `petab_problem` instead.
- **condition_table** (typing.Union[str, pathlib.Path, pandas.core.frame.DataFrame, None]) – PEtab condition table. If provided, parameters from there will be turned into AMICI constant parameters (i.e. parameters w.r.t. which no sensitivities will be computed). Deprecated, pass `petab_problem` instead.
- **observable_table** (typing.Union[str, pathlib.Path, pandas.core.frame.DataFrame, None]) – PEtab observable table. Deprecated, pass `petab_problem` instead.
- **measurement_table** (typing.Union[str, pathlib.Path, pandas.core.frame.DataFrame, None]) – PEtab measurement table. Deprecated, pass `petab_problem` instead.
- **petab_problem** (petab.problem.Problem) – PEtab problem.
- **model_name** (typing.Optional[str]) – Name of the generated model. If model file name was provided, this defaults to the file name without extension, otherwise the SBML model ID will be used.
- **model_output_dir** (typing.Union[pathlib.Path, str, None]) – Directory to write the model code to. Will be created if doesn't exist. Defaults to current directory.
- **verbose** (typing.Union[bool, int, None]) – Print/log extra information.
- **allow_reinit_fixpar_initcond** (bool) – See `amici.de_export.ODEExporter`. Must be enabled if initial states are to be reset after preequilibration.
- **validate** (bool) – Whether to validate the PEtab problem
- **non_estimated_parameters_as_constants** – Whether parameters marked as non-estimated in PEtab should be considered constant in AMICI. Setting this to `True` will reduce model size and simulation times. If sensitivities with respect to those parameters are required, this should be set to `False`.

- **output_parameter_defaults** (typing.Optional[dict[str, float]]) – Optional default parameter values for output parameters introduced in the PEtab observables table, in particular for placeholder parameters. dictionary mapping parameter IDs to default values.
- **discard_sbml_annotations** (bool) – Discard information contained in AMICI SBML annotations (debug).
- **kwargs** – Additional keyword arguments to be passed to *amici.sbml_import.SbmlImporter.sbml2amici()*.

Return type
amici.sbml_import.SbmlImporter

Returns
The created *amici.sbml_import.SbmlImporter* instance.

amici.petab_import.**import_petab_problem**(*petab_problem*, *model_output_dir=None*, *model_name=None*, *compile_=None*, *non_estimated_parameters_as_constants=True*, ***kwargs*)

Create an AMICI model for a PEtab problem.

Parameters

- **petab_problem** (petab.problem.Problem) – A petab problem containing all relevant information on the model.
- **model_output_dir** (typing.Union[str, pathlib.Path, None]) – Directory to write the model code to. It will be created if it doesn't exist. Defaults to current directory.
- **model_name** (str) – Name of the generated model module. Defaults to the ID of the model or the model file name without the extension.
- **compile** – If True, the model will be compiled. If False, the model will not be compiled. If None, the model will be compiled if it cannot be imported.
- **non_estimated_parameters_as_constants** – Whether parameters marked as non-estimated in PEtab should be considered constant in AMICI. Setting this to True will reduce model size and simulation times. If sensitivities with respect to those parameters are required, this should be set to False.
- **kwargs** – Additional keyword arguments to be passed to *amici.sbml_import.SbmlImporter.sbml2amici()* or *amici.pysb_import.pysb2amici()*, depending on the model type.

Return type
amici.amici.Model

Returns
The imported model.

amici.petab_import.**petab_noise_distributions_to_amici**(*observable_df*)

Map from the petab to the amici format of noise distribution identifiers.

Parameters
observable_df (pandas.core.frame.DataFrame) – PEtab observable table

Return type
dict[str, str]

Returns
dictionary of observable_id => AMICI noise-distributions

amici.petab_import.**petab_scale_to_amici_scale**(*scale_str*)

Convert PEtab parameter scaling string to AMICI scaling integer

Return type
int

amici.petab_import.**species_to_parameters**(*species_ids*, *sbml_model*)

Turn a SBML species into parameters and replace species references inside the model instance.

Parameters

- **species_ids** (list[str]) – list of SBML species ID to convert to parameters with the same ID as the replaced species.
- **sbml_model** (libsbml.Model) – SBML model to modify

Return type
list[str]

Returns
list of IDs of species which have been converted to parameters

10.5.16 amici.petab_import_pysb

PEtab import for PySB models

Deprecated since version 0.21.0: Use *amici.petab.pysb_import* instead.

amici.petab_import_pysb.**import_model_pysb**(*petab_problem*, *model_output_dir=None*, *verbose=True*, *model_name=None*, ***kwargs*)

Create AMICI model from PySB-PEtab problem

Parameters

- **petab_problem** (petab.problem.Problem) – PySB PEtab problem
- **model_output_dir** (typing.Union[pathlib.Path, str, None]) – Directory to write the model code to. Will be created if doesn't exist. Defaults to current directory.
- **verbose** (typing.Union[bool, int, None]) – Print/log extra information.
- **model_name** (typing.Optional[str]) – Name of the generated model module
- **kwargs** – Additional keyword arguments to be passed to *amici.pysb_import.pysb2amici()*.

Return type
None

10.5.17 amici.petab_objective

Evaluate a PEtab objective function.

Deprecated since version 0.21.0: Use *amici.petab.simulations* instead.

amici.petab_objective.**aggregate_sllh**(*amici_model*, *rdatas*, *parameter_mapping*, *edatas*, *petab_scale=True*, *petab_problem=None*)

Aggregate likelihood gradient for all conditions, according to PEtab parameter mapping.

Parameters

- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model from which `rdatas` were obtained.
- **rdatas** (collections.abc.Sequence[*amici.numpy.ReturnDataView*]) – Simulation results.
- **parameter_mapping** (typing.Optional[*amici.petab.parameter_mapping.ParameterMapping*]) – PEtab parameter mapping to condition-specific simulation parameters.
- **edatas** (list[typing.Union[amici.swig_wrappers.ExpData, *amici.amici.ExpDataPtr*]]) – Experimental data used for simulation.
- **petab_scale** (bool) – Whether to check that sensitivities were computed with parameters on the scales provided in the PEtab parameters table.
- **petab_problem** (petab.problem.Problem) – The PEtab problem that defines the parameter scales.

Return type
typing.Optional[dict[str, float]]

Returns
Aggregated likelihood sensitivities.

amici.petab_objective.**create_edatas**(*amici_model*, *petab_problem*, *simulation_conditions=None*)

Create list of *amici.amici.ExpData* objects for PEtab problem.

Parameters

- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model.
- **petab_problem** (petab.problem.Problem) – Underlying PEtab problem.
- **simulation_conditions** (typing.Union[pandas.core.frame.DataFrame, dict]) – Result of `petab.get_simulation_conditions()`. Can be provided to save time if this has be obtained before.

Return type
list[amici.swig_wrappers.ExpData]

Returns
List with one *amici.amici.ExpData* per simulation condition, with filled in timepoints and data.

amici.petab_objective.**create_parameter_mapping**(*petab_problem*, *simulation_conditions*, *scaled_parameters*, *amici_model*, ***parameter_mapping_kwargs*)

Generate AMICI specific parameter mapping.

Parameters

- **petab_problem** (petab.problem.Problem) – PEtab problem
- **simulation_conditions** (pandas.core.frame.DataFrame | list[dict]) – Result of `petab.get_simulation_conditions()`. Can be provided to save time if this has been obtained before.
- **scaled_parameters** (bool) – If `True`, problem_parameters are assumed to be on the scale provided in the PEtab parameter table and will be unscaled. If `False`, they are assumed to be in linear scale.

- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model.
- **parameter_mapping_kwargs** – Optional keyword arguments passed to petab.get_optimization_to_simulation_parameter_mapping(). To allow changing fixed PEtab problem parameters (`estimate=0`), use `fill_fixed_parameters=False`.

Return type
amici.petab.parameter_mapping.ParameterMapping

Returns
List of the parameter mappings.

amici.petab_objective.**fill_in_parameters**(*edatas*, *problem_parameters*, *scaled_parameters*, *parameter_mapping*, *amici_model*)

Fill fixed and dynamic parameters into the edatas (in-place).

Parameters

- **edatas** (list[amici.swig_wrappers.ExpData]) – List of experimental datas *amici.amici.ExpData* with everything except parameters filled.
- **problem_parameters** (dict[str, numbers.Number]) – Problem parameters as parameterId=>value dict. Only parameters included here will be set. Remaining parameters will be used as currently set in *amici_model*.
- **scaled_parameters** (bool) – If True, problem_parameters are assumed to be on the scale provided in the parameter mapping. If False, they are assumed to be in linear scale.
- **parameter_mapping** (*amici.petab.parameter_mapping.ParameterMapping*) – Parameter mapping for all conditions.
- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model.

Return type
None

amici.petab_objective.**rdatas_to_measurement_df**(*rdatas*, *model*, *measurement_df*)

Create a measurement dataframe in the PEtab format from the passed `rdatas` and own information.

Parameters

- **rdatas** (collections.abc.Sequence[*amici.amici.ReturnData*]) – A sequence of rdatas with the ordering of petab.get_simulation_conditions().
- **model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model used to generate `rdatas`.
- **measurement_df** (pandas.core.frame.DataFrame) – PEtab measurement table used to generate `rdatas`.

Return type
pandas.core.frame.DataFrame

Returns
A dataframe built from the rdatas in the format of `measurement_df`.

amici.petab_objective.**rdatas_to_simulation_df**(*rdatas*, *model*, *measurement_df*)

Create a PEtab simulation dataframe from *amici.amici.ReturnData* s.

See *rdatas_to_measurement_df()* for details, only that model outputs will appear in column `simulation` instead of `measurement`.

Return type
pandas.core.frame.DataFrame

amici.petab_objective.**rescale_sensitivity**(*sensitivity*, *parameter_value*, *old_scale*, *new_scale*)

Rescale a sensitivity between parameter scales.

Parameters

- **sensitivity** (float) – The sensitivity corresponding to the parameter value.
- **parameter_value** (float) – The parameter vector element, on old_scale.
- **old_scale** (str) – The scale of the parameter value.
- **new_scale** (str) – The parameter scale on which to rescale the sensitivity.

Return type
float

Returns
The rescaled sensitivity.

amici.petab_objective.**simulate_petab**(*petab_problem*, *amici_model*, *solver=None*, *problem_parameters=None*, *simulation_conditions=None*, *edatas=None*, *parameter_mapping=None*, *scaled_parameters=False*, *log_level=30*, *num_threads=1*, *failfast=True*, *scaled_gradients=False*)

Simulate PEtab model.

Note: Regardless of *scaled_parameters*, unscaled sensitivities are returned, unless *scaled_gradients=True*.

Parameters

- **petab_problem** (petab.problem.Problem) – PEtab problem to work on.
- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI Model assumed to be compatible with petab_problem.
- **solver** (typing.Optional[*amici.amici.Solver*]) – An AMICI solver. Will use default options if None.
- **problem_parameters** (typing.Optional[dict[str, float]]) – Run simulation with these parameters. If None, PEtab nominalValues will be used. To be provided as dict, mapping PEtab problem parameters to SBML IDs.
- **simulation_conditions** (typing.Union[pandas.core.frame.DataFrame, dict]) – Result of petab.get_simulation_conditions(). Can be provided to save time if this has be obtained before. Not required if edatas and parameter_mapping are provided.
- **edatas** (list[typing.Union[amici.swig_wrappers.ExpData, *amici.amici.ExpDataPtr*]]) – Experimental data. Parameters are inserted in-place for simulation.
- **parameter_mapping** (*amici.petab.parameter_mapping.ParameterMapping*) – Optional precomputed PEtab parameter mapping for efficiency, as generated by *create_parameter_mapping()* with scaled_parameters=True.
- **scaled_parameters** (typing.Optional[bool]) – If True, problem_parameters are assumed to be on the scale provided in the PEtab parameter table and will be unscaled. If False, they are assumed to be in linear scale. If *parameter_mapping* is provided, this must match the value of *scaled_parameters* used to generate the mapping.

- **log_level** (int) – Log level, see *amici.logging* module.
- **num_threads** (int) – Number of threads to use for simulating multiple conditions (only used if compiled with OpenMP).
- **failfast** (bool) – Returns as soon as an integration failure is encountered, skipping any remaining simulations.
- **scaled_gradients** (bool) – Whether to compute gradients on parameter scale (True) or not (False).

Return type
dict[str, typing.Any]

Returns

Dictionary of

- cost function value (LLH),
- list of *amici.amici.ReturnData* (RDATAS),
- list of *amici.amici.ExpData* (EDATAS),

corresponding to the different simulation conditions. For ordering of simulation conditions, see petab.Problem.get_simulation_conditions_from_measurement_df().

10.5.18 amici.petab_simulate

Simulate a PEtab problem

Deprecated since version 0.21.0: Use *amici.petab.simulator* instead.

class amici.petab_simulate.**PetabSimulator**(**args*, *amici_model=None*, ***kwargs*)

Implementation of the PEtab *Simulator* class that uses AMICI.

__init__(**args*, *amici_model=None*, ***kwargs*)

Initialize the simulator.

Initialize the simulator with sufficient information to perform a simulation. If no working directory is specified, a temporary one is created.

Parameters

- **petab_problem** – A PEtab problem.
- **working_dir** – All simulator-specific output files will be saved here. This directory and its contents may be modified and deleted, and should be considered ephemeral.

add_noise(*simulation_df*, *noise_scaling_factor=1*, ***kwargs*)

Add noise to simulated data.

Parameters

- **simulation_df** (pandas.core.frame.DataFrame) – A PEtab measurements table that contains simulated data.
- **noise_scaling_factor** (float) – A multiplier of the scale of the noise distribution.
- ****kwargs** – Additional keyword arguments are passed to sample_noise().

Return type
pandas.core.frame.DataFrame

Returns
Simulated data with noise, as a PEtab measurements table.

remove_working_dir(*force=False*, ***kwargs*)

Remove the simulator working directory, and all files within.

See the `petab.simulate.Simulator.__init__()` method arguments.

Parameters

- **force** (`bool`) – If `True`, the working directory is removed regardless of whether it is a temporary directory.
- ****kwargs** – Additional keyword arguments are passed to `shutil.rmtree()`.

Return type
`None`

simulate(*noise=False*, *noise_scaling_factor=1*, *as_measurement=False*, ***kwargs*)

Simulate a PEtab problem, optionally with noise.

Parameters

- **noise** (`bool`) – If True, noise is added to simulated data.
- **noise_scaling_factor** (`float`) – A multiplier of the scale of the noise distribution.
- **as_measurement** (`bool`) – Whether the data column is named `petab.C.MEASUREMENT` (*True*) or `petab.C.SIMULATION` (*False*).
- ****kwargs** – Additional keyword arguments are passed to `petab.simulate.Simulator.simulate_without_noise()`.

Return type
`pandas.core.frame.DataFrame`

Returns
Simulated data, as a PEtab measurements table.

simulate_without_noise(***kwargs*)

See `petab.simulate.Simulator.simulate()` docstring.

Additional keyword arguments can be supplied to specify arguments for the AMICI PEtab import, simulate, and export methods. See the docstrings for the respective methods for argument options: - *amici.petab_import.import_petab_problem()*, and - *amici.petab_objective.simulate_petab()*.

Note that some arguments are expected to have already been specified in the Simulator constructor (including the PEtab problem).

Return type
`pandas.core.frame.DataFrame`

10.5.19 amici.import_utils

Miscellaneous functions related to model import, independent of any specific model format

Functions

cast_to_sym(value, input_name)	Typecasts the value to `sympy.Float` if possible, and ensures the value is a symbolic expression.
generate_flux_symbol(reaction_index[, name])	Generate identifier symbol for a reaction flux.
generate_measurement_symbol(observable_id)	Generates the appropriate measurement symbol for the provided observable
generate_regularization_symbol(observable_id)	Generates the appropriate regularization symbol for the provided observable
grouper(iterable, n[, fillvalue])	Collect data into fixed-length chunks or blocks
noise_distribution_to_cost_function(...)	Parse noise distribution string to a cost function definition amici can work with.
noise_distribution_to_observable_transformat	Parse noise distribution string and extract observable transformation
smart_subs(element, old, new)	Optimized substitution that checks whether anything needs to be done first
smart_subs_dict(sym, subs[, field, reverse])	Substitutes expressions completely flattening them out.
strip_pysb(symbol)	Strips pysb info from a `pysb.Component` object
symbol_with_assumptions(name)	Central function to create symbols with consistent, canonical assumptions
toposort_symbols(symbols[, field])	Topologically sort symbol definitions according to their interdependency
unique_preserve_order(seq)	Return a list of unique elements in Sequence, keeping only the first occurrence of each element

Classes

ObservableTransformation(value[, names, ...])	Different modes of observable transformation.

Exceptions

CircularDependencyError(data)	
SBMLException	

exception amici.import_utils.**CircularDependencyError**(*data*)

__init__(*data*)

class amici.import_utils.**ObservableTransformation**(*value*, *names=None*, ***, *module=None*, *qualname=None*, *type=None*, *start=1*, *boundary=None*)

Different modes of observable transformation.

LIN = 'lin'

LOG = 'log'

LOG10 = 'log10'

__init__(**args*, ***kwds*)

static maketrans()

Return a translation table usable for str.translate().

If there is only one argument, it must be a dictionary mapping Unicode ordinals (integers) or characters to Unicode ordinals, strings or None. Character keys will be then converted to ordinals. If there are two arguments, they must be strings of equal length, and in the resulting dictionary, each character in x will be mapped to the character at the same position in y. If there is a third argument, it must be a string, whose characters will be mapped to None in the result.

exception amici.import_utils.**SBMLException**

amici.import_utils.**cast_to_sym**(*value*, *input_name*)

Typecasts the value to `sympy.Float` if possible, and ensures the value is a symbolic expression.

Parameters

- **value** (typing.Union[typing.SupportsFloat, sympy.core.expr.Expr, sympy.logic.boolalg.BooleanAtom]) – value to be cast
- **input_name** (str) – name of input variable

Return type
sympy.core.expr.Expr

Returns
typecast value

amici.import_utils.**generate_flux_symbol**(*reaction_index*, *name=None*)

Generate identifier symbol for a reaction flux. This function will always return the same unique python object for a given entity.

Parameters

- **reaction_index** (int) – index of the reaction to which the flux corresponds
- **name** (typing.Optional[str]) – an optional identifier of the reaction to which the flux corresponds

Return type
sympy.core.symbol.Symbol

Returns
identifier symbol

amici.import_utils.**generate_measurement_symbol**(*observable_id*)

Generates the appropriate measurement symbol for the provided observable

Parameters
observable_id (typing.Union[str, sympy.core.symbol.Symbol]) – symbol (or string representation) of the observable

Returns
symbol for the corresponding measurement

amici.import_utils.**generate_regularization_symbol**(*observable_id*)

Generates the appropriate regularization symbol for the provided observable

Parameters
observable_id (typing.Union[str, sympy.core.symbol.Symbol]) – symbol (or string representation) of the observable

Returns
symbol for the corresponding regularization

amici.import_utils.**grouper**(*iterable*, *n*, *fillvalue=None*)

Collect data into fixed-length chunks or blocks

grouper('ABCDEFG', 3, 'x') –> ABC DEF Gxx"

Parameters

- **iterable** (collections.abc.Iterable) – any iterable
- **n** (int) – chunk length
- **fillvalue** (typing.Any) – padding for last chunk if length < n

Return type
collections.abc.Iterable[tuple[typing.Any]]

Returns
itertools.zip_longest of requested chunks

amici.import_utils.**noise_distribution_to_cost_function**(*noise_distribution*)

Parse noise distribution string to a cost function definition amici can work with.

The noise distributions listed in the following are supported. m denotes the measurement, y the simulation, and σ a distribution scale parameter (currently, AMICI only supports a single distribution parameter).

- *'normal'*, *'lin-normal'*: A normal distribution:

$$\pi(m|y,\sigma) = \frac{1}{\sqrt{2\pi}\sigma}\, exp\left(-\frac{(m-y)^2}{2\sigma^2}\right)$$

- *'log-normal'*: A log-normal distribution (i.e. log(m) is normally distributed):

$$\pi(m|y,\sigma) = \frac{1}{\sqrt{2\pi}\sigma m}\, exp\left(-\frac{(\log m - \log y)^2}{2\sigma^2}\right)$$

- *'log10-normal'*: A log10-normal distribution (i.e. log10(m) is normally distributed):

$$\pi(m|y,\sigma) = \frac{1}{\sqrt{2\pi}\sigma m \log(10)}\, exp\left(-\frac{(\log_{10} m - \log_{10} y)^2}{2\sigma^2}\right)$$

- *'laplace'*, *'lin-laplace'*: A laplace distribution:

$$\pi(m|y,\sigma) = \frac{1}{2\sigma}\exp\left(-\frac{|m-y|}{\sigma}\right)$$

- *'log-laplace'*: A log-Laplace distribution (i.e. log(m) is Laplace distributed):

$$\pi(m|y,\sigma) = \frac{1}{2\sigma m}\exp\left(-\frac{|\log m - \log y|}{\sigma}\right)$$

- *'log10-laplace'*: A log10-Laplace distribution (i.e. log10(m) is Laplace distributed):

$$\pi(m|y,\sigma) = \frac{1}{2\sigma m \log(10)} \exp\left(-\frac{|\log_{10} m - \log_{10} y|}{\sigma}\right)$$

- *'binomial'*, *'lin-binomial'*: A (continuation of a discrete) binomial distribution, parameterized via the success probability $p = \sigma$:

$$\pi(m|y,\sigma) = \text{Heaviside}(y-m) \cdot \frac{\Gamma(y+1)}{\Gamma(m+1)\Gamma(y-m+1)} \sigma^m (1-\sigma)^{(y-m)}$$

- *'negative-binomial'*, *'lin-negative-binomial'*: A (continuation of a discrete) negative binomial distribution, with with *mean* = *y*, parameterized via success probability *p*:

$$\pi(m|y,\sigma) = \frac{\Gamma(m+r)}{\Gamma(m+1)\Gamma(r)} (1-\sigma)^m \sigma^r$$

  where

$$r = \frac{1-\sigma}{\sigma} y$$

The distributions above are for a single data point. For a collection $D = \{m_i\}_i$ of data points and corresponding simulations $Y = \{y_i\}_i$ and noise parameters $\Sigma = \{\sigma_i\}_i$, AMICI assumes independence, i.e. the full distributions is

$$\pi(D|Y,\Sigma) = \prod_i \pi(m_i|y_i,\sigma_i)$$

AMICI uses the logarithm $\log(\pi(m|y,\sigma)$.

In addition to the above mentioned distributions, it is also possible to pass a function taking a symbol string and returning a log-distribution string with variables '{str_symbol}', 'm{str_symbol}', 'sigma{str_symbol}' for y, m, sigma, respectively.

Parameters
noise_distribution (typing.Union[str, typing.Callable]) – An identifier specifying a noise model. Possible values are

{*'normal'*, *'lin-normal'*, *'log-normal'*, *'log10-normal'*, *'laplace'*, *'lin-laplace'*, *'log-laplace'*, *'log10-laplace'*, *'binomial'*, *'lin-binomial'*, *'negative-binomial'*, *'lin-negative-binomial'*, *<Callable>*}

For the meaning of the values see above.

Return type
typing.Callable[[str], str]

Returns
A function that takes a strSymbol and then creates a cost function string (negative log-likelihood) from it, which can be sympified.

amici.import_utils.**noise_distribution_to_observable_transformation**(*noise_distribution*)

Parse noise distribution string and extract observable transformation

Parameters
noise_distribution (typing.Union[str, typing.Callable]) – see *noise_distribution_to_cost_function()*

Return type
amici.import_utils.ObservableTransformation

Returns
observable transformation

amici.import_utils.**smart_subs**(*element*, *old*, *new*)

Optimized substitution that checks whether anything needs to be done first

Parameters

- **element** (sympy.core.expr.Expr) – substitution target
- **old** (sympy.core.symbol.Symbol) – to be substituted
- **new** (sympy.core.expr.Expr) – subsitution value

Return type
sympy.core.expr.Expr

Returns
substituted expression

amici.import_utils.**smart_subs_dict**(*sym*, *subs*, *field=None*, *reverse=True*)

Substitutes expressions completely flattening them out. Requires sorting of expressions with toposort.

Parameters

- **sym** (sympy.core.expr.Expr) – Symbolic expression in which expressions will be substituted
- **subs** (dict[sympy.core.symbol.Symbol, typing.Union[dict[str, sympy.core.expr.Expr], sympy.core.expr.Expr]]) – Substitutions
- **field** (typing.Optional[str]) – Field of substitution expressions in subs.values(), if applicable
- **reverse** (bool) – Whether ordering in subs should be reversed. Note that substitution requires the reverse order of what is required for evaluation.

Return type
sympy.core.expr.Expr

Returns
Substituted symbolic expression

amici.import_utils.**strip_pysb**(*symbol*)

Strips pysb info from a pysb.Component object

Parameters
symbol (sympy.core.basic.Basic) – symbolic expression

Return type
sympy.core.basic.Basic

Returns
stripped expression

amici.import_utils.**symbol_with_assumptions**(*name*)

Central function to create symbols with consistent, canonical assumptions

Parameters
name (str) – name of the symbol

Returns
symbol with canonical assumptions

amici.import_utils.**toposort_symbols**(*symbols*, *field=None*)

Topologically sort symbol definitions according to their interdependency

Parameters

- **symbols** (dict[sympy.core.symbol.Symbol, typing.Union[dict[str, sympy.core.expr.Expr], sympy.core.expr.Expr]]) – symbol definitions
- **field** (typing.Optional[str]) – field of definition.values() that is used to compute interdependency

Return type
dict[sympy.core.symbol.Symbol, typing.Union[dict[str, sympy.core.expr.Expr], sympy.core.expr.Expr]]

Returns
ordered symbol definitions

amici.import_utils.**unique_preserve_order**(*seq*)

Return a list of unique elements in Sequence, keeping only the first occurrence of each element

Parameters
seq (collections.abc.Sequence) – Sequence to prune

Return type
list

Returns
List of unique elements in `seq`

10.5.20 amici.de_export

C++ Export

This module provides all necessary functionality to specify a differential equation model and generate executable C++ simulation code. The user generally won't have to directly call any function from this module as this will be done by *amici.pysb_import.pysb2amici()*, *amici.sbml_import.SbmlImporter.sbml2amici()* and *amici.petab_import.import_model()*.

Module Attributes

non_unique_id_symbols	list of equations that have ids which may not be unique
CUSTOM_FUNCTIONS	custom c++ function replacements
logger	python log manager

Functions

is_valid_identifier(x)	Check whether *x* is a valid identifier for conditions, parameters, observables.

Classes

DEExporter(de_model[, outdir, verbose, ...])	The DEExporter class generates AMICI C++ files for a model as defined in symbolic expressions.

amici.de_export.**CUSTOM_FUNCTIONS = [{'build_hint': 'Using polygamma requires libboost-math header files.', 'c++': 'boost::math::polygamma', 'include': '#include <boost/math/special_functions/polygamma.hpp>', 'sympy': 'polygamma'}, {'c++': 'amici::heaviside', 'sympy': 'Heaviside'}, {'c++': 'amici::dirac', 'sympy': 'DiracDelta'}]**

custom c++ function replacements

class amici.de_export.**DEExporter**(*de_model*, *outdir=None*, *verbose=False*, *assume_pow_positivity=False*, *compiler=None*, *allow_reinit_fixpar_initcond=True*, *generate_sensitivity_code=True*, *model_name='model'*)

The DEExporter class generates AMICI C++ files for a model as defined in symbolic expressions.

Variables

- **model** – DE definition
- **verbose** – more verbose output if True
- **assume_pow_positivity** – if set to true, a special pow function is used to avoid problems with state variables that may become negative due to numerical errors
- **compiler** – Absolute path to the compiler executable to be used to build the Python extension, e.g. `/usr/bin/clang`.
- **functions** – carries C++ function signatures and other specifications
- **model_name** – name of the model that will be used for compilation
- **model_path** – path to the generated model specific files
- **model_swig_path** – path to the generated swig files
- **allow_reinit_fixpar_initcond** – indicates whether reinitialization of initial states depending on fixedParameters is allowed for this model
- **_build_hints** – If the given model uses special functions, this set contains hints for model building.
- **_code_printer** – Code printer to generate C++ code
- **generate_sensitivity_code** – Specifies whether code for sensitivity computation is to be generated

Note: When importing large models (several hundreds of species or parameters), import time can potentially be reduced by using multiple CPU cores. This is controlled by setting the `AMICI_IMPORT_NPROCS` environment

variable to the number of parallel processes that are to be used (default: 1). Note that for small models this may (slightly) increase import times.

__init__(*de_model*, *outdir=None*, *verbose=False*, *assume_pow_positivity=False*, *compiler=None*, *allow_reinit_fixpar_initcond=True*, *generate_sensitivity_code=True*, *model_name='model'*)

Generate AMICI C++ files for the DE provided to the constructor.

Parameters

- **de_model** (*amici.de_model.DEModel*) – DE model definition
- **outdir** (pathlib.Path | str | None) – see *amici.de_export.DEExporter.set_paths()*
- **verbose** (bool | int | None) – verbosity level for logging, True/False default to logging.Error/logging.DEBUG
- **assume_pow_positivity** (bool | None) – if set to true, a special pow function is used to avoid problems with state variables that may become negative due to numerical errors
- **compiler** (str | None) – Absolute path to the compiler executable to be used to build the Python extension, e.g. /usr/bin/clang.
- **allow_reinit_fixpar_initcond** (bool | None) – see *amici.de_export.DEExporter*
- **generate_sensitivity_code** (bool | None) – specifies whether code required for sensitivity computation will be generated
- **model_name** (str | None) – name of the model to be used during code generation

compile_model()

Compiles the generated code it into a simulatable module

Return type
None

generate_model_code()

Generates the native C++ code for the loaded model and a Matlab script that can be run to compile a mex file from the C++ code

Return type
None

set_name(*model_name*)

Sets the model name

Parameters
model_name (str) – name of the model (may only contain upper and lower case letters, digits and underscores, and must not start with a digit)

Return type
None

set_paths(*output_dir=None*)

Set output paths for the model and create if necessary

Parameters
output_dir (str | pathlib.Path | None) – relative or absolute path where the generated model code is to be placed. If None, this will default to amici-{self.model_name} in the current working directory. will be created if it does not exist.

Return type
None

amici.de_export.**is_valid_identifier**(*x*)

Check whether *x* is a valid identifier for conditions, parameters, observables... . Identifiers may only contain upper and lower case letters, digits and underscores, and must not start with a digit.

Parameters
x (str) – string to check

Return type
bool

Returns
True if valid, False otherwise

amici.de_export.**logger = <Logger amici.de_export (ERROR)>**

python log manager

amici.de_export.**non_unique_id_symbols = ['x_rdata', 'y']**

list of equations that have ids which may not be unique

10.5.21 amici.de_model

Symbolic differential equation model.

Classes

DEModel([verbose, simplify, cache_simplify])	Defines a Differential Equation as set of ModelQuantities.

class amici.de_model.**DEModel**(*verbose=False*, *simplify=<function _default_simplify>*, *cache_simplify=False*)

Defines a Differential Equation as set of ModelQuantities. This class provides general purpose interfaces to compute arbitrary symbolic derivatives that are necessary for model simulation or sensitivity computation.

Variables

- **_differential_states** – list of differential state variables
- **_algebraic_states** – list of algebraic state variables
- **_observables** – list of observables
- **_event_observables** – list of event observables
- **_sigma_ys** – list of sigmas for observables
- **_sigma_zs** – list of sigmas for event observables
- **_parameters** – list of parameters
- **_log_likelihood_ys** – list of loglikelihoods for observables
- **_log_likelihood_zs** – list of loglikelihoods for event observables
- **_log_likelihood_rzs** – list of loglikelihoods for event observable regularizations
- **_expressions** – list of expressions instances

- **_conservation_laws** – list of conservation laws
- **_symboldim_funs** – define functions that compute model dimensions, these are functions as the underlying symbolic expressions have not been populated at compile time
- **_eqs** – carries symbolic formulas of the symbolic variables of the model
- **_sparseeqs** – carries linear list of all symbolic formulas for sparsified variables
- **_vals** – carries numeric values of symbolic identifiers of the symbolic variables of the model
- **_names** – carries the names of symbolic identifiers of the symbolic variables of the model
- **_syms** – carries symbolic identifiers of the symbolic variables of the model
- **_sparsesyms** – carries linear list of all symbolic identifiers for sparsified variables
- **_colptrs** – carries column pointers for sparsified variables. See SUNMatrixContent_Sparse definition in `sunmatrix/sunmatrix_sparse.h`
- **_rowvals** – carries row values for sparsified variables. See SUNMatrixContent_Sparse definition in `sunmatrix/sunmatrix_sparse.h`
- **_equation_prototype** – defines the attribute from which an equation should be generated via list comprehension (see `OEModel._generate_equation()`)
- **_variable_prototype** – defines the attribute from which a variable should be generated via list comprehension (see `DEModel._generate_symbol()`)
- **_value_prototype** – defines the attribute from which a value should be generated via list comprehension (see `DEModel._generate_value()`)
- **_total_derivative_prototypes** – defines how a total derivative equation is computed for an equation, key defines the name and values should be arguments for `DEModel.totalDerivative()`
- **_lock_total_derivative** – add chainvariables to this set when computing total derivative from a partial derivative call to enforce a partial derivative in the next recursion. prevents infinite recursion
- **_simplify** – If not None, this function will be used to simplify symbolic derivative expressions. Receives sympy expressions as only argument. To apply multiple simplifications, wrap them in a lambda expression.
- **_x0_fixedParameters_idx** – Index list of subset of states for which x0_fixedParameters was computed
- **_w_recursion_depth** – recursion depth in w, quantified as nilpotency of dwdw
- **_has_quadratic_nllh** – whether all observables have a gaussian noise model, i.e. whether res and FIM make sense.
- **_static_indices** – dict of lists list of indices of static variables for different model entities.
- **_z2event** – list of event indices for each event observable

__init__(*verbose=False*, *simplify=<function _default_simplify>*, *cache_simplify=False*)

Create a new DEModel instance.

Parameters

- **verbose** (`bool` | `int` | `None`) – verbosity level for logging, True/False default to `logging.DEBUG`/`logging.ERROR`
- **simplify** (`typing.Optional`[`typing.Callable`]) – see `DEModel._simplify()`

- **cache_simplify** (bool) – Whether to cache calls to the simplify method. Can e.g. decrease import times for models with events.

add_component(*component*, *insert_first=False*)

Adds a new ModelQuantity to the model.

Parameters

- **component** (*amici.de_model_components.ModelQuantity*) – model quantity to be added
- **insert_first** (bool | None) – whether to add quantity first or last, relevant when components may refer to other components of the same type.

Return type
None

add_conservation_law(*state*, *total_abundance*, *coefficients*)

Adds a new conservation law to the model. A conservation law is defined by the conserved quantity $T = \sum_i (a_i * x_i)$, where a_i are coefficients and x_i are different state variables.

Parameters

- **state** (sympy.core.symbol.Symbol) – symbolic identifier of the state that should be replaced by the conservation law (x_j)
- **total_abundance** (sympy.core.symbol.Symbol) – symbolic identifier of the total abundance (T/a_j)
- **coefficients** (dict[sympy.core.symbol.Symbol, sympy.core.expr.Expr]) – Dictionary of coefficients {x_i: a_i}

Return type
None

add_spline(*spline*, *spline_expr*)

Add a spline to the model.

Parameters

- **spline** (*amici.splines.AbstractSpline*) – Spline instance to be added
- **spline_expr** (sympy.core.expr.Expr) – Sympy function representation of *spline* from `spline.ode_model_symbol()`.

Return type
None

algebraic_states()

Get all algebraic states.

Return type
list[*amici.de_model_components.AlgebraicState*]

colptrs(*name*)

Returns (and constructs if necessary) the column pointers for a sparsified symbolic variable.

Parameters
name (str) – name of the symbolic variable

Return type
list[sympy.core.numbers.Number] | list[list[sympy.core.numbers.Number]]

Returns
list containing the column pointers

`conservation_law_has_multispecies`(*tcl*)

Checks whether a conservation law has multiple species or it just defines one constant species

Parameters
tcl (*amici.de_model_components.ConservationLaw*) – conservation law

Return type
bool

Returns
boolean indicating if conservation_law is not None

`conservation_laws`()

Get all conservation laws.

Return type
list[*amici.de_model_components.ConservationLaw*]

`constants`()

Get all constants.

Return type
list[*amici.de_model_components.Constant*]

`differential_states`()

Get all differential states.

Return type
list[*amici.de_model_components.DifferentialState*]

`dynamic_indices`(*name*)

Return the indices of dynamic expressions in the given model entity.

Parameters
name (str) – Name of the model entity.

Return type
list[int]

Returns
List of indices of dynamic expressions.

`eq`(*name*)

Returns (and constructs if necessary) the formulas for a symbolic entity.

Parameters
name (str) – name of the symbolic variable

Return type
sympy.matrices.dense.MutableDenseMatrix

Returns
matrix of symbolic formulas

`event_observables`()

Get all event observables.

Return type
list[*amici.de_model_components.EventObservable*]

events()

Get all events.

Return type
list[*amici.de_model_components.Event*]

expressions()

Get all expressions.

Return type
list[*amici.de_model_components.Expression*]

free_symbols()

Returns list of free symbols that appear in RHS and initial conditions.

Return type
set[sympy.core.basic.Basic]

generate_basic_variables()

Generates the symbolic identifiers for all variables in DEModel._variable_prototype

Return type
None

get_appearance_counts(*idxs*)

Counts how often a state appears in the time derivative of another state and expressions for a subset of states

Parameters
idxs (list[int]) – list of state indices for which counts are to be computed

Return type
list[int]

Returns
list of counts for the states ordered according to the provided indices

get_conservation_laws()

Returns a list of states with conservation law set

Return type
list[tuple[sympy.core.symbol.Symbol, sympy.core.expr.Expr]]

Returns
list of state identifiers

get_observable_transformations()

List of observable transformations

Return type
list[*amici.import_utils.ObservableTransformation*]

Returns
list of transformations

get_solver_indices()

Returns a mapping that maps rdata species indices to solver indices

Return type
dict[int, int]

Returns
dictionary mapping rdata species indices to solver indices

is_ode()

Check if model is ODE model.

Return type
bool

log_likelihood_rzs()

Get all event observable regularization log likelihoods.

Return type
list[*amici.de_model_components.LogLikelihoodRZ*]

log_likelihood_ys()

Get all observable log likelihoodss.

Return type
list[*amici.de_model_components.LogLikelihoodY*]

log_likelihood_zs()

Get all event observable log likelihoods.

Return type
list[*amici.de_model_components.LogLikelihoodZ*]

name(*name*)

Returns (and constructs if necessary) the names of a symbolic variable

Parameters
name (str) – name of the symbolic variable

Return type
list[str]

Returns
list of names

num_cons_law()

Number of conservation laws.

Return type
int

Returns
number of conservation laws

num_const()

Number of Constants.

Return type
int

Returns
number of constant symbols

num_eventobs()

Number of Event Observables.

Return type
int

Returns
number of event observable symbols

num_events()

Total number of Events (those for which root-functions are added and those without).

Return type
int

Returns
number of events

num_events_solver()

Number of Events.

Return type
int

Returns
number of event symbols (length of the root vector in AMICI)

num_expr()

Number of Expressions.

Return type
int

Returns
number of expression symbols

num_obs()

Number of Observables.

Return type
int

Returns
number of observable symbols

num_par()

Number of Parameters.

Return type
int

Returns
number of parameter symbols

num_state_reinits()

Number of solver states which would be reinitialized after preequilibration

Return type
int

Returns
number of state variable symbols with reinitialization

num_states_rdata()

Number of states.

Return type
int

Returns
number of state variable symbols

num_states_solver()

Number of states after applying conservation laws.

Return type
int

Returns
number of state variable symbols

observables()

Get all observables.

Return type
list[*amici.de_model_components.Observable*]

parameters()

Get all parameters.

Return type
list[*amici.de_model_components.Parameter*]

parse_events()

This function checks the right-hand side for roots of Heaviside functions or events, collects the roots, removes redundant roots, and replaces the formulae of the found roots by identifiers of AMICI's Heaviside function implementation in the right-hand side

Return type
None

rowvals(*name*)

Returns (and constructs if necessary) the row values for a sparsified symbolic variable.

Parameters
name (str) – name of the symbolic variable

Return type
list[sympy.core.numbers.Number] | list[list[sympy.core.numbers.Number]]

Returns
list containing the row values

sigma_ys()

Get all observable sigmas.

Return type
list[*amici.de_model_components.SigmaY*]

sigma_zs()

Get all event observable sigmas.

Return type
list[*amici.de_model_components.SigmaZ*]

sparseeq(*name*)

Returns (and constructs if necessary) the sparsified formulas for a sparsified symbolic variable.

Parameters
name – name of the symbolic variable

Return type
sympy.matrices.dense.MutableDenseMatrix

Returns
linearized matrix containing the symbolic formulas

`sparsesym`(*name*, *force_generate=True*)

Returns (and constructs if necessary) the sparsified identifiers for a sparsified symbolic variable.

Parameters

- **name** (str) – name of the symbolic variable
- **force_generate** (bool) – whether the symbols should be generated if not available

Return type
list[str]

Returns
linearized Matrix containing the symbolic identifiers

`state_has_conservation_law`(*ix*)

Checks whether the state at specified index has a conservation law set

Parameters
ix (int) – state index

Return type
bool

Returns
boolean indicating if conservation_law is not None

`state_has_fixed_parameter_initial_condition`(*ix*)

Checks whether the state at specified index has a fixed parameter initial condition

Parameters
ix (int) – state index

Return type
bool

Returns
boolean indicating if any of the initial condition free variables is contained in the model constants

`state_is_constant`(*ix*)

Checks whether the temporal derivative of the state is zero

Parameters
ix (int) – state index

Return type
bool

Returns
boolean indicating if constant over time

`states`()

Get all states.

Return type
list[*amici.de_model_components.State*]

`static_indices`(*name*)

Returns the indices of static expressions in the given model entity.

Static expressions are those that do not depend on time, neither directly nor indirectly.

Parameters
name (str) – Name of the model entity.

Return type
list[int]

Returns
List of indices of static expressions.

`sym`(*name*)

Returns (and constructs if necessary) the identifiers for a symbolic entity.

Parameters
name (str) – name of the symbolic variable

Return type
sympy.matrices.dense.MutableDenseMatrix

Returns
matrix of symbolic identifiers

`sym_names`()

Returns a list of names of generated symbolic variables

Return type
list[str]

Returns
list of names

`sym_or_eq`(*name*, *varname*)

Returns symbols or equations depending on whether a given variable appears in the function signature or not.

Parameters

- **name** (str) – name of function for which the signature should be checked
- **varname** (str) – name of the variable which should be contained in the function signature

Return type
sympy.matrices.dense.MutableDenseMatrix

Returns
the variable symbols if the variable is part of the signature and the variable equations otherwise.

`val`(*name*)

Returns (and constructs if necessary) the numeric values of a symbolic entity

Parameters
name (str) – name of the symbolic variable

Return type
list[sympy.core.numbers.Number]

Returns
list containing the numeric values

10.5.22 amici.de_model_components

Objects for AMICI's internal differential equation model representation

Classes

AlgebraicEquation(identifier, value)	An AlgebraicEquation defines an algebraic equation.
AlgebraicState(identifier, name, init)	An AlgebraicState defines an entity that is algebraically determined
ConservationLaw(identifier, name, value, ...)	A conservation law defines the absolute the total amount of a (weighted) sum of states
Constant(identifier, name, value)	A Constant is a fixed variable in the model with respect to which sensitivities cannot be computed, abbreviated by `k`.
DifferentialState(identifier, name, init, dt)	A State variable defines an entity that evolves with time according to the provided time derivative, abbreviated by `x`.
Event(identifier, name, value, state_update)	An Event defines either a SBML event or a root of the argument of a Heaviside function.
EventObservable(identifier, name, value, event)	An Event Observable links model simulations to event related experimental measurements, abbreviated by `z`.
Expression(identifier, name, value)	An Expression is a recurring elements in symbolic formulas.
LogLikelihood(identifier, name, value)	A LogLikelihood defines the distance between measurements and experiments for a particular observable.
LogLikelihoodRZ(identifier, name, value)	Loglikelihood for event observables regularization
LogLikelihoodY(identifier, name, value)	Loglikelihood for observables
LogLikelihoodZ(identifier, name, value)	Loglikelihood for event observables
ModelQuantity(identifier, name, value)	Base class for model components
Observable(identifier, name, value[, ...])	An Observable links model simulations to experimental measurements, abbreviated by `y`.
Parameter(identifier, name, value)	A Parameter is a free variable in the model with respect to which sensitivities may be computed, abbreviated by `p`.
Sigma(identifier, name, value)	A Standard Deviation Sigma rescales the distance between simulations and measurements when computing residuals or objective functions, abbreviated by `sigma{y,z}`.
SigmaY(identifier, name, value)	Standard deviation for observables
SigmaZ(identifier, name, value)	Standard deviation for event observables
State(identifier, name, value)	Base class for differential and algebraic model states

class amici.de_model_components.**AlgebraicEquation**(*identifier*, *value*)

An AlgebraicEquation defines an algebraic equation.

__init__(*identifier*, *value*)

Create a new AlgebraicEquation instance.

Parameters

value (sympy.core.expr.Expr) – Formula of the algebraic equation, the solution is given by `formula == 0`

get_free_symbols()

get_id()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

get_name()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

get_val()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

set_val(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

class amici.de_model_components.**AlgebraicState**(*identifier*, *name*, *init*)

An AlgebraicState defines an entity that is algebraically determined

__init__(*identifier*, *name*, *init*)

Create a new AlgebraicState instance.

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the AlgebraicState
- **name** (str) – individual name of the AlgebraicState (does not need to be unique)
- **init** (sympy.core.expr.Expr) – initial value of the AlgebraicState

get_dx_rdata_dx_solver(*state_id*)

Returns the expression that allows computation of dx_rdata_dx_solver for this state, accounting for conservation laws.

Returns
dx_rdata_dx_solver expression

get_free_symbols()

get_id()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

`get_name()`

ModelQuantity name

Return type
`str`

Returns
name of the ModelQuantity

`get_val()`

ModelQuantity value

Return type
`sympy.core.expr.Expr`

Returns
value of the ModelQuantity

`get_x_rdata()`

Returns the expression that allows computation of x_rdata for this state, accounting for conservation laws.

Returns
x_rdata expression

`has_conservation_law()`

Checks whether this state has a conservation law assigned.

Returns
True if assigned, False otherwise

`set_val(val)`

Set ModelQuantity value

Returns
value of the ModelQuantity

`class amici.de_model_components.ConservationLaw(identifier, name, value, coefficients, state_id)`

A conservation law defines the absolute the total amount of a (weighted) sum of states

`__init__(identifier, name, value, coefficients, state_id)`

Create a new ConservationLaw instance.

Parameters

- **identifier** (`sympy.core.symbol.Symbol`) – unique identifier of the ConservationLaw
- **name** (`str`) – individual name of the ConservationLaw (does not need to be unique)
- **value** (`sympy.core.expr.Expr`) – formula (sum of states)
- **coefficients** (`dict[sympy.core.symbol.Symbol, sympy.core.expr.Expr]`) – coefficients of the states in the sum
- **state_id** (`sympy.core.symbol.Symbol`) – identifier of the state that this conservation law replaces

`get_id()`

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

get_name()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

get_ncoeff(*state_id*)

Computes the normalized coefficient a_i/a_j where i is the index of the provided state_id and j is the index of the state that is replaced by this conservation law. This can be used to compute both dtotal_cl/dx_rdata (=ncoeff) and dx_rdata/dx_solver (=-ncoeff).

Parameters
state_id – identifier of the state

Return type
typing.Union[sympy.core.expr.Expr, int, float]

Returns
normalized coefficent of the state

get_val()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

get_x_rdata()

Returns the expression that allows computation of x_rdata for the state that this conservation law replaces.

Returns
x_rdata expression

set_val(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

class amici.de_model_components.**Constant**(*identifier*, *name*, *value*)

A Constant is a fixed variable in the model with respect to which sensitivities cannot be computed, abbreviated by k.

__init__(*identifier*, *name*, *value*)

Create a new Expression instance.

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the Constant
- **name** (str) – individual name of the Constant (does not need to be unique)

- **value** (numbers.Number) – numeric value

get_id()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

get_name()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

get_val()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

set_val(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

class amici.de_model_components.**DifferentialState**(*identifier*, *name*, *init*, *dt*)

A State variable defines an entity that evolves with time according to the provided time derivative, abbreviated by `x`.

Variables

- **_conservation_law** – algebraic formula that allows computation of this state according to a conservation law
- **_dt** – algebraic formula that defines the temporal derivative of this state

__init__(*identifier*, *name*, *init*, *dt*)

Create a new State instance. Extends *ModelQuantity.__init__()* by `dt`

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the state
- **name** (str) – individual name of the state (does not need to be unique)
- **init** (sympy.core.expr.Expr) – initial value
- **dt** (sympy.core.expr.Expr) – time derivative

get_dt()

Gets the time derivative

Return type
sympy.core.expr.Expr

Returns
time derivative

`get_dx_rdata_dx_solver`(*state_id*)

Returns the expression that allows computation of `dx_rdata_dx_solver` for this state, accounting for conservation laws.

Returns
dx_rdata_dx_solver expression

`get_free_symbols`()

Gets the set of free symbols in time derivative and initial conditions

Return type
`set`[`sympy.core.basic.Basic`]

Returns
free symbols

`get_id`()

ModelQuantity identifier

Return type
`sympy.core.symbol.Symbol`

Returns
identifier of the ModelQuantity

`get_name`()

ModelQuantity name

Return type
`str`

Returns
name of the ModelQuantity

`get_val`()

ModelQuantity value

Return type
`sympy.core.expr.Expr`

Returns
value of the ModelQuantity

`get_x_rdata`()

Returns the expression that allows computation of x_rdata for this state, accounting for conservation laws.

Returns
x_rdata expression

`has_conservation_law`()

Checks whether this state has a conservation law assigned.

Returns
True if assigned, False otherwise

`set_conservation_law`(*law*)

Sets the conservation law of a state.

If a conservation law is set, the respective state will be replaced by an algebraic formula according to the respective conservation law.

Parameters
law (*amici.de_model_components.ConservationLaw*) – linear sum of states that if added to this state remain constant over time

Return type
None

`set_dt`(*dt*)

Sets the time derivative

Parameters
dt (sympy.core.expr.Expr) – time derivative

Return type
None

`set_val`(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

`class amici.de_model_components.Event`(*identifier*, *name*, *value*, *state_update*, *initial_value=True*)

An Event defines either a SBML event or a root of the argument of a Heaviside function. The Heaviside functions will be tracked via the vector `h` during simulation and are needed to inform the solver about a discontinuity in either the right-hand side or the states themselves, causing a reinitialization of the solver.

`__init__`(*identifier*, *name*, *value*, *state_update*, *initial_value=True*)

Create a new Event instance.

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the Event
- **name** (str) – individual name of the Event (does not need to be unique)
- **value** (sympy.core.expr.Expr) – formula for the root / trigger function
- **state_update** (typing.Optional[sympy.core.expr.Expr]) – formula for the bolus function (None for Heaviside functions, zero vector for events without bolus)
- **initial_value** (typing.Optional[bool]) – initial boolean value of the trigger function at t0. If set to *False*, events may trigger at `t==t0`, otherwise not.

`get_id`()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

`get_initial_value`()

Return the initial value for the root function.

Return type
bool

Returns
initial value formula

get_name()
ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

get_trigger_time()
Get the time at which the event triggers.

Only for events that trigger at a single fixed time-point.

Return type
sympy.core.numbers.Float

get_val()
ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

set_val(*val*)
Set ModelQuantity value

Returns
value of the ModelQuantity

triggers_at_fixed_timepoint()
Check whether the event triggers at a (single) fixed time-point.

Return type
bool

class amici.de_model_components.**EventObservable**(*identifier*, *name*, *value*, *event*, *measurement_symbol=None*, *transformation='lin'*)
An Event Observable links model simulations to event related experimental measurements, abbreviated by `z`.

Variables
_event – symbolic event identifier

__init__(*identifier*, *name*, *value*, *event*, *measurement_symbol=None*, *transformation='lin'*)
Create a new EventObservable instance.

Parameters
- **identifier** (sympy.core.symbol.Symbol) – See *Observable.__init__()*.
- **name** (str) – See *Observable.__init__()*.
- **value** (sympy.core.expr.Expr) – See *Observable.__init__()*.
- **transformation** (typing.Optional[*amici.import_utils.ObservableTransformation*]) – See *Observable.__init__()*.
- **event** (sympy.core.symbol.Symbol) – Symbolic identifier of the corresponding event.

get_event()

Get the symbolic identifier of the corresponding event.

Return type
sympy.core.symbol.Symbol

Returns
symbolic identifier

get_id()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

get_measurement_symbol()

Return type
sympy.core.symbol.Symbol

get_name()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

get_regularization_symbol()

Return type
sympy.core.symbol.Symbol

get_val()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

set_val(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

class amici.de_model_components.**Expression**(*identifier*, *name*, *value*)

An Expression is a recurring elements in symbolic formulas. Specifying this may yield more compact expression which may lead to substantially shorter model compilation times, but may also reduce model simulation time. Abbreviated by `w`.

__init__(*identifier*, *name*, *value*)

Create a new Expression instance.

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the Expression
- **name** (str) – individual name of the Expression (does not need to be unique)
- **value** (sympy.core.expr.Expr) – formula

get_id()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

get_name()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

get_val()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

set_val(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

class amici.de_model_components.**LogLikelihoodRZ**(*identifier*, *name*, *value*)

Loglikelihood for event observables regularization

__init__(*identifier*, *name*, *value*)

Create a new Expression instance.

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the LogLikelihood
- **name** (str) – individual name of the LogLikelihood (does not need to be unique)
- **value** (sympy.core.expr.Expr) – formula

get_id()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

get_name()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

get_val()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

set_val(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

class amici.de_model_components.**LogLikelihoodY**(*identifier*, *name*, *value*)

Loglikelihood for observables

__init__(*identifier*, *name*, *value*)

Create a new Expression instance.

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the LogLikelihood
- **name** (str) – individual name of the LogLikelihood (does not need to be unique)
- **value** (sympy.core.expr.Expr) – formula

get_id()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

get_name()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

get_val()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

`set_val`(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

`class amici.de_model_components.LogLikelihoodZ`(*identifier*, *name*, *value*)

Loglikelihood for event observables

`__init__`(*identifier*, *name*, *value*)

Create a new Expression instance.

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the LogLikelihood
- **name** (str) – individual name of the LogLikelihood (does not need to be unique)
- **value** (sympy.core.expr.Expr) – formula

`get_id`()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

`get_name`()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

`get_val`()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

`set_val`(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

`class amici.de_model_components.ModelQuantity`(*identifier*, *name*, *value*)

Base class for model components

`__init__`(*identifier*, *name*, *value*)

Create a new ModelQuantity instance.

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the quantity
- **name** (str) – individual name of the quantity (does not need to be unique)
- **value** (typing.Union[typing.SupportsFloat, numbers.Number, sympy.core.expr.Expr]) – either formula, numeric value or initial value

get_id()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

get_name()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

get_val()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

set_val(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

class amici.de_model_components.**Observable**(*identifier*, *name*, *value*, *measurement_symbol=None*, *transformation=ObservableTransformation.LIN*)

An Observable links model simulations to experimental measurements, abbreviated by `y`.

Variables

- **_measurement_symbol** – sympy symbol used in the objective function to represent measurements to this observable
- **trafo** – observable transformation, only applies when evaluating objective function or residuals

__init__(*identifier*, *name*, *value*, *measurement_symbol=None*, *transformation=ObservableTransformation.LIN*)

Create a new Observable instance.

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the Observable
- **name** (str) – individual name of the Observable (does not need to be unique)
- **value** (sympy.core.expr.Expr) – formula

- **transformation** (typing.Optional[*amici.import_utils.ObservableTransformation*]) – observable transformation, only applies when evaluating objective function or residuals

get_id()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

get_measurement_symbol()

Return type
sympy.core.symbol.Symbol

get_name()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

get_regularization_symbol()

Return type
sympy.core.symbol.Symbol

get_val()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

set_val(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

class amici.de_model_components.**Parameter**(*identifier*, *name*, *value*)

A Parameter is a free variable in the model with respect to which sensitivities may be computed, abbreviated by p.

__init__(*identifier*, *name*, *value*)

Create a new Expression instance.

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the Parameter
- **name** (str) – individual name of the Parameter (does not need to be unique)
- **value** (numbers.Number) – numeric value

get_id()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

get_name()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

get_val()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

set_val(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

class amici.de_model_components.**SigmaY**(*identifier*, *name*, *value*)

Standard deviation for observables

__init__(*identifier*, *name*, *value*)

Create a new Standard Deviation instance.

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the Standard Deviation
- **name** (str) – individual name of the Standard Deviation (does not need to be unique)
- **value** (sympy.core.expr.Expr) – formula

get_id()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

get_name()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

`get_val`()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

`set_val`(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

`class` amici.de_model_components.`SigmaZ`(*identifier*, *name*, *value*)

Standard deviation for event observables

`__init__`(*identifier*, *name*, *value*)

Create a new Standard Deviation instance.

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the Standard Deviation
- **name** (str) – individual name of the Standard Deviation (does not need to be unique)
- **value** (sympy.core.expr.Expr) – formula

`get_id`()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

`get_name`()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

`get_val`()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

set_val(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

class amici.de_model_components.**State**(*identifier*, *name*, *value*)

Base class for differential and algebraic model states

__init__(*identifier*, *name*, *value*)

Create a new ModelQuantity instance.

Parameters

- **identifier** (sympy.core.symbol.Symbol) – unique identifier of the quantity
- **name** (str) – individual name of the quantity (does not need to be unique)
- **value** (typing.Union[typing.SupportsFloat, numbers.Number, sympy.core.expr.Expr]) – either formula, numeric value or initial value

get_dx_rdata_dx_solver(*state_id*)

Returns the expression that allows computation of dx_rdata_dx_solver for this state, accounting for conservation laws.

Returns
dx_rdata_dx_solver expression

get_id()

ModelQuantity identifier

Return type
sympy.core.symbol.Symbol

Returns
identifier of the ModelQuantity

get_name()

ModelQuantity name

Return type
str

Returns
name of the ModelQuantity

get_val()

ModelQuantity value

Return type
sympy.core.expr.Expr

Returns
value of the ModelQuantity

get_x_rdata()

Returns the expression that allows computation of x_rdata for this state, accounting for conservation laws.

Returns
x_rdata expression

abstract has_conservation_law()

Checks whether this state has a conservation law assigned.

Returns
True if assigned, False otherwise

set_val(*val*)

Set ModelQuantity value

Returns
value of the ModelQuantity

10.5.23 amici.plotting

Plotting

Plotting related functions

Functions

plotObservableTrajectories(rdata[, ...])	Plot observable trajectories.
plotStateTrajectories(rdata[, ...])	Plot state trajectories.
plot_expressions(exprs, rdata)	Plot the given expressions evaluated on the given simulation outputs.
plot_jacobian(rdata)	Plot Jacobian as heatmap.
plot_observable_trajectories(rdata[, ...])	Plot observable trajectories.
plot_state_trajectories(rdata[, ...])	Plot state trajectories.

amici.plotting.**plotObservableTrajectories**(*rdata*, *observable_indices=None*, *ax=None*, *model=None*, *prefer_names=True*, *marker=None*)

Plot observable trajectories.

Parameters

- **rdata** (*amici.numpy.ReturnDataView*) – AMICI simulation results as returned by *amici.amici.runAmiciSimulation()*.
- **observable_indices** (typing.Optional[collections.abc.Iterable[int]]) – Indices of observables for which trajectories are to be plotted.
- **ax** (typing.Optional[matplotlib.axes._axes.Axes]) – matplotlib.pyplot.Axes instance to plot into.
- **model** (*amici.amici.Model*) – The model *rdata* was generated from.
- **prefer_names** (bool) – Whether observable names should be preferred over IDs, if available.
- **marker** – Point marker for plotting (see matplotlib documentation).

Return type
None

amici.plotting.**plotStateTrajectories**(*rdata*, *state_indices=None*, *ax=None*, *model=None*, *prefer_names=True*, *marker=None*)

Plot state trajectories.

Parameters

- **rdata** (*amici.numpy.ReturnDataView*) – AMICI simulation results as returned by *amici.amici.runAmiciSimulation()*.
- **state_indices** (typing.Optional[collections.abc.Sequence[int]]) – Indices of state variables for which trajectories are to be plotted.
- **ax** (typing.Optional[matplotlib.axes._axes.Axes]) – matplotlib.pyplot.Axes instance to plot into.
- **model** (*amici.amici.Model*) – The model *rdata* was generated from.
- **prefer_names** (bool) – Whether state names should be preferred over IDs, if available.
- **marker** – Point marker for plotting (see matplotlib documentation).

Return type
None

amici.plotting.**plot_expressions**(*exprs*, *rdata*)

Plot the given expressions evaluated on the given simulation outputs.

Parameters

- **exprs** (typing.Union[collections.abc.Sequence[typing.Union[str, sympy.core.expr.Expr]], str, sympy.core.expr.Expr]) – A symbolic expression, e.g., a sympy expression or a string that can be sympified. It Can include state variable, expression, and observable IDs, depending on whether the respective data is available in the simulation results. Parameters are not yet supported.
- **rdata** (*amici.numpy.ReturnDataView*) – The simulation results.

Return type
None

amici.plotting.**plot_jacobian**(*rdata*)

Plot Jacobian as heatmap.

amici.plotting.**plot_observable_trajectories**(*rdata*, *observable_indices=None*, *ax=None*, *model=None*, *prefer_names=True*, *marker=None*)

Plot observable trajectories.

Parameters

- **rdata** (*amici.numpy.ReturnDataView*) – AMICI simulation results as returned by *amici.amici.runAmiciSimulation()*.
- **observable_indices** (typing.Optional[collections.abc.Iterable[int]]) – Indices of observables for which trajectories are to be plotted.
- **ax** (typing.Optional[matplotlib.axes._axes.Axes]) – matplotlib.pyplot.Axes instance to plot into.
- **model** (*amici.amici.Model*) – The model *rdata* was generated from.
- **prefer_names** (bool) – Whether observable names should be preferred over IDs, if available.
- **marker** – Point marker for plotting (see matplotlib documentation).

Return type
None

amici.plotting.**plot_state_trajectories**(*rdata*, *state_indices=None*, *ax=None*, *model=None*, *prefer_names=True*, *marker=None*)

Plot state trajectories.

Parameters

- **rdata** (*amici.numpy.ReturnDataView*) – AMICI simulation results as returned by *amici.amici.runAmiciSimulation()*.
- **state_indices** (typing.Optional[collections.abc.Sequence[int]]) – Indices of state variables for which trajectories are to be plotted.
- **ax** (typing.Optional[matplotlib.axes._axes.Axes]) – matplotlib.pyplot.Axes instance to plot into.
- **model** (*amici.amici.Model*) – The model *rdata* was generated from.
- **prefer_names** (bool) – Whether state names should be preferred over IDs, if available.
- **marker** – Point marker for plotting (see matplotlib documentation).

Return type
None

10.5.24 amici.pandas

Pandas Wrappers

This module contains convenience wrappers that allow for easy interconversion between C++ objects from *amici.amici* and pandas DataFrames

Functions

constructEdataFromDataFrame(df, model, condition)	Constructs an ExpData instance according to the provided Model and DataFrame.
getDataObservablesAsDataFrame(model, edata_list)	Write Observables from experimental data as DataFrame.
getEdataFromDataFrame(model, df[, by_id])	Constructs a ExpData instances according to the provided Model and DataFrame.
getResidualsAsDataFrame(model, edata_list, ...)	Convert a list of ReturnData and ExpData to pandas DataFrame with residuals.
getSimulationObservablesAsDataFrame(model, ...)	Write Observables from simulation results as DataFrame.
getSimulationStatesAsDataFrame(model, ...[, ...])	Get model state according to lists of ReturnData and ExpData.
get_expressions_as_dataframe(model, ...[, by_id])	Get values of model expressions from lists of ReturnData as DataFrame.

amici.pandas.**getDataObservablesAsDataFrame**(*model*, *edata_list*, *by_id=False*)

Write Observables from experimental data as DataFrame.

Parameters

- **model** (typing.Union[*amici.amici.ModelPtr*, *amici.amici.Model*]) – Model instance.
- **edata_list** (typing.Union[list[*amici.amici.ExpData*], list[*amici.amici.ExpDataPtr*], *amici.amici.ExpData*, *amici.amici.ExpDataPtr*]) – list of ExpData instances with experimental data. May also be a single ExpData instance.
- **by_id** (typing.Optional[bool]) – If True, uses observable ids as column names in the generated DataFrame, otherwise the possibly more descriptive observable names are used.

Return type
pandas.core.frame.DataFrame

Returns
pandas DataFrame with conditions/timepoints as rows and observables as columns.

amici.pandas.**getEdataFromDataFrame**(*model*, *df*, *by_id=False*)

Constructs a ExpData instances according to the provided Model and DataFrame.

Parameters

- **df** (pandas.core.frame.DataFrame) – dataframe with Observable Names/Ids, FixedParameter Names/Ids and time as columns. Standard deviations may be specified by appending '_std' as suffix. Preequilibration fixedParameters may be specified by appending '_preeq' as suffix. Presimulation fixedParameters may be specified by appending '_presim' as suffix. Presimulation time may be specified as 't_presim' column.
- **model** (typing.Union[*amici.amici.ModelPtr*, *amici.amici.Model*]) – Model instance.
- **by_id** (typing.Optional[bool]) – Whether the column names in *df* are based on ids or names, corresponding to how the dataframe was created in the first place.

Return type
list[*amici.amici.ExpData*]

Returns
list of ExpData instances.

amici.pandas.**getResidualsAsDataFrame**(*model*, *edata_list*, *rdata_list*, *by_id=False*)

Convert a list of ReturnData and ExpData to pandas DataFrame with residuals.

Parameters

- **model** (*amici.amici.Model*) – Model instance.
- **edata_list** (typing.Union[list[*amici.amici.ExpData*], list[*amici.amici.ExpDataPtr*], *amici.amici.ExpData*, *amici.amici.ExpDataPtr*]) – list of ExpData instances with experimental data. May also be a single ExpData instance.
- **rdata_list** (typing.Union[list[*amici.numpy.ReturnDataView*], *amici.numpy.ReturnDataView*]) – list of ReturnData instances corresponding to ExpData. May also be a single ReturnData instance.
- **by_id** (typing.Optional[bool]) – bool, optional (default = False) If True, ids are used as identifiers, otherwise the possibly more descriptive names.

Return type
pandas.core.frame.DataFrame

Returns
pandas DataFrame with conditions and residuals.

amici.pandas.**getSimulationObservablesAsDataFrame**(*model*, *edata_list*, *rdata_list*, *by_id=False*)

Write Observables from simulation results as DataFrame.

Parameters

- **model** (*amici.amici.Model*) – Model instance.
- **edata_list** (typing.Union[list[*amici.amici.ExpData*], list[*amici.amici.ExpDataPtr*], *amici.amici.ExpData*, *amici.amici.ExpDataPtr*]) – list of ExpData instances with experimental data. May also be a single ExpData instance.
- **rdata_list** (typing.Union[list[*amici.numpy.ReturnDataView*], *amici.numpy.ReturnDataView*]) – list of ReturnData instances corresponding to ExpData. May also be a single ReturnData instance.
- **by_id** (typing.Optional[bool]) – If True, ids are used as identifiers, otherwise the possibly more descriptive names.

Return type
pandas.core.frame.DataFrame

Returns
pandas DataFrame with conditions/timepoints as rows and observables as columns.

amici.pandas.**getSimulationStatesAsDataFrame**(*model*, *edata_list*, *rdata_list*, *by_id=False*)

Get model state according to lists of ReturnData and ExpData.

Parameters

- **model** (*amici.amici.Model*) – Model instance.
- **edata_list** (typing.Union[list[*amici.amici.ExpData*], list[*amici.amici.ExpDataPtr*], *amici.amici.ExpData*, *amici.amici.ExpDataPtr*]) – list of ExpData instances with experimental data. May also be a single ExpData instance.
- **rdata_list** (typing.Union[list[*amici.numpy.ReturnDataView*], *amici.numpy.ReturnDataView*]) – list of ReturnData instances corresponding to ExpData. May also be a single ReturnData instance.
- **by_id** (typing.Optional[bool]) – If True, ids are used as identifiers, otherwise the possibly more descriptive names.

Return type
pandas.core.frame.DataFrame

Returns
pandas DataFrame with conditions/timepoints as rows and state variables as columns.

amici.pandas.**get_expressions_as_dataframe**(*model*, *edata_list*, *rdata_list*, *by_id=False*)

Get values of model expressions from lists of ReturnData as DataFrame.

Parameters

- **model** (*amici.amici.Model*) – Model instance.
- **edata_list** (typing.Union[list[*amici.amici.ExpData*], list[*amici.amici.ExpDataPtr*], *amici.amici.ExpData*, *amici.amici.ExpDataPtr*]) – list of ExpData instances with experimental data. May also be a single ExpData instance.
- **rdata_list** (typing.Union[list[*amici.numpy.ReturnDataView*], *amici.numpy.ReturnDataView*]) – list of ReturnData instances corresponding to ExpData. May also be a single ReturnData instance.

- **by_id** (typing.Optional[bool]) – If True, ids are used as identifiers, otherwise the possibly more descriptive names.

Return type
pandas.core.frame.DataFrame

Returns
pandas DataFrame with conditions/timepoints as rows and model expressions as columns.

10.5.25 amici.logging

Logging

This module provides custom logging functionality for other amici modules

Functions

get_logger([logger_name, log_level])	Returns (if extistant) or creates an AMICI logger
log_execution_time(description, logger)	Parameterized function decorator that enables automatic execution time tracking
set_log_level(logger, log_level)	**rtype** None

amici.logging.**get_logger**(*logger_name='amici'*, *log_level=None*, ***kwargs*)

Returns (if extistant) or creates an AMICI logger

If the AMICI base logger has already been set up, this method will return it or any of its descendant loggers without overriding the settings - i.e. any values supplied as kwargs will be ignored.

Parameters

- **logger_name** (typing.Optional[str]) – Get a logger for a specific namespace, typically __name__ for code outside of classes or self.__module__ inside a class
- **log_level** (typing.Optional[int]) – Override the default or preset log level for the requested logger. None or False uses the default or preset value. True evaluates to logging.DEBUG. Any integer is used directly.
- **console_output** – Set up a default console log handler if True (default). Only used when the AMICI logger hasn't been set up yet.
- **file_output** – Supply a filename to copy all log output to that file, or set to False to disable (default). Only used when the AMICI logger hasn't been set up yet.
- **capture_warnings** – Capture warnings from Python's warnings module if True (default). Only used when the AMICI logger hasn't been set up yet..

Return type
logging.Logger

Returns
A logging.Logger object with the requested name

amici.logging.**log_execution_time**(*description*, *logger*)

Parameterized function decorator that enables automatic execution time tracking

Parameters

- **description** (str) – Description of what the decorated function does
- **logger** (logging.Logger) – Logger to which execution timing will be printed

Return type
typing.Callable

amici.logging.**set_log_level**(*logger*, *log_level*)

Return type
None

10.5.26 amici.gradient_check

Finite Difference Check

This module provides functions to automatically check correctness of amici computed sensitivities using finite difference approximations

Functions

check_derivatives(model, solver[, edata, ...])	Finite differences check for likelihood gradient.
check_finite_difference(x0, model, solver, ...)	Checks the computed sensitivity based derivatives against a finite difference approximation.

amici.gradient_check.**check_derivatives**(*model*, *solver*, *edata=None*, *atol=0.0001*, *rtol=0.0001*, *epsilon=0.001*, *check_least_squares=True*, *skip_zero_pars=False*)

Finite differences check for likelihood gradient.

Parameters

- **model** (*amici.amici.Model*) – amici model
- **solver** (*amici.amici.Solver*) – amici solver
- **edata** (typing.Optional[amici.swig_wrappers.ExpData]) – exp data
- **atol** (typing.Optional[float]) – absolute tolerance for comparison
- **rtol** (typing.Optional[float]) – relative tolerance for comparison
- **epsilon** (typing.Optional[float]) – finite difference step-size
- **check_least_squares** (bool) – whether to check least squares related values.
- **skip_zero_pars** (bool) – whether to perform FD checks for parameters that are zero

Return type
None

amici.gradient_check.**check_finite_difference**(*x0*, *model*, *solver*, *edata*, *ip*, *fields*, *atol=0.0001*, *rtol=0.0001*, *epsilon=0.001*)

Checks the computed sensitivity based derivatives against a finite difference approximation.

Parameters

- **x0** (collections.abc.Sequence[float]) – parameter value at which to check finite difference approximation
- **model** (*amici.amici.Model*) – amici model
- **solver** (*amici.amici.Solver*) – amici solver
- **edata** (amici.swig_wrappers.ExpData) – exp data
- **ip** (int) – parameter index
- **fields** (list[str]) – rdata fields for which to check the gradient
- **atol** (typing.Optional[float]) – absolute tolerance for comparison
- **rtol** (typing.Optional[float]) – relative tolerance for comparison
- **epsilon** (typing.Optional[float]) – finite difference step-size

Return type
None

10.5.27 amici.parameter_mapping

Parameter mapping between AMICI and PEtab.

Deprecated since version 0.21.0: Use *amici.petab.parameter_mapping* instead.

class amici.parameter_mapping.**ParameterMapping**(*parameter_mappings=None*)

Parameter mapping for multiple conditions.

This can be used like a list of *ParameterMappingForCondition*s.

Parameters
parameter_mappings (list[*amici.petab.parameter_mapping.ParameterMappingForCondition*]) – List of parameter mappings for specific conditions.

__init__(*parameter_mappings=None*)

append(*parameter_mapping_for_condition*)

Append a condition specific parameter mapping.

count(*value*) → integer -- return number of occurrences of value

property free_symbols: set[str]

Get IDs of all (symbolic) parameters present in this mapping

index(*value*[, *start*[, *stop*]]) → integer -- return first index of value.

Raises ValueError if the value is not present.

Supporting start and stop arguments is optional, but recommended.

class amici.parameter_mapping.**ParameterMappingForCondition**(*map_sim_var=None*, *scale_map_sim_var=None*, *map_preeq_fix=None*, *scale_map_preeq_fix=None*, *map_sim_fix=None*, *scale_map_sim_fix=None*)

Parameter mapping for condition.

Contains mappings for free parameters, fixed parameters, and fixed preequilibration parameters, both for parameters and scales.

In the scale mappings, for each simulation parameter the scale on which the value is passed (and potentially gradients are to be returned) is given. In the parameter mappings, for each simulation parameter a corresponding optimization parameter (or a numeric value) is given.

If a mapping is not passed, the parameter mappings are assumed to be empty, and if a scale mapping is not passed, all scales are set to linear.

Parameters

- **map_sim_var** (dict[str, typing.Union[numbers.Number, str]]) – Mapping for free simulation parameters.
- **scale_map_sim_var** (dict[str, str]) – Scales for free simulation parameters.
- **map_preeq_fix** (dict[str, typing.Union[numbers.Number, str]]) – Mapping for fixed preequilibration parameters.
- **scale_map_preeq_fix** (dict[str, str]) – Scales for fixed preequilibration parameters.
- **map_sim_fix** (dict[str, typing.Union[numbers.Number, str]]) – Mapping for fixed simulation parameters.
- **scale_map_sim_fix** (dict[str, str]) – Scales for fixed simulation parameters.

__init__(*map_sim_var=None*, *scale_map_sim_var=None*, *map_preeq_fix=None*, *scale_map_preeq_fix=None*, *map_sim_fix=None*, *scale_map_sim_fix=None*)

property free_symbols: set[str]

Get IDs of all (symbolic) parameters present in this mapping

amici.parameter_mapping.**amici_to_petab_scale**(*amici_scale*)

Convert amici scale id to petab scale id.

Return type
str

amici.parameter_mapping.**fill_in_parameters**(*edatas*, *problem_parameters*, *scaled_parameters*, *parameter_mapping*, *amici_model*)

Fill fixed and dynamic parameters into the edatas (in-place).

Parameters

- **edatas** (list[amici.swig_wrappers.ExpData]) – List of experimental datas *amici.amici.ExpData* with everything except parameters filled.
- **problem_parameters** (dict[str, numbers.Number]) – Problem parameters as parameterId=>value dict. Only parameters included here will be set. Remaining parameters will be used as currently set in *amici_model*.
- **scaled_parameters** (bool) – If True, problem_parameters are assumed to be on the scale provided in the parameter mapping. If False, they are assumed to be in linear scale.

- **parameter_mapping** (*amici.petab.parameter_mapping.ParameterMapping*) – Parameter mapping for all conditions.
- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model.

Return type
None

amici.parameter_mapping.**fill_in_parameters_for_condition**(*edata*, *problem_parameters*, *scaled_parameters*, *parameter_mapping*, *amici_model*)

Fill fixed and dynamic parameters into the edata for condition (in-place).

Parameters

- **edata** (amici.swig_wrappers.ExpData) – Experimental data object to fill parameters into.
- **problem_parameters** (dict[str, numbers.Number]) – Problem parameters as parameterId=>value dict. Only parameters included here will be set. Remaining parameters will be used as already set in *amici_model* and *edata*.
- **scaled_parameters** (bool) – If True, problem_parameters are assumed to be on the scale provided in the parameter mapping. If False, they are assumed to be in linear scale.
- **parameter_mapping** (*amici.petab.parameter_mapping.ParameterMappingForCondition*) – Parameter mapping for current condition.
- **amici_model** (typing.Union[*amici.amici.Model*, *amici.amici.ModelPtr*]) – AMICI model

Return type
None

amici.parameter_mapping.**petab_to_amici_scale**(*petab_scale*)

Convert petab scale id to amici scale id.

Return type
int

amici.parameter_mapping.**scale_parameter**(*value*, *petab_scale*)

Bring parameter from linear scale to target scale.

Parameters

- **value** (numbers.Number) – Value to scale
- **petab_scale** (str) – Target scale of value

Return type
numbers.Number

Returns
value on target scale

amici.parameter_mapping.**scale_parameters_dict**(*value_dict*, *petab_scale_dict*)

Bring parameters from linear scale to target scale.

Bring values in value_dict from linear scale to the scale provided in petab_scale_dict (in-place). Both arguments are expected to have the same length and matching keys.

Parameters

- **value_dict** (dict[typing.Any, numbers.Number]) – Values to scale
- **petab_scale_dict** (dict[typing.Any, str]) – Target scales of values

Return type
None

amici.parameter_mapping.**unscale_parameter**(*value*, *petab_scale*)

Bring parameter from scale to linear scale.

Parameters

- **value** (numbers.Number) – Value to scale
- **petab_scale** (str) – Target scale of value

Return type
numbers.Number

Returns
value on linear scale

amici.parameter_mapping.**unscale_parameters_dict**(*value_dict*, *petab_scale_dict*)

Bring parameters from target scale to linear scale.

Bring values in value_dict from linear scale to the scale provided in petab_scale_dict (in-place). Both arguments are expected to have the same length and matching keys.

Parameters

- **value_dict** (dict[typing.Any, numbers.Number]) – Values to scale
- **petab_scale_dict** (dict[typing.Any, str]) – Target scales of values

Return type
None

10.5.28 amici.conserved_quantities_demartino

Functions

compute_moiety_conservation_laws(...[, ...])	Compute moiety conservation laws.

amici.conserved_quantities_demartino.**compute_moiety_conservation_laws**(*stoichiometric_list*, *num_species*, *num_reactions*, *max_num_monte_carlo=20*, *rng_seed=False*, *species_names=None*)

Compute moiety conservation laws.

According to the algorithm proposed by De Martino et al. (2014) https://doi.org/10.1371/journal.pone.0100750

Parameters

- **stoichiometric_list** (collections.abc.Sequence[float]) – the stoichiometric matrix as a list (species x reactions, column-major ordering)
- **num_species** (int) – total number of species in the reaction network

- **num_reactions** (int) – total number of reactions in the reaction network
- **max_num_monte_carlo** (int) – maximum number of MonteCarlo steps before changing to relaxation
- **rng_seed** (typing.Union[None, bool, int]) – Seed for the random number generator. If *False*, the RNG will not be re-initialized. Other values will be passed to random.seed().
- **species_names** (typing.Optional[collections.abc.Sequence[str]]) – Species names. Optional and only used for logging.

Return type
tuple[list[list[int]], list[list[float]]]

Returns
Integer MCLs as list of lists of indices of involved species and list of lists of corresponding coefficients.

10.5.29 amici.conserved_quantities_rref

Find conserved quantities deterministically

Functions

nullspace_by_rref(mat)	Compute basis of the nullspace of mat based on the reduced row echelon form
pivots(mat)	Get indices of pivot columns in mat, assumed to be in reduced row echelon form
rref(mat[, round_ndigits])	Bring matrix mat to reduced row echelon form

amici.conserved_quantities_rref.**nullspace_by_rref**(*mat*)

Compute basis of the nullspace of mat based on the reduced row echelon form

Return type
numpy.array

amici.conserved_quantities_rref.**pivots**(*mat*)

Get indices of pivot columns in mat, assumed to be in reduced row echelon form

Return type
list[int]

amici.conserved_quantities_rref.**rref**(*mat*, *round_ndigits=None*)

Bring matrix mat to reduced row echelon form

see https://en.wikipedia.org/wiki/Row_echelon_form

Parameters

- **mat** (numpy.array) – Numpy float matrix to operate on (will be copied)
- **round_ndigits** (typing.Union[typing.Literal[False], int, None]) – Number of digits to round intermediary results to, or False to disable rounding completely. Helps to avoid numerical artifacts.

Return type
numpy.array

Returns
`mat` in rref form.

10.5.30 amici.numpy

C++ object views

This module provides views on C++ objects for efficient access.

Functions

evaluate(expr, rdata)	Evaluate a symbolic expression based on the given simulation outputs.

Classes

ExpDataView(edata)	Interface class for C++ Exp Data objects that avoids possibly costly copies of member data.
ReturnDataView(rdata)	Interface class for C++ `amici.ReturnData` objects that avoids possibly costly copies of member data.
SwigPtrView(swigptr)	Interface class to expose `std::vector<double>` and scalar members of swig wrapped C++ objects as numpy array attributes and fields.

class amici.numpy.**ExpDataView**(*edata*)

Interface class for C++ Exp Data objects that avoids possibly costly copies of member data.

NOTE: This currently assumes that the underlying `ExpData` does not change after instantiating an *ExpDataView*.

__init__(*edata*)

Constructor

Parameters
edata (typing.Union[*amici.amici.ExpDataPtr*, *amici.amici.ExpData*]) – pointer to the ExpData instance

get(*k*[, *d*]) → D[k] if k in D, else d. d defaults to None.

items() → a set-like object providing a view on D's items

keys() → a set-like object providing a view on D's keys

values() → an object providing a view on D's values

class amici.numpy.**ReturnDataView**(*rdata*)

Interface class for C++ `amici.ReturnData` objects that avoids possibly costly copies of member data.

__init__(*rdata*)

Constructor

Parameters

rdata (typing.Union[*amici.amici.ReturnDataPtr*, *amici.amici.ReturnData*]) – pointer to the ReturnData instance

by_id(*entity_id*, *field=None*, *model=None*)

Get the value of a given field for a named entity.

Parameters

- **entity_id** (str) – The ID of the model entity that is to be extracted from field (e.g. a state ID).
- **field** (str) – The requested field, e.g. 'x' for model states. This is optional if field would be one of {'x', 'y', 'w'}
- **model** (*amici.amici.Model*) – The model from which this ReturnDataView was generated. This is optional if this ReturnData was generated with solver.getReturnDataReportingMode() == amici.RDataReporting.full.

Return type

numpy.array

get(*k*[, *d*]) → D[k] if k in D, else d. d defaults to None.

items() → a set-like object providing a view on D's items

keys() → a set-like object providing a view on D's keys

values() → an object providing a view on D's values

class amici.numpy.SwigPtrView(*swigptr*)

Interface class to expose std::vector<double> and scalar members of swig wrapped C++ objects as numpy array attributes and fields. This class is memory efficient as copies of the underlying C++ objects is only created when respective fields are accessed for the first time. Cached copies are used for all subsequent calls.

Variables

- **_swigptr** – pointer to the C++ object
- **_field_names** – names of members that will be exposed as numpy arrays
- **_field_dimensions** – dimensions of numpy arrays
- **_cache** – dictionary with cached values

__init__(*swigptr*)

Constructor

Parameters

swigptr – pointer to the C++ object

get(*k*[, *d*]) → D[k] if k in D, else d. d defaults to None.

items() → a set-like object providing a view on D's items

keys() → a set-like object providing a view on D's keys

values() → an object providing a view on D's values

amici.numpy.**evaluate**(*expr*, *rdata*)

Evaluate a symbolic expression based on the given simulation outputs.

Parameters

- **expr** (typing.Union[str, sympy.core.expr.Expr]) – A symbolic expression, e.g. a sympy expression or a string that can be sympified. Can include state variable, expression, and observable IDs, depending on whether the respective data is available in the simulation results. Parameters are not yet supported.
- **rdata** (*amici.numpy.ReturnDataView*) – The simulation results.

Return type
numpy.array

Returns
The evaluated expression for the simulation output timepoints.

10.5.31 amici.sbml_utils

SBML Utilities

This module provides helper functions for working with SBML.

Functions

add_assignment_rule(model, variable_id, formula)	Helper for adding an assignment rule to a SBML model.
add_compartment(model, compartment_id, *[, size])	Helper for adding a compartment to a SBML model.
add_inflow(model, species_id, rate, *[, ...])	**rtype** libsbml.Reaction
add_parameter(model, parameter_id, *[, ...])	Helper for adding a parameter to a SBML model.
add_rate_rule(model, variable_id, formula[, ...])	Helper for adding a rate rule to a SBML model.
add_species(model, species_id, *[, ...])	Helper for adding a species to a SBML model.
create_sbml_model(model_id[, level, version])	Helper for creating an empty SBML model.
get_sbml_units(model, x)	Try to get the units for expression *x*.
mathml2sympy(mathml, *[, evaluate, locals, ...])	**rtype** sympy.core.basic.Basic
pretty_xml(ugly_xml)	Prettifies an XML document (given as a string).
sbml_math_ast(expr, **kwargs)	Convert a SymPy expression to SBML math AST.
sbml_mathml(expr, *[, replace_time, pretty])	Prints a SymPy expression to a MathML expression parsable by libSBML.
set_sbml_math(obj, expr, **kwargs)	Set the math attribute of a SBML node using a SymPy expression.

Classes

MathMLSbmlPrinter([settings])	Prints a SymPy expression to a MathML expression parsable by libSBML.

Exceptions

SbmlAnnotationError
SbmlDuplicateComponentIdError
SbmlInvalidIdSyntax
SbmlMathError
SbmlMissingComponentIdError

class amici.sbml_utils.**MathMLSbmlPrinter**(*settings=None*)

Prints a SymPy expression to a MathML expression parsable by libSBML.

Differences from *sympy.MathMLContentPrinter*: 1. underscores in symbol names are not converted to subscripts 2. symbols with name 'time' are converted to the SBML time symbol

__init__(*settings=None*)

apply_patch()

doprint(*expr*, *, *pretty=False*)

Prints the expression as MathML.

Return type
str

emptyPrinter(*expr*)

mathml_tag(*e*)

Returns the MathML tag for an expression.

property order

printmethod: str = '_mathml_content'

restore_patch()

classmethod set_global_settings(**settings*)

Set system-wide printing settings.

exception amici.sbml_utils.**SbmlAnnotationError**

exception amici.sbml_utils.**SbmlDuplicateComponentIdError**

exception amici.sbml_utils.**SbmlInvalidIdSyntax**

exception amici.sbml_utils.**SbmlMathError**

exception amici.sbml_utils.**SbmlMissingComponentIdError**

amici.sbml_utils.**add_assignment_rule**(*model*, *variable_id*, *formula*, *rule_id=None*)

Helper for adding an assignment rule to a SBML model.

Parameters

- **model** (libsbml.Model) – SBML model to which the assignment rule is to be added.
- **variable_id** (typing.Union[str, sympy.core.symbol.Symbol]) – SBML ID of the quantity for which the assignment rule is to be added.
- **formula** – Formula for the assignment rule (it will be sympified).
- **rule_id** (str | None) – SBML ID of the new assignment rule. Defaults to *'assignment_' + variableId*.

Return type
libsbml.AssignmentRule

Returns
The assignment rule as a libsbml.AssignmentRule object.

amici.sbml_utils.**add_compartment**(*model*, *compartment_id*, ***, *size=1.0*)

Helper for adding a compartment to a SBML model.

Parameters

- **model** (libsbml.Model) – SBML model to which the compartment is to be added.
- **compartment_id** (typing.Union[str, sympy.core.symbol.Symbol]) – SBML ID of the new compartment.
- **size** (float) – Size of the new compartment. Defaults to *1.0*.

Return type
libsbml.Species

Returns
The new compartment as a libsbml.Compartment object.

amici.sbml_utils.**add_inflow**(*model*, *species_id*, *rate*, ***, *reaction_id=None*, *reversible=False*)

Return type
libsbml.Reaction

amici.sbml_utils.**add_parameter**(*model*, *parameter_id*, ***, *name=False*, *value=None*, *units=None*, *constant=None*)

Helper for adding a parameter to a SBML model.

Parameters

- **model** (libsbml.Model) – SBML model to which the parameter is to be added.
- **parameter_id** (typing.Union[str, sympy.core.symbol.Symbol]) – SBML ID of the new parameter.
- **name** (bool | str) – SBML name of the new parameter.
- **value** (float | None) – Value attribute for the new parameter.
- **units** (str | None) – Units attribute for the new parameter.

- **constant** (bool | None) – Constant attribute for the new parameter.

Return type
libsbml.Parameter

Returns
The new parameter as a libsbml.Parameter object.

amici.sbml_utils.**add_rate_rule**(*model*, *variable_id*, *formula*, *rule_id=None*)

Helper for adding a rate rule to a SBML model.

Parameters

- **model** (libsbml.Model) – SBML model to which the rate rule is to be added.
- **variable_id** (typing.Union[str, sympy.core.symbol.Symbol]) – SBML ID of the quantity for which the rate rule is to be added.
- **formula** – Formula for the rate rule (it will be sympified).
- **rule_id** (str | None) – SBML ID of the new rate rule. Defaults to *'rate_' + variableId*.

Return type
libsbml.RateRule

Returns
The new rate rule as a libsbml.RateRule object.

amici.sbml_utils.**add_species**(*model*, *species_id*, ***, *compartment_id=None*, *name=False*, *initial_amount=0.0*, *units=None*)

Helper for adding a species to a SBML model.

Parameters

- **model** (libsbml.Model) – SBML model to which the species is to be added.
- **species_id** (typing.Union[str, sympy.core.symbol.Symbol]) – SBML ID of the new species.
- **compartment_id** (str | None) – Compartment ID for the new species. If there is only one compartment it can be auto-selected.
- **initial_amount** (float) – Initial amount of the new species.
- **units** (str | None) – Units attribute for the new species.

Return type
libsbml.Species

Returns
The new species as a libsbml.Species object.

amici.sbml_utils.**create_sbml_model**(*model_id*, *level=2*, *version=5*)

Helper for creating an empty SBML model.

Parameters

- **model_id** (str) – SBML ID of the new model.
- **level** (int) – Level of the new SBML document.
- **version** (int) – Version of the new SBML document.

Return type
tuple[libsbml.SBMLDocument, libsbml.Model]

Returns
A tuple containing the newly created `libsbml.SBMLDocument` and `libsbml.Model`.

`amici.sbml_utils.get_sbml_units(model, x)`
Try to get the units for expression *x*.

Parameters
- **model** (`libsbml.Model`) – SBML model.
- **x** (`typing.Union[str, sympy.core.symbol.Symbol, sympy.core.basic.Basic]`) – Expression to get the units of.

Return type
`None | str`

Returns
A string if the units could be determined, otherwise *None*.

`amici.sbml_utils.mathml2sympy(mathml, *, evaluate=False, locals=None, expression_type='mathml2sympy')`

Return type
`sympy.core.basic.Basic`

`amici.sbml_utils.pretty_xml(ugly_xml)`
Prettifies an XML document (given as a string).

Return type
`str`

`amici.sbml_utils.sbml_math_ast(expr, **kwargs)`
Convert a SymPy expression to SBML math AST.

Parameters
- **expr** – expression to be converted (will be sympified).
- **kwargs** – extra options for MathML conversion.

Return type
`libsbml.ASTNode`

`amici.sbml_utils.sbml_mathml(expr, *, replace_time=False, pretty=False, **settings)`
Prints a SymPy expression to a MathML expression parsable by libSBML.

Parameters
- **expr** – expression to be converted to MathML (will be sympified).
- **replace_time** (`bool`) – replace the AMICI time symbol with the SBML time symbol.
- **pretty** (`bool`) – prettify the resulting MathML.

Return type
`str`

`amici.sbml_utils.set_sbml_math(obj, expr, **kwargs)`
Set the math attribute of a SBML node using a SymPy expression.

Parameters
- **obj** (`libsbml.SBase`) – SBML node supporting *setMath* method.
- **expr** – expression to which the math attribute of *obj* should be se to (will be sympified).
- **kwargs** – extra options for MathML conversion.

Return type
None

10.5.32 amici.splines

Splines

This module provides helper functions for reading/writing splines with AMICI annotations from/to SBML files and for adding such splines to the AMICI C++ code.

Functions

spline_user_functions(splines, p_index)	Custom user functions to be used in *ODEExporter* for linking spline expressions to C++ code.
sympify_noeval(x)	

Classes

AbstractSpline(sbml_id, nodes, ...[, ...])	Base class for spline functions which can be computed efficiently thanks to tailored C++ implementations in AMICI.
CubicHermiteSpline(sbml_id, nodes, ...[, ...])	
UniformGrid(start, stop[, step, ...])	A grid of uniformly-spaced real points, computed with rational arithmetic.

class amici.splines.**AbstractSpline**(*sbml_id*, *nodes*, *values_at_nodes*, ***, *evaluate_at=None*, *bc=None*, *extrapolate=None*, *logarithmic_parametrization=False*)

Base class for spline functions which can be computed efficiently thanks to tailored C++ implementations in AMICI. Inside an SBML file, such splines are implemented with an assignment rule containing both a symbolic piecewise formula for the spline (allowing compatibility with any SBML-aware software) and annotations which encode the necessary information for AMICI to recreate the spline object (allowing for fast computations when the SBML file is used together with AMICI).

__init__(*sbml_id*, *nodes*, *values_at_nodes*, ***, *evaluate_at=None*, *bc=None*, *extrapolate=None*, *logarithmic_parametrization=False*)

Base constructor for `AbstractSpline` objects.

Parameters

- **sbml_id** (`str` | `sympy.core.symbol.Symbol`) – The SBML ID of the parameter associated to the spline as a string or a SymPy symbol.
- **nodes** (`collections.abc.Sequence`) – The points at which the spline values are known. Currently, they must be numeric or only depend on constant parameters. These points should be strictly increasing. This argument will be sympified.
- **values_at_nodes** (`collections.abc.Sequence`) – The spline values at each of the points in `nodes`. They must not depend on model species. This argument will be sympified.

- **evaluate_at** (str | sympy.core.basic.Basic | None) – The point at which the spline is evaluated. It will be sympified. Defaults to model time.
- **bc** (typing.Union[None, str, tuple[typing.Optional[str], typing.Optional[str]]]) – Tuple of applied boundary conditions, one for each side of the spline domain. If a single boundary condition is given it will be applied to both sides. Possible boundary conditions (allowed values depend on the AbstractSpline subclass):

  ***None* or *'no_bc'*:**
  Boundary conditions are not needed for this spline object;

  ***'zeroderivative'*:**
  first derivative set to zero;

  ***'natural'*:**
  second derivative set to zero;

  ***'zeroderivative+natural'*:**
  first and second derivatives set to zero;

  ***'periodic'*:**
  periodic bc.
- **extrapolate** (typing.Union[None, str, tuple[typing.Optional[str], typing.Optional[str]]]) – Whether to extrapolate the spline outside the base interval defined by (nodes[0], nodes[-1]). It is a tuple of extrapolation methods, one for each side of the base interval. If it is not a tuple, then the same extrapolation will be applied on both sides. Extrapolation methods supported:

  ***None* or *'no_extrapolation'*:**
  no extrapolation should be performed. An exception will be raised in the C++ code if the spline is evaluated outside the base interval. In the fallback SBML symbolic expression *'polynomial'* extrapolation will be used.

  ***'polynomial'*:**
  the cubic polynomial used in the nearest spline segment will be used.

  ***'constant'*:**
  constant extrapolation will be used. Requires *'zeroderivative'* boundary condition. For splines which are continuous up to the second derivative, it requires the stricter *'zeroderivative+natural'* boundary condition.

  ***'linear'*:**
  linear extrapolation will be used. For splines which are continuous up to the second derivative, this requires the *'natural'* boundary condition.

  ***'periodic'*:**
  Periodic extrapolation. Requires *'periodic'* boundary conditions.
- **logarithmic_parametrization** (bool) – Whether interpolation should be done in log-scale.

add_to_sbml_model(*model*, ***, *auto_add=False*, *x_nominal=None*, *y_nominal=None*, *x_units=None*, *y_units=None*, *y_constant=None*)

Function to add the spline to an SBML model using an assignment rule with AMICI-specific annotations.

Parameters

- **model** (libsbml.Model) – A libsbml.Model to which the spline is to be added.

- **auto_add** (bool | str) – Automatically add missing parameters to the SBML model (defaults to *False*). Only used for expressions consisting in a single symbol. If equal to *'spline'*, only the parameter representing the spline will be added.
- **x_nominal** (collections.abc.Sequence[float] | None) – Nominal values used when auto-adding parameters for *nodes*.
- **y_nominal** (collections.abc.Sequence[float] | float | None) – Nominal values used when auto-adding parameters for *values_at_nodes*.
- **x_units** (str | None) – Units used when auto-adding parameters for *nodes*.
- **y_units** (str | None) – Units used when auto-adding parameters for *values_at_nodes*.
- **y_constant** (collections.abc.Sequence[bool] | bool | None) – Constant flags used when auto-adding parameters for *values_at_nodes*.

Return type
None

property amici_annotation: str

An SBML annotation describing the spline.

property bc: tuple[None | str, None | str]

Boundary conditions applied to this spline.

check_if_valid(*importer*)

Check if the spline described by this object can be correctly be implemented by AMICI. E.g., check whether the formulas for spline grid points, values, ... contain species symbols.

Return type
None

derivative(*x*, ***kwargs*)

Evaluate the spline derivative at the point *x*.

Return type
sympy.core.expr.Expr

evaluate(*x*)

Evaluate the spline at the point *x*.

Return type
sympy.core.basic.Basic

property evaluate_at: Basic

The symbolic argument at which the spline is evaluated.

property extrapolate: tuple[None | str, None | str]

Whether to extrapolate the spline outside the base interval.

property extrapolation_formulas: tuple[None | Basic, None | Basic]

Returns the extrapolation formulas on the left and right side of the interval `(nodes[0], nodes[-1])`. A value of `None` means that no extrapolation is required.

property formula: Piecewise

Compute a symbolic piecewise formula for the spline.

static from_annotation(*sbml_id*, *annotation*, *, *locals_*)

Create a spline object from a SBML annotation.

This function extracts annotation and children from the XML annotation and gives them to the `_fromAnnotation` function for parsing. Subclass behaviour should be implemented by extending `_fromAnnotation`. However, the mapping between method strings and subclasses must be hard-coded into this function here (at the moment).

Return type
amici.splines.AbstractSpline

static get_annotation(*rule*)

Extract AMICI spline annotation from an SBML assignment rule (given as a `libsbml.AssignmentRule` object). Return `None` if any such annotation could not be found.

Return type
`xml.etree.ElementTree.Element` | `None`

integrate(*x0*, *x1*)

Integrate the spline between the points *x0* and *x1*.

Return type
`sympy.core.basic.Basic`

static is_spline(*rule*)

Determine if an SBML assignment rule (given as a `libsbml.AssignmentRule` object) is an AMICI-annotated spline formula.

Return type
`bool`

property logarithmic_parametrization: bool

Whether interpolation is done in log-scale.

property mathml_formula: Piecewise

Compute a symbolic piecewise formula for the spline for use inside a SBML assignment rule: SBML symbol naming will be used and operations not supported by SBML MathML will be avoided.

abstract property method: str

Spline method.

property nodes: ndarray

The points at which the spline values are known.

ode_model_symbol(*importer*)

Returns the *sympy* object to be used by `amici.de_export.ODEModel`. This expression can be differentiated and easily mapped to the C++ code.

Return type
`sympy.core.function.Function`

parameters(*importer*)

Returns the SBML parameters used by this spline

Return type
`set`[`sympy.core.symbol.Symbol`]

property period: Basic | None

Period of a periodic spline. *None* if the spline is not periodic.

plot(*parameters=None*, ***, *xlim=None*, *npoints=100*, *xlabel=None*, *ylabel='spline value'*, *ax=None*)

Plots the spline, highlighting the nodes positions.

poly(*i*, ***, *x=None*)

Get the polynomial interpolant on the `(nodes[i], nodes[i+1])` interval. The polynomial is written in Horner form with respect to the scaled variable `poly_variable(x, i)`. If no variable `x` is provided, it will default to the one given at initialization time.

Return type
sympy.core.basic.Basic

poly_variable(*x*, *i*)

Given an evaluation point, return the value of the variable in which the polynomial on the `i`-th interval is expressed.

Return type
sympy.core.basic.Basic

property sbml_formula: Piecewise

Compute a symbolic piecewise formula for the spline, using SBML symbol naming (the AMICI time symbol will be replaced with its SBML counterpart).

property sbml_id: Symbol

SBML ID of the spline parameter.

second_derivative(*x*)

Evaluate the spline second derivative at the point *x*.

Return type
sympy.core.basic.Basic

segment_formula(*i*, ***, *x=None*)

Return the formula for the actual value of the spline expression on the `(nodes[i], nodes[i+1])` interval. Unless logarithmic parametrization is used, this is equal to the interpolating polynomial.

Return type
sympy.core.basic.Basic

abstract property smoothness: int

Smoothness of this spline.

squared_L2_norm_of_curvature()

Return the squared L2 norm of the spline's curvature (commonly used as a regularizer). This is always computed in the spline native scale (i.e., in log-scale for positivity enforcing splines).

Return type
sympy.core.basic.Basic

property values_at_nodes: ndarray

The spline values at each of the points in `nodes`.

y_scaled(*i*)

Return the values which should be interpolated by a polynomial. Unless logarithmic parametrization is used, they are equal to the values given at initialization time.

class amici.splines.**CubicHermiteSpline**(*sbml_id*, *nodes*, *values_at_nodes*, *derivatives_at_nodes=None*, ***, *evaluate_at=None*, *bc='auto'*, *extrapolate=None*, *logarithmic_parametrization=False*)

__init__(*sbml_id*, *nodes*, *values_at_nodes*, *derivatives_at_nodes=None*, ***, *evaluate_at=None*, *bc='auto'*, *extrapolate=None*, *logarithmic_parametrization=False*)

Constructor for *CubicHermiteSpline* objects.

Parameters

- **sbml_id** (str | sympy.core.symbol.Symbol) – The SBML ID of the parameter associated to the spline as a string or a SymPy symbol.
- **x** – The point at which the spline is evaluated. It will be sympified.
- **nodes** (collections.abc.Sequence) – The points at which the spline values are known. Currently, they must be numeric or only depend on constant parameters. These points should be strictly increasing. This argument will be sympified.
- **values_at_nodes** (collections.abc.Sequence) – The spline values at each of the points in *nodes*. They must not depend on model species. This argument will be sympified.
- **derivatives_at_nodes** (collections.abc.Sequence) – The spline derivatives at each of the points in *nodes*. They must not depend on model species. This argument will be sympified. If not specified, it will be computed by finite differences.
- **evaluate_at** (str | sympy.core.basic.Basic | None) – The point at which the spline is evaluated. It will be sympified. Defaults to model time.
- **bc** (typing.Union[None, str, tuple[typing.Optional[str], typing.Optional[str]]]) – Applied boundary conditions (see *AbstractSpline* documentation). If *'auto'* (the default), the boundary conditions will be automatically set depending on the extrapolation methods.
- **extrapolate** (typing.Union[None, str, tuple[typing.Optional[str], typing.Optional[str]]]) – Extrapolation method (see *AbstractSpline* documentation).
- **logarithmic_parametrization** (bool) – Whether interpolation should be done in log-scale.

add_to_sbml_model(*model*, ***, *auto_add=False*, *x_nominal=None*, *y_nominal=None*, *x_units=None*, *y_units=None*, *y_constant=None*)

Function to add the spline to an SBML model using an assignment rule with AMICI-specific annotations.

Parameters

- **model** (libsbml.Model) – A libsbml.Model to which the spline is to be added.
- **auto_add** (bool | str) – Automatically add missing parameters to the SBML model (defaults to *False*). Only used for expressions consisting in a single symbol. If equal to *'spline'*, only the parameter representing the spline will be added.
- **x_nominal** (collections.abc.Sequence[float] | None) – Nominal values used when auto-adding parameters for *nodes*.
- **y_nominal** (collections.abc.Sequence[float] | float | None) – Nominal values used when auto-adding parameters for *values_at_nodes*.
- **x_units** (str | None) – Units used when auto-adding parameters for *nodes*.
- **y_units** (str | None) – Units used when auto-adding parameters for *values_at_nodes*.
- **y_constant** (collections.abc.Sequence[bool] | bool | None) – Constant flags used when auto-adding parameters for *values_at_nodes*.

Return type

None

property amici_annotation: str

An SBML annotation describing the spline.

property bc: tuple[None | str, None | str]

Boundary conditions applied to this spline.

check_if_valid(*importer*)

Check if the spline described by this object can be correctly be implemented by AMICI. E.g., check whether the formulas for spline grid points, values, ... contain species symbols.

Return type
None

d_scaled(*i*)

Return the derivative of the polynomial interpolant at the *i*-th point. Unless logarithmic parametrization is used, it is equal to the derivative of the spline expression.

Return type
sympy.core.expr.Expr

derivative(*x*, ***kwargs*)

Evaluate the spline derivative at the point *x*.

Return type
sympy.core.expr.Expr

property derivatives_at_nodes: ndarray

The spline derivatives at each of the points in *nodes*.

property derivatives_by_fd: bool

evaluate(*x*)

Evaluate the spline at the point *x*.

Return type
sympy.core.basic.Basic

property evaluate_at: Basic

The symbolic argument at which the spline is evaluated.

property extrapolate: tuple[None | str, None | str]

Whether to extrapolate the spline outside the base interval.

property extrapolation_formulas: tuple[None | Basic, None | Basic]

Returns the extrapolation formulas on the left and right side of the interval `(nodes[0], nodes[-1])`. A value of `None` means that no extrapolation is required.

property formula: Piecewise

Compute a symbolic piecewise formula for the spline.

static from_annotation(*sbml_id*, *annotation*, *, *locals_*)

Create a spline object from a SBML annotation.

This function extracts annotation and children from the XML annotation and gives them to the `_fromAnnotation` function for parsing. Subclass behaviour should be implemented by extending `_fromAnnotation`. However, the mapping between method strings and subclasses must be hard-coded into this function here (at the moment).

Return type
amici.splines.AbstractSpline

static get_annotation(*rule*)

Extract AMICI spline annotation from an SBML assignment rule (given as a `libsbml.AssignmentRule` object). Return `None` if any such annotation could not be found.

Return type
xml.etree.ElementTree.Element | None

integrate(*x0*, *x1*)

Integrate the spline between the points *x0* and *x1*.

Return type
sympy.core.basic.Basic

static is_spline(*rule*)

Determine if an SBML assignment rule (given as a `libsbml.AssignmentRule` object) is an AMICI-annotated spline formula.

Return type
bool

property logarithmic_parametrization: bool

Whether interpolation is done in log-scale.

property mathml_formula: Piecewise

Compute a symbolic piecewise formula for the spline for use inside a SBML assignment rule: SBML symbol naming will be used and operations not supported by SBML MathML will be avoided.

property method: str

Spline method (cubic Hermite spline)

property nodes: ndarray

The points at which the spline values are known.

ode_model_symbol(*importer*)

Returns the *sympy* object to be used by `amici.de_export.ODEModel`. This expression can be differentiated and easily mapped to the C++ code.

Return type
sympy.core.function.Function

parameters(*importer*)

Returns the SBML parameters used by this spline

Return type
set[sympy.core.symbol.Symbol]

property period: Basic | None

Period of a periodic spline. *None* if the spline is not periodic.

plot(*parameters=None*, ***, *xlim=None*, *npoints=100*, *xlabel=None*, *ylabel='spline value'*, *ax=None*)

Plots the spline, highlighting the nodes positions.

poly(*i*, ***, *x=None*)

Get the polynomial interpolant on the `(nodes[i], nodes[i+1])` interval. The polynomial is written in Horner form with respect to the scaled variable `poly_variable(x, i)`. If no variable `x` is provided, it will default to the one given at initialization time.

Return type
sympy.core.basic.Basic

poly_variable(*x*, *i*)

Given an evaluation point, return the value of the variable in which the polynomial on the `i`-th interval is expressed.

Return type
sympy.core.basic.Basic

property sbml_formula: Piecewise

Compute a symbolic piecewise formula for the spline, using SBML symbol naming (the AMICI time symbol will be replaced with its SBML counterpart).

property sbml_id: Symbol

SBML ID of the spline parameter.

second_derivative(*x*)

Evaluate the spline second derivative at the point *x*.

Return type
sympy.core.basic.Basic

segment_formula(*i*, *, *x=None*)

Return the formula for the actual value of the spline expression on the `(nodes[i], nodes[i+1])` interval. Unless logarithmic parametrization is used, this is equal to the interpolating polynomial.

Return type
sympy.core.basic.Basic

property smoothness: int

Smoothness of this spline (equal to 1 for cubic Hermite splines since they are continuous up to the first derivative).

squared_L2_norm_of_curvature()

Return the squared L2 norm of the spline's curvature (commonly used as a regularizer). This is always computed in the spline native scale (i.e., in log-scale for positivity enforcing splines).

Return type
sympy.core.basic.Basic

property values_at_nodes: ndarray

The spline values at each of the points in `nodes`.

y_scaled(*i*)

Return the values which should be interpolated by a polynomial. Unless logarithmic parametrization is used, they are equal to the values given at initialization time.

class amici.splines.**UniformGrid**(*start*, *stop*, *step=None*, *, *number_of_nodes=None*, *always_include_stop=True*)

A grid of uniformly-spaced real points, computed with rational arithmetic.

Implements the `collections.abc.Sequence` interface and can be converted to a `numpy.ndarray` (conversion to float can be specified with `dtype=float`).

Variables

- **start** – first point.
- **stop** – last point.
- **step** – distance between consecutive points.
- **number_of_nodes** – number of grid nodes.

__init__(*start*, *stop*, *step=None*, ***, *number_of_nodes=None*, *always_include_stop=True*)

Create a new `UniformGrid`.

Note: A `UniformGrid` with a single node cannot be created.

Parameters

- **start** (`numbers.Real` | `sympy.core.basic.Basic`) – First point in the grid
- **stop** (`numbers.Real` | `sympy.core.basic.Basic`) – Last point in the grid (some caveats apply, see `always_include_stop`)
- **step** (`numbers.Real` | `sympy.core.basic.Basic` | `None`) – Desired step size of the grid. Mutually exclusive with `number_of_nodes`.
- **number_of_nodes** (`numbers.Integral` | `None`) – Number of grid nodes, i.e., the length of the grid. It must be greater than or equal to 2. Mutually exclusive with `step`.
- **always_include_stop** (`bool`) – Controls the behaviour when `step` is not `None`. If `True` (default), the endpoint is the smallest `start + k * step`, with `k` integer, which is greater than or equal to `stop`. Otherwise, the endpoint is the largest `start + k * step`, with `k` integer, which is smaller than or equal to `stop`.

count(*value*) → integer -- return number of occurrences of value

index(*value*[, *start*[, *stop*]]) → integer -- return first index of value.

Raises ValueError if the value is not present.

Supporting start and stop arguments is optional, but recommended.

property number_of_nodes: Basic

Number of grid nodes.

property start: Basic

First point.

property step: Basic

Distance between consecutive points.

property stop: Basic

Last point.

amici.splines.**spline_user_functions**(*splines*, *p_index*)

Custom user functions to be used in *ODEExporter* for linking spline expressions to C++ code.

Return type

`dict[str, list[tuple[typing.Callable[..., bool], typing.Callable[..., str]]]]`

amici.splines.**sympify_noeval**(*x*)

CHAPTER

ELEVEN

C++ INTERFACE

11.1 Building the C++ library

The following section describes building the AMICI C++ library:

Note: The AMICI C++ interface only supports simulation of models imported using the *Python interface* and *Matlab interface*. It cannot be used for model import itself.

Prerequisites:

- CBLAS compatible BLAS library
- a C++17 compatible compiler
- a C compiler
- Optional: * HDF5 libraries * boost for serialization

To use AMICI from C++, run the

```
./scripts/buildSuiteSparse.sh
./scripts/buildSundials.sh
./scripts/buildAmici.sh
```

script to build the AMICI library.

Note: On some systems, the CMake executable may be named something other than `cmake`. In this case, set the `CMAKE` environment variable to the correct name (e.g. `export CMAKE=cmake3`, in case you have CMake available as `cmake3`).

The static library can then be linked from

```
./build/libamici.a
```

In CMake-based packages, amici can be linked via

```
find_package(Amici)
```

For further usage, consult the AMICI *C++ interface documentation*.

11.1.1 Supported CBLAS libraries

The C++ interfaces require a system installation of a CBLAS-compatible *Basic Linear Algebra Subprograms* (BLAS) library. AMICI has been tested with various implementations such as Accelerate, Intel MKL, cblas, openblas and atlas.

11.1.2 Optional SuperLU_MT support

To build AMICI with SuperLU_MT support, run

```
./scripts/buildSuperLUMT.sh
./scripts/buildSundials.sh
cd build/
cmake -DSUNDIALS_SUPERLUMT_ENABLE=ON ..
make
```

11.2 Using AMICI's C++ interface

The various import functions in of the *Python interface* and *Matlab interface* translate models defined in different formats into C++ code. These generated model libraries, together with the AMICI base library can be used in any C++ application for model simulation and sensitivity analysis. This section will give a short overview over the generated files and provide a brief introduction of how this code can be included in other applications. Further details are available in the *C++ API reference*.

11.2.1 AMICI-generated C++ model files

After importing a model using either the *Python interface* or the *Matlab interface*, the specified output directory contains (among others) C++ code for the various model functions.

The content of a model source directory looks something like this (given *MODEL_NAME=model_steadystate*):

```
CMakeLists.txt
main.cpp
deltaqB.cpp
deltaqB.h
[... many more files *.(cpp|h|md5|o) ]
wrapfunctions.cpp
wrapfunctions.h
model_steadystate.h
model_steadystate.cpp
```

These files provide the implementation of a model-specific subclass of `amici::Model`. The `CMakeLists.txt` file can be used to build the model library using CMake. `main.cpp` contains a simple scaffold for running a model simulation from C++. See next section for more details on these files.

11.2.2 Running a model simulation

AMICI's public API is mostly available through amici/amici.h. This is the only header file that needs to be included for basic usage. All functions there are declared within the *amici namespace*. Additionally, amici/hdf5.h and amici/serialization.h may be handy for specific use cases. The former provides some functions for reading and writing HDF5 files, latter for serialization (requires Boost). All model-specific functions are defined in the namespace `model_$modelname`.

The main function for running an AMICI simulation is *amici::runAmiciSimulation()*. This function requires

- an instance of a *amici::Model* subclass as generated during model import. For the example *model_steadystate* the respective class is provided as `Model_model_steadystate` in `model_steadystate.h` in output directory for the given model.
- a *amici::Solver* instance. This solver instance needs to match the requirements of the model and can be obtained from *amici::AbstractModel::getSolver()*.
- optionally an *amici::ExpData* instance, which contains any experimental data (e.g. measurements, noise model parameters or model inputs) to evaluate residuals or an objective function.

This function returns a *amici::ReturnData* object, which contains all simulation results.

For running simulations for multiple experimental conditions (multiple *amici::ExpData* instances), *amici::runAmiciSimulations()* provides an alternative entry point. If AMICI (and your application) have been compiled with OpenMP support (see installation guide), this allows for running those simulations in parallel.

A scaffold for a standalone simulation program is automatically generated during model import in `main.cpp` in the model output directory. This program shows how to use the above-mentioned classes, how to obtain the simulation results, and may provide a starting point for your own simulation code.

Working with multiple or anonymous models

AMICI model import generates a *amici::Model* subclass for the specific model, based on the name used during import. One the one hand, this allows you to use multiple models with different names within a single application. On the other hand, this requires you to know the name of the model, which can be inconvenient in some cases.

When working with a single model, the `wrapfunctions.h` file generated during model import can be used to avoid specifying model names explicitly. It defines a function `amici::generic_model::getModel()`, that returns an instance of the model class by a generic name.

Note: Including multiple `wrapfunctions.h` files from different models in a single application is not possible. When using multiple models, explicit names have to be used or the different model libraries need to be loaded dynamically at runtime.

11.2.3 Compiling and linking

To run AMICI simulations from within your C++ application, you need to compile and link the following libraries:

- model library
- AMICI base library
- SUNDIALS libraries
- SuiteSparse libraries
- CBLAS-compatible BLAS

- optionally HDF5 (C, HL, and CXX components) set CMake option `ENABLE_HDF5` to `OFF` to build without HDF5-support
- optionally OpenMP (for parallel simulation of multiple conditions, see *amici::runAmiciSimulations()*)
- optionally boost (only when using serialization of AMICI object)

The simplest and recommended way is using the provide CMake files which take care of all these dependencies.

Considering the simple case, that you want to simulate one specific model in your CMake-based C++ application, you can copy or move the generated model directory containing the `CMakeLists.txt` file to your application directory, add *add_subdirectory(yourModelDirectory)* to your project's `CMakeLists.txt` file and build your project using CMake as usual.

11.2.4 Parameter estimation for AMICI models in high-performance computing environments

To perform parameter estimation for large or otherwise computationally demanding AMICI models from C++ in a high-performance computing environment, you may find the parPE library helpful. parPE allows for the private or shared memory parallel evaluation of a cost function requiring multiple simulations of the same model with different inputs. It provides interfaces to different optimizers, such as Ipopt.

11.3 AMICI C++ API

AMICI C++ library functions

11.3.1 Class Hierarchy

11.3.2 File Hierarchy

11.3.3 Full API

Namespaces

Namespace amici

Contents

Namespaces

- *Namespace amici::hdf5*

Classes

- *Struct LogItem*
- *Struct ModelDimensions*
- *Struct ModelState*
- *Struct ModelStateDerived*
- *Struct SimulationState*
- *Class AbstractModel*
- *Class AbstractSpline*
- *Class AmiException*
- *Class AmiVector*
- *Class AmiVectorArray*
- *Class BackwardProblem*
- *Class ConditionContext*
- *Class ContextManager*
- *Class CpuTimer*
- *Class CvodeException*
- *Class CVodeSolver*
- *Class ExpData*
- *Class FinalStateStorer*
- *Class ForwardProblem*
- *Class HermiteSpline*
- *Class IDAException*
- *Class IDASolver*
- *Class IntegrationFailure*
- *Class IntegrationFailureB*
- *Class Logger*
- *Class Model*
- *Class Model_DAE*
- *Class Model_ODE*
- *Class ModelContext*
- *Class NewtonFailure*
- *Class NewtonSolver*

- *Class NewtonSolverDense*
- *Class NewtonSolverSparse*
- *Class ReturnData*
- *Class SetupFailure*
- *Class SimulationParameters*
- *Class Solver*
- *Class SteadystateProblem*
- *Class SUNLinSolBand*
- *Class SUNLinSolDense*
- *Class SUNLinSolKLU*
- *Class SUNLinSolPCG*
- *Class SUNLinSolSPBCGS*
- *Class SUNLinSolSPFGMR*
- *Class SUNLinSolSPGMR*
- *Class SUNLinSolSPTFQMR*
- *Class SUNLinSolWrapper*
- *Class SUNMatrixWrapper*
- *Class SUNNonLinSolFixedPoint*
- *Class SUNNonLinSolNewton*
- *Class SUNNonLinSolWrapper*

Enums

- *Enum BLASLayout*
- *Enum BLASTranspose*
- *Enum Constraint*
- *Enum FixedParameterContext*
- *Enum InternalSensitivityMethod*
- *Enum InterpolationType*
- *Enum LinearMultistepMethod*
- *Enum LinearSolver*
- *Enum LogSeverity*
- *Enum ModelQuantity*
- *Enum NewtonDampingFactorMode*
- *Enum NonlinearSolverIteration*
- *Enum ObservableScaling*
- *Enum ParameterScaling*

- *Enum RDataReporting*
- *Enum SecondOrderMode*
- *Enum SensitivityMethod*
- *Enum SensitivityOrder*
- *Enum SplineBoundaryCondition*
- *Enum SplineExtrapolation*
- *Enum SteadyStateComputationMode*
- *Enum SteadyStateContext*
- *Enum SteadyStateSensitivityMode*
- *Enum SteadyStateStatus*

Functions

- *Template Function amici::addSlice(gsl::span<T const> const, gsl::span<T>)*
- *Template Function amici::addSlice(std::vector<T> const&, gsl::span<T>)*
- *Function amici::amici_daxpy*
- *Function amici::amici_dgemm*
- *Function amici::amici_dgemv*
- *Function amici::backtraceString*
- *Template Function amici::checkBufferSize*
- *Function amici::checkSigmaPositivity(realtype, char const *)*
- *Function amici::checkSigmaPositivity(std::vector<realtype> const&, char const *)*
- *Template Function amici::deserializeFromChar*
- *Template Function amici::deserializeFromString*
- *Function amici::dotProd*
- *Function amici::getScaledParameter*
- *Function amici::getUnscaledParameter*
- *Template Function amici::is_equal*
- *Function amici::linearSum*
- *Function amici::N_VGetArrayPointerConst*
- *Function amici::operator==(Model const&, Model const&)*
- *Function amici::operator==(ModelDimensions const&, ModelDimensions const&)*
- *Function amici::operator==(ExpData const&, ExpData const&)*
- *Function amici::operator==(ModelState const&, ModelState const&)*
- *Function amici::operator==(SimulationParameters const&, SimulationParameters const&)*
- *Function amici::operator==(Solver const&, Solver const&)*
- *Function amici::printfToString*

- *Function amici::regexErrorToString*
- *Function amici::runAmiciSimulation*
- *Function amici::runAmiciSimulations*
- *Function amici::scaleParameters*
- *Template Function amici::serializeToChar*
- *Template Function amici::serializeToStdVec*
- *Template Function amici::serializeToString*
- *Function amici::simulation_status_to_str*
- *Template Function amici::slice(std::vector<T> const&, int, unsigned)*
- *Template Function amici::slice(std::vector<T>&, int, unsigned)*
- *Function amici::unravel_index(size_t, size_t)*
- *Function amici::unravel_index(sunindextype, SUNMatrix)*
- *Function amici::unscaleParameters*
- *Function amici::wrapErrHandlerFn*
- *Template Function amici::writeSlice(gsl::span<T const> const, gsl::span<T>)*
- *Template Function amici::writeSlice(std::vector<T> const&, std::vector<T>&)*
- *Template Function amici::writeSlice(std::vector<T> const&, gsl::span<T>)*
- *Function amici::writeSlice(AmiVector const&, gsl::span<realtype>)*

Typedefs

- *Typedef amici::const_N_Vector*
- *Typedef amici::realtype*

Variables

- *Variable amici::AMICI_CONV_FAILURE*
- *Variable amici::AMICI_DAMPING_FACTOR_ERROR*
- *Variable amici::AMICI_DATA_RETURN*
- *Variable amici::AMICI_ERR_FAILURE*
- *Variable amici::AMICI_ERROR*
- *Variable amici::AMICI_FIRST_RHSFUNC_ERR*
- *Variable amici::AMICI_ILL_INPUT*
- *Variable amici::AMICI_LSETUP_FAIL*
- *Variable amici::AMICI_MAX_TIME_EXCEEDED*
- *Variable amici::AMICI_NO_STEADY_STATE*
- *Variable amici::AMICI_NORMAL*

Namespace amici::hdf5

Contents

Functions

- *Function amici::hdf5::getIntDataset1D*
- *Function amici::hdf5::getIntScalarAttribute*
- *Function amici::hdf5::getStringAttribute*
- *Function amici::hdf5::locationExists(std::string const&, std::string const&)*
- *Function amici::hdf5::locationExists(H5::H5File const&, std::string const&)*
- *Function amici::hdf5::readModelDataFromHDF5(H5::H5File const&, Model&, std::string const&)*
- *Function amici::hdf5::readModelDataFromHDF5(std::string const&, Model&, std::string const&)*
- *Function amici::hdf5::readSimulationExpData*
- *Function amici::hdf5::readSolverSettingsFromHDF5(std::string const&, Solver&, std::string const&)*
- *Function amici::hdf5::readSolverSettingsFromHDF5(const H5::H5File&, Solver&, std::string const&)*
- *Function amici::hdf5::writeReturnData(ReturnData const&, H5::H5File const&, std::string const&)*
- *Function amici::hdf5::writeReturnData(ReturnData const&, std::string const&, std::string const&)*
- *Function amici::hdf5::writeReturnDataDiagnosis*
- *Function amici::hdf5::writeSimulationExpData*
- *Function amici::hdf5::writeSolverSettingsToHDF5(Solver const&, H5::H5File const&, std::string const&)*
- *Function amici::hdf5::writeSolverSettingsToHDF5(Solver const&, std::string const&, std::string const&)*

Namespace boost

Contents

- *Namespaces*

Namespaces

- *Namespace boost::serialization*

Namespace boost::serialization

Contents

- *Functions*

Functions

- *Template Function boost::serialization::archiveVector*
- *Template Function boost::serialization::serialize(Archive&, amici::CVodeSolver&, unsigned int)*
- *Template Function boost::serialization::serialize(Archive&, amici::IDASolver&, unsigned int)*
- *Template Function boost::serialization::serialize(Archive&, amici::Solver&, unsigned int)*
- *Template Function boost::serialization::serialize(Archive&, amici::ReturnData&, unsigned int)*
- *Template Function boost::serialization::serialize(Archive&, amici::Model&, unsigned int)*
- *Template Function boost::serialization::serialize(Archive&, amici::AmiVector&, unsigned int)*

Namespace gsl

Contents

Functions

- *Function gsl::make_span(SUNMatrix)*
- *Function gsl::make_span(N_Vector)*
- *Function gsl::make_span(amici::AmiVector const&)*

Namespace std

STL namespace.

Classes and Structs

Struct LogItem

- Defined in file_include_amici_logging.h

Struct Documentation

struct **LogItem**

A log item.

Public Functions

LogItem() = default

Default ctor.

inline **LogItem**(*LogSeverity* severity, std::string const &identifier, std::string const &message)

Construct a *LogItem*.

Parameters

- **severity** –
- **identifier** –
- **message** –

Public Members

LogSeverity **severity** = *LogSeverity*::*error*

Severity level

std::string **identifier**

Short identifier for the logged event

std::string **message**

A more detailed and readable message

Struct ModelDimensions

- Defined in file_include_amici_model_dimensions.h

Inheritance Relationships

Derived Types

- `public amici::Model` (*Class Model*)
- `public amici::ReturnData` (*Class ReturnData*)

Struct Documentation

struct **ModelDimensions**

Container for model dimensions.

Holds number of states, observables, etc.

Subclassed by *amici::Model*, *amici::ReturnData*

Public Functions

ModelDimensions() = default

Default ctor

inline **ModelDimensions**(int const nx_rdata, int const nxtrue_rdata, int const nx_solver, int const nxtrue_solver, int const nx_solver_reinit, int const np, int const nk, int const ny, int const nytrue, int const nz, int const nztrue, int const ne, int const ne_solver, int const nspl, int const nJ, int const nw, int const ndwdx, int const ndwdp, int const ndwdw, int const ndxdotdw, std::vector<int> ndJydy, int const ndxrdatadxsolver, int const ndxrdatadtcl, int const ndtotal_cldx_rdata, int const nnz, int const ubw, int const lbw)

Constructor with model dimensions.

Parameters

- **nx_rdata** – Number of state variables
- **nxtrue_rdata** – Number of state variables of the non-augmented model
- **nx_solver** – Number of state variables with conservation laws applied
- **nxtrue_solver** – Number of state variables of the non-augmented model with conservation laws applied
- **nx_solver_reinit** – Number of state variables with conservation laws subject to reinitialization
- **np** – Number of parameters
- **nk** – Number of constants
- **ny** – Number of observables
- **nytrue** – Number of observables of the non-augmented model
- **nz** – Number of event observables
- **nztrue** – Number of event observables of the non-augmented model
- **ne** – Number of events
- **ne_solver** – Number of events that require root-finding
- **nspl** – Number of splines
- **nJ** – Number of objective functions
- **nw** – Number of repeating elements
- **ndwdx** – Number of nonzero elements in the `x` derivative of the repeating elements
- **ndwdp** – Number of nonzero elements in the `p` derivative of the repeating elements
- **ndwdw** – Number of nonzero elements in the `w` derivative of the repeating elements
- **ndxdotdw** – Number of nonzero elements in the w derivative of $xdot$
- **ndJydy** – Number of nonzero elements in the y derivative of dJy (shape `nytrue`)
- **ndxrdatadxsolver** – Number of nonzero elements in the x derivative of x_rdata
- **ndxrdatadtcl** – Number of nonzero elements in the tcl derivative of x_rdata
- **ndtotal_cldx_rdata** – Number of nonzero elements in the x_rdata derivative of $total_cl$
- **nnz** – Number of nonzero elements in Jacobian

- **ubw** – Upper matrix bandwidth in the Jacobian
- **lbw** – Lower matrix bandwidth in the Jacobian

Public Members

int **nx_rdata** = {0}

Number of states

int **nxtrue_rdata** = {0}

Number of states in the unaugmented system

int **nx_solver** = {0}

Number of states with conservation laws applied

int **nxtrue_solver** = {0}

Number of states in the unaugmented system with conservation laws applied

int **nx_solver_reinit** = {0}

Number of solver states subject to reinitialization

int **np** = {0}

Number of parameters

int **nk** = {0}

Number of constants

int **ny** = {0}

Number of observables

int **nytrue** = {0}

Number of observables in the unaugmented system

int **nz** = {0}

Number of event outputs

int **nztrue** = {0}

Number of event outputs in the unaugmented system

int **ne** = {0}

Number of events

int **ne_solver** = {0}

Number of events that require root-finding

int **nspl** = {0}

Number of spline functions in the model

int **nw** = {0}

Number of common expressions

int **ndwdx** = {0}

Number of nonzero elements in the x derivative of the repeating elements

int **ndwdp** = {0}

Number of nonzero elements in the p derivative of the repeating elements

int **ndwdw** = {0}

Number of nonzero elements in the w derivative of the repeating elements

int **ndxdotdw** = {0}

Number of nonzero elements in the w derivative of $xdot$

std::vector<int> **ndJydy**

Number of nonzero elements in the y derivative of dJy (dimension nytrue)

int **ndxrdatadxsolver** = {0}

Number of nonzero elements in the x derivative of x_rdata

int **ndxrdatadtcl** = {0}

Number of nonzero elements in the tcl derivative of x_rdata

int **ndtotal_cldx_rdata** = {0}

Number of nonzero elements in the x_rdata derivative of $total_cl$

int **nnz** = {0}

Number of nonzero entries in Jacobian

int **nJ** = {0}

Dimension of the augmented objective function for 2nd order ASA

int **ubw** = {0}

Upper bandwidth of the Jacobian

int **lbw** = {0}

Lower bandwidth of the Jacobian

Struct ModelState

- Defined in file_include_amici_model_state.h

Struct Documentation

struct **ModelState**

Exchange format to store and transfer the state of the model at a specific timepoint.

This is designed to only encompass the minimal number of attributes that need to be transferred.

Public Members

std::vector<*realtype*> **h**

Flag indicating whether a certain Heaviside function should be active or not (dimension: `ne`)

std::vector<*realtype*> **total_cl**

Total abundances for conservation laws (dimension: `nx_rdata - nx_solver`)

std::vector<*realtype*> **stotal_cl**

Sensitivities of total abundances for conservation laws (dimension: `(nx_rdata-nx_solver) x np`, row-major)

std::vector<*realtype*> **unscaledParameters**

Unscaled parameters (dimension: `np`)

std::vector<*realtype*> **fixedParameters**

Constants (dimension: `nk`)

std::vector<int> **plist**

Indexes of parameters wrt to which sensitivities are computed (dimension: nplist)

std::vector<*realtype*> **spl_**

temporary storage for spline values

Struct ModelStateDerived

- Defined in file_include_amici_model_state.h

Struct Documentation

struct **ModelStateDerived**

Storage for *amici::Model* quantities computed based on *amici::ModelState* for a specific timepoint.

Serves as workspace for a model simulation to avoid repeated reallocation.

Public Functions

ModelStateDerived() = default

explicit **ModelStateDerived**(*ModelDimensions* const &dim)

Constructor from model dimensions.

Parameters
dim – *Model* dimensions

Public Members

SUNMatrixWrapper **J_**

Sparse Jacobian (dimension: nx_solver x nx_solver, nnz: *amici::Model::nnz*)

SUNMatrixWrapper **JB_**

Sparse Backwards Jacobian (dimension: nx_solver x nx_solver, nnz:*amici::Model::nnz*)

SUNMatrixWrapper **dxdotdw_**

Sparse dxdotdw temporary storage (dimension: nx_solver x nw, nnz: ndxdotdw)

SUNMatrixWrapper **dwdx_**

Sparse dwdx temporary storage (dimension: nw x nx_solver, nnz:ndwdx)

SUNMatrixWrapper **dwdp_**

Sparse dwdp temporary storage (dimension: nw x np, nnz: ndwdp)

SUNMatrixWrapper **M_**

Dense Mass matrix (dimension: nx_solver x nx_solver)

SUNMatrixWrapper **MSparse_**

Sparse Mass matrix (dimension: nx_solver x nx_solver, nnz: sum(amici::Model::idlist))

SUNMatrixWrapper **dfdx_**

JSparse intermediate matrix (dimension: nx_solver x nx_solver, nnz: dynamic)

SUNMatrixWrapper **dxdotdp_full**

Temporary storage of dxdotdp_full data across functions (Python only) (dimension: nplist x nx_solver, nnz: dynamic, type CSC_MAT)

SUNMatrixWrapper **dxdotdp_explicit**

Temporary storage of dxdotdp_explicit data across functions (Python only) (dimension: nplist x nx_solver, nnz: ndxdotdp_explicit, type CSC_MAT)

SUNMatrixWrapper **dxdotdp_implicit**

Temporary storage of dxdotdp_implicit data across functions, Python-only (dimension: nplist x nx_solver, nnz: dynamic, type CSC_MAT)

SUNMatrixWrapper **dxdotdx_explicit**

Temporary storage of dxdotdx_explicit data across functions (Python only) (dimension: nplist x nx_solver, nnz: nxdotdotdx_explicit, type CSC_MAT)

SUNMatrixWrapper **dxdotdx_implicit**

Temporary storage of dxdotdx_implicit data across functions, Python-only (dimension: nplist x nx_solver, nnz: dynamic, type CSC_MAT)

SUNMatrixWrapper **dx_rdatadx_solver**

Temporary storage for dx_rdatadx_solver (dimension: nx_rdata x nx_solver, nnz: ndxrdatadxsolver, type: CSC_MAT)

SUNMatrixWrapper **dx_rdatadtcl**

Temporary storage for dx_rdatadtcl (dimension: nx_rdata x ncl, nnz: ndxrdatadtclr, type: CSC_MAT)

SUNMatrixWrapper **dtotal_cldx_rdata**

Temporary storage for dtotal_cldx_rdata (dimension: ncl x nx_rdata, nnz: ndtotal_cldx_rdata, type: CSC_MAT)

AmiVectorArray **dxdotdp** = {0, 0}

Temporary storage of dxdotdp data across functions, Matlab only (dimension: nplist x nx_solver , row-major)

std::vector<*SUNMatrixWrapper*> **dJydy_**

Sparse observable derivative of data likelihood, only used if pythonGenerated == true (dimension nytrue, nJ x ny, row-major)

std::vector<*realtype*> **dJydy_matlab_**

Observable derivative of data likelihood, only used if pythonGenerated == false (dimension nJ x ny x nytrue , row-major)

std::vector<*realtype*> **dJydsigma_**

Observable sigma derivative of data likelihood (dimension nJ x ny x nytrue, row-major)

std::vector<*realtype*> **dJydx_**

State derivative of data likelihood (dimension nJ x nx_solver, row-major)

std::vector<*realtype*> **dJydp_**

Parameter derivative of data likelihood for current timepoint (dimension: nJ x nplist, row-major)

std::vector<*realtype*> **dJzdz_**

event output derivative of event likelihood (dimension nJ x nz x nztrue, row-major)

std::vector<*realtype*> **dJzdsigma_**

event sigma derivative of event likelihood (dimension nJ x nz x nztrue, row-major)

std::vector<*realtype*> **dJrzdz_**

event output derivative of event likelihood at final timepoint (dimension nJ x nz x nztrue, row-major)

std::vector<*realtype*> **dJrzdsigma_**

event sigma derivative of event likelihood at final timepoint (dimension nJ x nz x nztrue, row-major)

std::vector<*realtype*> **dJzdx_**

state derivative of event likelihood (dimension `nJ` x `nx_solver`, row-major)

std::vector<*realtype*> **dJzdp_**

parameter derivative of event likelihood for current timepoint (dimension: nJ x nplist x, row-major)

std::vector<*realtype*> **dzdx_**

state derivative of event output (dimension: nz x `nx_solver`, row-major)

std::vector<*realtype*> **dzdp_**

parameter derivative of event output (dimension: nz x nplist, row-major)

std::vector<*realtype*> **drzdx_**

state derivative of event regularization variable (dimension: `nz` x `nx_solver`, row-major)

std::vector<*realtype*> **drzdp_**

parameter derivative of event regularization variable (dimension: nz x nplist, row-major)

std::vector<*realtype*> **dydp_**

parameter derivative of observable (dimension: ny x nplist, row-major)

std::vector<*realtype*> **dydx_**

state derivative of time-resolved observable (dimension: `nx_solver` x `ny`, row-major)

std::vector<*realtype*> **w_**

temporary storage of w data across functions (dimension: nw)

std::vector<*realtype*> **sx_**

temporary storage for flattened sx, (dimension: `nx_solver` x `nplist`, row-major)

std::vector<*realtype*> **sy_**

temporary storage for sy, (dimension: `ny` x `nplist`, row-major)

std::vector<*realtype*> **x_rdata_**

temporary storage for `x_rdata` (dimension: `nx_rdata`)

std::vector<*realtype*> **sx_rdata_**

temporary storage for `sx_rdata` slice (dimension: `nx_rdata`)

std::vector<*realtype*> **y_**

temporary storage for time-resolved observable (dimension: ny)

std::vector<*realtype*> **sigmay_**

data standard deviation for current timepoint (dimension: ny)

std::vector<*realtype*> **dsigmaydp_**

temporary storage for parameter derivative of data standard deviation, (dimension: ny x nplist, row-major)

std::vector<*realtype*> **dsigmaydy_**

temporary storage for observable derivative of data standard deviation, (dimension: ny x ny, row-major)

std::vector<*realtype*> **z_**

temporary storage for event-resolved observable (dimension: nz)

std::vector<*realtype*> **rz_**

temporary storage for event regularization (dimension: nz)

std::vector<*realtype*> **sigmaz_**

temporary storage for event standard deviation (dimension: nz)

std::vector<*realtype*> **dsigmazdp_**

temporary storage for parameter derivative of event standard deviation, (dimension: nz x nplist, row-major)

std::vector<*realtype*> **deltax_**

temporary storage for change in x after event (dimension: `nx_solver`)

std::vector<*realtype*> **deltasx_**

temporary storage for change in sx after event (dimension: `nx_solver` x `nplist`, row-major)

std::vector<*realtype*> **deltaxB_**

temporary storage for change in xB after event (dimension: `nx_solver`)

std::vector<*realtype*> **deltaqB_**

temporary storage for change in qB after event (dimension: nJ x nplist, row-major)

SUNMatrixWrapper **sspl_**

temporary storage for sensitivity values of splines

AmiVector **x_pos_tmp_** = {0}

temporary storage of positified state variables according to stateIsNonNegative (dimension: `nx_solver`)

Struct SimulationState

- Defined in file_include_amici_model_state.h

Struct Documentation

struct **SimulationState**

implements an exchange format to store and transfer the state of a simulation at a specific timepoint.

Public Members

realtype **t**

timepoint

AmiVector **x**

state variables

AmiVector **dx**

state variables

AmiVectorArray **sx**

state variable sensitivity

ModelState **state**

state of the model that was used for simulation

Class AbstractModel

- Defined in file_include_amici_abstract_model.h

Inheritance Relationships

Derived Type

- `public amici::Model` (*Class Model*)

Class Documentation

class **AbstractModel**

Abstract base class of *amici::Model* defining functions that need to be implemented in an AMICI model.

Some functions have empty default implementations or throw. This class shall not have any data members.

Subclassed by *amici::Model*

Public Functions

virtual **~AbstractModel**() = default

virtual std::unique_ptr<*Solver*> **getSolver**() = 0

Retrieves the solver object.

Returns
The *Solver* instance

virtual void **froot**(*realtype* const t, *AmiVector* const &x, *AmiVector* const &dx, gsl::span<*realtype*> root) = 0

Root function.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)
- **root** – array to which values of the root function will be written

virtual void **fxdot**(*realtype* const t, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* &xdot) = 0

Residual function.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xdot** – array to which values of the residual function will be written

virtual void **fsxdot**(*realtype* const t, *AmiVector* const &x, *AmiVector* const &dx, int ip, *AmiVector* const &sx, *AmiVector* const &sdx, *AmiVector* &sxdot) = 0

Sensitivity Residual function.

Parameters

- **t** – time

- **x** – state
- **dx** – time derivative of state (DAE only)
- **ip** – parameter index
- **sx** – sensitivity state
- **sdx** – time derivative of sensitivity state (DAE only)
- **sxdot** – array to which values of the sensitivity residual function will be written

virtual void **fxBdot_ss**(*realtype* const t, *AmiVector* const &xB, *AmiVector* const &dxB, *AmiVector* &xBdot) = 0

Residual function backward when running in steady state mode.

Parameters

- **t** – time
- **xB** – adjoint state
- **dxB** – time derivative of state (DAE only)
- **xBdot** – array to which values of the residual function will be written

virtual void **fJSparseB_ss**(SUNMatrix JB) = 0

Sparse Jacobian function backward, steady state case.

Parameters

JB – sparse matrix to which values of the Jacobian will be written

virtual void **writeSteadystateJB**(*realtype* const t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xB, *AmiVector* const &dxB, *AmiVector* const &xBdot) = 0

Computes the sparse backward Jacobian for steadystate integration and writes it to the model member.

Parameters

- **t** – timepoint
- **cj** – scalar in Jacobian
- **x** – Vector with the states
- **dx** – Vector with the derivative states
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **xBdot** – Vector with the adjoint state right hand side

virtual void **fJ**(*realtype* const t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xdot, SUNMatrix J) = 0

Dense Jacobian function.

Parameters

- **t** – time
- **cj** – scaling factor (inverse of timestep, DAE only)
- **x** – state
- **dx** – time derivative of state (DAE only)

- **xdot** – values of residual function (unused)
- **J** – dense matrix to which values of the jacobian will be written

virtual void **fJB**(*realtype* const t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xB, *AmiVector* const &dxB, *AmiVector* const &xBdot, SUNMatrix JB) = 0

Dense Jacobian function.

Parameters

- **t** – time
- **cj** – scaling factor (inverse of timestep, DAE only)
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **xBdot** – Vector with the adjoint right hand side (unused)
- **JB** – dense matrix to which values of the jacobian will be written

virtual void **fJSparse**(*realtype* const t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xdot, SUNMatrix J) = 0

Sparse Jacobian function.

Parameters

- **t** – time
- **cj** – scaling factor (inverse of timestep, DAE only)
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xdot** – values of residual function (unused)
- **J** – sparse matrix to which values of the Jacobian will be written

virtual void **fJSparseB**(*realtype* const t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xB, *AmiVector* const &dxB, *AmiVector* const &xBdot, SUNMatrix JB) = 0

Sparse Jacobian function.

Parameters

- **t** – time
- **cj** – scaling factor (inverse of timestep, DAE only)
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **xBdot** – Vector with the adjoint right hand side (unused)
- **JB** – dense matrix to which values of the jacobian will be written

virtual void **fJDiag**(*realtype* const t, *AmiVector* &Jdiag, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx) = 0

Diagonal Jacobian function.

Parameters

- **t** – time
- **Jdiag** – array to which the diagonal of the Jacobian will be written
- **cj** – scaling factor (inverse of timestep, DAE only)
- **x** – state
- **dx** – time derivative of state (DAE only)

virtual void **fdxdotdp**(*realtype* const t, *AmiVector* const &x, *AmiVector* const &dx) = 0

Model-specific sparse implementation of explicit parameter derivative of right hand side.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)

virtual void **fJv**(*realtype* const t, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xdot, *AmiVector* const &v, *AmiVector* &nJv, *realtype* cj) = 0

Jacobian multiply function.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xdot** – values of residual function (unused)
- **v** – multiplication vector (unused)
- **nJv** – array to which result of multiplication will be written
- **cj** – scaling factor (inverse of timestep, DAE only)

virtual std::string **getAmiciVersion**() const

Returns the AMICI version that was used to generate the model.

Returns
AMICI version string

virtual std::string **getAmiciCommit**() const

Returns the AMICI commit that was used to generate the model.

Returns
AMICI commit string

virtual void **fx0**(*realtype* *x0, *realtype* const t, *realtype* const *p, *realtype* const *k)

Model-specific implementation of fx0.

Parameters

- **x0** – initial state

- **t** – initial time
- **p** – parameter vector
- **k** – constant vector

virtual bool **isFixedParameterStateReinitializationAllowed**() const

Function indicating whether reinitialization of states depending on fixed parameters is permissible.

Returns
flag indicating whether reinitialization of states depending on fixed parameters is permissible

virtual void **fx0_fixedParameters**(*realtype* *x0, *realtype* const t, *realtype* const *p, *realtype* const *k, gsl::span<int const> reinitialization_state_idxs)

Model-specific implementation of fx0_fixedParameters.

Parameters

- **x0** – initial state
- **t** – initial time
- **p** – parameter vector
- **k** – constant vector
- **reinitialization_state_idxs** – Indices of states to be reinitialized based on provided constants / fixed parameters.

virtual void **fsx0_fixedParameters**(*realtype* *sx0, *realtype* const t, *realtype* const *x0, *realtype* const *p, *realtype* const *k, int ip, gsl::span<int const> reinitialization_state_idxs)

Model-specific implementation of fsx0_fixedParameters.

Parameters

- **sx0** – initial state sensitivities
- **t** – initial time
- **x0** – initial state
- **p** – parameter vector
- **k** – constant vector
- **ip** – sensitivity index
- **reinitialization_state_idxs** – Indices of states to be reinitialized based on provided constants / fixed parameters.

virtual void **fsx0**(*realtype* *sx0, *realtype* const t, *realtype* const *x0, *realtype* const *p, *realtype* const *k, int ip)

Model-specific implementation of fsx0.

Parameters

- **sx0** – initial state sensitivities
- **t** – initial time
- **x0** – initial state
- **p** – parameter vector
- **k** – constant vector

- **ip** – sensitivity index

virtual void **fdx0**(*AmiVector* &x0, *AmiVector* &dx0)

Initial value for time derivative of states (only necessary for DAEs)

Parameters

- **x0** – Vector with the initial states
- **dx0** – Vector to which the initial derivative states will be written (only DAE)

virtual void **fstau**(*realtype* *stau, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *tcl, *realtype* const *sx, int ip, int ie)

Model-specific implementation of fstau.

Parameters

- **stau** – total derivative of event timepoint
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **tcl** – total abundances for conservation laws
- **sx** – current state sensitivity
- **ip** – sensitivity index
- **ie** – event index

virtual void **fy**(*realtype* *y, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w)

Model-specific implementation of fy.

Parameters

- **y** – model output at current timepoint
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **w** – repeating elements vector

virtual void **fdydp**(*realtype* *dydp, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ip, *realtype* const *w, *realtype* const *dwdp)

Model-specific implementation of fdydp (MATLAB-only)

Parameters

- **dydp** – partial derivative of observables y w.r.t. model parameters p
- **t** – current time
- **x** – current state

- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **ip** – parameter index w.r.t. which the derivative is requested
- **w** – repeating elements vector
- **dwdp** – Recurring terms in xdot, parameter derivative

virtual void **fdydp**(*realtype* *dydp, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ip, *realtype* const *w, *realtype* const *tcl, *realtype* const *dtcldp, *realtype* const *spl, *realtype* const *sspl)

Model-specific implementation of fdydp (Python)

Parameters

- **dydp** – partial derivative of observables y w.r.t. model parameters p
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **ip** – parameter index w.r.t. which the derivative is requested
- **w** – repeating elements vector
- **tcl** – total abundances for conservation laws
- **dtcldp** – Sensitivities of total abundances for conservation laws
- **spl** – spline value vector
- **sspl** – sensitivities of spline values vector w.r.t. parameters p

virtual void **fdydx**(*realtype* *dydx, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w, *realtype* const *dwdx)

Model-specific implementation of fdydx.

Parameters

- **dydx** – partial derivative of observables y w.r.t. model states x
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **w** – repeating elements vector
- **dwdx** – Recurring terms in xdot, state derivative

virtual void **fz**(*realtype* *z, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h)

Model-specific implementation of fz.

Parameters

- **z** – value of event output
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector

virtual void **fsz**(*realtype* *sz, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *sx, int ip)

Model-specific implementation of fsz.

Parameters

- **sz** – Sensitivity of rz, total derivative
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **sx** – current state sensitivity
- **ip** – sensitivity index

virtual void **frz**(*realtype* *rz, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h)

Model-specific implementation of frz.

Parameters

- **rz** – value of root function at current timepoint (non-output events not included)
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector

virtual void **fsrz**(*realtype* *srz, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *sx, int ip)

Model-specific implementation of fsrz.

Parameters

- **srz** – Sensitivity of rz, total derivative
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **sx** – current state sensitivity
- **h** – Heaviside vector
- **ip** – sensitivity index

virtual void **fdzdp**(*realtype* *dzdp, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ip)

Model-specific implementation of fdzdp.

Parameters

- **dzdp** – partial derivative of event-resolved output z w.r.t. model parameters p
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **ip** – parameter index w.r.t. which the derivative is requested

virtual void **fdzdx**(*realtype* *dzdx, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h)

Model-specific implementation of fdzdx.

Parameters

- **dzdx** – partial derivative of event-resolved output z w.r.t. model states x
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector

virtual void **fdrzdp**(*realtype* *drzdp, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ip)

Model-specific implementation of fdrzdp.

Parameters

- **drzdp** – partial derivative of root output rz w.r.t. model parameters p
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **ip** – parameter index w.r.t. which the derivative is requested

virtual void **fdrzdx**(*realtype* *drzdx, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h)

Model-specific implementation of fdrzdx.

Parameters

- **drzdx** – partial derivative of root output rz w.r.t. model states x
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector

virtual void **fdeltax**(*realtype* *deltax, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ie, *realtype* const *xdot, *realtype* const *xdot_old)

Model-specific implementation of fdeltax.

Parameters

- **deltax** – state update
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **ie** – event index
- **xdot** – new model right hand side
- **xdot_old** – previous model right hand side

virtual void **fdeltasx**(*realtype* *deltasx, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w, int ip, int ie, *realtype* const *xdot, *realtype* const *xdot_old, *realtype* const *sx, *realtype* const *stau, *realtype* const *tcl)

Model-specific implementation of fdeltasx.

Parameters

- **deltasx** – sensitivity update
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **w** – repeating elements vector
- **ip** – sensitivity index
- **ie** – event index
- **xdot** – new model right hand side
- **xdot_old** – previous model right hand side
- **sx** – state sensitivity
- **stau** – event-time sensitivity
- **tcl** – total abundances for conservation laws

virtual void **fdeltaxB**(*realtype* *deltaxB, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ie, *realtype* const *xdot, *realtype* const *xdot_old, *realtype* const *xB)

Model-specific implementation of fdeltaxB.

Parameters

- **deltaxB** – adjoint state update
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **ie** – event index
- **xdot** – new model right hand side
- **xdot_old** – previous model right hand side
- **xB** – current adjoint state

virtual void **fdeltaqB**(*realtype* *deltaqB, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ip, int ie, *realtype* const *xdot, *realtype* const *xdot_old, *realtype* const *xB)

Model-specific implementation of fdeltaqB.

Parameters

- **deltaqB** – sensitivity update
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **ip** – sensitivity index
- **ie** – event index
- **xdot** – new model right hand side
- **xdot_old** – previous model right hand side
- **xB** – adjoint state

virtual void **fsigmay**(*realtype* *sigmay, *realtype* const t, *realtype* const *p, *realtype* const *k, *realtype* const *y)

Model-specific implementation of fsigmay.

Parameters

- **sigmay** – standard deviation of measurements
- **t** – current time
- **p** – parameter vector
- **k** – constant vector
- **y** – model output at timepoint t

virtual void **fdsigmaydp**(*realtype* *dsigmaydp, *realtype* const t, *realtype* const *p, *realtype* const *k, *realtype* const *y, int ip)

Model-specific implementation of fdsigmaydp.

Parameters

- **dsigmaydp** – partial derivative of standard deviation of measurements
- **t** – current time
- **p** – parameter vector
- **k** – constant vector
- **y** – model output at timepoint t
- **ip** – sensitivity index

virtual void **fdsigmaydy**(*realtype* *dsigmaydy, *realtype* const t, *realtype* const *p, *realtype* const *k, *realtype* const *y)

Model-specific implementation of fsigmay.

Parameters

- **dsigmaydy** – partial derivative of standard deviation of measurements w.r.t. model outputs
- **t** – current time

- **p** – parameter vector
- **k** – constant vector
- **y** – model output at timepoint t

virtual void **fsigmaz**(*realtype* *sigmaz, *realtype* const t, *realtype* const *p, *realtype* const *k)

Model-specific implementation of fsigmaz.

Parameters

- **sigmaz** – standard deviation of event measurements
- **t** – current time
- **p** – parameter vector
- **k** – constant vector

virtual void **fdsigmazdp**(*realtype* *dsigmazdp, *realtype* const t, *realtype* const *p, *realtype* const *k, int ip)

Model-specific implementation of fsigmaz.

Parameters

- **dsigmazdp** – partial derivative of standard deviation of event measurements
- **t** – current time
- **p** – parameter vector
- **k** – constant vector
- **ip** – sensitivity index

virtual void **fJy**(*realtype* *nllh, int iy, *realtype* const *p, *realtype* const *k, *realtype* const *y, *realtype* const *sigmay, *realtype* const *my)

Model-specific implementation of fJy.

Parameters

- **nllh** – negative log-likelihood for measurements y
- **iy** – output index
- **p** – parameter vector
- **k** – constant vector
- **y** – model output at timepoint
- **sigmay** – measurement standard deviation at timepoint
- **my** – measurements at timepoint

virtual void **fJz**(*realtype* *nllh, int iz, *realtype* const *p, *realtype* const *k, *realtype* const *z, *realtype* const *sigmaz, *realtype* const *mz)

Model-specific implementation of fJz.

Parameters

- **nllh** – negative log-likelihood for event measurements z
- **iz** – event output index
- **p** – parameter vector
- **k** – constant vector

- **z** – model event output at timepoint
- **sigmaz** – event measurement standard deviation at timepoint
- **mz** – event measurements at timepoint

virtual void **fJrz**(*realtype* *nllh, int iz, *realtype* const *p, *realtype* const *k, *realtype* const *z, *realtype* const *sigmaz)

Model-specific implementation of fJrz.

Parameters

- **nllh** – regularization for event measurements z
- **iz** – event output index
- **p** – parameter vector
- **k** – constant vector
- **z** – model event output at timepoint
- **sigmaz** – event measurement standard deviation at timepoint

virtual void **fdJydy**(*realtype* *dJydy, int iy, *realtype* const *p, *realtype* const *k, *realtype* const *y, *realtype* const *sigmay, *realtype* const *my)

Model-specific implementation of fdJydy.

Parameters

- **dJydy** – partial derivative of time-resolved measurement negative log-likelihood Jy
- **iy** – output index
- **p** – parameter vector
- **k** – constant vector
- **y** – model output at timepoint
- **sigmay** – measurement standard deviation at timepoint
- **my** – measurement at timepoint

virtual void **fdJydy_colptrs**(*SUNMatrixWrapper* &dJydy, int index)

Model-specific implementation of fdJydy colptrs.

Parameters

- **dJydy** – sparse matrix to which colptrs will be written
- **index** – ytrue index

virtual void **fdJydy_rowvals**(*SUNMatrixWrapper* &dJydy, int index)

Model-specific implementation of fdJydy rowvals.

Parameters

- **dJydy** – sparse matrix to which rowvals will be written
- **index** – `ytrue` index

virtual void **fdJydsigma**(*realtype* *dJydsigma, int iy, *realtype* const *p, *realtype* const *k, *realtype* const *y, *realtype* const *sigmay, *realtype* const *my)

Model-specific implementation of fdJydsigma.

Parameters

- **dJydsigma** – Sensitivity of time-resolved measurement negative log-likelihood Jy w.r.t. standard deviation sigmay
- **iy** – output index
- **p** – parameter vector
- **k** – constant vector
- **y** – model output at timepoint
- **sigmay** – measurement standard deviation at timepoint
- **my** – measurement at timepoint

virtual void **fdJzdz**(*realtype* *dJzdz, int iz, *realtype* const *p, *realtype* const *k, *realtype* const *z, *realtype* const *sigmaz, *realtype* const *mz)

Model-specific implementation of fdJzdz.

Parameters

- **dJzdz** – partial derivative of event measurement negative log-likelihood Jz
- **iz** – event output index
- **p** – parameter vector
- **k** – constant vector
- **z** – model event output at timepoint
- **sigmaz** – event measurement standard deviation at timepoint
- **mz** – event measurement at timepoint

virtual void **fdJzdsigma**(*realtype* *dJzdsigma, int iz, *realtype* const *p, *realtype* const *k, *realtype* const *z, *realtype* const *sigmaz, *realtype* const *mz)

Model-specific implementation of fdJzdsigma.

Parameters

- **dJzdsigma** – Sensitivity of event measurement negative log-likelihood Jz w.r.t. standard deviation sigmaz
- **iz** – event output index
- **p** – parameter vector
- **k** – constant vector
- **z** – model event output at timepoint
- **sigmaz** – event measurement standard deviation at timepoint
- **mz** – event measurement at timepoint

virtual void **fdJrzdz**(*realtype* *dJrzdz, int iz, *realtype* const *p, *realtype* const *k, *realtype* const *rz, *realtype* const *sigmaz)

Model-specific implementation of fdJrzdz.

Parameters

- **dJrzdz** – partial derivative of event penalization Jrz
- **iz** – event output index
- **p** – parameter vector

- **k** – constant vector
- **rz** – model root output at timepoint
- **sigmaz** – event measurement standard deviation at timepoint

virtual void **fdJrzdsigma**(*realtype* *dJrzdsigma, int iz, *realtype* const *p, *realtype* const *k, *realtype* const *rz, *realtype* const *sigmaz)

Model-specific implementation of fdJrzdsigma.

Parameters

- **dJrzdsigma** – Sensitivity of event penalization Jrz w.r.t. standard deviation sigmaz
- **iz** – event output index
- **p** – parameter vector
- **k** – constant vector
- **rz** – model root output at timepoint
- **sigmaz** – event measurement standard deviation at timepoint

virtual void **fw**(*realtype* *w, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *tcl, *realtype* const *spl, bool include_static = true)

Model-specific implementation of fw.

Parameters

- **w** – Recurring terms in xdot
- **t** – timepoint
- **x** – vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **tcl** – total abundances for conservation laws
- **spl** – spline value vector
- **include_static** – Whether to (re-)evaluate only dynamic expressions (false) or also static expressions (true). Dynamic expressions are those that depend directly or indirectly on time, static expressions are those that don't.

virtual void **fdwdp**(*realtype* *dwdp, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w, *realtype* const *tcl, *realtype* const *stcl, *realtype* const *spl, *realtype* const *sspl, bool include_static = true)

Model-specific sparse implementation of dwdp.

Parameters

- **dwdp** – Recurring terms in xdot, parameter derivative
- **t** – timepoint
- **x** – vector with the states
- **p** – parameter vector
- **k** – constants vector

- **h** – Heaviside vector
- **w** – vector with helper variables
- **tcl** – total abundances for conservation laws
- **stcl** – sensitivities of total abundances for conservation laws
- **spl** – spline value vector
- **sspl** – sensitivities of spline values vector w.r.t. parameters p
- **include_static** – Whether to (re-)evaluate only dynamic expressions (false) or also static expressions (true). Dynamic expressions are those that depend directly or indirectly on time, static expressions are those that don't.

virtual void **fdwdp_colptrs**(*SUNMatrixWrapper* &dwdp)

Model-specific implementation for dwdp, column pointers.

Parameters

dwdp – sparse matrix to which colptrs will be written

virtual void **fdwdp_rowvals**(*SUNMatrixWrapper* &dwdp)

Model-specific implementation for dwdp, row values.

Parameters

dwdp – sparse matrix to which rowvals will be written

virtual void **fdwdx**(*realtype* *dwdx, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w, *realtype* const *tcl, *realtype* const *spl, bool include_static = true)

Model-specific implementation of dwdx, data part.

Parameters

- **dwdx** – Recurring terms in xdot, state derivative
- **t** – timepoint
- **x** – vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **w** – vector with helper variables
- **tcl** – total abundances for conservation laws
- **spl** – spline value vector
- **include_static** – Whether to (re-)evaluate only dynamic expressions (false) or also static expressions (true). Dynamic expressions are those that depend directly or indirectly on time, static expressions are those that don't.

virtual void **fdwdx_colptrs**(*SUNMatrixWrapper* &dwdx)

Model-specific implementation for dwdx, column pointers.

Parameters

dwdx – sparse matrix to which colptrs will be written

virtual void **fdwdx_rowvals**(*SUNMatrixWrapper* &dwdx)

Model-specific implementation for dwdx, row values.

Parameters
dwdx – sparse matrix to which rowvals will be written

virtual void **fdwdw**(*realtype* *dwdw, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w, *realtype* const *tcl, bool include_static = true)

Model-specific implementation of fdwdw, no w chainrule (Py)

Parameters

- **dwdw** – partial derivative w wrt w
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **w** – vector with helper variables
- **tcl** – Total abundances for conservation laws
- **include_static** – Whether to (re-)evaluate only dynamic expressions (false) or also static expressions (true). Dynamic expressions are those that depend directly or indirectly on time, static expressions are those that don't.

virtual void **fdwdw_colptrs**(*SUNMatrixWrapper* &dwdw)

Model-specific implementation of fdwdw, colptrs part.

Parameters
dwdw – sparse matrix to which colptrs will be written

virtual void **fdwdw_rowvals**(*SUNMatrixWrapper* &dwdw)

Model-specific implementation of fdwdw, rowvals part.

Parameters
dwdw – sparse matrix to which rowvals will be written

virtual void **fdx_rdatadx_solver**(*realtype* *dx_rdatadx_solver, *realtype* const *x, *realtype* const *tcl, *realtype* const *p, *realtype* const *k)

Compute dx_rdata / dx_solver.

Parameters

- **dx_rdatadx_solver** – dx_rdata / dx_solver
- **p** – parameter vector
- **k** – constant vector
- **x** – State variables with conservation laws applied
- **tcl** – Total abundances for conservation laws

virtual void **fdx_rdatadx_solver_colptrs**(*SUNMatrixWrapper* &dxrdatadxsolver)

Model-specific implementation of fdx_rdatadx_solver, colptrs part.

Parameters
dxrdatadxsolver – sparse matrix to which colptrs will be written

virtual void **fdx_rdatadx_solver_rowvals**(*SUNMatrixWrapper* &dxrdatadxsolver)

Model-specific implementation of fdx_rdatadx_solver, rowvals part.

Parameters

dxrdatadxsolver – sparse matrix to which rowvals will be written

virtual void **fdx_rdatadp**(*realtype* *dx_rdatadp, *realtype* const *x, *realtype* const *tcl, *realtype* const *p, *realtype* const *k, int const ip)

Compute dx_rdata / dp.

Parameters

- **dx_rdatadp** – dx_rdata / dp
- **p** – parameter vector
- **k** – constant vector
- **x** – State variables with conservation laws applied
- **tcl** – Total abundances for conservation laws
- **ip** – Sensitivity index

virtual void **fdx_rdatadtcl**(*realtype* *dx_rdatadtcl, *realtype* const *x, *realtype* const *tcl, *realtype* const *p, *realtype* const *k)

Compute dx_rdata / dtcl.

Parameters

- **dx_rdatadtcl** – dx_rdata / dtcl
- **p** – parameter vector
- **k** – constant vector
- **x** – State variables with conservation laws applied
- **tcl** – Total abundances for conservation laws

virtual void **fdx_rdatadtcl_colptrs**(*SUNMatrixWrapper* &dx_rdatadtcl)

Model-specific implementation of fdx_rdatadtcl, colptrs part.

Parameters

dx_rdatadtcl – sparse matrix to which colptrs will be written

virtual void **fdx_rdatadtcl_rowvals**(*SUNMatrixWrapper* &dx_rdatadtcl)

Model-specific implementation of fdx_rdatadtcl, rowvals part.

Parameters

dx_rdatadtcl – sparse matrix to which rowvals will be written

virtual void **fdtotal_cldp**(*realtype* *dtotal_cldp, *realtype* const *x_rdata, *realtype* const *p, *realtype* const *k, int const ip)

Compute dtotal_cl / dp.

Parameters

- **dtotal_cldp** – dtotal_cl / dp
- **x_rdata** – State variables with conservation laws applied
- **p** – parameter vector
- **k** – constant vector

- **ip** – Sensitivity index

virtual void **fdtotal_cldx_rdata**(*realtype* *dtotal_cldx_rdata, *realtype* const *x_rdata, *realtype* const *p, *realtype* const *k, *realtype* const *tcl)

Compute dtotal_cl / dx_rdata.

Parameters

- **dtotal_cldx_rdata** – dtotal_cl / dx_rdata
- **x_rdata** – State variables with conservation laws applied
- **p** – parameter vector
- **k** – constant vector
- **tcl** – Total abundances for conservation laws

virtual void **fdtotal_cldx_rdata_colptrs**(*SUNMatrixWrapper* &dtotal_cldx_rdata)

Model-specific implementation of fdtotal_cldx_rdata, colptrs part.

Parameters
dtotal_cldx_rdata – sparse matrix to which colptrs will be written

virtual void **fdtotal_cldx_rdata_rowvals**(*SUNMatrixWrapper* &dtotal_cldx_rdata)

Model-specific implementation of fdtotal_cldx_rdata, rowvals part.

Parameters
dtotal_cldx_rdata – sparse matrix to which rowvals will be written

virtual std::vector<*HermiteSpline*> **fcreate_splines**(*realtype* const *p, *realtype* const *k)

Model-specific implementation of spline creation.

Parameters

- **p** – parameter vector
- **k** – constants vector

Returns
Vector of splines used in the model

virtual void **fdspline_valuesdp**(*realtype* *dspline_valuesdp, *realtype* const *p, *realtype* const *k, int const ip)

Model-specific implementation the parametric derivatives of spline node values.

Parameters

- **dspline_valuesdp** – vector to which derivatives will be written
- **p** – parameter vector
- **k** – constants vector
- **ip** – Sensitivity index

virtual void **fdspline_slopesdp**(*realtype* *dspline_slopesdp, *realtype* const *p, *realtype* const *k, int const ip)

Model-specific implementation the parametric derivatives of slopevalues at spline nodes.

Parameters

- **dspline_slopesdp** – vector to which derivatives will be written
- **p** – parameter vector

- **k** – constants vector
- **ip** – Sensitivity index

Class AbstractSpline

- Defined in file_include_amici_splinefunctions.h

Inheritance Relationships

Derived Type

- `public amici::HermiteSpline` (*Class HermiteSpline*)

Class Documentation

class **AbstractSpline**

AMICI spline base class.

Instances of this class are created upon solver setup and the needed splines are set up (e.g., interpolation of the nodes is performed). Upon call to a spline function, only the evaluation of the spline polynomial is carried out.

Subclassed by *amici::HermiteSpline*

Public Functions

AbstractSpline() = default

default constructor

AbstractSpline(std::vector<*realtype*> nodes, std::vector<*realtype*> node_values, bool equidistant_spacing, bool logarithmic_parametrization)

Common constructor for *AbstractSpline* instances.

Parameters

- **nodes** – the nodes defining the position at which the value of the spline is known (if `equidistant_spacing` is true, it must contain only the first and the last node; the other nodes will be automatically inserted, assuming they are uniformly spaced)
- **node_values** – the values assumed by the spline at the nodes
- **equidistant_spacing** – whether equidistant nodes are to be computed
- **logarithmic_parametrization** – if true, the spline interpolation will occur in log-space in order to ensure positivity of the interpolant (which strictly speaking will no longer be a spline)

virtual **~AbstractSpline**() = default

virtual void **compute_coefficients**() = 0

Compute the coefficients for all polynomial segments of this spline.

virtual void **compute_coefficients_sensi**(int nplist, int spline_offset, gsl::span<*realtype*> dvaluesdp, gsl::span<*realtype*> dslopesdp) = 0

Compute the coefficients for all polynomial segments of the derivatives of this spline with respect to the parameters.

Remark

The contents of `dvaluesdp` and `dslopesdp` may be modified by this function.

Parameters

- **nplist** – number of parameters
- **spline_offset** – offset of this spline inside `dvaluesdp` and `dslopesdp`
- **dvaluesdp** – derivatives of the spline values with respect to the parameters (for all splines in the model, not just this one)
- **dslopesdp** – derivatives of the spline derivatives with respect to the parameters (for all splines in the model, not just this one)

realtype **get_value**(*realtype* const t) const

Get the value of this spline at a given point.

Parameters
t – point at which the spline is to be evaluated

Returns
value of the spline at `t`

virtual *realtype* **get_value_scaled**(*realtype* const t) const = 0

Get the value of this spline at a given point in the scale in which interpolation is carried out (e.g., log-scale)

Parameters
t – point at which the spline is to be evaluated

Returns
scaled value of the spline at `t`

realtype **get_node_value**(int const i) const

Get the value of this spline at a given node.

Parameters
i – index of the node at which the spline is to be evaluated

Returns
value of the spline at the `i`-th node

realtype **get_node_value_scaled**(int const i) const

Get the value of this spline at a given node in the scale in which interpolation is carried out (e.g., log-scale)

Parameters
i – index of the node at which the spline is to be evaluated

Returns
scaled value of the spline at the `i`-th node

realtype **get_sensitivity**(*realtype* const t, int const ip) const

Get the derivative of this spline with respect to a given parameter at a given point.

Parameters

- **t** – point at which the sensitivity is to be evaluated
- **ip** – index of the parameter

Returns

sensitivity of the spline with respect to the ipth parameter at t

realtype **get_sensitivity**(*realtype* const t, int const ip, *realtype* const value) const

Get the derivative of this spline with respect to a given parameter at a given point.

Parameters

- **t** – point at which the sensitivity is to be evaluated
- **ip** – index of the parameter
- **value** – value of the spline at the given time point. It is used e.g. when interpolation is carried out in log-space. If omitted it will be computed.

Returns

sensitivity of the spline with respect to the ipth parameter at t

virtual *realtype* **get_sensitivity_scaled**(*realtype* const t, int const ip) const = 0

Get the derivative of this spline with respect to a given parameter at a given point in the scale in which interpolation is carried out (e.g., log-scale)

Parameters

- **t** – point at which the sensitivity is to be evaluated
- **ip** – index of the parameter

Returns

scaled sensitivity of the spline with respect to the ipth parameter at t

virtual void **compute_final_value**() = 0

Compute the limit value of the spline as the evaluation point tends to positive infinity.

virtual void **compute_final_sensitivity**(int nplist, int spline_offset, gsl::span<*realtype*> dspline_valuesdp, gsl::span<*realtype*> dspline_slopesdp) = 0

Compute the limit of the value of the sensitivity as the evaluation point tends to positive infinity.

Parameters

- **nplist** – number of parameters
- **spline_offset** – offset of this spline inside dspline_valuesdp and dspline_slopesdp
- **dspline_valuesdp** – derivatives of the spline values with respect to the parameters (for all splines in the model, not just this one)
- **dspline_slopesdp** – derivatives of the spline derivatives with respect to the parameters (for all splines in the model, not just this one)

realtype **get_final_value**() const

Get the limit value of the spline as the evaluation point tends to positive infinity.

Returns

limit value

realtype **get_final_value_scaled**() const

Get the limit value of the spline (in the scale in which interpolation is carried out) as the evaluation point tends to positive infinity.

Returns
limit value

realtype **get_final_sensitivity**(int const ip) const

Get the limit value of the sensitivity with respect to the given parameter as the evaluation point tends to positive infinity.

Parameters
ip – parameter index

Returns
limit value

realtype **get_final_sensitivity_scaled**(int const ip) const

Get the limit value of the sensitivity with respect to the given parameter (in the scale in which interpolation is carried out) as the evaluation point tends to positive infinity.

Parameters
ip – parameter index

Returns
limit value

bool **get_equidistant_spacing**() const

Whether nodes are uniformly spaced.

Returns
boolean flag

bool **get_logarithmic_parametrization**() const

Whether spline interpolation is carried out in log-space.

Returns
boolean flag

inline int **n_nodes**() const

The number of interpolation nodes for this spline.

Returns
number of nodes

Protected Functions

void **set_final_value_scaled**(*realtype* finalValue)

Set the limit value of the spline (in the scale in which interpolation is carried out) as the evaluation point tends to positive infinity.

Parameters
finalValue – final value

void **set_final_sensitivity_scaled**(std::vector<*realtype*> finalSensitivity)

Set the limit value of the sensitivity (in the scale in which interpolation is carried out) as the evaluation point tends to positive infinity.

Parameters
finalSensitivity – final value of the sensitivity for each parameter

Protected Attributes

std::vector<*realtype*> **nodes_**

The nodes at which this spline is interpolated.

std::vector<*realtype*> **node_values_**

The values the spline assumes at the nodes.

std::vector<*realtype*> **coefficients**

Coefficients for each polynomial segment of the spline.

std::vector<*realtype*> **coefficients_extrapolate**

Polynomial coefficients for the extrapolating the spline values.

std::vector<*realtype*> **coefficients_sensi**

Coefficients for each polynomial segment of the sensitivities with respect to the parameters.

std::vector<*realtype*> **coefficients_extrapolate_sensi**

Polynomial coefficients for the extrapolating the sensitivities.

Class AmiException

- Defined in file_include_amici_exception.h

Inheritance Relationships

Base Type

- `public std::exception`

Derived Types

- `public amici::CvodeException` (*Class CvodeException*)
- `public amici::IDAException` (*Class IDAException*)
- `public amici::IntegrationFailure` (*Class IntegrationFailure*)
- `public amici::IntegrationFailureB` (*Class IntegrationFailureB*)
- `public amici::NewtonFailure` (*Class NewtonFailure*)
- `public amici::SetupFailure` (*Class SetupFailure*)

Class Documentation

class **AmiException** : public std::exception

AMICI exception class.

Has a printf style interface to allow easy generation of error messages

Subclassed by *amici::CvodeException*, *amici::IDAException*, *amici::IntegrationFailure*, *amici::IntegrationFailureB*, *amici::NewtonFailure*, *amici::SetupFailure*

Public Functions

AmiException(int const first_frame = 3)

Default ctor.

Parameters
first_frame – Index of first frame to include

explicit **AmiException**(char const *fmt, ...)

Constructor with printf style interface.

Parameters

- **fmt** – error message with printf format
- **...** – printf formatting variables

char const ***what**() const noexcept override

Override of default error message function.

Returns
msg error message

char const ***getBacktrace**() const

Returns the stored backtrace.

Returns
trace backtrace

void **storeBacktrace**(int nMaxFrames, int const first_frame)

Stores the current backtrace.

Parameters

- **nMaxFrames** – number of frames to go back in stacktrace
- **first_frame** – Index of first frame to include

Protected Functions

void **storeMessage**(char const *fmt, va_list argptr)

Store the provided message.

Parameters

- **fmt** – error message with printf format
- **argptr** – pointer to variadic argument list

Class AmiVector

- Defined in file_include_amici_vector.h

Class Documentation

class **AmiVector**

AmiVector class provides a generic interface to the NVector_Serial struct

Public Functions

AmiVector() = default

Default constructor.

inline explicit **AmiVector**(long int const length)

empty constructor

Creates an std::vector<realtype> and attaches the data pointer to a newly created N_Vector_Serial. Using N_VMake_Serial ensures that the N_Vector module does not try to deallocate the data vector when calling N_VDestroy_Serial

Parameters
length – number of elements in vector

inline explicit **AmiVector**(std::vector<*realtype*> rvec)

constructor from std::vector,

Moves data from std::vector and constructs an nvec that points to the data

Parameters
rvec – vector from which the data will be moved

inline explicit **AmiVector**(gsl::span<*realtype* const> rvec)

constructor from gsl::span,

Copy data from gsl::span and constructs a vector

Parameters
rvec – vector from which the data will be copied

inline **AmiVector**(*AmiVector* const &vold)

copy constructor

Parameters
vold – vector from which the data will be copied

inline **AmiVector**(*AmiVector* &&other) noexcept

move constructor

Parameters
other – vector from which the data will be moved

~AmiVector()

destructor

AmiVector &**operator=**(*AmiVector* const &other)

copy assignment operator

Parameters
other – right hand side

Returns
left hand side

inline *AmiVector* &**operator*=**(*AmiVector* const &multiplier)

operator *= (element-wise multiplication)

Parameters
multiplier – multiplier

Returns
result

inline *AmiVector* &**operator/=**(*AmiVector* const &divisor)

operator /= (element-wise division)

Parameters
divisor – divisor

Returns
result

inline auto **begin**()

Returns an iterator that points to the first element of the vector.

Returns
iterator that points to the first element

inline auto **end**()

Returns an iterator that points to one element after the last element of the vector.

Returns
iterator that points to one element after the last element

realtype ***data**()

data accessor

Returns
pointer to data array

realtype const ***data**() const

const data accessor

Returns
const pointer to data array

N_Vector **getNVector**()

N_Vector accessor.

Returns
N_Vector

const_N_Vector **getNVector**() const

N_Vector accessor.

Returns
N_Vector

std::vector<*realtype*> const &**getVector**() const

Vector accessor.

Returns
Vector

int **getLength**() const

returns the length of the vector

Returns
length

void **zero**()

fills vector with zero values

void **minus**()

changes the sign of data elements

void **set**(*realtype* val)

sets all data elements to a specific value

Parameters
val – value for data elements

realtype &**operator[]**(int pos)

accessor to data elements of the vector

Parameters
pos – index of element

Returns
element

realtype &**at**(int pos)

accessor to data elements of the vector

Parameters
pos – index of element

Returns
element

realtype const &**at**(int pos) const

accessor to data elements of the vector

Parameters
pos – index of element

Returns
element

void **copy**(*AmiVector* const &other)

copies data from another *AmiVector*

Parameters
other – data source

inline void **abs**()

Take absolute value (in-place)

Friends

template<class **Archive**>
friend void **serialize**(*Archive* &ar, *AmiVector* &s, unsigned int version)

Serialize *AmiVector* (see boost::serialization::serialize)

Parameters

- **ar** – Archive to serialize to
- **s** – Data to serialize
- **version** – Version number

Class AmiVectorArray

- Defined in file_include_amici_vector.h

Class Documentation

class **AmiVectorArray**

AmiVectorArray class.

Provides a generic interface to arrays of NVector_Serial structs

Public Functions

AmiVectorArray() = default

Default constructor.

AmiVectorArray(long int length_inner, long int length_outer)

empty constructor

Creates an std::vector<realype> and attaches the data pointer to a newly created N_VectorArray using CloneVectorArrayEmpty ensures that the N_Vector module does not try to deallocate the data vector when calling N_VDestroyVectorArray_Serial

Parameters

- **length_inner** – length of vectors
- **length_outer** – number of vectors

AmiVectorArray(*AmiVectorArray* const &vaold)

copy constructor

Parameters
vaold – object to copy from

~AmiVectorArray() = default

AmiVectorArray &**operator=**(*AmiVectorArray* const &other)

copy assignment operator

Parameters
other – right hand side

Returns
left hand side

realtype ***data**(int pos)

accessor to data of *AmiVector* elements

Parameters
pos – index of *AmiVector*

Returns
pointer to data array

realtype const ***data**(int pos) const

const accessor to data of *AmiVector* elements

Parameters
pos – index of *AmiVector*

Returns
const pointer to data array

realtype &**at**(int ipos, int jpos)

accessor to elements of *AmiVector* elements

Parameters

- **ipos** – inner index in *AmiVector*
- **jpos** – outer index in *AmiVectorArray*

Returns
element

realtype const &**at**(int ipos, int jpos) const

const accessor to elements of *AmiVector* elements

Parameters

- **ipos** – inner index in *AmiVector*
- **jpos** – outer index in *AmiVectorArray*

Returns
element

N_Vector ***getNVectorArray**()

accessor to NVectorArray

Returns
N_VectorArray

N_Vector **getNVector**(int pos)

accessor to NVector element

Parameters
pos – index of corresponding *AmiVector*

Returns
N_Vector

const_N_Vector **getNVector**(int pos) const

const accessor to NVector element

Parameters
pos – index of corresponding *AmiVector*

Returns
N_Vector

AmiVector &**operator[]**(int pos)

accessor to *AmiVector* elements

Parameters
pos – index of *AmiVector*

Returns
AmiVector

AmiVector const &**operator[]**(int pos) const

const accessor to *AmiVector* elements

Parameters
pos – index of *AmiVector*

Returns
const *AmiVector*

int **getLength**() const

length of *AmiVectorArray*

Returns
length

void **zero**()

set every *AmiVector* in *AmiVectorArray* to zero

void **flatten_to_vector**(std::vector<*realtype*> &vec) const

flattens the *AmiVectorArray* to a vector in row-major format

Parameters
vec – vector into which the *AmiVectorArray* will be flattened. Must have length equal to number of elements.

void **copy**(*AmiVectorArray* const &other)

copies data from another *AmiVectorArray*

Parameters
other – data source

Class BackwardProblem

- Defined in file_include_amici_backwardproblem.h

Class Documentation

class **BackwardProblem**

class to solve backwards problems.

solves the backwards problem for adjoint sensitivity analysis and handles events and data-points

Public Functions

explicit **BackwardProblem**(*ForwardProblem* const &fwd, *SteadystateProblem* const *posteq)

Construct backward problem from forward problem.

Parameters

- **fwd** – pointer to corresponding forward problem
- **posteq** – pointer to postequilibration problem, can be nullptr

void **workBackwardProblem**()

Solve the backward problem.

If adjoint sensitivities are enabled this will also compute sensitivities. workForwardProblem must be called before this is function is called.

inline *realtype* **gett**() const

Accessor for current time t.

Returns
t

inline int **getwhich**() const

Accessor for which.

Returns
which

inline int ***getwhichptr**()

Accessor for pointer to which.

Returns
which

inline std::vector<*realtype*> const &**getdJydx**() const

Accessor for dJydx.

Returns
dJydx

inline *AmiVector* const &**getAdjointState**() const

Accessor for xB.

Returns
xB

inline *AmiVector* const &**getAdjointQuadrature**() const

Accessor for xQB.

Returns
xQB

Class ConditionContext

- Defined in file_include_amici_edata.h

Inheritance Relationships

Base Type

- `public amici::ContextManager` (*Class ContextManager*)

Class Documentation

class **ConditionContext** : public amici::*ContextManager*

The *ConditionContext* class applies condition-specific *amici::Model* settings and restores them when going out of scope.

Public Functions

explicit **ConditionContext**(*Model* *model, *ExpData* const *edata = nullptr, *FixedParameterContext* fpc = *FixedParameterContext*::*simulation*)

Apply condition-specific settings from edata to model while keeping a backup of the original values.

Parameters

- **model** –
- **edata** –
- **fpc** – flag indicating which fixedParameter from edata to apply

ConditionContext &**operator=**(*ConditionContext* const &other) = delete

~ConditionContext()

void **applyCondition**(*ExpData* const *edata, *FixedParameterContext* fpc)

Apply condition-specific settings from edata to the constructor-supplied model, not changing the settings which were backed-up in the constructor call.

Parameters

- **edata** –
- **fpc** – flag indicating which fixedParameter from edata to apply

void **restore**()

Restore original settings on constructor-supplied *amici::Model*. Will be called during destruction. Explicit call is generally not necessary.

Class ContextManager

- Defined in file_include_amici_misc.h

Inheritance Relationships

Derived Types

- `public amici::ConditionContext` (*Class ConditionContext*)
- `public amici::FinalStateStorer` (*Class FinalStateStorer*)
- `public amici::ModelContext` (*Class ModelContext*)

Class Documentation

class **ContextManager**

Generic implementation for a context manager, explicitly deletes copy and move operators for derived classes.

Subclassed by *amici::ConditionContext*, *amici::FinalStateStorer*, *amici::ModelContext*

Public Functions

ContextManager() = default

ContextManager(*ContextManager* &other) = delete

ContextManager(*ContextManager* &&other) = delete

Class CpuTimer

- Defined in file_include_amici_misc.h

Class Documentation

class **CpuTimer**

Tracks elapsed CPU time using std::clock.

Public Functions

inline **CpuTimer**()

Constructor.

inline void **reset**()

Reset the timer.

inline double **elapsed_seconds**() const

Get elapsed CPU time in seconds since initialization or last reset.

Returns
CPU time in seconds

inline double **elapsed_milliseconds**() const

Get elapsed CPU time in milliseconds since initialization or last reset.

Returns
CPU time in milliseconds

Public Static Attributes

static bool const **uses_thread_clock** = false

Whether the timer uses a thread clock (i.e. provides proper, thread-specific CPU time).

Class CvodeException

- Defined in file_include_amici_exception.h

Inheritance Relationships

Base Type

- `public amici::AmiException` (*Class AmiException*)

Class Documentation

class **CvodeException** : public amici::*AmiException*

CVODE exception handler class.

Public Functions

CvodeException(int error_code, char const *function, char const *extra = nullptr)

Constructor.

Parameters

- **error_code** – error code returned by CVODE function
- **function** – CVODE function name
- **extra** – Extra text to append to error message

Class CVodeSolver

- Defined in file_include_amici_solver_cvodes.h

Inheritance Relationships

Base Type

- `public amici::Solver` (*Class Solver*)

Class Documentation

class **CVodeSolver** : public amici::*Solver*

The *CVodeSolver* class is a wrapper around the SUNDIALS CVODES solver.

Public Functions

~CVodeSolver() override = default

virtual *Solver* ***clone**() const override

Clone this instance.

Returns
The clone

virtual void **reInit**(*realtype* t0, *AmiVector* const &yy0, *AmiVector* const &yp0) const override

Reinitializes the states in the solver after an event occurrence.

Parameters

- **t0** – reinitialization timepoint
- **yy0** – initial state variables
- **yp0** – initial derivative state variables (DAE only)

virtual void **sensReInit**(*AmiVectorArray* const &yyS0, *AmiVectorArray* const &ypS0) const override

Reinitializes the state sensitivities in the solver after an event occurrence.

Parameters

- **yyS0** – new state sensitivity
- **ypS0** – new derivative state sensitivities (DAE only)

virtual void **sensToggleOff**() const override

Switches off computation of state sensitivities without deallocating the memory for sensitivities.

virtual void **reInitB**(int which, *realtype* tB0, *AmiVector* const &yyB0, *AmiVector* const &ypB0) const override

Reinitializes the adjoint states after an event occurrence.

Parameters

- **which** – identifier of the backwards problem

- **tB0** – reinitialization timepoint
- **yyB0** – new adjoint state
- **ypB0** – new adjoint derivative state

virtual void **quadReInitB**(int which, *AmiVector* const &yQB0) const override

Reinitialize the adjoint states after an event occurrence.

Parameters

- **which** – identifier of the backwards problem
- **yQB0** – new adjoint quadrature state

virtual int **solve**(*realtype* tout, int itask) const override

Solves the forward problem until a predefined timepoint.

Parameters

- **tout** – timepoint until which simulation should be performed
- **itask** – task identifier, can be CV_NORMAL or CV_ONE_STEP

Returns

status flag indicating success of execution

virtual int **solveF**(*realtype* tout, int itask, int *ncheckPtr) const override

Solves the forward problem until a predefined timepoint (adjoint only)

Parameters

- **tout** – timepoint until which simulation should be performed
- **itask** – task identifier, can be CV_NORMAL or CV_ONE_STEP
- **ncheckPtr** – pointer to a number that counts the internal checkpoints

Returns

status flag indicating success of execution

virtual void **solveB**(*realtype* tBout, int itaskB) const override

Solves the backward problem until a predefined timepoint (adjoint only)

Parameters

- **tBout** – timepoint until which simulation should be performed
- **itaskB** – task identifier, can be CV_NORMAL or CV_ONE_STEP

virtual void **getDky**(*realtype* t, int k) const override

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order

virtual void **getSensDky**(*realtype* t, int k) const override

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order

virtual void **getQuadDkyB**(*realtype* t, int k, int which) const override

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order
- **which** – index of backward problem

virtual void **getDkyB**(*realtype* t, int k, int which) const override

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order
- **which** – index of backward problem

virtual void **getRootInfo**(int *rootsfound) const override

getRootInfo extracts information which event occurred

Parameters

rootsfound – array with flags indicating whether the respective event occurred

virtual void **setStopTime**(*realtype* tstop) const override

Sets a timepoint at which the simulation will be stopped.

Parameters

tstop – timepoint until which simulation should be performed

virtual void **turnOffRootFinding**() const override

Disable rootfinding.

virtual *Model* const ***getModel**() const override

Accessor function to the model stored in the user data

Returns

user data model

virtual void **setLinearSolver**() const override

Sets the linear solver for the forward problem.

virtual void **setLinearSolverB**(int which) const override

Sets the linear solver for the backward problem.

Parameters

which – index of the backward problem

virtual void **setNonLinearSolver**() const override

Set the non-linear solver for the forward problem.

virtual void **setNonLinearSolverSens**() const override

Set the non-linear solver for sensitivities.

virtual void **setNonLinearSolverB**(int which) const override

Set the non-linear solver for the backward problem.

Parameters

which – index of the backward problem

Solver() = default

Default constructor.

Solver(*Solver* const &other)

Solver copy constructor.

Parameters
other –

Protected Functions

virtual void **calcIC**(*realtype* tout1) const override

Calculates consistent initial conditions, assumes initial states to be correct (DAE only)

Parameters
tout1 – next timepoint to be computed (sets timescale)

virtual void **calcICB**(int which, *realtype* tout1) const override

Calculates consistent initial conditions for the backwards problem, assumes initial states to be correct (DAE only)

Parameters

- **which** – identifier of the backwards problem
- **tout1** – next timepoint to be computed (sets timescale)

virtual void **getB**(int which) const override

extracts the adjoint state at the current timepoint from solver memory and writes it to the xB member variable

Parameters
which – index of the backwards problem

virtual void **getSens**() const override

extracts the state sensitivity at the current timepoint from solver memory and writes it to the sx member variable

virtual void **getQuadB**(int which) const override

extracts the adjoint quadrature state at the current timepoint from solver memory and writes it to the xQB member variable

Parameters
which – index of the backwards problem

virtual void **getQuad**(*realtype* &t) const override

extracts the quadrature at the current timepoint from solver memory and writes it to the xQ member variable

Parameters
t – timepoint for quadrature extraction

virtual void **getQuadDky**(*realtype* t, int k) const override

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order

virtual void **reInitPostProcessF**(*realtype* tnext) const override

reInitPostProcessF postprocessing of the solver memory after a discontinuity in the forward problem

Parameters
tnext – next timepoint (defines integration direction)

virtual void **reInitPostProcessB**(*realtype* tnext) const override

reInitPostProcessB postprocessing of the solver memory after a discontinuity in the backward problem

Parameters
tnext – next timepoint (defines integration direction)

void **reInitPostProcess**(void *cv_mem, *realtype* *t, *AmiVector* *yout, *realtype* tout) const

Postprocessing of the solver memory after a discontinuity.

Parameters

- **cv_mem** – pointer to CVODES solver memory object
- **t** – pointer to integration time
- **yout** – new state vector
- **tout** – anticipated next integration timepoint.

virtual void **allocateSolver**() const override

Create specifies solver method and initializes solver memory for the forward problem.

virtual void **setSStolerances**(double rtol, double atol) const override

sets scalar relative and absolute tolerances for the forward problem

Parameters

- **rtol** – relative tolerances
- **atol** – absolute tolerances

virtual void **setSensSStolerances**(double rtol, double const *atol) const override

activates sets scalar relative and absolute tolerances for the sensitivity variables

Parameters

- **rtol** – relative tolerances
- **atol** – array of absolute tolerances for every sensitivity variable

virtual void **setSensErrCon**(bool error_corr) const override

SetSensErrCon specifies whether error control is also enforced for sensitivities for the forward problem

Parameters
error_corr – activation flag

virtual void **setQuadErrConB**(int which, bool flag) const override

Specifies whether error control is also enforced for the backward quadrature problem.

Parameters

- **which** – identifier of the backwards problem
- **flag** – activation flag

virtual void **setQuadErrCon**(bool flag) const override

Specifies whether error control is also enforced for the forward quadrature problem.

Parameters
flag – activation flag

virtual void **setErrHandlerFn**() const override

Attaches the error handler function (errMsgIdAndTxt) to the solver.

virtual void **setUserData**() const override

Attaches the user data to the forward problem.

virtual void **setUserDataB**(int which) const override

attaches the user data to the backward problem

Parameters
which – identifier of the backwards problem

virtual void **setMaxNumSteps**(long int mxsteps) const override

specifies the maximum number of steps for the forward problem

---

Note: in contrast to the SUNDIALS method, this sets the overall maximum, not the maximum between output times.

Parameters
mxsteps – number of steps

virtual void **setStabLimDet**(int stldet) const override

activates stability limit detection for the forward problem

Parameters
stldet – flag for stability limit detection (TRUE or FALSE)

virtual void **setStabLimDetB**(int which, int stldet) const override

activates stability limit detection for the backward problem

Parameters

- **which** – identifier of the backwards problem
- **stldet** – flag for stability limit detection (TRUE or FALSE)

virtual void **setId**(*Model* const *model) const override

specify algebraic/differential components (DAE only)

Parameters
model – model specification

virtual void **setSuppressAlg**(bool flag) const override

deactivates error control for algebraic components (DAE only)

Parameters
flag – deactivation flag

void **resetState**(void *cv_mem, *const_N_Vector* y0) const

resetState reset the CVODES solver to restart integration after a rhs discontinuity.

Parameters

- **cv_mem** – pointer to CVODES solver memory object
- **y0** – new state vector

virtual void **setSensParams**(*realtype* const *p, *realtype* const *pbar, int const *plist) const override

specifies the scaling and indexes for sensitivity computation

Parameters

- **p** – parameters
- **pbar** – parameter scaling constants
- **plist** – parameter index list

virtual void **adjInit**() const override

initializes the adjoint problem

virtual void **quadInit**(*AmiVector* const &xQ0) const override

initializes the quadratures

Parameters

xQ0 – vector with initial values for xQ

virtual void **allocateSolverB**(int *which) const override

Specifies solver method and initializes solver memory for the backward problem.

Parameters

which – identifier of the backwards problem

virtual void **setSStolerancesB**(int which, *realtype* relTolB, *realtype* absTolB) const override

sets relative and absolute tolerances for the backward problem

Parameters

- **which** – identifier of the backwards problem
- **relTolB** – relative tolerances
- **absTolB** – absolute tolerances

virtual void **quadSStolerancesB**(int which, *realtype* reltolQB, *realtype* abstolQB) const override

sets relative and absolute tolerances for the quadrature backward problem

Parameters

- **which** – identifier of the backwards problem
- **reltolQB** – relative tolerances
- **abstolQB** – absolute tolerances

virtual void **quadSStolerances**(*realtype* reltolQ, *realtype* abstolQ) const override

sets relative and absolute tolerances for the quadrature problem

Parameters

- **reltolQB** – relative tolerances
- **abstolQB** – absolute tolerances

virtual void **setMaxNumStepsB**(int which, long int mxstepsB) const override

specifies the maximum number of steps for the forward problem

---

Note: in contrast to the SUNDIALS method, this sets the overall maximum, not the maximum between output times.

Parameters

- **which** – identifier of the backwards problem
- **mxstepsB** – number of steps

virtual void **diag**() const override

attaches a diagonal linear solver to the forward problem

virtual void **diagB**(int which) const override

attaches a diagonal linear solver to the backward problem

Parameters

which – identifier of the backwards problem

virtual void **getNumSteps**(void const *ami_mem, long int *numsteps) const override

reports the number of solver steps

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **numsteps** – output array

virtual void **getNumRhsEvals**(void const *ami_mem, long int *numrhsevals) const override

reports the number of right hand evaluations

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **numrhsevals** – output array

virtual void **getNumErrTestFails**(void const *ami_mem, long int *numerrtestfails) const override

reports the number of local error test failures

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **numerrtestfails** – output array

virtual void **getNumNonlinSolvConvFails**(void const *ami_mem, long int *numnonlinsolvconvfails) const override

reports the number of nonlinear convergence failures

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **numnonlinsolvconvfails** – output array

virtual void **getLastOrder**(void const *ami_ami_mem, int *order) const override

Reports the order of the integration method during the last internal step.

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **order** – output array

virtual void ***getAdjBmem**(void *ami_mem, int which) const override

Retrieves the solver memory instance for the backward problem.

Parameters

- **which** – identifier of the backwards problem
- **ami_mem** – pointer to the forward solver memory instance

Returns

A (void *) pointer to the CVODES memory allocated for the backward problem.

virtual void **init**(*realtype* t0, *AmiVector* const &x0, *AmiVector* const &dx0) const override

Initializes the states at the specified initial timepoint.

Parameters

- **t0** – initial timepoint
- **x0** – initial states
- **dx0** – initial derivative states

virtual void **initSteadystate**(*realtype* const t0, *AmiVector* const &x0, *AmiVector* const &dx0) const override

Initializes the states at the specified initial timepoint.

Parameters

- **t0** – initial timepoint
- **x0** – initial states
- **dx0** – initial derivative states

virtual void **sensInit1**(*AmiVectorArray* const &sx0, *AmiVectorArray* const &sdx0) const override

Initializes the forward sensitivities.

Parameters

- **sx0** – initial states sensitivities
- **sdx0** – initial derivative states sensitivities

virtual void **binit**(int which, *realtype* tf, *AmiVector* const &xB0, *AmiVector* const &dxB0) const override

Initialize the adjoint states at the specified final timepoint.

Parameters

- **which** – identifier of the backwards problem
- **tf** – final timepoint
- **xB0** – initial adjoint state
- **dxB0** – initial adjoint derivative state

virtual void **qbinit**(int which, *AmiVector* const &xQB0) const override

Initialize the quadrature states at the specified final timepoint.

Parameters

- **which** – identifier of the backwards problem
- **xQB0** – initial adjoint quadrature state

virtual void **rootInit**(int ne) const override

Initializes the rootfinding for events.

Parameters

ne – number of different events

virtual void **setDenseJacFn**() const override

Set the dense Jacobian function.

virtual void **setSparseJacFn**() const override

sets the sparse Jacobian function

virtual void **setBandJacFn**() const override

sets the banded Jacobian function

virtual void **setJacTimesVecFn**() const override

sets the Jacobian vector multiplication function

virtual void **setDenseJacFnB**(int which) const override

sets the dense Jacobian function

Parameters

which – identifier of the backwards problem

virtual void **setSparseJacFnB**(int which) const override

sets the sparse Jacobian function

Parameters

which – identifier of the backwards problem

virtual void **setBandJacFnB**(int which) const override

sets the banded Jacobian function

Parameters

which – identifier of the backwards problem

virtual void **setJacTimesVecFnB**(int which) const override

sets the Jacobian vector multiplication function

Parameters

which – identifier of the backwards problem

virtual void **setSparseJacFn_ss**() const override

sets the sparse Jacobian function for backward steady state case

virtual void **apply_max_nonlin_iters**() const override

Apply the maximum number of nonlinear solver iterations permitted per step.

virtual void **apply_max_conv_fails**() const override

Apply the maximum number of nonlinear solver convergence failures permitted per step.

virtual void **apply_constraints**() const override

Apply the constraints to the solver.

virtual void **apply_max_step_size**() const override

Apply the allowed maximum stepsize to the solver.

Friends

template<class **Archive**>
friend void **serialize**(*Archive* &ar, *CVodeSolver* &s, unsigned int)

Serialize *amici::CVodeSolver* to boost archive.

Parameters

- **ar** – Archive
- **s** – *Solver* instance to serialize

friend bool **operator==**(*CVodeSolver* const &a, *CVodeSolver* const &b)

Equality operator.

Parameters

- **a** –
- **b** –

Returns

Whether a and b are equal

Class ExpData

- Defined in file_include_amici_edata.h

Inheritance Relationships

Base Type

- `public amici::SimulationParameters` (*Class SimulationParameters*)

Class Documentation

class **ExpData** : public amici::*SimulationParameters*

ExpData carries all information about experimental or condition-specific data.

Public Functions

ExpData() = default

Default constructor.

ExpData(*ExpData* const&) = default

Copy constructor.

ExpData(int nytrue, int nztrue, int nmaxevent)

Constructor that only initializes dimensions.

Parameters

- **nytrue** – Number of observables
- **nztrue** – Number of event outputs
- **nmaxevent** – Maximal number of events to track

ExpData(int nytrue, int nztrue, int nmaxevent, std::vector<*realtype*> ts)

constructor that initializes timepoints from vectors

Parameters

- **nytrue** – Number of observables
- **nztrue** – Number of event outputs
- **nmaxevent** – Maximal number of events to track
- **ts** – Timepoints (dimension: nt)

ExpData(int nytrue, int nztrue, int nmaxevent, std::vector<*realtype*> ts, std::vector<*realtype*> fixedParameters)

constructor that initializes timepoints and fixed parameters from vectors

Parameters

- **nytrue** – Number of observables
- **nztrue** – Number of event outputs
- **nmaxevent** – Maximal number of events to track
- **ts** – Timepoints (dimension: nt)
- **fixedParameters** – *Model* constants (dimension: nk)

ExpData(int nytrue, int nztrue, int nmaxevent, std::vector<*realtype*> ts, std::vector<*realtype*> const &observedData, std::vector<*realtype*> const &observedDataStdDev, std::vector<*realtype*> const &observedEvents, std::vector<*realtype*> const &observedEventsStdDev)

constructor that initializes timepoints and data from vectors

Parameters

- **nytrue** – Number of observables
- **nztrue** – Number of event outputs
- **nmaxevent** – Maximal number of events to track
- **ts** – Timepoints (dimension: nt)
- **observedData** – observed data (dimension: nt x nytrue, row-major)
- **observedDataStdDev** – standard deviation of observed data (dimension: nt x nytrue, row-major)

- **observedEvents** – observed events (dimension: nmaxevents x nztrue, row-major)
- **observedEventsStdDev** – standard deviation of observed events/roots (dimension: nmaxevents x nztrue, row-major)

explicit **ExpData**(*Model* const &model)

constructor that initializes with *Model*

Parameters
model – pointer to model specification object

ExpData(*ReturnData* const &rdata, *realtype* sigma_y, *realtype* sigma_z)

constructor that initializes with returnData, adds noise according to specified sigmas

Parameters

- **rdata** – return data pointer with stored simulation results
- **sigma_y** – scalar standard deviations for all observables
- **sigma_z** – scalar standard deviations for all event observables

ExpData(*ReturnData* const &rdata, std::vector<*realtype*> sigma_y, std::vector<*realtype*> sigma_z)

constructor that initializes with returnData, adds noise according to specified sigmas

Parameters

- **rdata** – return data pointer with stored simulation results
- **sigma_y** – vector of standard deviations for observables (dimension: nytrue or nt x nytrue, row-major)
- **sigma_z** – vector of standard deviations for event observables (dimension: nztrue or nmaxevent x nztrue, row-major)

~ExpData() = default

int **nytrue**() const

number of observables of the non-augmented model

Returns
number of observables of the non-augmented model

int **nztrue**() const

number of event observables of the non-augmented model

Returns
number of event observables of the non-augmented model

int **nmaxevent**() const

maximal number of events to track

Returns
maximal number of events to track

int **nt**() const

number of timepoints

Returns
number of timepoints

void **setTimepoints**(std::vector<*realtype*> const &ts)

Set output timepoints.

If the number of timepoint increases, this will grow the observation/sigma matrices and fill new entries with NaN. If the number of timepoints decreases, this will shrink the observation/sigma matrices.

Note that the mapping from timepoints to measurements will not be preserved. E.g., say there are measurements at t = 2, and this function is called with [1, 2], then the old measurements will belong to t = 1.

Parameters
ts – timepoints

std::vector<*realtype*> const &**getTimepoints**() const

Get output timepoints.

Returns
ExpData::ts

realtype **getTimepoint**(int it) const

Get timepoint for the given index.

Parameters
it – timepoint index

Returns
timepoint timepoint at index

void **setObservedData**(std::vector<*realtype*> const &observedData)

Set all measurements.

Parameters
observedData – observed data (dimension: nt x nytrue, row-major)

void **setObservedData**(std::vector<*realtype*> const &observedData, int iy)

Set measurements for a given observable index.

Parameters

- **observedData** – observed data (dimension: nt)
- **iy** – observed data index

bool **isSetObservedData**(int it, int iy) const

Whether there is a measurement for the given time- and observable- index.

Parameters

- **it** – time index
- **iy** – observable index

Returns
boolean specifying if data was set

std::vector<*realtype*> const &**getObservedData**() const

Get all measurements.

Returns
observed data (dimension: nt x nytrue, row-major)

realtype const ***getObservedDataPtr**(int it) const

Get measurements for a given timepoint index.

Parameters
it – timepoint index

Returns
pointer to observed data at index (dimension: nytrue)

void **setObservedDataStdDev**(std::vector<*realtype*> const &observedDataStdDev)

Set standard deviations for measurements.

Parameters
observedDataStdDev – standard deviation of observed data (dimension: nt x nytrue, row-major)

void **setObservedDataStdDev**(*realtype* stdDev)

Set identical standard deviation for all measurements.

Parameters
stdDev – standard deviation (dimension: scalar)

void **setObservedDataStdDev**(std::vector<*realtype*> const &observedDataStdDev, int iy)

Set standard deviations of observed data for a specific observable index.

Parameters

- **observedDataStdDev** – standard deviation of observed data (dimension: nt)
- **iy** – observed data index

void **setObservedDataStdDev**(*realtype* stdDev, int iy)

Set all standard deviation for a given observable index to the input value.

Parameters

- **stdDev** – standard deviation (dimension: scalar)
- **iy** – observed data index

bool **isSetObservedDataStdDev**(int it, int iy) const

Whether standard deviation for a measurement at specified timepoint- and observable index has been set.

Parameters

- **it** – time index
- **iy** – observable index

Returns
boolean specifying if standard deviation of data was set

std::vector<*realtype*> const &**getObservedDataStdDev**() const

Get measurement standard deviations.

Returns
standard deviation of observed data

realtype const ***getObservedDataStdDevPtr**(int it) const

Get pointer to measurement standard deviations.

Parameters
it – timepoint index

Returns
pointer to standard deviation of observed data at index

void **setObservedEvents**(std::vector<*realtype*> const &observedEvents)

Set observed event data.

Parameters
observedEvents – observed data (dimension: nmaxevent x nztrue, row-major)

void **setObservedEvents**(std::vector<*realtype*> const &observedEvents, int iz)

Set observed event data for specific event observable.

Parameters

- **observedEvents** – observed data (dimension: nmaxevent)
- **iz** – observed event data index

bool **isSetObservedEvents**(int ie, int iz) const

Check whether event data at specified indices has been set.

Parameters

- **ie** – event index
- **iz** – event observable index

Returns
boolean specifying if data was set

std::vector<*realtype*> const &**getObservedEvents**() const

Get observed event data.

Returns
observed event data

realtype const ***getObservedEventsPtr**(int ie) const

Get pointer to observed data at ie-th occurrence.

Parameters
ie – event occurrence

Returns
pointer to observed event data at ie-th occurrence

void **setObservedEventsStdDev**(std::vector<*realtype*> const &observedEventsStdDev)

Set standard deviation of observed event data.

Parameters
observedEventsStdDev – standard deviation of observed event data

void **setObservedEventsStdDev**(*realtype* stdDev)

Set standard deviation of observed event data.

Parameters
stdDev – standard deviation (dimension: scalar)

void **setObservedEventsStdDev**(std::vector<*realtype*> const &observedEventsStdDev, int iz)

Set standard deviation of observed data for a specific observable.

Parameters

- **observedEventsStdDev** – standard deviation of observed data (dimension: nmaxevent)

- **iz** – observed data index

void **setObservedEventsStdDev**(*realtype* stdDev, int iz)

Set all standard deviations of a specific event-observable.

Parameters

- **stdDev** – standard deviation (dimension: scalar)
- **iz** – observed data index

bool **isSetObservedEventsStdDev**(int ie, int iz) const

Check whether standard deviation of event data at specified indices has been set.

Parameters

- **ie** – event index
- **iz** – event observable index

Returns

boolean specifying if standard deviation of event data was set

std::vector<*realtype*> const &**getObservedEventsStdDev**() const

Get standard deviation of observed event data.

Returns

standard deviation of observed event data

realtype const ***getObservedEventsStdDevPtr**(int ie) const

Get pointer to standard deviation of observed event data at ie-th occurrence.

Parameters

ie – event occurrence

Returns

pointer to standard deviation of observed event data at ie-th occurrence

void **clear_observations**()

Set all observations and their standard deviations to NaN.

Useful, e.g., after calling *ExpData::setTimepoints*.

Public Members

std::string **id**

Arbitrary (not necessarily unique) identifier.

Protected Functions

void **applyDimensions**()

resizes observedData, observedDataStdDev, observedEvents and observedEventsStdDev

void **applyDataDimension**()

resizes observedData and observedDataStdDev

void **applyEventDimension**()

resizes observedEvents and observedEventsStdDev

void **checkDataDimension**(std::vector<*realtype*> const &input, char const *fieldname) const
checker for dimensions of input observedData or observedDataStdDev

Parameters

- **input** – vector input to be checked
- **fieldname** – name of the input

void **checkEventsDimension**(std::vector<*realtype*> const &input, char const *fieldname) const
checker for dimensions of input observedEvents or observedEventsStdDev

Parameters

- **input** – vector input to be checked
- **fieldname** – name of the input

Protected Attributes

int **nytrue_** = {0}
number of observables

int **nztrue_** = {0}
number of event observables

int **nmaxevent_** = {0}
maximal number of event occurrences

std::vector<*realtype*> **observed_data_**
observed data (dimension: nt x nytrue, row-major)

std::vector<*realtype*> **observed_data_std_dev_**
standard deviation of observed data (dimension: nt x nytrue, row-major)

std::vector<*realtype*> **observed_events_**
observed events (dimension: nmaxevents x nztrue, row-major)

std::vector<*realtype*> **observed_events_std_dev_**
standard deviation of observed events/roots (dimension: nmaxevents x nztrue, row-major)

Friends

inline friend bool **operator==**(*ExpData* const &lhs, *ExpData* const &rhs)
Equality operator.

Parameters

- **lhs** – some object
- **rhs** – another object

Returns
`true`, if both arguments are equal; `false` otherwise.

Class FinalStateStorer

- Defined in file_include_amici_forwardproblem.h

Inheritance Relationships

Base Type

- `public amici::ContextManager` (*Class ContextManager*)

Class Documentation

class **FinalStateStorer** : public amici::*ContextManager*

stores the stimulation state when it goes out of scope

Public Functions

inline explicit **FinalStateStorer**(*ForwardProblem* *fwd)

constructor, attaches problem pointer

Parameters

fwd – problem from which the simulation state is to be stored

FinalStateStorer &**operator=**(*FinalStateStorer* const &other) = delete

inline **~FinalStateStorer**()

destructor, stores simulation state

Class ForwardProblem

- Defined in file_include_amici_forwardproblem.h

Class Documentation

class **ForwardProblem**

The *ForwardProblem* class groups all functions for solving the forward problem.

Public Functions

ForwardProblem(*ExpData* const *edata, *Model* *model, *Solver* *solver, *SteadystateProblem* const *preeq)

Constructor.

Parameters

- **edata** – pointer to *ExpData* instance
- **model** – pointer to *Model* instance

- **solver** – pointer to *Solver* instance
- **preeq** – preequilibration with which to initialize the forward problem, pass nullptr for no initialization

~ForwardProblem() = default

void **workForwardProblem**()

Solve the forward problem.

If forward sensitivities are enabled this will also compute sensitivities.

void **getAdjointUpdates**(*Model* &model, *ExpData* const &edata)

computes adjoint updates dJydx according to provided model and expdata

Parameters

- **model** – *Model* instance
- **edata** – experimental data

inline *realtype* **getTime**() const

Accessor for t.

Returns
t

inline *AmiVector* const &**getState**() const

Accessor for x.

Returns
x

inline *AmiVector* const &**getStateDerivative**() const

Accessor for dx.

Returns
dx

inline *AmiVectorArray* const &**getStateSensitivity**() const

Accessor for sx.

Returns
sx

inline std::vector<*AmiVector*> const &**getStatesAtDiscontinuities**() const

Accessor for x_disc.

Returns
x_disc

inline std::vector<*AmiVector*> const &**getRHSAtDiscontinuities**() const

Accessor for xdot_disc.

Returns
xdot_disc

inline std::vector<*AmiVector*> const &**getRHSBeforeDiscontinuities**() const

Accessor for xdot_old_disc.

Returns
xdot_old_disc

inline std::vector<int> const &**getNumberOfRoots**() const

Accessor for nroots.

Returns
nroots

inline std::vector<*realtype*> const &**getDiscontinuities**() const

Accessor for discs.

Returns
discs

inline std::vector<std::vector<int>> const &**getRootIndexes**() const

Accessor for rootidx.

Returns
rootidx

inline std::vector<*realtype*> const &**getDJydx**() const

Accessor for dJydx.

Returns
dJydx

inline std::vector<*realtype*> const &**getDJzdx**() const

Accessor for dJzdx.

Returns
dJzdx

inline *AmiVector* ***getStatePointer**()

Accessor for pointer to x.

Returns
&x

inline *AmiVector* ***getStateDerivativePointer**()

Accessor for pointer to dx.

Returns
&dx

inline *AmiVectorArray* ***getStateSensitivityPointer**()

accessor for pointer to sx

Returns
&sx

inline *AmiVectorArray* ***getStateDerivativeSensitivityPointer**()

Accessor for pointer to sdx.

Returns
&sdx

inline int **getCurrentTimeIteration**() const

Accessor for it.

Returns
it

inline *realtype* **getFinalTime**() const

Returns final time point for which simulations are available.

Returns
time point

inline int **getEventCounter**() const

Returns maximal event index for which simulations are available.

Returns
index

inline int **getRootCounter**() const

Returns maximal event index for which the timepoint is available.

Returns
index

inline *SimulationState* const &**getSimulationStateTimepoint**(int it) const

Retrieves the carbon copy of the simulation state variables at the specified timepoint index.

Parameters
it – timepoint index

Returns
state

inline *SimulationState* const &**getSimulationStateEvent**(int iroot) const

Retrieves the carbon copy of the simulation state variables at the specified event index.

Parameters
iroot – event index

Returns
SimulationState

inline *SimulationState* const &**getInitialSimulationState**() const

Retrieves the carbon copy of the simulation state variables at the initial timepoint.

Returns
SimulationState

inline *SimulationState* const &**getFinalSimulationState**() const

Retrieves the carbon copy of the simulation state variables at the final timepoint (or when simulation failed)

Returns
SimulationState

Public Members

Model ***model**

pointer to model instance

Solver ***solver**

pointer to solver instance

ExpData const ***edata**

pointer to experimental data instance

Class HermiteSpline

- Defined in file_include_amici_splinefunctions.h

Inheritance Relationships

Base Type

- `public amici::AbstractSpline` (*Class AbstractSpline*)

Class Documentation

class **HermiteSpline** : public amici::*AbstractSpline*

AMICI Hermite spline class.

Instances of this class represent Hermite splines, which are uniquely determined by their nodes, the values at their nodes, the derivatives at their nodes (defaulting to finite difference approximations from the node values), boundary conditions and extrapolation conditions. Optionally, the spline can be defined in log-space in order to ensure positivity.

Public Functions

HermiteSpline() = default

HermiteSpline(std::vector<*realtype*> nodes, std::vector<*realtype*> node_values, std::vector<*realtype*> node_values_derivative, *SplineBoundaryCondition* firstNodeBC, *SplineBoundaryCondition* lastNodeBC, *SplineExtrapolation* firstNodeExtrapol, *SplineExtrapolation* lastNodeExtrapol, bool node_derivative_by_FD, bool equidistant_spacing, bool logarithmic_parametrization)

Construct a *HermiteSpline*.

Parameters

- **nodes** – the nodes defining the position at which the value of the spline is known (if `equidistant_spacing` is true, it must contain only the first and the last node; the other nodes will be automatically inserted, assuming they are uniformly spaced)
- **node_values** – the values assumed by the spline at the nodes
- **node_values_derivative** – the derivatives of the spline at the nodes (if `node_derivative_by_FD` is true, it will resized and filled with finite difference approximations computed from `node_values`)
- **firstNodeBC** – boundary condition at the first node
- **lastNodeBC** – boundary condition at the last node
- **firstNodeExtrapol** – extrapolation method on the left side
- **lastNodeExtrapol** – extrapolation method on the right side
- **node_derivative_by_FD** – whether derivatives are to be computed by finite differences
- **equidistant_spacing** – whether equidistant nodes are to be computed

- **logarithmic_parametrization** – if true, the spline interpolation will occur in log-space in order to ensure positivity of the interpolant (which strictly speaking will no longer be a spline)

virtual void **compute_coefficients**() override

Compute the coefficients for all polynomial segments of this spline.

virtual void **compute_coefficients_sensi**(int nplist, int spline_offset, gsl::span<*realtype*> dvaluesdp, gsl::span<*realtype*> dslopesdp) override

Compute the coefficients for all polynomial segments of the derivatives of this spline with respect to the parameters.

Remark

The contents of `dvaluesdp` and `dslopesdp` may be modified by this function.

Parameters

- **nplist** – number of parameters
- **spline_offset** – offset of this spline inside `dvaluesdp` and `dslopesdp`
- **dvaluesdp** – derivatives of the spline values with respect to the parameters (for all splines in the model, not just this one)
- **dslopesdp** – derivatives of the spline derivatives with respect to the parameters (for all splines in the model, not just this one)

virtual void **compute_final_value**() override

Compute the limit value of the spline as the evaluation point tends to positive infinity.

virtual void **compute_final_sensitivity**(int nplist, int spline_offset, gsl::span<*realtype*> dspline_valuesdp, gsl::span<*realtype*> dspline_slopesdp) override

Compute the limit of the value of the sensitivity as the evaluation point tends to positive infinity.

Parameters

- **nplist** – number of parameters
- **spline_offset** – offset of this spline inside `dspline_valuesdp` and `dspline_slopesdp`
- **dspline_valuesdp** – derivatives of the spline values with respect to the parameters (for all splines in the model, not just this one)
- **dspline_slopesdp** – derivatives of the spline derivatives with respect to the parameters (for all splines in the model, not just this one)

virtual *realtype* **get_value_scaled**(*realtype* const t) const override

Get the value of this spline at a given point in the scale in which interpolation is carried out (e.g., log-scale)

Parameters

t – point at which the spline is to be evaluated

Returns

scaled value of the spline at `t`

realtype **get_node_derivative**(int const i) const

Get the derivative of the spline at a given node.

Parameters
i – index of the node at which the spline is to be evaluated

Returns
value of the derivative at the i-th node

realtype **get_node_derivative_scaled**(int const i) const

Get the derivative of the spline at a given node in the scale in which interpolation is carried out (e.g., log-scale)

Parameters
i – index of the node at which the spline is to be evaluated

Returns
scaled value of the derivative at the i-th node

virtual *realtype* **get_sensitivity_scaled**(*realtype* const t, int const ip) const override

Get the derivative of this spline with respect to a given parameter at a given point in the scale in which interpolation is carried out (e.g., log-scale)

Parameters

- **t** – point at which the sensitivity is to be evaluated
- **ip** – index of the parameter

Returns
scaled sensitivity of the spline with respect to the ipth parameter at t

inline bool **get_node_derivative_by_fd**() const

Whether derivatives of this spline are computed by finite differences.

Returns
boolean flag

Class IDAException

- Defined in file_include_amici_exception.h

Inheritance Relationships

Base Type

- public amici::AmiException (*Class AmiException*)

Class Documentation

class **IDAException** : public amici::*AmiException*

IDA exception handler class.

Public Functions

IDAException(int error_code, char const *function, char const *extra = nullptr)

Constructor.

Parameters

- **error_code** – error code returned by IDA function
- **function** – IDA function name
- **extra** – Extra text to append to error message

Class IDASolver

- Defined in file_include_amici_solver_idas.h

Inheritance Relationships

Base Type

- `public amici::Solver` (*Class Solver*)

Class Documentation

class **IDASolver** : public amici::*Solver*

The *IDASolver* class is a wrapper around the SUNDIALS IDAS solver.

Public Functions

~IDASolver() override = default

virtual *Solver* ***clone**() const override

Clone this instance.

Returns
The clone

virtual void **reInitPostProcessF**(*realtype* tnext) const override

reInitPostProcessF postprocessing of the solver memory after a discontinuity in the forward problem

Parameters
tnext – next timepoint (defines integration direction)

virtual void **reInitPostProcessB**(*realtype* tnext) const override

reInitPostProcessB postprocessing of the solver memory after a discontinuity in the backward problem

Parameters

tnext – next timepoint (defines integration direction)

virtual void **reInit**(*realtype* t0, *AmiVector* const &yy0, *AmiVector* const &yp0) const override

Reinitializes the states in the solver after an event occurrence.

Parameters

- **t0** – reinitialization timepoint
- **yy0** – initial state variables
- **yp0** – initial derivative state variables (DAE only)

virtual void **sensReInit**(*AmiVectorArray* const &yyS0, *AmiVectorArray* const &ypS0) const override

Reinitializes the state sensitivities in the solver after an event occurrence.

Parameters

- **yyS0** – new state sensitivity
- **ypS0** – new derivative state sensitivities (DAE only)

virtual void **sensToggleOff**() const override

Switches off computation of state sensitivities without deallocating the memory for sensitivities.

virtual void **reInitB**(int which, *realtype* tB0, *AmiVector* const &yyB0, *AmiVector* const &ypB0) const override

Reinitializes the adjoint states after an event occurrence.

Parameters

- **which** – identifier of the backwards problem
- **tB0** – reinitialization timepoint
- **yyB0** – new adjoint state
- **ypB0** – new adjoint derivative state

virtual void **quadReInitB**(int which, *AmiVector* const &yQB0) const override

Reinitialize the adjoint states after an event occurrence.

Parameters

- **which** – identifier of the backwards problem
- **yQB0** – new adjoint quadrature state

virtual void **quadSStolerancesB**(int which, *realtype* reltolQB, *realtype* abstolQB) const override

sets relative and absolute tolerances for the quadrature backward problem

Parameters

- **which** – identifier of the backwards problem
- **reltolQB** – relative tolerances
- **abstolQB** – absolute tolerances

virtual void **quadSStolerances**(*realtype* reltolQ, *realtype* abstolQ) const override

sets relative and absolute tolerances for the quadrature problem

Parameters

- **reltolQB** – relative tolerances
- **abstolQB** – absolute tolerances

virtual int **solve**(*realtype* tout, int itask) const override

Solves the forward problem until a predefined timepoint.

Parameters

- **tout** – timepoint until which simulation should be performed
- **itask** – task identifier, can be CV_NORMAL or CV_ONE_STEP

Returns

status flag indicating success of execution

virtual int **solveF**(*realtype* tout, int itask, int *ncheckPtr) const override

Solves the forward problem until a predefined timepoint (adjoint only)

Parameters

- **tout** – timepoint until which simulation should be performed
- **itask** – task identifier, can be CV_NORMAL or CV_ONE_STEP
- **ncheckPtr** – pointer to a number that counts the internal checkpoints

Returns

status flag indicating success of execution

virtual void **solveB**(*realtype* tBout, int itaskB) const override

Solves the backward problem until a predefined timepoint (adjoint only)

Parameters

- **tBout** – timepoint until which simulation should be performed
- **itaskB** – task identifier, can be CV_NORMAL or CV_ONE_STEP

virtual void **getRootInfo**(int *rootsfound) const override

getRootInfo extracts information which event occurred

Parameters

rootsfound – array with flags indicating whether the respective event occurred

virtual void **getDky**(*realtype* t, int k) const override

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order

virtual void **getSens**() const override

extracts the state sensitivity at the current timepoint from solver memory and writes it to the sx member variable

virtual void **getSensDky**(*realtype* t, int k) const override

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order

virtual void **getB**(int which) const override

extracts the adjoint state at the current timepoint from solver memory and writes it to the xB member variable

Parameters
which – index of the backwards problem

virtual void **getDkyB**(*realtype* t, int k, int which) const override

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order
- **which** – index of backward problem

virtual void **getQuadB**(int which) const override

extracts the adjoint quadrature state at the current timepoint from solver memory and writes it to the xQB member variable

Parameters
which – index of the backwards problem

virtual void **getQuadDkyB**(*realtype* t, int k, int which) const override

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order
- **which** – index of backward problem

virtual void **getQuad**(*realtype* &t) const override

extracts the quadrature at the current timepoint from solver memory and writes it to the xQ member variable

Parameters
t – timepoint for quadrature extraction

virtual void **getQuadDky**(*realtype* t, int k) const override

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order

virtual void **calcIC**(*realtype* tout1) const override

Calculates consistent initial conditions, assumes initial states to be correct (DAE only)

Parameters
tout1 – next timepoint to be computed (sets timescale)

virtual void **calcICB**(int which, *realtype* tout1) const override

Calculates consistent initial conditions for the backwards problem, assumes initial states to be correct (DAE only)

Parameters

- **which** – identifier of the backwards problem
- **tout1** – next timepoint to be computed (sets timescale)

virtual void **setStopTime**(*realtype* tstop) const override

Sets a timepoint at which the simulation will be stopped.

Parameters
tstop – timepoint until which simulation should be performed

virtual void **turnOffRootFinding**() const override

Disable rootfinding.

virtual *Model* const ***getModel**() const override

Accessor function to the model stored in the user data

Returns
user data model

virtual void **setLinearSolver**() const override

Sets the linear solver for the forward problem.

virtual void **setLinearSolverB**(int which) const override

Sets the linear solver for the backward problem.

Parameters
which – index of the backward problem

virtual void **setNonLinearSolver**() const override

Set the non-linear solver for the forward problem.

virtual void **setNonLinearSolverSens**() const override

Set the non-linear solver for sensitivities.

virtual void **setNonLinearSolverB**(int which) const override

Set the non-linear solver for the backward problem.

Parameters
which – index of the backward problem

Solver() = default

Default constructor.

Solver(*Solver* const &other)

Solver copy constructor.

Parameters
other –

Protected Functions

void **reInitPostProcess**(void *ida_mem, *realtype* *t, *AmiVector* *yout, *AmiVector* *ypout, *realtype* tout) const

Postprocessing of the solver memory after a discontinuity.

Parameters

- **ida_mem** – pointer to IDAS solver memory object
- **t** – pointer to integration time
- **yout** – new state vector
- **ypout** – new state derivative vector
- **tout** – anticipated next integration timepoint.

virtual void **allocateSolver**() const override

Create specifies solver method and initializes solver memory for the forward problem.

virtual void **setSStolerances**(*realtype* rtol, *realtype* atol) const override

sets scalar relative and absolute tolerances for the forward problem

Parameters

- **rtol** – relative tolerances
- **atol** – absolute tolerances

virtual void **setSensSStolerances**(*realtype* rtol, *realtype* const *atol) const override

activates sets scalar relative and absolute tolerances for the sensitivity variables

Parameters

- **rtol** – relative tolerances
- **atol** – array of absolute tolerances for every sensitivity variable

virtual void **setSensErrCon**(bool error_corr) const override

SetSensErrCon specifies whether error control is also enforced for sensitivities for the forward problem

Parameters
error_corr – activation flag

virtual void **setQuadErrConB**(int which, bool flag) const override

Specifies whether error control is also enforced for the backward quadrature problem.

Parameters

- **which** – identifier of the backwards problem
- **flag** – activation flag

virtual void **setQuadErrCon**(bool flag) const override

Specifies whether error control is also enforced for the forward quadrature problem.

Parameters
flag – activation flag

virtual void **setErrHandlerFn**() const override

Attaches the error handler function (errMsgIdAndTxt) to the solver.

virtual void **setUserData**() const override

Attaches the user data to the forward problem.

virtual void **setUserDataB**(int which) const override

attaches the user data to the backward problem

Parameters
which – identifier of the backwards problem

virtual void **setMaxNumSteps**(long int mxsteps) const override

specifies the maximum number of steps for the forward problem

---

Note: in contrast to the SUNDIALS method, this sets the overall maximum, not the maximum between output times.

Parameters
mxsteps – number of steps

virtual void **setStabLimDet**(int stldet) const override

activates stability limit detection for the forward problem

Parameters
stldet – flag for stability limit detection (TRUE or FALSE)

virtual void **setStabLimDetB**(int which, int stldet) const override

activates stability limit detection for the backward problem

Parameters

- **which** – identifier of the backwards problem
- **stldet** – flag for stability limit detection (TRUE or FALSE)

virtual void **setId**(*Model* const *model) const override

specify algebraic/differential components (DAE only)

Parameters
model – model specification

virtual void **setSuppressAlg**(bool flag) const override

deactivates error control for algebraic components (DAE only)

Parameters
flag – deactivation flag

void **resetState**(void *ida_mem, *const_N_Vector* yy0, *const_N_Vector* yp0) const

resetState reset the IDAS solver to restart integration after a rhs discontinuity.

Parameters

- **ida_mem** – pointer to IDAS solver memory object
- **yy0** – new state vector
- **yp0** – new state derivative vector

virtual void **setSensParams**(*realtype* const *p, *realtype* const *pbar, int const *plist) const override

specifies the scaling and indexes for sensitivity computation

Parameters

- **p** – parameters
- **pbar** – parameter scaling constants
- **plist** – parameter index list

virtual void **adjInit**() const override

initializes the adjoint problem

virtual void **quadInit**(*AmiVector* const &xQ0) const override

initializes the quadratures

Parameters

xQ0 – vector with initial values for xQ

virtual void **allocateSolverB**(int *which) const override

Specifies solver method and initializes solver memory for the backward problem.

Parameters

which – identifier of the backwards problem

virtual void **setMaxNumStepsB**(int which, long int mxstepsB) const override

specifies the maximum number of steps for the forward problem

---

Note: in contrast to the SUNDIALS method, this sets the overall maximum, not the maximum between output times.

Parameters

- **which** – identifier of the backwards problem
- **mxstepsB** – number of steps

virtual void **setSStolerancesB**(int which, *realtype* relTolB, *realtype* absTolB) const override

sets relative and absolute tolerances for the backward problem

Parameters

- **which** – identifier of the backwards problem
- **relTolB** – relative tolerances
- **absTolB** – absolute tolerances

virtual void **diag**() const override

attaches a diagonal linear solver to the forward problem

virtual void **diagB**(int which) const override

attaches a diagonal linear solver to the backward problem

Parameters

which – identifier of the backwards problem

virtual void **getNumSteps**(void const *ami_mem, long int *numsteps) const override

reports the number of solver steps

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)

- **numsteps** – output array

virtual void **getNumRhsEvals**(void const *ami_mem, long int *numrhsevals) const override

reports the number of right hand evaluations

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **numrhsevals** – output array

virtual void **getNumErrTestFails**(void const *ami_mem, long int *numerrtestfails) const override

reports the number of local error test failures

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **numerrtestfails** – output array

virtual void **getNumNonlinSolvConvFails**(void const *ami_mem, long int *numnonlinsolvconvfails) const override

reports the number of nonlinear convergence failures

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **numnonlinsolvconvfails** – output array

virtual void **getLastOrder**(void const *ami_mem, int *order) const override

Reports the order of the integration method during the last internal step.

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **order** – output array

virtual void ***getAdjBmem**(void *ami_mem, int which) const override

Retrieves the solver memory instance for the backward problem.

Parameters

- **which** – identifier of the backwards problem
- **ami_mem** – pointer to the forward solver memory instance

Returns

A (void *) pointer to the CVODES memory allocated for the backward problem.

virtual void **init**(*realtype* t0, *AmiVector* const &x0, *AmiVector* const &dx0) const override

Initializes the states at the specified initial timepoint.

Parameters

- **t0** – initial timepoint
- **x0** – initial states
- **dx0** – initial derivative states

virtual void **initSteadystate**(*realtype* const t0, *AmiVector* const &x0, *AmiVector* const &dx0) const override

Initializes the states at the specified initial timepoint.

Parameters

- **t0** – initial timepoint
- **x0** – initial states
- **dx0** – initial derivative states

virtual void **sensInit1**(*AmiVectorArray* const &sx0, *AmiVectorArray* const &sdx0) const override

Initializes the forward sensitivities.

Parameters

- **sx0** – initial states sensitivities
- **sdx0** – initial derivative states sensitivities

virtual void **binit**(int which, *realtype* tf, *AmiVector* const &xB0, *AmiVector* const &dxB0) const override

Initialize the adjoint states at the specified final timepoint.

Parameters

- **which** – identifier of the backwards problem
- **tf** – final timepoint
- **xB0** – initial adjoint state
- **dxB0** – initial adjoint derivative state

virtual void **qbinit**(int which, *AmiVector* const &xQB0) const override

Initialize the quadrature states at the specified final timepoint.

Parameters

- **which** – identifier of the backwards problem
- **xQB0** – initial adjoint quadrature state

virtual void **rootInit**(int ne) const override

Initializes the rootfinding for events.

Parameters

ne – number of different events

virtual void **setDenseJacFn**() const override

Set the dense Jacobian function.

virtual void **setSparseJacFn**() const override

sets the sparse Jacobian function

virtual void **setBandJacFn**() const override

sets the banded Jacobian function

virtual void **setJacTimesVecFn**() const override

sets the Jacobian vector multiplication function

virtual void **setDenseJacFnB**(int which) const override

sets the dense Jacobian function

Parameters
which – identifier of the backwards problem

virtual void **setSparseJacFnB**(int which) const override

sets the sparse Jacobian function

Parameters
which – identifier of the backwards problem

virtual void **setBandJacFnB**(int which) const override

sets the banded Jacobian function

Parameters
which – identifier of the backwards problem

virtual void **setJacTimesVecFnB**(int which) const override

sets the Jacobian vector multiplication function

Parameters
which – identifier of the backwards problem

virtual void **setSparseJacFn_ss**() const override

sets the sparse Jacobian function for backward steady state case

virtual void **apply_max_nonlin_iters**() const override

Apply the maximum number of nonlinear solver iterations permitted per step.

virtual void **apply_max_conv_fails**() const override

Apply the maximum number of nonlinear solver convergence failures permitted per step.

virtual void **apply_constraints**() const override

Apply the constraints to the solver.

virtual void **apply_max_step_size**() const override

Apply the allowed maximum stepsize to the solver.

Class IntegrationFailure

- Defined in file_include_amici_exception.h

Inheritance Relationships

Base Type

- `public amici::AmiException` (*Class AmiException*)

Class Documentation

class **IntegrationFailure** : public amici::*AmiException*

Integration failure exception for the forward problem.

This exception should be thrown when an integration failure occurred for this exception we can assume that we can recover from the exception and return a solution struct to the user

Public Functions

IntegrationFailure(int code, *realtype* t)

Constructor.

Parameters

- **code** – error code returned by cvode/ida
- **t** – time of integration failure

Public Members

int **error_code**

error code returned by cvodes/idas

realtype **time**

time of integration failure

Class IntegrationFailureB

- Defined in file_include_amici_exception.h

Inheritance Relationships

Base Type

- `public amici::AmiException` (*Class AmiException*)

Class Documentation

class **IntegrationFailureB** : public amici::*AmiException*

Integration failure exception for the backward problem.

This exception should be thrown when an integration failure occurred for this exception we can assume that we can recover from the exception and return a solution struct to the user

Public Functions

IntegrationFailureB(int code, *realtype* t)

Constructor.

Parameters

- **code** – error code returned by cvode/ida
- **t** – time of integration failure

Public Members

int **error_code**

error code returned by cvode/ida

realtype **time**

time of integration failure

Class Logger

- Defined in file_include_amici_logging.h

Class Documentation

class **Logger**

A logger, holding a list of error messages.

Public Functions

Logger() = default

void **log**(*LogSeverity* severity, std::string const &identifier, std::string const &message)

Add a log entry.

Parameters

- **severity** – Severity level
- **identifier** – Short identifier for the logged event
- **message** – A more detailed message

void **log**(*LogSeverity* severity, std::string const &identifier, char const *format, ...)

Add a log entry with printf-like message formatting.

Parameters

- **severity** – Severity level
- **identifier** – Short identifier for the logged event
- **format** – printf format string

Public Members

std::vector<*LogItem*> **items**

The log items

Class Model

- Defined in file_include_amici_model.h

Inheritance Relationships

Base Types

- `public amici::AbstractModel` (*Class AbstractModel*)
- `public amici::ModelDimensions` (*Struct ModelDimensions*)

Derived Types

- `public amici::Model_DAE` (*Class Model_DAE*)
- `public amici::Model_ODE` (*Class Model_ODE*)

Class Documentation

class **Model** : public amici::*AbstractModel*, public amici::*ModelDimensions*

The *Model* class represents an AMICI ODE/DAE model.

The model can compute various model related quantities based on symbolically generated code.

Subclassed by *amici::Model_DAE*, *amici::Model_ODE*

Public Functions

Model() = default

Default constructor

Model(*ModelDimensions* const &model_dimensions, *SimulationParameters* simulation_parameters, amici::*SecondOrderMode* o2mode, std::vector<amici::*realtype*> idlist, std::vector<int> z2event, bool pythonGenerated = false, int ndxdotdp_explicit = 0, int ndxdotdx_explicit = 0, int w_recursion_depth = 0, std::map<*realtype*, std::vector<int>> state_independent_events = {})

Constructor with model dimensions.

Parameters

- **model_dimensions** – *Model* dimensions
- **simulation_parameters** – Simulation parameters
- **o2mode** – Second order sensitivity mode

- **idlist** – Indexes indicating algebraic components (DAE only)
- **z2event** – Mapping of event outputs to events
- **pythonGenerated** – Flag indicating matlab or python wrapping
- **ndxdotdp_explicit** – Number of nonzero elements in dxdotdp_explicit
- **ndxdotdx_explicit** – Number of nonzero elements in dxdotdx_explicit
- **w_recursion_depth** – Recursion depth of fw
- **state_independent_events** – Map of events with state-independent triggers functions, mapping trigger timepoints to event indices.

~Model() override = default

Destructor.

Model &**operator=**(*Model* const &other) = delete

Copy assignment is disabled until const members are removed.

Parameters
other – Object to copy from

Returns

virtual *Model* ***clone**() const = 0

Clone this instance.

Returns
The clone

void **initialize**(*AmiVector* &x, *AmiVector* &dx, *AmiVectorArray* &sx, *AmiVectorArray* &sdx, bool computeSensitivities, std::vector<int> &roots_found)

Initialize model properties.

Parameters

- **x** – Reference to state variables
- **dx** – Reference to time derivative of states (DAE only)
- **sx** – Reference to state variable sensitivities
- **sdx** – Reference to time derivative of state sensitivities (DAE only)
- **computeSensitivities** – Flag indicating whether sensitivities are to be computed
- **roots_found** – boolean indicators indicating whether roots were found at t0 by this fun

void **reinitialize**(*realtype* t, *AmiVector* &x, *AmiVectorArray* &sx, bool computeSensitivities)

Re-initialize model properties after changing simulation context.

Parameters

- **t** – Timepoint
- **x** – Reference to state variables
- **sx** – Reference to state variable sensitivities
- **computeSensitivities** – Flag indicating whether sensitivities are to be computed

void **initializeB**(*AmiVector* &xB, *AmiVector* &dxB, *AmiVector* &xQB, bool posteq) const

Initialize model properties.

Parameters

- **xB** – Adjoint state variables
- **dxB** – Time derivative of adjoint states (DAE only)
- **xQB** – Adjoint quadratures
- **posteq** – Flag indicating whether postequilibration was performed

void **initializeStates**(*AmiVector* &x)

Initialize initial states.

Parameters

x – State vector to be initialized

void **initializeStateSensitivities**(*AmiVectorArray* &sx, *AmiVector* const &x)

Initialize initial state sensitivities.

Parameters

- **sx** – Reference to state variable sensitivities
- **x** – Reference to state variables

void **initializeSplines**()

Initialization of spline functions.

void **initializeSplineSensitivities**()

Initialization of spline sensitivity functions.

void **initEvents**(*AmiVector* const &x, *AmiVector* const &dx, std::vector<int> &roots_found)

Initialize the Heaviside variables `h` at the initial time `t0`.

Heaviside variables activate/deactivate on event occurrences.

Parameters

- **x** – Reference to state variables
- **dx** – Reference to time derivative of states (DAE only)
- **roots_found** – boolean indicators indicating whether roots were found at t0 by this fun

int **nplist**() const

Get number of parameters wrt to which sensitivities are computed.

Returns

Length of sensitivity index vector

int **np**() const

Get total number of model parameters.

Returns

Length of parameter vector

int **nk**() const

Get number of constants.

Returns

Length of constant vector

int **ncl**() const

Get number of conservation laws.

Returns
Number of conservation laws (i.e., difference between `nx_rdata` and `nx_solver`).

int **nx_reinit**() const

Get number of solver states subject to reinitialization.

Returns
Model member `nx_solver_reinit`

double const ***k**() const

Get fixed parameters.

Returns
Pointer to constants array

int **nMaxEvent**() const

Get maximum number of events that may occur for each type.

Returns
Maximum number of events that may occur for each type

void **setNMaxEvent**(int nmaxevent)

Set maximum number of events that may occur for each type.

Parameters
nmaxevent – Maximum number of events that may occur for each type

int **nt**() const

Get number of timepoints.

Returns
Number of timepoints

std::vector<*ParameterScaling*> const &**getParameterScale**() const

Get parameter scale for each parameter.

Returns
Vector of parameter scales

void **setParameterScale**(*ParameterScaling* pscale)

Set parameter scale for each parameter.

NOTE: Resets initial state sensitivities.

Parameters
pscale – Scalar parameter scale to be set for all parameters

void **setParameterScale**(std::vector<*ParameterScaling*> const &pscaleVec)

Set parameter scale for each parameter.

NOTE: Resets initial state sensitivities.

Parameters
pscaleVec – Vector of parameter scales

std::vector<*realtype*> const &**getUnscaledParameters**() const

Get parameters with transformation according to parameter scale applied.

Returns
Unscaled parameters

std::vector<*realtype*> const &**getParameters**() const

Get parameter vector.

Returns
The user-set parameters (see also *Model::getUnscaledParameters*)

realtype **getParameterById**(std::string const &par_id) const

Get value of first model parameter with the specified ID.

Parameters
par_id – Parameter ID

Returns
Parameter value

realtype **getParameterByName**(std::string const &par_name) const

Get value of first model parameter with the specified name.

Parameters
par_name – Parameter name

Returns
Parameter value

void **setParameters**(std::vector<*realtype*> const &p)

Set the parameter vector.

Parameters
p – Vector of parameters

void **setParameterById**(std::map<std::string, *realtype*> const &p, bool ignoreErrors = false)

Set model parameters according to the parameter IDs and mapped values.

Parameters

- **p** – Map of parameters IDs and values
- **ignoreErrors** – Ignore errors such as parameter IDs in p which are not model parameters

void **setParameterById**(std::string const &par_id, *realtype* value)

Set value of first model parameter with the specified ID.

Parameters

- **par_id** – Parameter ID
- **value** – Parameter value

int **setParametersByIdRegex**(std::string const &par_id_regex, *realtype* value)

Set all values of model parameters with IDs matching the specified regular expression.

Parameters

- **par_id_regex** – Parameter ID regex
- **value** – Parameter value

Returns
Number of parameter IDs that matched the regex

void **setParameterByName**(std::string const &par_name, *realtype* value)

Set value of first model parameter with the specified name.

Parameters

- **par_name** – Parameter name
- **value** – Parameter value

void **setParameterByName**(std::map<std::string, *realtype*> const &p, bool ignoreErrors = false)

Set model parameters according to the parameter name and mapped values.

Parameters

- **p** – Map of parameters names and values
- **ignoreErrors** – Ignore errors such as parameter names in p which are not model parameters

int **setParametersByNameRegex**(std::string const &par_name_regex, *realtype* value)

Set all values of all model parameters with names matching the specified regex.

Parameters

- **par_name_regex** – Parameter name regex
- **value** – Parameter value

Returns

Number of fixed parameter names that matched the regex

std::vector<*realtype*> const &**getFixedParameters**() const

Get values of fixed parameters.

Returns

Vector of fixed parameters with same ordering as in *Model::getFixedParameterIds*

realtype **getFixedParameterById**(std::string const &par_id) const

Get value of fixed parameter with the specified ID.

Parameters

par_id – Parameter ID

Returns

Parameter value

realtype **getFixedParameterByName**(std::string const &par_name) const

Get value of fixed parameter with the specified name.

If multiple parameters have the same name, the first parameter with matching name is returned.

Parameters

par_name – Parameter name

Returns

Parameter value

void **setFixedParameters**(std::vector<*realtype*> const &k)

Set values for constants.

Parameters

k – Vector of fixed parameters

void **setFixedParameterById**(std::string const &par_id, *realtype* value)

Set value of first fixed parameter with the specified ID.

Parameters

- **par_id** – Fixed parameter id
- **value** – Fixed parameter value

int **setFixedParametersByIdRegex**(std::string const &par_id_regex, *realtype* value)

Set values of all fixed parameters with the ID matching the specified regex.

Parameters

- **par_id_regex** – Fixed parameter name regex
- **value** – Fixed parameter value

Returns

Number of fixed parameter IDs that matched the regex

void **setFixedParameterByName**(std::string const &par_name, *realtype* value)

Set value of first fixed parameter with the specified name.

Parameters

- **par_name** – Fixed parameter ID
- **value** – Fixed parameter value

int **setFixedParametersByNameRegex**(std::string const &par_name_regex, *realtype* value)

Set value of all fixed parameters with name matching the specified regex.

Parameters

- **par_name_regex** – Fixed parameter name regex
- **value** – Fixed parameter value

Returns

Number of fixed parameter names that matched the regex

virtual std::string **getName**() const

Get the model name.

Returns

Model name

virtual bool **hasParameterNames**() const

Report whether the model has parameter names set.

Returns

Boolean indicating whether parameter names were set. Also returns `true` if the number of corresponding variables is just zero.

virtual std::vector<std::string> **getParameterNames**() const

Get names of the model parameters.

Returns

The parameter names

virtual bool **hasStateNames**() const

Report whether the model has state names set.

Returns
Boolean indicating whether state names were set. Also returns `true` if the number of corresponding variables is just zero.

virtual std::vector<std::string> **getStateNames**() const

Get names of the model states.

Returns
State names

virtual std::vector<std::string> **getStateNamesSolver**() const

Get names of the solver states.

Returns
State names

virtual bool **hasFixedParameterNames**() const

Report whether the model has fixed parameter names set.

Returns
Boolean indicating whether fixed parameter names were set. Also returns `true` if the number of corresponding variables is just zero.

virtual std::vector<std::string> **getFixedParameterNames**() const

Get names of the fixed model parameters.

Returns
Fixed parameter names

virtual bool **hasObservableNames**() const

Report whether the model has observable names set.

Returns
Boolean indicating whether observable names were set. Also returns `true` if the number of corresponding variables is just zero.

virtual std::vector<std::string> **getObservableNames**() const

Get names of the observables.

Returns
Observable names

virtual bool **hasExpressionNames**() const

Report whether the model has expression names set.

Returns
Boolean indicating whether expression names were set. Also returns `true` if the number of corresponding variables is just zero.

virtual std::vector<std::string> **getExpressionNames**() const

Get names of the expressions.

Returns
Expression names

virtual bool **hasParameterIds**() const

Report whether the model has parameter IDs set.

Returns
Boolean indicating whether parameter IDs were set. Also returns `true` if the number of corresponding variables is just zero.

virtual std::vector<std::string> **getParameterIds**() const

Get IDs of the model parameters.

Returns
Parameter IDs

virtual bool **hasStateIds**() const

Report whether the model has state IDs set.

Returns
Boolean indicating whether state IDs were set. Also returns `true` if the number of corresponding variables is just zero.

virtual std::vector<std::string> **getStateIds**() const

Get IDs of the model states.

Returns
State IDs

virtual std::vector<std::string> **getStateIdsSolver**() const

Get IDs of the solver states.

Returns
State IDs

virtual bool **hasFixedParameterIds**() const

Report whether the model has fixed parameter IDs set.

Returns
Boolean indicating whether fixed parameter IDs were set. Also returns `true` if the number of corresponding variables is just zero.

virtual std::vector<std::string> **getFixedParameterIds**() const

Get IDs of the fixed model parameters.

Returns
Fixed parameter IDs

virtual bool **hasObservableIds**() const

Report whether the model has observable IDs set.

Returns
Boolean indicating whether observable ids were set. Also returns `true` if the number of corresponding variables is just zero.

virtual std::vector<std::string> **getObservableIds**() const

Get IDs of the observables.

Returns
Observable IDs

virtual bool **hasExpressionIds**() const

Report whether the model has expression IDs set.

Returns
Boolean indicating whether expression ids were set. Also returns `true` if the number of corresponding variables is just zero.

virtual std::vector<std::string> **getExpressionIds**() const

Get IDs of the expression.

Returns
Expression IDs

virtual bool **hasQuadraticLLH**() const

Checks whether the defined noise model is gaussian, i.e., the nllh is quadratic.

Returns
boolean flag

std::vector<*realtype*> const &**getTimepoints**() const

Get the timepoint vector.

Returns
Timepoint vector

realtype **getTimepoint**(int it) const

Get simulation timepoint for time index `it`.

Parameters
it – Time index

Returns
Timepoint

void **setTimepoints**(std::vector<*realtype*> const &ts)

Set the timepoint vector.

Parameters
ts – New timepoint vector

double **t0**() const

Get simulation start time.

Returns
Simulation start time

void **setT0**(double t0)

Set simulation start time.

Output timepoints are absolute timepoints, independent of t_0. For output timepoints $t < t_0$, the initial state will be returned.

Parameters
t0 – Simulation start time

std::vector<bool> const &**getStateIsNonNegative**() const

Get flags indicating whether states should be treated as non-negative.

Returns
Vector of flags

void **setStateIsNonNegative**(std::vector<bool> const &stateIsNonNegative)

Set flags indicating whether states should be treated as non-negative.

Parameters
stateIsNonNegative – Vector of flags

void **setAllStatesNonNegative**()

Set flags indicating that all states should be treated as non-negative.

inline *ModelState* const &**getModelState**() const

Get the current model state.

Returns
Current model state

inline void **setModelState**(*ModelState* const &state)

Set the current model state.

Parameters
state – *Model* state

inline void **setMinimumSigmaResiduals**(double min_sigma)

Sets the estimated lower boundary for sigma_y. When :meth:`setAddSigmaResiduals` is activated, this lower boundary must ensure that log(sigma) + min_sigma > 0.

Parameters
min_sigma – lower boundary

inline *realtype* **getMinimumSigmaResiduals**() const

Gets the specified estimated lower boundary for sigma_y.

Returns
lower boundary

inline void **setAddSigmaResiduals**(bool sigma_res)

Specifies whether residuals should be added to account for parameter dependent sigma.

If set to true, additional residuals of the form $\sqrt{\log(\sigma) + C}$ will be added. This enables least-squares optimization for variables with Gaussian noise assumption and parameter dependent standard deviation sigma. The constant C can be set via :meth:`setMinimumSigmaResiduals`.

Parameters
sigma_res – if true, additional residuals are added

inline bool **getAddSigmaResiduals**() const

Checks whether residuals should be added to account for parameter dependent sigma.

Returns
sigma_res

std::vector<int> const &**getParameterList**() const

Get the list of parameters for which sensitivities are computed.

Returns
List of parameter indices

int **plist**(int pos) const

Get entry in parameter list by index.

Parameters
pos – Index in sensitivity parameter list

Returns
Index in parameter list

void **setParameterList**(std::vector<int> const &plist)

Set the list of parameters for which sensitivities are to be computed.

NOTE: Resets initial state sensitivities.

Parameters
plist – List of parameter indices

std::vector<*realtype*> **getInitialStates**()

Get the initial states.

Returns
Initial state vector

void **setInitialStates**(std::vector<*realtype*> const &x0)

Set the initial states.

Parameters
x0 – Initial state vector

bool **hasCustomInitialStates**() const

Return whether custom initial states have been set.

Returns
`true` if has custom initial states, otherwise `false`

std::vector<*realtype*> **getInitialStateSensitivities**()

Get the initial states sensitivities.

Returns
vector of initial state sensitivities

void **setInitialStateSensitivities**(std::vector<*realtype*> const &sx0)

Set the initial state sensitivities.

Parameters
sx0 – vector of initial state sensitivities with chainrule applied. This could be a slice of *ReturnData::sx* or *ReturnData::sx0*

bool **hasCustomInitialStateSensitivities**() const

Return whether custom initial state sensitivities have been set.

Returns
`true` if has custom initial state sensitivities, otherwise `false`.

void **setUnscaledInitialStateSensitivities**(std::vector<*realtype*> const &sx0)

Set the initial state sensitivities.

Parameters
sx0 – Vector of initial state sensitivities without chainrule applied. This could be the readin from a `model.sx0data` saved to HDF5.

void **setSteadyStateComputationMode**(*SteadyStateComputationMode* mode)

Set the mode how steady state is computed in the steadystate simulation.

Parameters
mode – Steadystate computation mode

SteadyStateComputationMode **getSteadyStateComputationMode**() const

Gets the mode how steady state is computed in the steadystate simulation.

Returns
Mode

void **setSteadyStateSensitivityMode**(*SteadyStateSensitivityMode* mode)

Set the mode how sensitivities are computed in the steadystate simulation.

Parameters
mode – Steadystate sensitivity mode

SteadyStateSensitivityMode **getSteadyStateSensitivityMode**() const

Gets the mode how sensitivities are computed in the steadystate simulation.

Returns
Mode

void **setReinitializeFixedParameterInitialStates**(bool flag)

Set whether initial states depending on fixed parameters are to be reinitialized after preequilibration and presimulation.

Parameters
flag – Fixed parameters reinitialized?

bool **getReinitializeFixedParameterInitialStates**() const

Get whether initial states depending on fixedParameters are to be reinitialized after preequilibration and presimulation.

Returns
flag `true` / `false`

void **requireSensitivitiesForAllParameters**()

Require computation of sensitivities for all parameters p [0..np[in natural order.

NOTE: Resets initial state sensitivities.

void **getExpression**(gsl::span<*realtype*> w, *realtype* const t, *AmiVector* const &x)

Get time-resolved `w`.

Parameters

- **w** – Buffer (shape `nw`)
- **t** – Current timepoint
- **x** – Current state

void **getObservable**(gsl::span<*realtype*> y, *realtype* const t, *AmiVector* const &x)

Get time-resolved observables.

Parameters

- **y** – Buffer (shape `ny`)
- **t** – Current timepoint
- **x** – Current state

virtual *ObservableScaling* **getObservableScaling**(int iy) const

Get scaling type for observable.

Parameters
iy – observable index

Returns
scaling type

void **getObservableSensitivity**(gsl::span<*realtype*> sy, *realtype* const t, *AmiVector* const &x, *AmiVectorArray* const &sx)

Get sensitivity of time-resolved observables.

Total derivative $sy = dydx * sx + dydp$ (only for forward sensitivities).

Parameters

- **sy** – buffer (shape ny x nplist, row-major)
- **t** – Timpoint
- **x** – State variables
- **sx** – State sensitivities

void **getObservableSigma**(gsl::span<*realtype*> sigmay, int const it, *ExpData* const *edata)

Get time-resolved observable standard deviations.

Parameters

- **sigmay** – Buffer (shape ny)
- **it** – Timepoint index
- **edata** – Pointer to experimental data instance (optional, pass nullptr to ignore)

void **getObservableSigmaSensitivity**(gsl::span<*realtype*> ssigmay, gsl::span<*realtype* const> sy, int const it, *ExpData* const *edata)

Sensitivity of time-resolved observable standard deviation.

Total derivative (can be used with both adjoint and forward sensitivity).

Parameters

- **ssigmay** – Buffer (shape ny x nplist, row-major)
- **sy** – Sensitivity of time-resolved observables for current timepoint
- **it** – Timepoint index
- **edata** – Pointer to experimental data instance (optional, pass nullptr to ignore)

void **addObservableObjective**(*realtype* &Jy, int const it, *AmiVector* const &x, *ExpData* const &edata)

Add time-resolved measurement negative log-likelihood Jy.

Parameters

- **Jy** – Buffer (shape 1)
- **it** – Timepoint index
- **x** – State variables
- **edata** – Experimental data

void **addObservableObjectiveSensitivity**(std::vector<*realtype*> &sllh, std::vector<*realtype*> &s2llh, int const it, *AmiVector* const &x, *AmiVectorArray* const &sx, *ExpData* const &edata)

Add sensitivity of time-resolved measurement negative log-likelihood Jy.

Parameters

- **sllh** – First-order buffer (shape nplist)
- **s2llh** – Second-order buffer (shape nJ - 1 x nplist, row-major)

- **it** – Timepoint index
- **x** – State variables
- **sx** – State sensitivities
- **edata** – Experimental data

void **addPartialObservableObjectiveSensitivity**(std::vector<*realtype*> &sllh, std::vector<*realtype*> &s2llh, int const it, *AmiVector* const &x, *ExpData* const &edata)

Add sensitivity of time-resolved measurement negative log-likelihood Jy.

Partial derivative (to be used with adjoint sensitivities).

Parameters

- **sllh** – First order output buffer (shape nplist)
- **s2llh** – Second order output buffer (shape nJ - 1 x nplist, row-major)
- **it** – Timepoint index
- **x** – State variables
- **edata** – Experimental data

void **getAdjointStateObservableUpdate**(gsl::span<*realtype*> dJydx, int const it, *AmiVector* const &x, *ExpData* const &edata)

Get state sensitivity of the negative loglikelihood Jy, partial derivative (to be used with adjoint sensitivities).

Parameters

- **dJydx** – Output buffer (shape nJ x nx_solver, row-major)
- **it** – Timepoint index
- **x** – State variables
- **edata** – Experimental data instance

void **getEvent**(gsl::span<*realtype*> z, int const ie, *realtype* const t, *AmiVector* const &x)

Get event-resolved observables.

Parameters

- **z** – Output buffer (shape nz)
- **ie** – Event index
- **t** – Timepoint
- **x** – State variables

void **getEventSensitivity**(gsl::span<*realtype*> sz, int const ie, *realtype* const t, *AmiVector* const &x, *AmiVectorArray* const &sx)

Get sensitivities of event-resolved observables.

Total derivative (only forward sensitivities).

Parameters

- **sz** – Output buffer (shape nz x nplist, row-major)
- **ie** – Event index

- **t** – Timepoint
- **x** – State variables
- **sx** – State sensitivities

void **getUnobservedEventSensitivity**(gsl::span<*realtype*> sz, int const ie)

Get sensitivity of z at final timepoint.

Ignores sensitivity of timepoint. Total derivative.

Parameters

- **sz** – Output buffer (shape nz x nplist, row-major)
- **ie** – Event index

void **getEventRegularization**(gsl::span<*realtype*> rz, int const ie, *realtype* const t, *AmiVector* const &x)

Get regularization for event-resolved observables.

Parameters

- **rz** – Output buffer (shape nz)
- **ie** – Event index
- **t** – Timepoint
- **x** – State variables

void **getEventRegularizationSensitivity**(gsl::span<*realtype*> srz, int const ie, *realtype* const t, *AmiVector* const &x, *AmiVectorArray* const &sx)

Get sensitivities of regularization for event-resolved observables.

Total derivative. Only forward sensitivities.

Parameters

- **srz** – Output buffer (shape nz x nplist, row-major)
- **ie** – Event index
- **t** – Timepoint
- **x** – State variables
- **sx** – State sensitivities

void **getEventSigma**(gsl::span<*realtype*> sigmaz, int const ie, int const nroots, *realtype* const t, *ExpData* const *edata)

Get event-resolved observable standard deviations.

Parameters

- **sigmaz** – Output buffer (shape nz)
- **ie** – Event index
- **nroots** – Event occurrence
- **t** – Timepoint
- **edata** – Pointer to experimental data (optional, pass nullptr to ignore)

void **getEventSigmaSensitivity**(gsl::span<*realtype*> ssigmaz, int const ie, int const nroots, *realtype* const t, *ExpData* const *edata)

Get sensitivities of event-resolved observable standard deviations.

Total derivative (only forward sensitivities).

Parameters

- **ssigmaz** – Output buffer (shape `nz x nplist`, row-major)
- **ie** – Event index
- **nroots** – Event occurrence
- **t** – Timepoint
- **edata** – Pointer to experimental data (optional, pass `nullptr` to ignore)

void **addEventObjective**(*realtype* &Jz, int const ie, int const nroots, *realtype* const t, *AmiVector* const &x, *ExpData* const &edata)

Add event-resolved observable negative log-likelihood.

Parameters

- **Jz** – Output buffer (shape 1)
- **ie** – Event index
- **nroots** – Event occurrence
- **t** – Timepoint
- **x** – State variables
- **edata** – Experimental data

void **addEventObjectiveRegularization**(*realtype* &Jrz, int const ie, int const nroots, *realtype* const t, *AmiVector* const &x, *ExpData* const &edata)

Add event-resolved observable negative log-likelihood.

Parameters

- **Jrz** – Output buffer (shape 1)
- **ie** – Event index
- **nroots** – Event occurrence
- **t** – Timepoint
- **x** – State variables
- **edata** – Experimental data

void **addEventObjectiveSensitivity**(std::vector<*realtype*> &sllh, std::vector<*realtype*> &s2llh, int const ie, int const nroots, *realtype* const t, *AmiVector* const &x, *AmiVectorArray* const &sx, *ExpData* const &edata)

Add sensitivity of time-resolved measurement negative log-likelihood Jy.

Total derivative (to be used with forward sensitivities).

Parameters

- **sllh** – First order buffer (shape `nplist`)
- **s2llh** – Second order buffer (shape `nJ-1` x `nplist`, row-major)

- **ie** – Event index
- **nroots** – Event occurrence
- **t** – Timepoint
- **x** – State variables
- **sx** – State sensitivities
- **edata** – Experimental data

void **addPartialEventObjectiveSensitivity**(std::vector<*realtype*> &sllh, std::vector<*realtype*> &s2llh, int const ie, int const nroots, *realtype* const t, *AmiVector* const &x, *ExpData* const &edata)

Add sensitivity of time-resolved measurement negative log-likelihood Jy.

Partial derivative (to be used with adjoint sensitivities).

Parameters

- **sllh** – First order buffer (shape `nplist`)
- **s2llh** – Second order buffer (shape `(nJ-1)` x `nplist`, row-major)
- **ie** – Event index
- **nroots** – Event occurrence
- **t** – Timepoint
- **x** – State variables
- **edata** – Experimental data

void **getAdjointStateEventUpdate**(gsl::span<*realtype*> dJzdx, int const ie, int const nroots, *realtype* const t, *AmiVector* const &x, *ExpData* const &edata)

State sensitivity of the negative loglikelihood Jz.

Partial derivative (to be used with adjoint sensitivities).

Parameters

- **dJzdx** – Output buffer (shape `nJ` x `nx_solver`, row-major)
- **ie** – Event index
- **nroots** – Event occurrence
- **t** – Timepoint
- **x** – State variables
- **edata** – Experimental data

void **getEventTimeSensitivity**(std::vector<*realtype*> &stau, *realtype* const t, int const ie, *AmiVector* const &x, *AmiVectorArray* const &sx)

Sensitivity of event timepoint, total derivative.

Only forward sensitivities.

Parameters

- **stau** – Timepoint sensitivity (shape `nplist`)
- **t** – Timepoint
- **ie** – Event index

- **x** – State variables
- **sx** – State sensitivities

void **addStateEventUpdate**(*AmiVector* &x, int const ie, *realtype* const t, *AmiVector* const &xdot, *AmiVector* const &xdot_old)

Update state variables after event.

Parameters

- **x** – Current state (will be overwritten)
- **ie** – Event index
- **t** – Current timepoint
- **xdot** – Current residual function values
- **xdot_old** – Value of residual function before event

void **addStateSensitivityEventUpdate**(*AmiVectorArray* &sx, int const ie, *realtype* const t, *AmiVector* const &x_old, *AmiVector* const &xdot, *AmiVector* const &xdot_old, std::vector<*realtype*> const &stau)

Update state sensitivity after event.

Parameters

- **sx** – Current state sensitivity (will be overwritten)
- **ie** – Event index
- **t** – Current timepoint
- **x_old** – Current state
- **xdot** – Current residual function values
- **xdot_old** – Value of residual function before event
- **stau** – Timepoint sensitivity, to be computed with *Model::getEventTimeSensitivity*

void **addAdjointStateEventUpdate**(*AmiVector* &xB, int const ie, *realtype* const t, *AmiVector* const &x, *AmiVector* const &xdot, *AmiVector* const &xdot_old)

Update adjoint state after event.

Parameters

- **xB** – Current adjoint state (will be overwritten)
- **ie** – Event index
- **t** – Current timepoint
- **x** – Current state
- **xdot** – Current residual function values
- **xdot_old** – Value of residual function before event

void **addAdjointQuadratureEventUpdate**(*AmiVector* xQB, int const ie, *realtype* const t, *AmiVector* const &x, *AmiVector* const &xB, *AmiVector* const &xdot, *AmiVector* const &xdot_old)

Update adjoint quadratures after event.

Parameters

- **xQB** – Current quadrature state (will be overwritten)

- **ie** – Event index
- **t** – Current timepoint
- **x** – Current state
- **xB** – Current adjoint state
- **xdot** – Current residual function values
- **xdot_old** – Value of residual function before event

void **updateHeaviside**(std::vector<int> const &rootsfound)

Update the Heaviside variables h on event occurrences.

Parameters

rootsfound – Provides the direction of the zero-crossing, so adding it will give the right update to the Heaviside variables (zero if no root was found)

void **updateHeavisideB**(int const *rootsfound)

Updates the Heaviside variables h on event occurrences in the backward problem.

Parameters

rootsfound – Provides the direction of the zero-crossing, so adding it will give the right update to the Heaviside variables (zero if no root was found)

int **checkFinite**(gsl::span<*realtype* const> array, *ModelQuantity* model_quantity, *realtype* t) const

Check if the given array has only finite elements.

For (1D) spans.

Parameters

- **array** –
- **model_quantity** – The model quantity array corresponds to
- **t** – Current timepoint

Returns

int **checkFinite**(gsl::span<*realtype* const> array, *ModelQuantity* model_quantity, size_t num_cols, *realtype* t) const

Check if the given array has only finite elements.

For flattened 2D arrays.

Parameters

- **array** – Flattened matrix
- **model_quantity** – The model quantity array corresponds to
- **num_cols** – Number of columns of the non-flattened matrix
- **t** – Current timepoint

Returns

int **checkFinite**(SUNMatrix m, *ModelQuantity* model_quantity, *realtype* t) const

Check if the given array has only finite elements.

For SUNMatrix.

Parameters

- **m** – Matrix to check

- **model_quantity** – The model quantity m corresponds to
- **t** – current timepoint

Returns

void **setAlwaysCheckFinite**(bool alwaysCheck)

Set whether the result of every call to Model::f* should be checked for finiteness.

Parameters
alwaysCheck –

bool **getAlwaysCheckFinite**() const

Get setting of whether the result of every call to Model::f* should be checked for finiteness.

Returns
that

void **fx0**(*AmiVector* &x)

Compute/get initial states.

Parameters
x – Output buffer.

void **fx0_fixedParameters**(*AmiVector* &x)

Set only those initial states that are specified via fixed parameters.

Parameters
x – Output buffer.

void **fsx0**(*AmiVectorArray* &sx, *AmiVector* const &x)

Compute/get initial value for initial state sensitivities.

Parameters

- **sx** – Output buffer for state sensitivities
- **x** – State variables

void **fsx0_fixedParameters**(*AmiVectorArray* &sx, *AmiVector* const &x)

Get only those initial states sensitivities that are affected from *amici::Model::fx0_fixedParameters*.

Parameters

- **sx** – Output buffer for state sensitivities
- **x** – State variables

virtual void **fsdx0**()

Compute sensitivity of derivative initial states sensitivities **sdx0**.

Only necessary for DAEs.

void **fx_rdata**(*AmiVector* &x_rdata, *AmiVector* const &x_solver)

Expand conservation law for states.

Parameters

- **x_rdata** – Output buffer for state variables with conservation laws expanded (stored in *amici::ReturnData*).
- **x_solver** – State variables with conservation laws applied (solver returns this)

void **fsx_rdata**(*AmiVectorArray* &sx_rdata, *AmiVectorArray* const &sx_solver, *AmiVector* const &x_solver)

Expand conservation law for state sensitivities.

Parameters

- **sx_rdata** – Output buffer for state variables sensitivities with conservation laws expanded (stored in *amici::ReturnData*).
- **sx_solver** – State variables sensitivities with conservation laws applied (solver returns this)
- **x_solver** – State variables with conservation laws applied (solver returns this)

void **setReinitializationStateIdxs**(std::vector<int> const &idxs)

Set indices of states to be reinitialized based on provided constants / fixed parameters.

Parameters

idxs – Array of state indices

std::vector<int> const &**getReinitializationStateIdxs**() const

Return indices of states to be reinitialized based on provided constants / fixed parameters.

Returns

Those indices.

AmiVectorArray const &**get_dxdotdp**() const

getter for dxdotdp (matlab generated)

Returns

dxdotdp

SUNMatrixWrapper const &**get_dxdotdp_full**() const

getter for dxdotdp (python generated)

Returns

dxdotdp

virtual std::vector<double> **get_trigger_timepoints**() const

Get trigger times for events that don't require root-finding.

Returns

List of unique trigger points for events that don't require root-finding (i.e. that trigger at predetermined timepoints), in ascending order.

virtual void **fdeltaqB**(*realtype* *deltaqB, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ip, int ie, *realtype* const *xdot, *realtype* const *xdot_old, *realtype* const *xB)

Model-specific implementation of fdeltaqB.

Parameters

- **deltaqB** – sensitivity update
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **ip** – sensitivity index

- **ie** – event index
- **xdot** – new model right hand side
- **xdot_old** – previous model right hand side
- **xB** – adjoint state

virtual void **fdeltasx**(*realtype* *deltasx, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w, int ip, int ie, *realtype* const *xdot, *realtype* const *xdot_old, *realtype* const *sx, *realtype* const *stau, *realtype* const *tcl)

Model-specific implementation of fdeltasx.

Parameters

- **deltasx** – sensitivity update
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **w** – repeating elements vector
- **ip** – sensitivity index
- **ie** – event index
- **xdot** – new model right hand side
- **xdot_old** – previous model right hand side
- **sx** – state sensitivity
- **stau** – event-time sensitivity
- **tcl** – total abundances for conservation laws

virtual void **fdeltax**(*realtype* *deltax, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ie, *realtype* const *xdot, *realtype* const *xdot_old)

Model-specific implementation of fdeltax.

Parameters

- **deltax** – state update
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **ie** – event index
- **xdot** – new model right hand side
- **xdot_old** – previous model right hand side

virtual void **fdeltaxB**(*realtype* *deltaxB, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ie, *realtype* const *xdot, *realtype* const *xdot_old, *realtype* const *xB)

Model-specific implementation of fdeltaxB.

Parameters

- **deltaxB** – adjoint state update
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **ie** – event index
- **xdot** – new model right hand side
- **xdot_old** – previous model right hand side
- **xB** – current adjoint state

virtual void **fdJrzdsigma**(*realtype* *dJrzdsigma, int iz, *realtype* const *p, *realtype* const *k, *realtype* const *rz, *realtype* const *sigmaz)

Model-specific implementation of fdJrzdsigma.

Parameters

- **dJrzdsigma** – Sensitivity of event penalization Jrz w.r.t. standard deviation sigmaz
- **iz** – event output index
- **p** – parameter vector
- **k** – constant vector
- **rz** – model root output at timepoint
- **sigmaz** – event measurement standard deviation at timepoint

virtual void **fdJrzdz**(*realtype* *dJrzdz, int iz, *realtype* const *p, *realtype* const *k, *realtype* const *rz, *realtype* const *sigmaz)

Model-specific implementation of fdJrzdz.

Parameters

- **dJrzdz** – partial derivative of event penalization Jrz
- **iz** – event output index
- **p** – parameter vector
- **k** – constant vector
- **rz** – model root output at timepoint
- **sigmaz** – event measurement standard deviation at timepoint

virtual void **fdJydsigma**(*realtype* *dJydsigma, int iy, *realtype* const *p, *realtype* const *k, *realtype* const *y, *realtype* const *sigmay, *realtype* const *my)

Model-specific implementation of fdJydsigma.

Parameters

- **dJydsigma** – Sensitivity of time-resolved measurement negative log-likelihood Jy w.r.t. standard deviation sigmay
- **iy** – output index
- **p** – parameter vector
- **k** – constant vector
- **y** – model output at timepoint
- **sigmay** – measurement standard deviation at timepoint
- **my** – measurement at timepoint

virtual void **fdJydy**(*realtype* *dJydy, int iy, *realtype* const *p, *realtype* const *k, *realtype* const *y, *realtype* const *sigmay, *realtype* const *my)

Model-specific implementation of fdJydy.

Parameters

- **dJydy** – partial derivative of time-resolved measurement negative log-likelihood Jy
- **iy** – output index
- **p** – parameter vector
- **k** – constant vector
- **y** – model output at timepoint
- **sigmay** – measurement standard deviation at timepoint
- **my** – measurement at timepoint

virtual void **fdJydy_colptrs**(*SUNMatrixWrapper* &dJydy, int index)

Model-specific implementation of fdJydy colptrs.

Parameters

- **dJydy** – sparse matrix to which colptrs will be written
- **index** – ytrue index

virtual void **fdJydy_rowvals**(*SUNMatrixWrapper* &dJydy, int index)

Model-specific implementation of fdJydy rowvals.

Parameters

- **dJydy** – sparse matrix to which rowvals will be written
- **index** – `ytrue` index

virtual void **fdJzdsigma**(*realtype* *dJzdsigma, int iz, *realtype* const *p, *realtype* const *k, *realtype* const *z, *realtype* const *sigmaz, *realtype* const *mz)

Model-specific implementation of fdJzdsigma.

Parameters

- **dJzdsigma** – Sensitivity of event measurement negative log-likelihood Jz w.r.t. standard deviation sigmaz
- **iz** – event output index
- **p** – parameter vector

- **k** – constant vector
- **z** – model event output at timepoint
- **sigmaz** – event measurement standard deviation at timepoint
- **mz** – event measurement at timepoint

virtual void **fdJzdz**(*realtype* *dJzdz, int iz, *realtype* const *p, *realtype* const *k, *realtype* const *z, *realtype* const *sigmaz, *realtype* const *mz)

Model-specific implementation of fdJzdz.

Parameters

- **dJzdz** – partial derivative of event measurement negative log-likelihood Jz
- **iz** – event output index
- **p** – parameter vector
- **k** – constant vector
- **z** – model event output at timepoint
- **sigmaz** – event measurement standard deviation at timepoint
- **mz** – event measurement at timepoint

virtual void **fdrzdp**(*realtype* *drzdp, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ip)

Model-specific implementation of fdrzdp.

Parameters

- **drzdp** – partial derivative of root output rz w.r.t. model parameters p
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **ip** – parameter index w.r.t. which the derivative is requested

virtual void **fdrzdx**(*realtype* *drzdx, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h)

Model-specific implementation of fdrzdx.

Parameters

- **drzdx** – partial derivative of root output rz w.r.t. model states x
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector

- **h** – Heaviside vector

virtual void **fdsigmaydp**(*realtype* *dsigmaydp, *realtype* const t, *realtype* const *p, *realtype* const *k, *realtype* const *y, int ip)

Model-specific implementation of fdsigmaydp.

Parameters

- **dsigmaydp** – partial derivative of standard deviation of measurements
- **t** – current time
- **p** – parameter vector
- **k** – constant vector
- **y** – model output at timepoint t
- **ip** – sensitivity index

virtual void **fdsigmaydy**(*realtype* *dsigmaydy, *realtype* const t, *realtype* const *p, *realtype* const *k, *realtype* const *y)

Model-specific implementation of fsigmay.

Parameters

- **dsigmaydy** – partial derivative of standard deviation of measurements w.r.t. model outputs
- **t** – current time
- **p** – parameter vector
- **k** – constant vector
- **y** – model output at timepoint t

virtual void **fdsigmazdp**(*realtype* *dsigmazdp, *realtype* const t, *realtype* const *p, *realtype* const *k, int ip)

Model-specific implementation of fsigmaz.

Parameters

- **dsigmazdp** – partial derivative of standard deviation of event measurements
- **t** – current time
- **p** – parameter vector
- **k** – constant vector
- **ip** – sensitivity index

virtual void **fdtotal_cldp**(*realtype* *dtotal_cldp, *realtype* const *x_rdata, *realtype* const *p, *realtype* const *k, int const ip)

Compute dtotal_cl / dp.

Parameters

- **dtotal_cldp** – dtotal_cl / dp
- **x_rdata** – State variables with conservation laws applied
- **p** – parameter vector
- **k** – constant vector
- **ip** – Sensitivity index

virtual void **fdtotal_cldx_rdata**(*realtype* *dtotal_cldx_rdata, *realtype* const *x_rdata, *realtype* const *p, *realtype* const *k, *realtype* const *tcl)

Compute dtotal_cl / dx_rdata.

Parameters

- **dtotal_cldx_rdata** – dtotal_cl / dx_rdata
- **x_rdata** – State variables with conservation laws applied
- **p** – parameter vector
- **k** – constant vector
- **tcl** – Total abundances for conservation laws

virtual void **fdtotal_cldx_rdata_colptrs**(*SUNMatrixWrapper* &dtotal_cldx_rdata)

Model-specific implementation of fdtotal_cldx_rdata, colptrs part.

Parameters

dtotal_cldx_rdata – sparse matrix to which colptrs will be written

virtual void **fdtotal_cldx_rdata_rowvals**(*SUNMatrixWrapper* &dtotal_cldx_rdata)

Model-specific implementation of fdtotal_cldx_rdata, rowvals part.

Parameters

dtotal_cldx_rdata – sparse matrix to which rowvals will be written

virtual void **fdwdp**(*realtype* *dwdp, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w, *realtype* const *tcl, *realtype* const *stcl, *realtype* const *spl, *realtype* const *sspl, bool include_static = true)

Model-specific sparse implementation of dwdp.

Parameters

- **dwdp** – Recurring terms in xdot, parameter derivative
- **t** – timepoint
- **x** – vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **w** – vector with helper variables
- **tcl** – total abundances for conservation laws
- **stcl** – sensitivities of total abundances for conservation laws
- **spl** – spline value vector
- **sspl** – sensitivities of spline values vector w.r.t. parameters p
- **include_static** – Whether to (re-)evaluate only dynamic expressions (false) or also static expressions (true). Dynamic expressions are those that depend directly or indirectly on time, static expressions are those that don't.

virtual void **fdwdp_colptrs**(*SUNMatrixWrapper* &dwdp)

Model-specific implementation for dwdp, column pointers.

Parameters

dwdp – sparse matrix to which colptrs will be written

virtual void **fdwdp_rowvals**(*SUNMatrixWrapper* &dwdp)

Model-specific implementation for dwdp, row values.

Parameters

dwdp – sparse matrix to which rowvals will be written

virtual void **fdwdw**(*realtype* *dwdw, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w, *realtype* const *tcl, bool include_static = true)

Model-specific implementation of fdwdw, no w chainrule (Py)

Parameters

- **dwdw** – partial derivative w wrt w
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **w** – vector with helper variables
- **tcl** – Total abundances for conservation laws
- **include_static** – Whether to (re-)evaluate only dynamic expressions (false) or also static expressions (true). Dynamic expressions are those that depend directly or indirectly on time, static expressions are those that don't.

virtual void **fdwdw_colptrs**(*SUNMatrixWrapper* &dwdw)

Model-specific implementation of fdwdw, colptrs part.

Parameters

dwdw – sparse matrix to which colptrs will be written

virtual void **fdwdw_rowvals**(*SUNMatrixWrapper* &dwdw)

Model-specific implementation of fdwdw, rowvals part.

Parameters

dwdw – sparse matrix to which rowvals will be written

virtual void **fdwdx**(*realtype* *dwdx, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w, *realtype* const *tcl, *realtype* const *spl, bool include_static = true)

Model-specific implementation of dwdx, data part.

Parameters

- **dwdx** – Recurring terms in xdot, state derivative
- **t** – timepoint
- **x** – vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **w** – vector with helper variables
- **tcl** – total abundances for conservation laws

- **spl** – spline value vector
- **include_static** – Whether to (re-)evaluate only dynamic expressions (false) or also static expressions (true). Dynamic expressions are those that depend directly or indirectly on time, static expressions are those that don't.

virtual void **fdwdx_colptrs**(*SUNMatrixWrapper* &dwdx)

Model-specific implementation for dwdx, column pointers.

Parameters
dwdx – sparse matrix to which colptrs will be written

virtual void **fdwdx_rowvals**(*SUNMatrixWrapper* &dwdx)

Model-specific implementation for dwdx, row values.

Parameters
dwdx – sparse matrix to which rowvals will be written

virtual void **fdx_rdatadp**(*realtype* *dx_rdatadp, *realtype* const *x, *realtype* const *tcl, *realtype* const *p, *realtype* const *k, int const ip)

Compute dx_rdata / dp.

Parameters

- **dx_rdatadp** – dx_rdata / dp
- **p** – parameter vector
- **k** – constant vector
- **x** – State variables with conservation laws applied
- **tcl** – Total abundances for conservation laws
- **ip** – Sensitivity index

virtual void **fdx_rdatadtcl**(*realtype* *dx_rdatadtcl, *realtype* const *x, *realtype* const *tcl, *realtype* const *p, *realtype* const *k)

Compute dx_rdata / dtcl.

Parameters

- **dx_rdatadtcl** – dx_rdata / dtcl
- **p** – parameter vector
- **k** – constant vector
- **x** – State variables with conservation laws applied
- **tcl** – Total abundances for conservation laws

virtual void **fdx_rdatadtcl_colptrs**(*SUNMatrixWrapper* &dx_rdatadtcl)

Model-specific implementation of fdx_rdatadtcl, colptrs part.

Parameters
dx_rdatadtcl – sparse matrix to which colptrs will be written

virtual void **fdx_rdatadtcl_rowvals**(*SUNMatrixWrapper* &dx_rdatadtcl)

Model-specific implementation of fdx_rdatadtcl, rowvals part.

Parameters
dx_rdatadtcl – sparse matrix to which rowvals will be written

virtual void **fdx_rdatadx_solver**(*realtype* *dx_rdatadx_solver, *realtype* const *x, *realtype* const *tcl, *realtype* const *p, *realtype* const *k)

Compute dx_rdata / dx_solver.

Parameters

- **dx_rdatadx_solver** – dx_rdata / dx_solver
- **p** – parameter vector
- **k** – constant vector
- **x** – State variables with conservation laws applied
- **tcl** – Total abundances for conservation laws

virtual void **fdx_rdatadx_solver_colptrs**(*SUNMatrixWrapper* &dxrdatadxsolver)

Model-specific implementation of fdx_rdatadx_solver, colptrs part.

Parameters

dxrdatadxsolver – sparse matrix to which colptrs will be written

virtual void **fdx_rdatadx_solver_rowvals**(*SUNMatrixWrapper* &dxrdatadxsolver)

Model-specific implementation of fdx_rdatadx_solver, rowvals part.

Parameters

dxrdatadxsolver – sparse matrix to which rowvals will be written

virtual void **fdydp**(*realtype* *dydp, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ip, *realtype* const *w, *realtype* const *dwdp)

Model-specific implementation of fdydp (MATLAB-only)

Parameters

- **dydp** – partial derivative of observables y w.r.t. model parameters p
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **ip** – parameter index w.r.t. which the derivative is requested
- **w** – repeating elements vector
- **dwdp** – Recurring terms in xdot, parameter derivative

virtual void **fdydp**(*realtype* *dydp, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ip, *realtype* const *w, *realtype* const *tcl, *realtype* const *dtcldp, *realtype* const *spl, *realtype* const *sspl)

Model-specific implementation of fdydp (Python)

Parameters

- **dydp** – partial derivative of observables y w.r.t. model parameters p
- **t** – current time
- **x** – current state
- **p** – parameter vector

- **k** – constant vector
- **h** – Heaviside vector
- **ip** – parameter index w.r.t. which the derivative is requested
- **w** – repeating elements vector
- **tcl** – total abundances for conservation laws
- **dtcldp** – Sensitivities of total abundances for conservation laws
- **spl** – spline value vector
- **sspl** – sensitivities of spline values vector w.r.t. parameters p

virtual void **fdydx**(*realtype* *dydx, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w, *realtype* const *dwdx)

Model-specific implementation of fdydx.

Parameters

- **dydx** – partial derivative of observables y w.r.t. model states x
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **w** – repeating elements vector
- **dwdx** – Recurring terms in xdot, state derivative

virtual void **fdzdp**(*realtype* *dzdp, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ip)

Model-specific implementation of fdzdp.

Parameters

- **dzdp** – partial derivative of event-resolved output z w.r.t. model parameters p
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **ip** – parameter index w.r.t. which the derivative is requested

virtual void **fdzdx**(*realtype* *dzdx, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h)

Model-specific implementation of fdzdx.

Parameters

- **dzdx** – partial derivative of event-resolved output z w.r.t. model states x

- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector

virtual void **fJrz**(*realtype* *nllh, int iz, *realtype* const *p, *realtype* const *k, *realtype* const *z, *realtype* const *sigmaz)

Model-specific implementation of fJrz.

Parameters

- **nllh** – regularization for event measurements z
- **iz** – event output index
- **p** – parameter vector
- **k** – constant vector
- **z** – model event output at timepoint
- **sigmaz** – event measurement standard deviation at timepoint

virtual void **fJy**(*realtype* *nllh, int iy, *realtype* const *p, *realtype* const *k, *realtype* const *y, *realtype* const *sigmay, *realtype* const *my)

Model-specific implementation of fJy.

Parameters

- **nllh** – negative log-likelihood for measurements y
- **iy** – output index
- **p** – parameter vector
- **k** – constant vector
- **y** – model output at timepoint
- **sigmay** – measurement standard deviation at timepoint
- **my** – measurements at timepoint

virtual void **fJz**(*realtype* *nllh, int iz, *realtype* const *p, *realtype* const *k, *realtype* const *z, *realtype* const *sigmaz, *realtype* const *mz)

Model-specific implementation of fJz.

Parameters

- **nllh** – negative log-likelihood for event measurements z
- **iz** – event output index
- **p** – parameter vector
- **k** – constant vector
- **z** – model event output at timepoint
- **sigmaz** – event measurement standard deviation at timepoint

- **mz** – event measurements at timepoint

virtual void **frz**(*realtype* *rz, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h)

Model-specific implementation of frz.

Parameters

- **rz** – value of root function at current timepoint (non-output events not included)
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector

virtual void **fsigmay**(*realtype* *sigmay, *realtype* const t, *realtype* const *p, *realtype* const *k, *realtype* const *y)

Model-specific implementation of fsigmay.

Parameters

- **sigmay** – standard deviation of measurements
- **t** – current time
- **p** – parameter vector
- **k** – constant vector
- **y** – model output at timepoint t

virtual void **fsigmaz**(*realtype* *sigmaz, *realtype* const t, *realtype* const *p, *realtype* const *k)

Model-specific implementation of fsigmaz.

Parameters

- **sigmaz** – standard deviation of event measurements
- **t** – current time
- **p** – parameter vector
- **k** – constant vector

virtual void **fsrz**(*realtype* *srz, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *sx, int ip)

Model-specific implementation of fsrz.

Parameters

- **srz** – Sensitivity of rz, total derivative
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector

- **sx** – current state sensitivity
- **h** – Heaviside vector
- **ip** – sensitivity index

virtual void **fstau**(*realtype* *stau, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *tcl, *realtype* const *sx, int ip, int ie)

Model-specific implementation of fstau.

Parameters

- **stau** – total derivative of event timepoint
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **tcl** – total abundances for conservation laws
- **sx** – current state sensitivity
- **ip** – sensitivity index
- **ie** – event index

virtual void **fsx0**(*realtype* *sx0, *realtype* const t, *realtype* const *x0, *realtype* const *p, *realtype* const *k, int ip)

Model-specific implementation of fsx0.

Parameters

- **sx0** – initial state sensitivities
- **t** – initial time
- **x0** – initial state
- **p** – parameter vector
- **k** – constant vector
- **ip** – sensitivity index

virtual void **fsx0_fixedParameters**(*realtype* *sx0, *realtype* const t, *realtype* const *x0, *realtype* const *p, *realtype* const *k, int ip, gsl::span<int const> reinitialization_state_idxs)

Model-specific implementation of fsx0_fixedParameters.

Parameters

- **sx0** – initial state sensitivities
- **t** – initial time
- **x0** – initial state
- **p** – parameter vector
- **k** – constant vector
- **ip** – sensitivity index

- **reinitialization_state_idxs** – Indices of states to be reinitialized based on provided constants / fixed parameters.

virtual void **fsz**(*realtype* *sz, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *sx, int ip)

Model-specific implementation of fsz.

Parameters

- **sz** – Sensitivity of rz, total derivative
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **sx** – current state sensitivity
- **ip** – sensitivity index

virtual void **fw**(*realtype* *w, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *tcl, *realtype* const *spl, bool include_static = true)

Model-specific implementation of fw.

Parameters

- **w** – Recurring terms in xdot
- **t** – timepoint
- **x** – vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **tcl** – total abundances for conservation laws
- **spl** – spline value vector
- **include_static** – Whether to (re-)evaluate only dynamic expressions (false) or also static expressions (true). Dynamic expressions are those that depend directly or indirectly on time, static expressions are those that don't.

virtual void **fx0**(*realtype* *x0, *realtype* const t, *realtype* const *p, *realtype* const *k)

Model-specific implementation of fx0.

Parameters

- **x0** – initial state
- **t** – initial time
- **p** – parameter vector
- **k** – constant vector

virtual void **fx0_fixedParameters**(*realtype* *x0, *realtype* const t, *realtype* const *p, *realtype* const *k, gsl::span<int const> reinitialization_state_idxs)

Model-specific implementation of fx0_fixedParameters.

Parameters

- **x0** – initial state
- **t** – initial time
- **p** – parameter vector
- **k** – constant vector
- **reinitialization_state_idxs** – Indices of states to be reinitialized based on provided constants / fixed parameters.

virtual void **fy**(*realtype* *y, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w)

Model-specific implementation of fy.

Parameters

- **y** – model output at current timepoint
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector
- **w** – repeating elements vector

virtual void **fz**(*realtype* *z, int ie, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h)

Model-specific implementation of fz.

Parameters

- **z** – value of event output
- **ie** – event index
- **t** – current time
- **x** – current state
- **p** – parameter vector
- **k** – constant vector
- **h** – Heaviside vector

Public Members

bool **pythonGenerated** = false

Flag indicating Matlab- or Python-based model generation

SecondOrderMode **o2mode** = {*SecondOrderMode*::*none*}

Flag indicating whether for `amici::Solver::sensi_ == amici::SensitivityOrder::second` directional or full second order derivative will be computed

std::vector<*realtype*> **idlist**

Flag array for DAE equations

Logger ***logger** = nullptr

Logger

std::map<*realtype*, std::vector<int>> **state_independent_events_** = {}

Map of trigger timepoints to event indices for events that don't require root-finding.

Protected Functions

void **writeSliceEvent**(gsl::span<*realtype* const> slice, gsl::span<*realtype*> buffer, int const ie)

Write part of a slice to a buffer according to indices specified in z2event.

Parameters

- **slice** – Input data slice
- **buffer** – Output data slice
- **ie** – Event index

void **writeSensitivitySliceEvent**(gsl::span<*realtype* const> slice, gsl::span<*realtype*> buffer, int const ie)

Write part of a sensitivity slice to a buffer according to indices specified in z2event.

Parameters

- **slice** – source data slice
- **buffer** – output data slice
- **ie** – event index

void **writeLLHSensitivitySlice**(std::vector<*realtype*> const &dLLhdp, std::vector<*realtype*> &sllh, std::vector<*realtype*> &s2llh)

Separate first and second order objective sensitivity information and write them into the respective buffers.

Parameters

- **dLLhdp** – Data with mangled first- and second-order information
- **sllh** – First order buffer
- **s2llh** – Second order buffer

void **checkLLHBufferSize**(std::vector<*realtype*> const &sllh, std::vector<*realtype*> const &s2llh) const

Verify that the provided buffers have the expected size.

Parameters

- **sllh** – first order buffer
- **s2llh** – second order buffer

void **initializeVectors**()

Set the nplist-dependent vectors to their proper sizes.

void **fy**(*realtype* t, *AmiVector* const &x)

Compute observables / measurements.

Parameters

- **t** – Current timepoint
- **x** – Current state

void **fdydp**(*realtype* t, *AmiVector* const &x)

Compute partial derivative of observables y w.r.t. model parameters `p`.

Parameters

- **t** – Current timepoint
- **x** – Current state

void **fdydx**(*realtype* t, *AmiVector* const &x)

Compute partial derivative of observables y w.r.t. state variables `x`.

Parameters

- **t** – Current timepoint
- **x** – Current state

void **fsigmay**(int it, *ExpData* const *edata)

Compute standard deviation of measurements.

Parameters

- **it** – Timepoint index
- **edata** – Experimental data

void **fdsigmaydp**(int it, *ExpData* const *edata)

Compute partial derivative of standard deviation of measurements w.r.t. model parameters.

Parameters

- **it** – Timepoint index
- **edata** – pointer to *amici::ExpData* data instance holding sigma values

void **fdsigmaydy**(int it, *ExpData* const *edata)

Compute partial derivative of standard deviation of measurements w.r.t. model outputs.

Parameters

- **it** – Timepoint index
- **edata** – pointer to *amici::ExpData* data instance holding sigma values

void **fJy**(*realtype* &Jy, int it, *AmiVector* const &y, *ExpData* const &edata)

Compute negative log-likelihood of measurements y.

Parameters

- **Jy** – Variable to which llh will be added
- **it** – Timepoint index
- **y** – Simulated observable
- **edata** – Pointer to experimental data instance

void **fdJydy**(int it, *AmiVector* const &x, *ExpData* const &edata)

Compute partial derivative of time-resolved measurement negative log-likelihood Jy.

Parameters

- **it** – timepoint index
- **x** – state variables
- **edata** – Pointer to experimental data

void **fdJydsigma**(int it, *AmiVector* const &x, *ExpData* const &edata)

Sensitivity of time-resolved measurement negative log-likelihood Jy w.r.t. standard deviation sigma.

Parameters

- **it** – timepoint index
- **x** – state variables
- **edata** – pointer to experimental data instance

void **fdJydp**(int const it, *AmiVector* const &x, *ExpData* const &edata)

Compute sensitivity of time-resolved measurement negative log-likelihood Jy w.r.t. parameters for the given timepoint.

Parameters

- **it** – timepoint index
- **x** – state variables
- **edata** – pointer to experimental data instance

void **fdJydx**(int const it, *AmiVector* const &x, *ExpData* const &edata)

Sensitivity of time-resolved measurement negative log-likelihood Jy w.r.t. state variables.

Parameters

- **it** – Timepoint index
- **x** – State variables
- **edata** – Pointer to experimental data instance

void **fz**(int ie, *realtype* t, *AmiVector* const &x)

Compute event-resolved output.

Parameters

- **ie** – Event index
- **t** – Current timepoint
- **x** – Current state

void **fdzdp**(int ie, *realtype* t, *AmiVector* const &x)

Compute partial derivative of event-resolved output `z` w.r.t. model parameters `p`

Parameters

- **ie** – event index
- **t** – current timepoint
- **x** – current state

void **fdzdx**(int ie, *realtype* t, *AmiVector* const &x)

Compute partial derivative of event-resolved output `z` w.r.t. model states `x`.

Parameters

- **ie** – Event index
- **t** – Current timepoint
- **x** – Current state

void **frz**(int ie, *realtype* t, *AmiVector* const &x)

Compute event root function of events.

Equal to *Model::froot* but does not include non-output events.

Parameters

- **ie** – Event index
- **t** – Current timepoint
- **x** – Current state

void **fdrzdp**(int ie, *realtype* t, *AmiVector* const &x)

Compute sensitivity of event-resolved root output w.r.t. model parameters `p`.

Parameters

- **ie** – Event index
- **t** – Current timepoint
- **x** – Current state

void **fdrzdx**(int ie, *realtype* t, *AmiVector* const &x)

Compute sensitivity of event-resolved measurements rz w.r.t. model states `x`.

Parameters

- **ie** – Event index
- **t** – Current timepoint
- **x** – Current state

void **fsigmaz**(int const ie, int const nroots, *realtype* const t, *ExpData* const *edata)

Compute standard deviation of events.

Parameters

- **ie** – Event index
- **nroots** – Event index
- **t** – Current timepoint

- **edata** – Experimental data

void **fdsigmazdp**(int ie, int nroots, *realtype* t, *ExpData* const *edata)

Compute sensitivity of standard deviation of events measurements w.r.t. model parameters p.

Parameters

- **ie** – Event index
- **nroots** – Event occurrence
- **t** – Current timepoint
- **edata** – Pointer to experimental data instance

void **fJz**(*realtype* &Jz, int nroots, *AmiVector* const &z, *ExpData* const &edata)

Compute negative log-likelihood of event-resolved measurements z.

Parameters

- **Jz** – Variable to which llh will be added
- **nroots** – Event index
- **z** – Simulated event
- **edata** – Experimental data

void **fdJzdz**(int const ie, int const nroots, *realtype* const t, *AmiVector* const &x, *ExpData* const &edata)

Compute partial derivative of event measurement negative log-likelihood Jz.

Parameters

- **ie** – Event index
- **nroots** – Event index
- **t** – Current timepoint
- **x** – State variables
- **edata** – Experimental data

void **fdJzdsigma**(int const ie, int const nroots, *realtype* const t, *AmiVector* const &x, *ExpData* const &edata)

Compute sensitivity of event measurement negative log-likelihood Jz w.r.t. standard deviation sigmaz.

Parameters

- **ie** – Event index
- **nroots** – Event index
- **t** – Current timepoint
- **x** – State variables
- **edata** – Pointer to experimental data instance

void **fdJzdp**(int const ie, int const nroots, *realtype* t, *AmiVector* const &x, *ExpData* const &edata)

Compute sensitivity of event-resolved measurement negative log-likelihood Jz w.r.t. parameters.

Parameters

- **ie** – Event index
- **nroots** – Event index
- **t** – Current timepoint

- **x** – State variables
- **edata** – Pointer to experimental data instance

void **fdJzdx**(int const ie, int const nroots, *realtype* t, *AmiVector* const &x, *ExpData* const &edata)

Compute sensitivity of event-resolved measurement negative log-likelihood Jz w.r.t. state variables.

Parameters

- **ie** – Event index
- **nroots** – Event index
- **t** – Current timepoint
- **x** – State variables
- **edata** – Experimental data

void **fJrz**(*realtype* &Jrz, int nroots, *AmiVector* const &rz, *ExpData* const &edata)

Compute regularization of negative log-likelihood with roots of event-resolved measurements rz.

Parameters

- **Jrz** – Variable to which regularization will be added
- **nroots** – Event index
- **rz** – Regularization variable
- **edata** – Experimental data

void **fdJrzdz**(int const ie, int const nroots, *realtype* const t, *AmiVector* const &x, *ExpData* const &edata)

Compute partial derivative of event measurement negative log-likelihood J.

Parameters

- **ie** – Event index
- **nroots** – Event index
- **t** – Current timepoint
- **x** – State variables
- **edata** – Experimental data

void **fdJrzdsigma**(int const ie, int const nroots, *realtype* const t, *AmiVector* const &x, *ExpData* const &edata)

Compute sensitivity of event measurement negative log-likelihood Jz w.r.t. standard deviation sigmaz.

Parameters

- **ie** – event index
- **nroots** – event index
- **t** – current timepoint
- **x** – state variables
- **edata** – pointer to experimental data instance

void **fspl**(*realtype* t)

Spline functions.

Parameters

t – timepoint

void **fsspl**(*realtype* t)

Parametric derivatives of splines functions.

Parameters
t – timepoint

void **fw**(*realtype* t, *realtype* const *x, bool include_static = true)

Compute recurring terms in xdot.

Parameters

- **t** – Timepoint
- **x** – Array with the states
- **include_static** – Whether to (re-)evaluate only dynamic expressions (false) or also static expressions (true). Dynamic expressions are those that depend directly or indirectly on time, static expressions are those that don't.

void **fdwdp**(*realtype* t, *realtype* const *x, bool include_static = true)

Compute parameter derivative for recurring terms in xdot.

Parameters

- **t** – Timepoint
- **x** – Array with the states
- **include_static** – Whether to (re-)evaluate only dynamic expressions (false) or also static expressions (true). Dynamic expressions are those that depend directly or indirectly on time, static expressions are those that don't.

void **fdwdx**(*realtype* t, *realtype* const *x, bool include_static = true)

Compute state derivative for recurring terms in xdot.

Parameters

- **t** – Timepoint
- **x** – Array with the states
- **include_static** – Whether to (re-)evaluate only dynamic expressions (false) or also static expressions (true). Dynamic expressions are those that depend directly or indirectly on time, static expressions are those that don't.

void **fdwdw**(*realtype* t, *realtype* const *x, bool include_static = true)

Compute self derivative for recurring terms in xdot.

Parameters

- **t** – Timepoint
- **x** – Array with the states
- **include_static** – Whether to (re-)evaluate only dynamic expressions (false) or also static expressions (true). Dynamic expressions are those that depend directly or indirectly on time, static expressions are those that don't.

virtual void **fx_rdata**(*realtype* *x_rdata, *realtype* const *x_solver, *realtype* const *tcl, *realtype* const *p, *realtype* const *k)

Compute fx_rdata.

To be implemented by derived class if applicable.

Parameters

- **x_rdata** – State variables with conservation laws expanded
- **x_solver** – State variables with conservation laws applied
- **tcl** – Total abundances for conservation laws
- **p** – parameter vector
- **k** – constant vector

virtual void **fsx_rdata**(*realtype* *sx_rdata, *realtype* const *sx_solver, *realtype* const *stcl, *realtype* const *p, *realtype* const *k, *realtype* const *x_solver, *realtype* const *tcl, int const ip)

Compute fsx_solver.

To be implemented by derived class if applicable.

Parameters

- **sx_rdata** – State sensitivity variables with conservation laws expanded
- **sx_solver** – State sensitivity variables with conservation laws applied
- **stcl** – Sensitivities of total abundances for conservation laws
- **p** – parameter vector
- **k** – constant vector
- **x_solver** – State variables with conservation laws applied
- **tcl** – Total abundances for conservation laws
- **ip** – Sensitivity index

virtual void **fx_solver**(*realtype* *x_solver, *realtype* const *x_rdata)

Compute fx_solver.

To be implemented by derived class if applicable.

Parameters

- **x_solver** – State variables with conservation laws applied
- **x_rdata** – State variables with conservation laws expanded

virtual void **fsx_solver**(*realtype* *sx_solver, *realtype* const *sx_rdata)

Compute fsx_solver.

To be implemented by derived class if applicable.

Parameters

- **sx_rdata** – State sensitivity variables with conservation laws expanded
- **sx_solver** – State sensitivity variables with conservation laws applied

virtual void **ftotal_cl**(*realtype* *total_cl, *realtype* const *x_rdata, *realtype* const *p, *realtype* const *k)

Compute ftotal_cl.

To be implemented by derived class if applicable.

Parameters

- **total_cl** – Total abundances of conservation laws
- **x_rdata** – State variables with conservation laws expanded

- **p** – parameter vector
- **k** – constant vector

virtual void **fstotal_cl**(*realtype* *stotal_cl, *realtype* const *sx_rdata, int const ip, *realtype* const *x_rdata, *realtype* const *p, *realtype* const *k, *realtype* const *tcl)

Compute fstotal_cl.

To be implemented by derived class if applicable.

Parameters

- **stotal_cl** – Sensitivities for the total abundances of conservation laws
- **sx_rdata** – State sensitivity variables with conservation laws expanded
- **ip** – Sensitivity index
- **x_rdata** – State variables with conservation laws expanded
- **p** – parameter vector
- **k** – constant vector
- **tcl** – Total abundances for conservation laws

const_N_Vector **computeX_pos**(*const_N_Vector* x)

Compute non-negative state vector.

Compute non-negative state vector according to stateIsNonNegative. If anyStateNonNegative is set to `false`, i.e., all entries in stateIsNonNegative are `false`, this function directly returns `x`, otherwise all entries of x are copied in to `amici::Model::x_pos_tmp_` and negative values are replaced by `0` where applicable.

Parameters

x – State vector possibly containing negative values

Returns

State vector with negative values replaced by `0` according to stateIsNonNegative

realtype const ***computeX_pos**(*AmiVector* const &x)

Compute non-negative state vector.

Compute non-negative state vector according to stateIsNonNegative. If anyStateNonNegative is set to `false`, i.e., all entries in stateIsNonNegative are `false`, this function directly returns `x`, otherwise all entries of x are copied in to `amici::Model::x_pos_tmp_` and negative values are replaced by `0` where applicable.

Parameters

x – State vector possibly containing negative values

Returns

State vector with negative values replaced by `0` according to stateIsNonNegative

Protected Attributes

ModelState **state_**

All variables necessary for function evaluation

ModelStateDerived **derived_state_**

Storage for model quantities beyond *ModelState* for the current timepoint

std::vector<*HermiteSpline*> **splines_**

Storage for splines of the model

std::vector<int> **z2event_**

index indicating to which event an event output belongs

std::vector<*realtype*> **x0data_**

state initialization (size nx_solver)

std::vector<*realtype*> **sx0data_**

sensitivity initialization (size nx_rdata x nplist, row-major)

std::vector<bool> **state_is_non_negative_**

vector of bools indicating whether state variables are to be assumed to be positive

std::vector<bool> **root_initial_values_**

Vector of booleans indicating the initial boolean value for every event trigger function. Events at t0 can only trigger if the initial value is set to `false`. Must be specified during model compilation by setting the `initialValue` attribute of an event trigger.

bool **any_state_non_negative_** = {false}

boolean indicating whether any entry in stateIsNonNegative is `true`

int **nmaxevent_** = {10}

maximal number of events to track

SteadyStateComputationMode
steadystate_computation_mode_{*SteadyStateComputationMode*::*integrateIfNewtonFails*}

method for steady-state computation

SteadyStateSensitivityMode
steadystate_sensitivity_mode_{*SteadyStateSensitivityMode*::*integrateIfNewtonFails*}

method for steadystate sensitivities computation

bool **always_check_finite_** = {true}

Indicates whether the result of every call to `Model::f*` should be checked for finiteness

bool **sigma_res_** = {false}

indicates whether sigma residuals are to be added for every datapoint

realtype **min_sigma_** = {50.0}

offset to ensure positivity of sigma residuals, only has an effect when `sigma_res_` is `true`

Friends

template<class **Archive**>
friend void **serialize**(*Archive* &ar, *Model* &m, unsigned int version)

Serialize *Model* (see `boost::serialization::serialize`).

Parameters

- **ar** – Archive to serialize to
- **m** – Data to serialize
- **version** – Version number

friend bool **operator==**(*Model* const &a, *Model* const &b)

Check equality of data members.

Parameters

- **a** – First model instance
- **b** – Second model instance

Returns
Equality

Class Model_DAE

- Defined in file_include_amici_model_dae.h

Inheritance Relationships

Base Type

- `public amici::Model` (*Class Model*)

Class Documentation

class **Model_DAE** : public amici::*Model*

The *Model* class represents an AMICI DAE model.

The model does not contain any data, but represents the state of the model at a specific time t. The states must not always be in sync, but may be updated asynchronously.

Public Functions

Model_DAE() = default

default constructor

inline **Model_DAE**(*ModelDimensions* const &model_dimensions, *SimulationParameters* simulation_parameters, *SecondOrderMode* const o2mode, std::vector<*realtype*> const &idlist, std::vector<int> const &z2event, bool const pythonGenerated = false, int const ndxdotdp_explicit = 0, int const ndxdotdx_explicit = 0, int const w_recursion_depth = 0, std::map<*realtype*, std::vector<int>> state_independent_events = {})

Constructor with model dimensions.

Parameters

- **model_dimensions** – *Model* dimensions
- **simulation_parameters** – Simulation parameters
- **o2mode** – second order sensitivity mode
- **idlist** – indexes indicating algebraic components (DAE only)
- **z2event** – mapping of event outputs to events
- **pythonGenerated** – flag indicating matlab or python wrapping
- **ndxdotdp_explicit** – number of nonzero elements dxdotdp_explicit
- **ndxdotdx_explicit** – number of nonzero elements dxdotdx_explicit
- **w_recursion_depth** – Recursion depth of fw
- **state_independent_events** – Map of events with state-independent triggers functions, mapping trigger timepoints to event indices.

virtual void **fJ**(*realtype* t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xdot, SUNMatrix J) override

Dense Jacobian function.

Parameters

- **t** – time
- **cj** – scaling factor (inverse of timestep, DAE only)
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xdot** – values of residual function (unused)
- **J** – dense matrix to which values of the jacobian will be written

void **fJ**(*realtype* t, *realtype* cj, *const_N_Vector* x, *const_N_Vector* dx, *const_N_Vector* xdot, SUNMatrix J)

Jacobian of xdot with respect to states x.

Parameters

- **t** – timepoint
- **cj** – scaling factor, inverse of the step size
- **x** – Vector with the states
- **dx** – Vector with the derivative states

- **xdot** – Vector with the right hand side
- **J** – Matrix to which the Jacobian will be written

virtual void **fJB**(*realtype* const t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xB, *AmiVector* const &dxB, *AmiVector* const &xBdot, SUNMatrix JB) override

Dense Jacobian function.

Parameters

- **t** – time
- **cj** – scaling factor (inverse of timestep, DAE only)
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **xBdot** – Vector with the adjoint right hand side (unused)
- **JB** – dense matrix to which values of the jacobian will be written

void **fJB**(*realtype* t, *realtype* cj, *const_N_Vector* x, *const_N_Vector* dx, *const_N_Vector* xB, *const_N_Vector* dxB, SUNMatrix JB)

Jacobian of xBdot with respect to adjoint state xB.

Parameters

- **t** – timepoint
- **cj** – scaling factor, inverse of the step size
- **x** – Vector with the states
- **dx** – Vector with the derivative states
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **JB** – Matrix to which the Jacobian will be written

virtual void **fJSparse**(*realtype* t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xdot, SUNMatrix J) override

Sparse Jacobian function.

Parameters

- **t** – time
- **cj** – scaling factor (inverse of timestep, DAE only)
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xdot** – values of residual function (unused)
- **J** – sparse matrix to which values of the Jacobian will be written

void **fJSparse**(*realtype* t, *realtype* cj, *const_N_Vector* x, *const_N_Vector* dx, SUNMatrix J)

J in sparse form (for sparse solvers from the SuiteSparse Package)

Parameters

- **t** – timepoint
- **cj** – scalar in Jacobian (inverse stepsize)
- **x** – Vector with the states
- **dx** – Vector with the derivative states
- **J** – Matrix to which the Jacobian will be written

virtual void **fJSparseB**(*realtype* const t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xB, *AmiVector* const &dxB, *AmiVector* const &xBdot, SUNMatrix JB) override

Sparse Jacobian function.

Parameters

- **t** – time
- **cj** – scaling factor (inverse of timestep, DAE only)
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **xBdot** – Vector with the adjoint right hand side (unused)
- **JB** – dense matrix to which values of the jacobian will be written

void **fJSparseB**(*realtype* t, *realtype* cj, *const_N_Vector* x, *const_N_Vector* dx, *const_N_Vector* xB, *const_N_Vector* dxB, SUNMatrix JB)

JB in sparse form (for sparse solvers from the SuiteSparse Package)

Parameters

- **t** – timepoint
- **cj** – scalar in Jacobian
- **x** – Vector with the states
- **dx** – Vector with the derivative states
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **JB** – Matrix to which the Jacobian will be written

virtual void **fJDiag**(*realtype* t, *AmiVector* &JDiag, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx) override

Diagonal of the Jacobian (for preconditioning)

Parameters

- **t** – timepoint
- **JDiag** – Vector to which the Jacobian diagonal will be written

- **cj** – scaling factor, inverse of the step size
- **x** – Vector with the states
- **dx** – Vector with the derivative states

virtual void **fJv**(*realtype* t, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xdot, *AmiVector* const &v, *AmiVector* &nJv, *realtype* cj) override

Jacobian multiply function.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xdot** – values of residual function (unused)
- **v** – multiplication vector (unused)
- **nJv** – array to which result of multiplication will be written
- **cj** – scaling factor (inverse of timestep, DAE only)

void **fJv**(*realtype* t, *const_N_Vector* x, *const_N_Vector* dx, *const_N_Vector* v, N_Vector Jv, *realtype* cj)

Matrix vector product of J with a vector v (for iterative solvers)

Parameters

- **t** – timepoint
- **cj** – scaling factor, inverse of the step size
- **x** – Vector with the states
- **dx** – Vector with the derivative states
- **v** – Vector with which the Jacobian is multiplied
- **Jv** – Vector to which the Jacobian vector product will be written

void **fJvB**(*realtype* t, *const_N_Vector* x, *const_N_Vector* dx, *const_N_Vector* xB, *const_N_Vector* dxB, *const_N_Vector* vB, N_Vector JvB, *realtype* cj)

Matrix vector product of JB with a vector v (for iterative solvers)

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **dx** – Vector with the derivative states
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **vB** – Vector with which the Jacobian is multiplied
- **JvB** – Vector to which the Jacobian vector product will be written
- **cj** – scalar in Jacobian (inverse stepsize)

virtual void **froot**(*realtype* t, *AmiVector* const &x, *AmiVector* const &dx, gsl::span<*realtype*> root) override

Root function.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)
- **root** – array to which values of the root function will be written

void **froot**(*realtype* t, *const_N_Vector* x, *const_N_Vector* dx, gsl::span<*realtype*> root)

Event trigger function for events.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **dx** – Vector with the derivative states
- **root** – array with root function values

virtual void **fxdot**(*realtype* t, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* &xdot) override

Residual function.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xdot** – array to which values of the residual function will be written

void **fxdot**(*realtype* t, *const_N_Vector* x, *const_N_Vector* dx, N_Vector xdot)

Residual function of the DAE.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **dx** – Vector with the derivative states
- **xdot** – Vector with the right hand side

void **fxBdot**(*realtype* t, *const_N_Vector* x, *const_N_Vector* dx, *const_N_Vector* xB, *const_N_Vector* dxB, N_Vector xBdot)

Right hand side of differential equation for adjoint state xB.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **dx** – Vector with the derivative states
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states

- **xBdot** – Vector with the adjoint right hand side

void **fqBdot**(*realtype* t, *const_N_Vector* x, *const_N_Vector* dx, *const_N_Vector* xB, *const_N_Vector* dxB, N_Vector qBdot)

Right hand side of integral equation for quadrature states qB.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **dx** – Vector with the derivative states
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **qBdot** – Vector with the adjoint quadrature right hand side

virtual void **fxBdot_ss**(*realtype* const t, *AmiVector* const &xB, *AmiVector* const &dxB, *AmiVector* &xBdot) override

Residual function backward when running in steady state mode.

Parameters

- **t** – time
- **xB** – adjoint state
- **dxB** – time derivative of state (DAE only)
- **xBdot** – array to which values of the residual function will be written

void **fxBdot_ss**(*realtype* t, *const_N_Vector* xB, *const_N_Vector* dxB, N_Vector xBdot) const

Implementation of fxBdot for steady state case at the N_Vector level.

Parameters

- **t** – timepoint
- **xB** – Vector with the adjoint state
- **dxB** – Vector with the adjoint derivative states
- **xBdot** – Vector with the adjoint right hand side

void **fqBdot_ss**(*realtype* t, *const_N_Vector* xB, *const_N_Vector* dxB, N_Vector qBdot) const

Implementation of fqBdot for steady state at the N_Vector level.

Parameters

- **t** – timepoint
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **qBdot** – Vector with the adjoint quadrature right hand side

virtual void **fJSparseB_ss**(SUNMatrix JB) override

Sparse Jacobian function backward, steady state case.

Parameters

JB – sparse matrix to which values of the Jacobian will be written

virtual void **writeSteadystateJB**(*realtype* const t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xB, *AmiVector* const &dxB, *AmiVector* const &xBdot) override

Computes the sparse backward Jacobian for steadystate integration and writes it to the model member.

Parameters

- **t** – timepoint
- **cj** – scalar in Jacobian
- **x** – Vector with the states
- **dx** – Vector with the derivative states
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **xBdot** – Vector with the adjoint state right hand side

void **fdxdotdp**(*realtype* t, *const_N_Vector* const x, *const_N_Vector* const dx)

Sensitivity of dx/dt wrt model parameters p.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **dx** – Vector with the derivative states

inline virtual void **fdxdotdp**(*realtype* const t, *AmiVector* const &x, *AmiVector* const &dx) override

Model-specific sparse implementation of explicit parameter derivative of right hand side.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)

virtual void **fsxdot**(*realtype* t, *AmiVector* const &x, *AmiVector* const &dx, int ip, *AmiVector* const &sx, *AmiVector* const &sdx, *AmiVector* &sxdot) override

Sensitivity Residual function.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)
- **ip** – parameter index
- **sx** – sensitivity state
- **sdx** – time derivative of sensitivity state (DAE only)
- **sxdot** – array to which values of the sensitivity residual function will be written

void **fsxdot**(*realtype* t, *const_N_Vector* x, *const_N_Vector* dx, int ip, *const_N_Vector* sx, *const_N_Vector* sdx, N_Vector sxdot)

Right hand side of differential equation for state sensitivities sx.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **dx** – Vector with the derivative states
- **ip** – parameter index
- **sx** – Vector with the state sensitivities
- **sdx** – Vector with the derivative state sensitivities
- **sxdot** – Vector with the sensitivity right hand side

void **fM**(*realtype* t, *const_N_Vector* x)

Mass matrix for DAE systems.

Parameters

- **t** – timepoint
- **x** – Vector with the states

virtual std::unique_ptr<*Solver*> **getSolver**() override

Retrieves the solver object.

Returns

The *Solver* instance

Protected Functions

virtual void **fJSparse**(SUNMatrixContent_Sparse JSparse, *realtype* t, *realtype* const *x, double const *p, double const *k, *realtype* const *h, *realtype* cj, *realtype* const *dx, *realtype* const *w, *realtype* const *dwdx)

Model specific implementation for fJSparse.

Parameters

- **JSparse** – Matrix to which the Jacobian will be written
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **cj** – scaling factor, inverse of the step size
- **dx** – Vector with the derivative states
- **w** – vector with helper variables
- **dwdx** – derivative of w wrt x

virtual void **froot**(*realtype* *root, *realtype* t, *realtype* const *x, double const *p, double const *k, *realtype* const *h, *realtype* const *dx)

Model specific implementation for froot.

Parameters

- **root** – values of the trigger function
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **dx** – Vector with the derivative states

virtual void **fxdot**(*realtype* *xdot, *realtype* t, *realtype* const *x, double const *p, double const *k, *realtype* const *h, *realtype* const *dx, *realtype* const *w) = 0

Model specific implementation for fxdot.

Parameters

- **xdot** – residual function
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **w** – vector with helper variables
- **dx** – Vector with the derivative states

virtual void **fdxdotdp**(*realtype* *dxdotdp, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ip, *realtype* const *dx, *realtype* const *w, *realtype* const *dwdp)

Model specific implementation of fdxdotdp.

Parameters

- **dxdotdp** – partial derivative xdot wrt p
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **ip** – parameter index
- **dx** – Vector with the derivative states
- **w** – vector with helper variables
- **dwdp** – derivative of w wrt p

virtual void **fdxdotdp_explicit**(*realtype* *dxdotdp_explicit, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *dx, *realtype* const *w)

Model specific implementation of fdxdotdp_explicit, no w chainrule (Py)

Parameters

- **dxdotdp_explicit** – partial derivative xdot wrt p
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **dx** – Vector with the derivative states
- **w** – vector with helper variables

virtual void **fdxdotdp_explicit_colptrs**(*SUNMatrixWrapper* &dxdotdp)

Model specific implementation of fdxdotdp_explicit, colptrs part.

Parameters
dxdotdp – sparse matrix to which colptrs will be written

virtual void **fdxdotdp_explicit_rowvals**(*SUNMatrixWrapper* &dxdotdp)

Model specific implementation of fdxdotdp_explicit, rowvals part.

Parameters
dxdotdp – sparse matrix to which rowvals will be written

virtual void **fdxdotdx_explicit**(*realtype* *dxdotdx_explicit, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *dx, *realtype* const *w)

Model specific implementation of fdxdotdx_explicit, no w chainrule (Py)

Parameters

- **dxdotdx_explicit** – partial derivative xdot wrt x
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – heavyside vector
- **dx** – Vector with the derivative states
- **w** – vector with helper variables

virtual void **fdxdotdx_explicit_colptrs**(*SUNMatrixWrapper* &dxdotdx)

Model specific implementation of fdxdotdx_explicit, colptrs part.

Parameters
dxdotdx – sparse matrix to which colptrs will be written

virtual void **fdxdotdx_explicit_rowvals**(*SUNMatrixWrapper* &dxdotdx)

Model specific implementation of fdxdotdx_explicit, rowvals part.

Parameters
dxdotdx – sparse matrix to which rowvals will be written

virtual void **fdxdotdw**(*realtype* *dxdotdw, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *dx, *realtype* const *w)

Model specific implementation of fdxdotdw, data part.

Parameters

- **dxdotdw** – partial derivative xdot wrt w
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **dx** – Vector with the derivative states
- **w** – vector with helper variables

virtual void **fdxdotdw_colptrs**(*SUNMatrixWrapper* &dxdotdw)

Model specific implementation of fdxdotdw, colptrs part.

Parameters

dxdotdw – sparse matrix to which colptrs will be written

virtual void **fdxdotdw_rowvals**(*SUNMatrixWrapper* &dxdotdw)

Model specific implementation of fdxdotdw, rowvals part.

Parameters

dxdotdw – sparse matrix to which rowvals will be written

void **fdxdotdw**(*realtype* t, *const_N_Vector* x, *const_N_Vector* dx)

Sensitivity of dx/dt wrt model parameters w.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **dx** – Vector with the derivative states

virtual void **fM**(*realtype* *M, *realtype* const t, *realtype* const *x, *realtype* const *p, *realtype* const *k)

Model specific implementation of fM.

Parameters

- **M** – mass matrix
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector

Class Model_ODE

- Defined in file_include_amici_model_ode.h

Inheritance Relationships

Base Type

- `public amici::Model` (*Class Model*)

Class Documentation

class **Model_ODE** : public amici::*Model*

The *Model* class represents an AMICI ODE model.

The model does not contain any data, but represents the state of the model at a specific time t. The states must not always be in sync, but may be updated asynchronously.

Public Functions

Model_ODE() = default

default constructor

inline **Model_ODE**(*ModelDimensions* const &model_dimensions, *SimulationParameters* simulation_parameters, *SecondOrderMode* const o2mode, std::vector<*realtype*> const &idlist, std::vector<int> const &z2event, bool const pythonGenerated = false, int const ndxdotdp_explicit = 0, int const ndxdotdx_explicit = 0, int const w_recursion_depth = 0, std::map<*realtype*, std::vector<int>> state_independent_events = {})

Constructor with model dimensions.

Parameters

- **model_dimensions** – *Model* dimensions
- **simulation_parameters** – Simulation parameters
- **o2mode** – second order sensitivity mode
- **idlist** – indexes indicating algebraic components (DAE only)
- **z2event** – mapping of event outputs to events
- **pythonGenerated** – flag indicating matlab or python wrapping
- **ndxdotdp_explicit** – number of nonzero elements dxdotdp_explicit
- **ndxdotdx_explicit** – number of nonzero elements dxdotdx_explicit
- **w_recursion_depth** – Recursion depth of fw
- **state_independent_events** – Map of events with state-independent triggers functions, mapping trigger timepoints to event indices.

virtual void **fJ**(*realtype* t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xdot, SUNMatrix J) override

Dense Jacobian function.

Parameters

- **t** – time
- **cj** – scaling factor (inverse of timestep, DAE only)
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xdot** – values of residual function (unused)
- **J** – dense matrix to which values of the jacobian will be written

void **fJ**(*realtype* t, *const_N_Vector* x, *const_N_Vector* xdot, SUNMatrix J)

Implementation of fJ at the N_Vector level.

This function provides an interface to the model specific routines for the solver implementation as well as the *AmiVector* level implementation

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **xdot** – Vector with the right hand side
- **J** – Matrix to which the Jacobian will be written

virtual void **fJB**(*realtype* const t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xB, *AmiVector* const &dxB, *AmiVector* const &xBdot, SUNMatrix JB) override

Dense Jacobian function.

Parameters

- **t** – time
- **cj** – scaling factor (inverse of timestep, DAE only)
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **xBdot** – Vector with the adjoint right hand side (unused)
- **JB** – dense matrix to which values of the jacobian will be written

void **fJB**(*realtype* t, *const_N_Vector* x, *const_N_Vector* xB, *const_N_Vector* xBdot, SUNMatrix JB)

Implementation of fJB at the N_Vector level, this function provides an interface to the model specific routines for the solver implementation.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **xB** – Vector with the adjoint states

- **xBdot** – Vector with the adjoint right hand side
- **JB** – Matrix to which the Jacobian will be written

virtual void **fJSparse**(*realtype* t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xdot, SUNMatrix J) override

Sparse Jacobian function.

Parameters

- **t** – time
- **cj** – scaling factor (inverse of timestep, DAE only)
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xdot** – values of residual function (unused)
- **J** – sparse matrix to which values of the Jacobian will be written

void **fJSparse**(*realtype* t, *const_N_Vector* x, SUNMatrix J)

Implementation of fJSparse at the N_Vector level, this function provides an interface to the model specific routines for the solver implementation as well as the *AmiVector* level implementation.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **J** – Matrix to which the Jacobian will be written

virtual void **fJSparseB**(*realtype* const t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xB, *AmiVector* const &dxB, *AmiVector* const &xBdot, SUNMatrix JB) override

Sparse Jacobian function.

Parameters

- **t** – time
- **cj** – scaling factor (inverse of timestep, DAE only)
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **xBdot** – Vector with the adjoint right hand side (unused)
- **JB** – dense matrix to which values of the jacobian will be written

void **fJSparseB**(*realtype* t, *const_N_Vector* x, *const_N_Vector* xB, *const_N_Vector* xBdot, SUNMatrix JB)

Implementation of fJSparseB at the N_Vector level, this function provides an interface to the model specific routines for the solver implementation.

Parameters

- **t** – timepoint
- **x** – Vector with the states

- **xB** – Vector with the adjoint states
- **xBdot** – Vector with the adjoint right hand side
- **JB** – Matrix to which the Jacobian will be written

void **fJDiag**(*realtype* t, N_Vector JDiag, *const_N_Vector* x)

Implementation of fJDiag at the N_Vector level, this function provides an interface to the model specific routines for the solver implementation.

Parameters

- **t** – timepoint
- **JDiag** – Vector to which the Jacobian diagonal will be written
- **x** – Vector with the states

virtual void **fJDiag**(*realtype* t, *AmiVector* &JDiag, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx) override

Diagonal of the Jacobian (for preconditioning)

Parameters

- **t** – timepoint
- **JDiag** – Vector to which the Jacobian diagonal will be written
- **cj** – scaling factor, inverse of the step size
- **x** – Vector with the states
- **dx** – Vector with the derivative states

virtual void **fJv**(*realtype* t, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xdot, *AmiVector* const &v, *AmiVector* &nJv, *realtype* cj) override

Jacobian multiply function.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xdot** – values of residual function (unused)
- **v** – multiplication vector (unused)
- **nJv** – array to which result of multiplication will be written
- **cj** – scaling factor (inverse of timestep, DAE only)

void **fJv**(*const_N_Vector* v, N_Vector Jv, *realtype* t, *const_N_Vector* x)

Implementation of fJv at the N_Vector level.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **v** – Vector with which the Jacobian is multiplied
- **Jv** – Vector to which the Jacobian vector product will be written

void **fJvB**(*const_N_Vector* vB, N_Vector JvB, *realtype* t, *const_N_Vector* x, *const_N_Vector* xB)

Implementation of fJvB at the N_Vector level.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **xB** – Vector with the adjoint states
- **vB** – Vector with which the Jacobian is multiplied
- **JvB** – Vector to which the Jacobian vector product will be written

virtual void **froot**(*realtype* t, *AmiVector* const &x, *AmiVector* const &dx, gsl::span<*realtype*> root) override

Root function.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)
- **root** – array to which values of the root function will be written

void **froot**(*realtype* t, *const_N_Vector* x, gsl::span<*realtype*> root)

Implementation of froot at the N_Vector level This function provides an interface to the model specific routines for the solver implementation as well as the *AmiVector* level implementation.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **root** – array with root function values

virtual void **fxdot**(*realtype* t, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* &xdot) override

Residual function.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)
- **xdot** – array to which values of the residual function will be written

void **fxdot**(*realtype* t, *const_N_Vector* x, N_Vector xdot)

Implementation of fxdot at the N_Vector level, this function provides an interface to the model specific routines for the solver implementation as well as the *AmiVector* level implementation.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **xdot** – Vector with the right hand side

void **fxBdot**(*realtype* t, N_Vector x, N_Vector xB, N_Vector xBdot)

Implementation of fxBdot at the N_Vector level.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **xB** – Vector with the adjoint states
- **xBdot** – Vector with the adjoint right hand side

void **fqBdot**(*realtype* t, *const_N_Vector* x, *const_N_Vector* xB, N_Vector qBdot)

Implementation of fqBdot at the N_Vector level.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **xB** – Vector with the adjoint states
- **qBdot** – Vector with the adjoint quadrature right hand side

virtual void **fxBdot_ss**(*realtype* const t, *AmiVector* const &xB, *AmiVector* const&, *AmiVector* &xBdot) override

Residual function backward when running in steady state mode.

Parameters

- **t** – time
- **xB** – adjoint state
- **dxB** – time derivative of state (DAE only)
- **xBdot** – array to which values of the residual function will be written

void **fxBdot_ss**(*realtype* t, *const_N_Vector* xB, N_Vector xBdot) const

Implementation of fxBdot for steady state at the N_Vector level.

Parameters

- **t** – timepoint
- **xB** – Vector with the states
- **xBdot** – Vector with the adjoint right hand side

void **fqBdot_ss**(*realtype* t, N_Vector xB, N_Vector qBdot) const

Implementation of fqBdot for steady state case at the N_Vector level.

Parameters

- **t** – timepoint
- **xB** – Vector with the adjoint states
- **qBdot** – Vector with the adjoint quadrature right hand side

virtual void **fJSparseB_ss**(SUNMatrix JB) override

Sparse Jacobian function backward, steady state case.

Parameters

JB – sparse matrix to which values of the Jacobian will be written

virtual void **writeSteadystateJB**(*realtype* const t, *realtype* cj, *AmiVector* const &x, *AmiVector* const &dx, *AmiVector* const &xB, *AmiVector* const &dxB, *AmiVector* const &xBdot) override

Computes the sparse backward Jacobian for steadystate integration and writes it to the model member.

Parameters

- **t** – timepoint
- **cj** – scalar in Jacobian
- **x** – Vector with the states
- **dx** – Vector with the derivative states
- **xB** – Vector with the adjoint states
- **dxB** – Vector with the adjoint derivative states
- **xBdot** – Vector with the adjoint state right hand side

virtual void **fsxdot**(*realtype* t, *AmiVector* const &x, *AmiVector* const &dx, int ip, *AmiVector* const &sx, *AmiVector* const &sdx, *AmiVector* &sxdot) override

Sensitivity Residual function.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)
- **ip** – parameter index
- **sx** – sensitivity state
- **sdx** – time derivative of sensitivity state (DAE only)
- **sxdot** – array to which values of the sensitivity residual function will be written

void **fsxdot**(*realtype* t, *const_N_Vector* x, int ip, *const_N_Vector* sx, N_Vector sxdot)

Implementation of fsxdot at the N_Vector level.

Parameters

- **t** – timepoint
- **x** – Vector with the states
- **ip** – parameter index
- **sx** – Vector with the state sensitivities
- **sxdot** – Vector with the sensitivity right hand side

virtual std::unique_ptr<*Solver*> **getSolver**() override

Retrieves the solver object.

Returns

The *Solver* instance

Protected Functions

virtual void **fJSparse**(SUNMatrixContent_Sparse JSparse, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w, *realtype* const *dwdx)

Model specific implementation for fJSparse (Matlab)

Parameters

- **JSparse** – Matrix to which the Jacobian will be written
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **w** – vector with helper variables
- **dwdx** – derivative of w wrt x

virtual void **fJSparse**(*realtype* *JSparse, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w, *realtype* const *dwdx)

Model specific implementation for fJSparse, data only (Py)

Parameters

- **JSparse** – Matrix to which the Jacobian will be written
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **w** – vector with helper variables
- **dwdx** – derivative of w wrt x

virtual void **fJSparse_colptrs**(*SUNMatrixWrapper* &JSparse)

Model specific implementation for fJSparse, column pointers.

Parameters
JSparse – sparse matrix to which colptrs will be written

virtual void **fJSparse_rowvals**(*SUNMatrixWrapper* &JSparse)

Model specific implementation for fJSparse, row values.

Parameters
JSparse – sparse matrix to which rowvals will be written

virtual void **froot**(*realtype* *root, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *tcl)

Model specific implementation for froot.

Parameters

- **root** – values of the trigger function

- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **tcl** – total abundances for conservation laws

virtual void **fxdot**(*realtype* *xdot, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w) = 0

Model specific implementation for fxdot.

Parameters

- **xdot** – residual function
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **w** – vector with helper variables

virtual void **fdxdotdp**(*realtype* *dxdotdp, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, int ip, *realtype* const *w, *realtype* const *dwdp)

Model specific implementation of fdxdotdp, with w chainrule (Matlab)

Parameters

- **dxdotdp** – partial derivative xdot wrt p
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **ip** – parameter index
- **w** – vector with helper variables
- **dwdp** – derivative of w wrt p

virtual void **fdxdotdp_explicit**(*realtype* *dxdotdp_explicit, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w)

Model specific implementation of fdxdotdp_explicit, no w chainrule (Py)

Parameters

- **dxdotdp_explicit** – partial derivative xdot wrt p
- **t** – timepoint
- **x** – Vector with the states

- **p** – parameter vector
- **k** – constants vector
- **h** – Heaviside vector
- **w** – vector with helper variables

virtual void **fdxdotdp_explicit_colptrs**(*SUNMatrixWrapper* &dxdotdp)

Model specific implementation of fdxdotdp_explicit, colptrs part.

Parameters
dxdotdp – sparse matrix to which colptrs will be written

virtual void **fdxdotdp_explicit_rowvals**(*SUNMatrixWrapper* &dxdotdp)

Model specific implementation of fdxdotdp_explicit, rowvals part.

Parameters
dxdotdp – sparse matrix to which rowvals will be written

virtual void **fdxdotdx_explicit**(*realtype* *dxdotdx_explicit, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w)

Model specific implementation of fdxdotdx_explicit, no w chainrule (Py)

Parameters

- **dxdotdx_explicit** – partial derivative xdot wrt x
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector
- **k** – constants vector
- **h** – heavyside vector
- **w** – vector with helper variables

virtual void **fdxdotdx_explicit_colptrs**(*SUNMatrixWrapper* &dxdotdx)

Model specific implementation of fdxdotdx_explicit, colptrs part.

Parameters
dxdotdx – sparse matrix to which colptrs will be written

virtual void **fdxdotdx_explicit_rowvals**(*SUNMatrixWrapper* &dxdotdx)

Model specific implementation of fdxdotdx_explicit, rowvals part.

Parameters
dxdotdx – sparse matrix to which rowvals will be written

virtual void **fdxdotdw**(*realtype* *dxdotdw, *realtype* t, *realtype* const *x, *realtype* const *p, *realtype* const *k, *realtype* const *h, *realtype* const *w)

Model specific implementation of fdxdotdw, data part.

Parameters

- **dxdotdw** – partial derivative xdot wrt w
- **t** – timepoint
- **x** – Vector with the states
- **p** – parameter vector

- **k** – constants vector
- **h** – Heaviside vector
- **w** – vector with helper variables

virtual void **fdxdotdw_colptrs**(*SUNMatrixWrapper* &dxdotdw)

Model specific implementation of fdxdotdw, colptrs part.

Parameters
dxdotdw – sparse matrix to which colptrs will be written

virtual void **fdxdotdw_rowvals**(*SUNMatrixWrapper* &dxdotdw)

Model specific implementation of fdxdotdw, rowvals part.

Parameters
dxdotdw – sparse matrix to which rowvals will be written

void **fdxdotdw**(*realtype* t, *const_N_Vector* x)

Sensitivity of dx/dt wrt model parameters w.

Parameters

- **t** – timepoint
- **x** – Vector with the states

void **fdxdotdp**(*realtype* t, *const_N_Vector* x)

Explicit sensitivity of dx/dt wrt model parameters p

Parameters

- **t** – timepoint
- **x** – Vector with the states

virtual void **fdxdotdp**(*realtype* t, *AmiVector* const &x, *AmiVector* const &dx) override

Model-specific sparse implementation of explicit parameter derivative of right hand side.

Parameters

- **t** – time
- **x** – state
- **dx** – time derivative of state (DAE only)

Class ModelContext

- Defined in file_include_amici_rdata.h

Inheritance Relationships

Base Type

- `public amici::ContextManager` (*Class ContextManager*)

Class Documentation

class **ModelContext** : public amici::*ContextManager*

The *ModelContext* temporarily stores amici::Model::state and restores it when going out of scope.

Public Functions

explicit **ModelContext**(*Model* *model)

initialize backup of the original values.

Parameters
model –

ModelContext &**operator=**(*ModelContext* const &other) = delete

~ModelContext()

void **restore**()

Restore original state on constructor-supplied *amici::Model*. Will be called during destruction. Explicit call is generally not necessary.

Class NewtonFailure

- Defined in file_include_amici_exception.h

Inheritance Relationships

Base Type

- `public amici::AmiException` (*Class AmiException*)

Class Documentation

class **NewtonFailure** : public amici::*AmiException*

Newton failure exception.

This exception should be thrown when the steady state computation failed to converge for this exception we can assume that we can recover from the exception and return a solution struct to the user

Public Functions

NewtonFailure(int code, char const *function)

Constructor, simply calls *AmiException* constructor.

Parameters

- **function** – name of the function in which the error occurred
- **code** – error code

Public Members

int **error_code**

error code returned by solver

Class NewtonSolver

- Defined in file_include_amici_newton_solver.h

Inheritance Relationships

Derived Types

- `public amici::NewtonSolverDense` (*Class NewtonSolverDense*)
- `public amici::NewtonSolverSparse` (*Class NewtonSolverSparse*)

Class Documentation

class **NewtonSolver**

The *NewtonSolver* class sets up the linear solver for the Newton method.

Subclassed by *amici::NewtonSolverDense*, *amici::NewtonSolverSparse*

Public Functions

explicit **NewtonSolver**(*Model* const &model)

Initializes solver according to the dimensions in the provided model.

Parameters
model – pointer to the model object

void **getStep**(*AmiVector* &delta, *Model* &model, *SimulationState* const &state)

Computes the solution of one Newton iteration.

Parameters

- **delta** – containing the RHS of the linear system, will be overwritten by solution to the linear system
- **model** – pointer to the model instance
- **state** – current simulation state

void **computeNewtonSensis**(*AmiVectorArray* &sx, *Model* &model, *SimulationState* const &state)

Computes steady state sensitivities.

Parameters

- **sx** – pointer to state variable sensitivities
- **model** – pointer to the model instance
- **state** – current simulation state

virtual void **prepareLinearSystem**(*Model* &model, *SimulationState* const &state) = 0

Writes the Jacobian for the Newton iteration and passes it to the linear solver.

Parameters

- **model** – pointer to the model instance
- **state** – current simulation state

virtual void **prepareLinearSystemB**(*Model* &model, *SimulationState* const &state) = 0

Writes the Jacobian (JB) for the Newton iteration and passes it to the linear solver

Parameters

- **model** – pointer to the model instance
- **state** – current simulation state

virtual void **solveLinearSystem**(*AmiVector* &rhs) = 0

Solves the linear system for the Newton step.

Parameters

rhs – containing the RHS of the linear system, will be overwritten by solution to the linear system

virtual void **reinitialize**() = 0

Reinitialize the linear solver.

virtual bool **is_singular**(*Model* &model, *SimulationState* const &state) const = 0

Checks whether linear system is singular.

Parameters

- **model** – pointer to the model instance
- **state** – current simulation state

Returns

boolean indicating whether the linear system is singular (condition number < 1/machine precision)

virtual **~NewtonSolver**() = default

Public Static Functions

static std::unique_ptr<*NewtonSolver*> **getSolver**(*Solver* const &simulationSolver, *Model* const &model)

Factory method to create a *NewtonSolver* based on linsolType.

Parameters

- **simulationSolver** – solver with settings
- **model** – pointer to the model instance

Returns

solver *NewtonSolver* according to the specified linsolType

Protected Attributes

AmiVector **xdot_**

dummy rhs, used as dummy argument when computing J and JB

AmiVector **x_**

dummy state, attached to linear solver

AmiVector **xB_**

dummy adjoint state, used as dummy argument when computing JB

AmiVector **dxB_**

dummy differential adjoint state, used as dummy argument when computing JB

Class NewtonSolverDense

- Defined in file_include_amici_newton_solver.h

Inheritance Relationships

Base Type

- `public amici::NewtonSolver` (*Class NewtonSolver*)

Class Documentation

class **NewtonSolverDense** : public amici::*NewtonSolver*

The *NewtonSolverDense* provides access to the dense linear solver for the Newton method.

Public Functions

explicit **NewtonSolverDense**(*Model* const &model)

constructor for sparse solver

Parameters
model – model instance that provides problem dimensions

NewtonSolverDense(*NewtonSolverDense* const&) = delete

NewtonSolverDense &**operator=**(*NewtonSolverDense* const &other) = delete

~NewtonSolverDense() override

virtual void **solveLinearSystem**(*AmiVector* &rhs) override

Solves the linear system for the Newton step.

Parameters
rhs – containing the RHS of the linear system, will be overwritten by solution to the linear system

virtual void **prepareLinearSystem**(*Model* &model, *SimulationState* const &state) override

Writes the Jacobian for the Newton iteration and passes it to the linear solver.

Parameters

- **model** – pointer to the model instance
- **state** – current simulation state

virtual void **prepareLinearSystemB**(*Model* &model, *SimulationState* const &state) override

Writes the Jacobian (JB) for the Newton iteration and passes it to the linear solver

Parameters

- **model** – pointer to the model instance
- **state** – current simulation state

virtual void **reinitialize**() override

Reinitialize the linear solver.

virtual bool **is_singular**(*Model* &model, *SimulationState* const &state) const override

Checks whether linear system is singular.

Parameters

- **model** – pointer to the model instance
- **state** – current simulation state

Returns
boolean indicating whether the linear system is singular (condition number < 1/machine precision)

Class NewtonSolverSparse

- Defined in file_include_amici_newton_solver.h

Inheritance Relationships

Base Type

- public amici::NewtonSolver (*Class NewtonSolver*)

Class Documentation

class **NewtonSolverSparse** : public amici::*NewtonSolver*

The *NewtonSolverSparse* provides access to the sparse linear solver for the Newton method.

Public Functions

explicit **NewtonSolverSparse**(*Model* const &model)

constructor for dense solver

Parameters

model – model instance that provides problem dimensions

NewtonSolverSparse(*NewtonSolverSparse* const&) = delete

NewtonSolverSparse &**operator=**(*NewtonSolverSparse* const &other) = delete

~NewtonSolverSparse() override

virtual void **solveLinearSystem**(*AmiVector* &rhs) override

Solves the linear system for the Newton step.

Parameters

rhs – containing the RHS of the linear system, will be overwritten by solution to the linear system

virtual void **prepareLinearSystem**(*Model* &model, *SimulationState* const &state) override

Writes the Jacobian for the Newton iteration and passes it to the linear solver.

Parameters

- **model** – pointer to the model instance
- **state** – current simulation state

virtual void **prepareLinearSystemB**(*Model* &model, *SimulationState* const &state) override

Writes the Jacobian (JB) for the Newton iteration and passes it to the linear solver

Parameters

- **model** – pointer to the model instance
- **state** – current simulation state

virtual bool **is_singular**(*Model* &model, *SimulationState* const &state) const override

Checks whether linear system is singular.

Parameters

- **model** – pointer to the model instance
- **state** – current simulation state

Returns

boolean indicating whether the linear system is singular (condition number < 1/machine precision)

virtual void **reinitialize**() override

Reinitialize the linear solver.

Class ReturnData

- Defined in file_include_amici_rdata.h

Inheritance Relationships

Base Type

- `public amici::ModelDimensions` (*Struct ModelDimensions*)

Class Documentation

class **ReturnData** : public amici::*ModelDimensions*

Stores all data to be returned by amici::runAmiciSimulation.

NOTE: multi-dimensional arrays are stored in row-major order (C-style)

Public Functions

ReturnData() = default

Default constructor.

ReturnData(std::vector<*realtype*> ts, *ModelDimensions* const &model_dimensions, int nplist, int nmaxevent, int nt, int newton_maxsteps, std::vector<*ParameterScaling*> pscale, *SecondOrderMode* o2mode, *SensitivityOrder* sensi, *SensitivityMethod* sensi_meth, *RDataReporting* rdrm, bool quadratic_llh, bool sigma_res, *realtype* sigma_offset)

Constructor.

Parameters

- **ts** – see amici::SimulationParameters::ts
- **model_dimensions** – *Model* dimensions
- **nplist** – see amici::ModelDimensions::nplist
- **nmaxevent** – see amici::ModelDimensions::nmaxevent
- **nt** – see amici::ModelDimensions::nt
- **newton_maxsteps** – see amici::Solver::newton_maxsteps
- **pscale** – see *amici::SimulationParameters::pscale*
- **o2mode** – see amici::SimulationParameters::o2mode
- **sensi** – see amici::Solver::sensi
- **sensi_meth** – see amici::Solver::sensi_meth
- **rdrm** – see amici::Solver::rdata_reporting
- **quadratic_llh** – whether model defines a quadratic nllh and computing res, sres and FIM makes sense
- **sigma_res** – indicates whether additional residuals are to be added for each sigma
- **sigma_offset** – offset to ensure real-valuedness of sigma residuals

ReturnData(*Solver* const &solver, *Model* const &model)

constructor that uses information from model and solver to appropriately initialize fields

Parameters

- **solver** – solver instance
- **model** – model instance

~ReturnData() = default

void **processSimulationObjects**(*SteadystateProblem* const *preeq, *ForwardProblem* const *fwd, *BackwardProblem* const *bwd, *SteadystateProblem* const *posteq, *Model* &model, *Solver* const &solver, *ExpData* const *edata)

constructor that uses information from model and solver to appropriately initialize fields

Parameters

- **preeq** – simulated preequilibration problem, pass `nullptr` to ignore
- **fwd** – simulated forward problem, pass `nullptr` to ignore
- **bwd** – simulated backward problem, pass `nullptr` to ignore
- **posteq** – simulated postequilibration problem, pass `nullptr` to ignore
- **model** – matching model instance
- **solver** – matching solver instance
- **edata** – matching experimental data

Public Members

std::string **id**

Arbitrary (not necessarily unique) identifier.

std::vector<*realtype*> **ts**

timepoints (shape `nt`)

std::vector<*realtype*> **xdot**

time derivative (shape `nx`) evaluated at `t_last`.

std::vector<*realtype*> **J**

Jacobian of differential equation right hand side (shape `nx` x `nx`, row-major) evaluated at `t_last`.

std::vector<*realtype*> **w**

w data from the model (recurring terms in xdot, for imported SBML models from python, this contains the flux vector) (shape `nt` x `nw`, row major)

std::vector<*realtype*> **z**

event output (shape `nmaxevent` x `nz`, row-major)

std::vector<*realtype*> **sigmaz**

event output sigma standard deviation (shape `nmaxevent` x `nz`, row-major)

std::vector<*realtype*> **sz**

parameter derivative of event output (shape `nmaxevent` x `nplist` x `nz`, row-major)

std::vector<*realtype*> **ssigmaz**

parameter derivative of event output standard deviation (shape `nmaxevent` x `nplist` x `nz`, row-major)

std::vector<*realtype*> **rz**

event trigger output (shape `nmaxevent` x `nz`, row-major)

std::vector<*realtype*> **srz**

parameter derivative of event trigger output (shape `nmaxevent` x `nplist` x `nz`, row-major)

std::vector<*realtype*> **s2rz**

second-order parameter derivative of event trigger output (shape `nmaxevent` x `nztrue` x `nplist` x `nplist`, row-major)

std::vector<*realtype*> **x**

state (shape `nt` x `nx`, row-major)

std::vector<*realtype*> **sx**

parameter derivative of state (shape `nt` x `nplist` x `nx`, row-major)

std::vector<*realtype*> **y**

observable (shape `nt` x `ny`, row-major)

std::vector<*realtype*> **sigmay**

observable standard deviation (shape `nt` x `ny`, row-major)

std::vector<*realtype*> **sy**

parameter derivative of observable (shape `nt` x `nplist` x `ny`, row-major)

std::vector<*realtype*> **ssigmay**

parameter derivative of observable standard deviation (shape `nt` x `nplist` x `ny`, row-major)

std::vector<*realtype*> **res**

observable (shape `nt*ny`, row-major)

std::vector<*realtype*> **sres**

parameter derivative of residual (shape `nt*ny` x `nplist`, row-major)

std::vector<*realtype*> **FIM**

fisher information matrix (shape `nplist` x `nplist`, row-major)

std::vector<int> **numsteps**

number of integration steps forward problem (shape `nt`)

std::vector<int> **numstepsB**

number of integration steps backward problem (shape `nt`)

std::vector<int> **numrhsevals**

number of right hand side evaluations forward problem (shape `nt`)

std::vector<int> **numrhsevalsB**

number of right hand side evaluations backward problem (shape `nt`)

std::vector<int> **numerrtestfails**

number of error test failures forward problem (shape `nt`)

std::vector<int> **numerrtestfailsB**

number of error test failures backward problem (shape `nt`)

std::vector<int> **numnonlinsolvconvfails**

number of linear solver convergence failures forward problem (shape `nt`)

std::vector<int> **numnonlinsolvconvfailsB**

number of linear solver convergence failures backward problem (shape `nt`)

std::vector<int> **order**

employed order forward problem (shape `nt`)

double **cpu_time** = 0.0

computation time of forward solve [ms]

.. warning:: If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

double **cpu_timeB** = 0.0

computation time of backward solve [ms]

.. warning:: If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

double **cpu_time_total** = 0.0

total CPU time from entering runAmiciSimulation until exiting [ms]

.. warning:: If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

std::vector<*SteadyStateStatus*> **preeq_status**

flags indicating success of steady state solver (preequilibration)

double **preeq_cpu_time** = 0.0

computation time of the steady state solver [ms] (preequilibration)

.. warning:: If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

double **preeq_cpu_timeB** = 0.0

computation time of the steady state solver of the backward problem [ms] (preequilibration)

.. warning:: If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

std::vector<*SteadyStateStatus*> **posteq_status**

flags indicating success of steady state solver (postequilibration)

double **posteq_cpu_time** = 0.0

computation time of the steady state solver [ms] (postequilibration)

.. warning:: If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

double **posteq_cpu_timeB** = 0.0

computation time of the steady state solver of the backward problem [ms] (postequilibration)

.. warning:: If AMICI was built without boost, this tracks the CPU-time of the current process. Therefore, in a multi-threaded context, this value may be incorrect.

std::vector<int> **preeq_numsteps**

number of Newton steps for steady state problem (preequilibration) [newton, simulation, newton] (length = 3)

int **preeq_numstepsB** = 0

number of simulation steps for adjoint steady state problem (preequilibration) [== 0 if analytical solution worked, > 0 otherwise]

std::vector<int> **posteq_numsteps**

number of Newton steps for steady state problem (preequilibration) [newton, simulation, newton] (shape 3) (postequilibration)

int **posteq_numstepsB** = 0

number of simulation steps for adjoint steady state problem (postequilibration) [== 0 if analytical solution worked, > 0 otherwise]

realtype **preeq_t** = NAN

time when steadystate was reached via simulation (preequilibration)

realtype **preeq_wrms** = NAN

weighted root-mean-square of the rhs when steadystate was reached (preequilibration)

realtype **posteq_t** = NAN

time when steadystate was reached via simulation (postequilibration)

realtype **posteq_wrms** = NAN

weighted root-mean-square of the rhs when steadystate was reached (postequilibration)

std::vector<*realtype*> **x0**

initial state (shape `nx`)

std::vector<*realtype*> **x_ss**

preequilibration steady state (shape `nx`)

std::vector<*realtype*> **sx0**

initial sensitivities (shape `nplist` x `nx`, row-major)

std::vector<*realtype*> **sx_ss**

preequilibration sensitivities (shape `nplist` x `nx`, row-major)

realtype **llh** = 0.0

log-likelihood value

realtype **chi2** = 0.0

χ^2 value

std::vector<*realtype*> **sllh**

parameter derivative of log-likelihood (shape `nplist`)

std::vector<*realtype*> **s2llh**

second-order parameter derivative of log-likelihood (shape `nJ-1` x `nplist`, row-major)

int **status** = *AMICI_NOT_RUN*

Simulation status code.

One of:

- AMICI_SUCCESS, indicating successful simulation
- AMICI_MAX_TIME_EXCEEDED, indicating that the simulation did not finish within the allowed time (see *Solver*.{set,get}MaxTime)
- AMICI_ERROR, indicating that some error occurred during simulation (a more detailed error message will have been printed).
- AMICI_NOT_RUN, if no simulation was started

int **nx** = {0}

number of states (alias `nx_rdata`, kept for backward compatibility)

int **nxtrue** = {0}

number of states in the unaugmented system (alias nxtrue_rdata, kept for backward compatibility)

int **nplist** = {0}

number of parameter for which sensitivities were requested

int **nmaxevent** = {0}

maximal number of occurring events (for every event type)

int **nt** = {0}

number of considered timepoints

int **newton_maxsteps** = {0}

maximal number of newton iterations for steady state calculation

std::vector<*ParameterScaling*> **pscale**

scaling of parameterization

SecondOrderMode **o2mode** = {*SecondOrderMode*::*none*}

flag indicating whether second-order sensitivities were requested

SensitivityOrder **sensi** = {*SensitivityOrder*::*none*}

sensitivity order

SensitivityMethod **sensi_meth** = {*SensitivityMethod*::*none*}

sensitivity method

RDataReporting **rdata_reporting** = {*RDataReporting*::*full*}

reporting mode

bool **sigma_res**

boolean indicating whether residuals for standard deviations have been added

std::vector<*LogItem*> **messages**

log messages

realtype **t_last** = {std::numeric_limits<*realtype*>::quiet_NaN()}

The final internal time of the solver.

Protected Functions

void **initializeLikelihoodReporting**(bool quadratic_llh)

initializes storage for likelihood reporting mode

Parameters

quadratic_llh – whether model defines a quadratic nllh and computing res, sres and FIM makes sense.

void **initializeResidualReporting**(bool enable_res)

initializes storage for residual reporting mode

Parameters

enable_res – whether residuals are to be computed

void **initializeFullReporting**(bool enable_fim)

initializes storage for full reporting mode

Parameters

enable_fim – whether FIM Hessian approximation is to be computed

void **initializeObjectiveFunction**(bool enable_chi2)

initialize values for chi2 and llh and derivatives

Parameters

enable_chi2 – whether chi2 values are to be computed

void **processPreEquilibration**(*SteadystateProblem* const &preeq, *Model* &model)

extracts data from a preequilibration *SteadystateProblem*

Parameters

- **preeq** – *SteadystateProblem* for preequilibration
- **model** – *Model* instance to compute return values

void **processPostEquilibration**(*SteadystateProblem* const &posteq, *Model* &model, *ExpData* const *edata)

extracts data from a preequilibration *SteadystateProblem*

Parameters

- **posteq** – *SteadystateProblem* for postequilibration
- **model** – *Model* instance to compute return values
- **edata** – *ExpData* instance containing observable data

void **processForwardProblem**(*ForwardProblem* const &fwd, *Model* &model, *ExpData* const *edata)

extracts results from forward problem

Parameters

- **fwd** – forward problem
- **model** – model that was used for forward simulation
- **edata** – *ExpData* instance containing observable data

void **processBackwardProblem**(*ForwardProblem* const &fwd, *BackwardProblem* const &bwd, *SteadystateProblem* const *preeq, *Model* &model)

extracts results from backward problem

Parameters

- **fwd** – forward problem
- **bwd** – backward problem
- **preeq** – *SteadystateProblem* for preequilibration
- **model** – model that was used for forward/backward simulation

void **processSolver**(*Solver* const &solver)

extracts results from solver

Parameters

solver – solver that was used for forward/backward simulation

template<class **T**>
inline void **storeJacobianAndDerivativeInReturnData**(*T* const &problem, *Model* &model)

Evaluates and stores the Jacobian and right hand side at final timepoint.

Parameters

- **problem** – forward problem or steadystate problem
- **model** – model that was used for forward/backward simulation

void **readSimulationState**(*SimulationState* const &state, *Model* &model)

sets member variables and model state according to provided simulation state

Parameters

- **state** – simulation state provided by Problem
- **model** – model that was used for forward/backward simulation

void **fres**(int it, *Model* &model, *ExpData* const &edata)

Residual function.

Parameters

- **it** – time index
- **model** – model that was used for forward/backward simulation
- **edata** – *ExpData* instance containing observable data

void **fchi2**(int it, *ExpData* const &edata)

Chi-squared function.

Parameters

- **it** – time index
- **edata** – *ExpData* instance containing observable data

void **fsres**(int it, *Model* &model, *ExpData* const &edata)

Residual sensitivity function.

Parameters

- **it** – time index
- **model** – model that was used for forward/backward simulation
- **edata** – *ExpData* instance containing observable data

void **fFIM**(int it, *Model* &model, *ExpData* const &edata)

Fisher information matrix function.

Parameters

- **it** – time index
- **model** – model that was used for forward/backward simulation
- **edata** – *ExpData* instance containing observable data

void **invalidate**(int it_start)

Set likelihood, state variables, outputs and respective sensitivities to NaN (typically after integration failure)

Parameters

it_start – time index at which to start invalidating

void **invalidateLLH**()

Set likelihood and chi2 to NaN (typically after integration failure)

void **invalidateSLLH**()

Set likelihood sensitivities to NaN (typically after integration failure)

void **applyChainRuleFactorToSimulationResults**(*Model* const &model)

applies the chain rule to account for parameter transformation in the sensitivities of simulation results

Parameters

model – *Model* from which the *ReturnData* was obtained

inline bool **computingFSA**() const

Checks whether forward sensitivity analysis is performed.

Returns

boolean indicator

void **getDataOutput**(int it, *Model* &model, *ExpData* const *edata)

Extracts output information for data-points, expects that x_solver_ and sx_solver_ were set appropriately.

Parameters

- **it** – timepoint index
- **model** – model that was used in forward solve
- **edata** – *ExpData* instance carrying experimental data

void **getDataSensisFSA**(int it, *Model* &model, *ExpData* const *edata)

Extracts data information for forward sensitivity analysis, expects that x_solver_ and sx_solver_ were set appropriately.

Parameters

- **it** – index of current timepoint
- **model** – model that was used in forward solve
- **edata** – *ExpData* instance carrying experimental data

void **getEventOutput**(*realtype* t, std::vector<int> const rootidx, *Model* &model, *ExpData* const *edata)

Extracts output information for events, expects that x_solver_ and sx_solver_ were set appropriately.

Parameters

- **t** – event timepoint

- **rootidx** – information about which roots fired (1 indicating fired, 0/-1 for not)
- **model** – model that was used in forward solve
- **edata** – *ExpData* instance carrying experimental data

void **getEventSensisFSA**(int ie, *realtype* t, *Model* &model, *ExpData* const *edata)

Extracts event information for forward sensitivity analysis, expects that x_solver_ and sx_solver_ were set appropriately.

Parameters

- **ie** – index of event type
- **t** – event timepoint
- **model** – model that was used in forward solve
- **edata** – *ExpData* instance carrying experimental data

void **handleSx0Backward**(*Model* const &model, *SteadystateProblem* const &preeq, std::vector<*realtype*> &llhS0, *AmiVector* &xQB) const

Updates contribution to likelihood from quadratures (xQB), if preequilibration was run in adjoint mode.

Parameters

- **model** – model that was used for forward/backward simulation
- **preeq** – *SteadystateProblem* for preequilibration
- **llhS0** – contribution to likelihood for initial state sensitivities of preequilibration
- **xQB** – vector with quadratures from adjoint computation

void **handleSx0Forward**(*Model* const &model, std::vector<*realtype*> &llhS0, *AmiVector* &xB) const

Updates contribution to likelihood for initial state sensitivities (llhS0), if no preequilibration was run or if forward sensitivities were used.

Parameters

- **model** – model that was used for forward/backward simulation
- **llhS0** – contribution to likelihood for initial state sensitivities
- **xB** – vector with final adjoint state (excluding conservation laws)

Protected Attributes

realtype **sigma_offset**

offset for sigma_residuals

realtype **t_**

timepoint for model evaluation

AmiVector **x_solver_**

partial state vector, excluding states eliminated from conservation laws

AmiVector **dx_solver_**

partial time derivative of state vector, excluding states eliminated from conservation laws

AmiVectorArray **sx_solver_**

partial sensitivity state vector array, excluding states eliminated from conservation laws

AmiVector **x_rdata_**

full state vector, including states eliminated from conservation laws

AmiVectorArray **sx_rdata_**

full sensitivity state vector array, including states eliminated from conservation laws

std::vector<int> **nroots_**

array of number of found roots for a certain event type (shape `ne`)

Friends

template<class **Archive**>
friend void **serialize**(*Archive* &ar, *ReturnData* &r, unsigned int version)

Serialize *ReturnData* (see boost::serialization::serialize)

Parameters

- **ar** – Archive to serialize to
- **r** – Data to serialize
- **version** – Version number

Class SetupFailure

- Defined in file_include_amici_exception.h

Inheritance Relationships

Base Type

- `public amici::AmiException` (*Class AmiException*)

Class Documentation

class **SetupFailure** : public amici::*AmiException*

Setup failure exception.

This exception should be thrown when the solver setup failed for this exception we can assume that we cannot recover from the exception and an error will be thrown

Public Functions

explicit **SetupFailure**(char const *fmt, ...)

Constructor with printf style interface.

Parameters

- **fmt** – error message with printf format
- **...** – printf formatting variables

Class SimulationParameters

- Defined in file_include_amici_simulation_parameters.h

Inheritance Relationships

Derived Type

- `public amici::ExpData` (*Class ExpData*)

Class Documentation

class **SimulationParameters**

Container for various simulation parameters.

Subclassed by *amici::ExpData*

Public Functions

SimulationParameters() = default

inline explicit **SimulationParameters**(std::vector<*realtype*> timepoints)

Constructor.

Parameters

timepoints – Timepoints for which simulation results are requested

inline **SimulationParameters**(std::vector<*realtype*> fixedParameters, std::vector<*realtype*> parameters)

Constructor.

Parameters

- **fixedParameters** – *Model* constants
- **parameters** – *Model* parameters

inline **SimulationParameters**(std::vector<*realtype*> fixedParameters, std::vector<*realtype*> parameters, std::vector<int> plist)

Constructor.

Parameters

- **fixedParameters** – *Model* constants

- **parameters** – *Model* parameters
- **plist** – *Model* parameter indices w.r.t. which sensitivities are to be computed

inline **SimulationParameters**(std::vector<*realtype*> timepoints, std::vector<*realtype*> fixedParameters, std::vector<*realtype*> parameters)

Constructor.

Parameters

- **timepoints** – Timepoints for which simulation results are requested
- **fixedParameters** – *Model* constants
- **parameters** – *Model* parameters

void **reinitializeAllFixedParameterDependentInitialStatesForPresimulation**(int nx_rdata)

Set reinitialization of all states based on model constants for presimulation (only meaningful if preequilibration is performed).

Convenience function to populate `reinitialization_state_idxs_presim` and `reinitialization_state_idxs_sim`

Parameters

nx_rdata – Number of states (*Model::nx_rdata*)

void **reinitializeAllFixedParameterDependentInitialStatesForSimulation**(int nx_rdata)

Set reinitialization of all states based on model constants for the 'main' simulation (only meaningful if presimulation or preequilibration is performed).

Convenience function to populate `reinitialization_state_idxs_presim` and `reinitialization_state_idxs_sim`

Parameters

nx_rdata – Number of states (*Model::nx_rdata*)

void **reinitializeAllFixedParameterDependentInitialStates**(int nx_rdata)

Set reinitialization of all states based on model constants for all simulation phases.

Convenience function to populate `reinitialization_state_idxs_presim` and `reinitialization_state_idxs_sim`

Parameters

nx_rdata – Number of states (*Model::nx_rdata*)

Public Members

std::vector<*realtype*> **fixedParameters**

Model constants.

Vector of size *Model::nk()* or empty

std::vector<*realtype*> **fixedParametersPreequilibration**

Model constants for pre-equilibration.

Vector of size *Model::nk()* or empty.

std::vector<*realtype*> **fixedParametersPresimulation**

Model constants for pre-simulation.

Vector of size *Model::nk()* or empty.

std::vector<*realtype*> **parameters**

Model parameters.

Vector of size *Model::np()* or empty with parameter scaled according to SimulationParameter::pscale.

std::vector<*realtype*> **x0**

Initial state.

Vector of size Model::nx() or empty

std::vector<*realtype*> **sx0**

Initial state sensitivities.

Dimensions: Model::nx() * *Model::nplist()*, Model::nx() * ExpData::plist.size(), if *ExpData::plist* is not empty, or empty

std::vector<*ParameterScaling*> **pscale**

Parameter scales.

Vector of parameter scale of size *Model::np()*, indicating how/if each parameter is to be scaled.

std::vector<int> **plist**

Parameter indices w.r.t. which to compute sensitivities.

realtype **tstart_** = {0.0}

Starting time of the simulation.

Output timepoints are absolute timepoints, independent of t_{start}. For output timepoints $t < t_{start}$, the initial state will be returned.

realtype **t_presim** = {0.0}

Duration of pre-simulation.

If this is > 0, presimulation will be performed from (model->t0 - t_presim) to model->t0 using the fixedParameters in fixedParametersPresimulation

std::vector<*realtype*> **ts_**

Timepoints for which model state/outputs/... are requested.

Vector of timepoints.

bool **reinitializeFixedParameterInitialStates** = {false}

Flag indicating whether reinitialization of states depending on fixed parameters is activated.

std::vector<int> **reinitialization_state_idxs_presim**

Indices of states to be reinitialized based on provided presimulation constants / fixed parameters.

std::vector<int> **reinitialization_state_idxs_sim**

Indices of states to be reinitialized based on provided constants / fixed parameters.

Class Solver

- Defined in file_include_amici_solver.h

Inheritance Relationships

Derived Types

- `public amici::CVodeSolver` (*Class CVodeSolver*)
- `public amici::IDASolver` (*Class IDASolver*)

Class Documentation

class **Solver**

The *Solver* class provides a generic interface to CVODES and IDAS solvers, individual realizations are realized in the *CVodeSolver* and the *IDASolver* class. All transient private/protected members (CVODES/IDAS memory, interface variables and status flags) are specified as mutable and not included in serialization or equality checks. No solver setting parameter should be marked mutable.

NOTE: Any changes in data members here must be propagated to copy ctor, equality operator, serialization functions in serialization.h, and amici::hdf5::(read/write)SolverSettings(From/To)HDF5 in hdf5.cpp.

Subclassed by *amici::CVodeSolver*, *amici::IDASolver*

Public Types

using **user_data_type** = std::pair<*Model**, *Solver* const*>

Type of what is passed to Sundials solvers as user_data

using **free_solver_ptr** = std::function<void(void*)>

Type of the function to free a raw sundials solver pointer

Public Functions

Solver() = default

Default constructor.

Solver(*Solver* const &other)

Solver copy constructor.

Parameters
other –

virtual **~Solver**() = default

virtual *Solver* ***clone**() const = 0

Clone this instance.

Returns
The clone

int **run**(*realtype* tout) const

runs a forward simulation until the specified timepoint

Parameters
tout – next timepoint

Returns
status flag

int **step**(*realtype* tout) const

makes a single step in the simulation

Parameters
tout – next timepoint

Returns
status flag

void **runB**(*realtype* tout) const

runs a backward simulation until the specified timepoint

Parameters
tout – next timepoint

void **setup**(*realtype* t0, *Model* *model, *AmiVector* const &x0, *AmiVector* const &dx0, *AmiVectorArray* const &sx0, *AmiVectorArray* const &sdx0) const

Initializes the ami memory object and applies specified options.

Parameters

- **t0** – initial timepoint
- **model** – pointer to the model instance
- **x0** – initial states
- **dx0** – initial derivative states
- **sx0** – initial state sensitivities
- **sdx0** – initial derivative state sensitivities

void **setupB**(int *which, *realtype* tf, *Model* *model, *AmiVector* const &xB0, *AmiVector* const &dxB0, *AmiVector* const &xQB0) const

Initializes the AMI memory object for the backwards problem.

Parameters

- **which** – index of the backward problem, will be set by this routine
- **tf** – final timepoint (initial timepoint for the bwd problem)
- **model** – pointer to the model instance
- **xB0** – initial adjoint states
- **dxB0** – initial adjoint derivative states

- **xQB0** – initial adjoint quadratures

void **setupSteadystate**(*realtype* const t0, *Model* *model, *AmiVector* const &x0, *AmiVector* const &dx0, *AmiVector* const &xB0, *AmiVector* const &dxB0, *AmiVector* const &xQ0) const

Initializes the ami memory for quadrature computation.

Parameters

- **t0** – initial timepoint
- **model** – pointer to the model instance
- **x0** – initial states
- **dx0** – initial derivative states
- **xB0** – initial adjoint states
- **dxB0** – initial derivative adjoint states
- **xQ0** – initial quadrature vector

void **updateAndReinitStatesAndSensitivities**(*Model* *model) const

Reinitializes state and respective sensitivities (if necessary) according to changes in fixedParameters.

Parameters

model – pointer to the model instance

virtual void **getRootInfo**(int *rootsfound) const = 0

getRootInfo extracts information which event occurred

Parameters

rootsfound – array with flags indicating whether the respective event occurred

virtual void **calcIC**(*realtype* tout1) const = 0

Calculates consistent initial conditions, assumes initial states to be correct (DAE only)

Parameters

tout1 – next timepoint to be computed (sets timescale)

virtual void **calcICB**(int which, *realtype* tout1) const = 0

Calculates consistent initial conditions for the backwards problem, assumes initial states to be correct (DAE only)

Parameters

- **which** – identifier of the backwards problem
- **tout1** – next timepoint to be computed (sets timescale)

virtual void **solveB**(*realtype* tBout, int itaskB) const = 0

Solves the backward problem until a predefined timepoint (adjoint only)

Parameters

- **tBout** – timepoint until which simulation should be performed
- **itaskB** – task identifier, can be CV_NORMAL or CV_ONE_STEP

virtual void **turnOffRootFinding**() const = 0

Disable rootfinding.

SensitivityMethod **getSensitivityMethod**() const

Return current sensitivity method.

Returns
method enum

void **setSensitivityMethod**(*SensitivityMethod* sensi_meth)

Set sensitivity method.

Parameters
sensi_meth –

SensitivityMethod **getSensitivityMethodPreequilibration**() const

Return current sensitivity method during preequilibration.

Returns
method enum

void **setSensitivityMethodPreequilibration**(*SensitivityMethod* sensi_meth_preeq)

Set sensitivity method for preequilibration.

Parameters
sensi_meth_preeq –

void **switchForwardSensisOff**() const

Disable forward sensitivity integration (used in steady state sim)

int **getNewtonMaxSteps**() const

Get maximum number of allowed Newton steps for steady state computation.

Returns

void **setNewtonMaxSteps**(int newton_maxsteps)

Set maximum number of allowed Newton steps for steady state computation.

Parameters
newton_maxsteps –

NewtonDampingFactorMode **getNewtonDampingFactorMode**() const

Get a state of the damping factor used in the Newton solver.

Returns

void **setNewtonDampingFactorMode**(*NewtonDampingFactorMode* dampingFactorMode)

Turn on/off a damping factor in the Newton method.

Parameters
dampingFactorMode –

double **getNewtonDampingFactorLowerBound**() const

Get a lower bound of the damping factor used in the Newton solver.

Returns

void **setNewtonDampingFactorLowerBound**(double dampingFactorLowerBound)

Set a lower bound of the damping factor in the Newton solver.

Parameters
dampingFactorLowerBound –

SensitivityOrder **getSensitivityOrder**() const

Get sensitivity order.

Returns
sensitivity order

void **setSensitivityOrder**(*SensitivityOrder* sensi)

Set the sensitivity order.

Parameters
sensi – sensitivity order

double **getRelativeTolerance**() const

Get the relative tolerances for the forward problem.

Same tolerance is used for the backward problem if not specified differently via setRelativeToleranceASA.

Returns
relative tolerances

void **setRelativeTolerance**(double rtol)

Sets the relative tolerances for the forward problem.

Same tolerance is used for the backward problem if not specified differently via setRelativeToleranceASA.

Parameters
rtol – relative tolerance (non-negative number)

double **getAbsoluteTolerance**() const

Get the absolute tolerances for the forward problem.

Same tolerance is used for the backward problem if not specified differently via setAbsoluteToleranceASA.

Returns
absolute tolerances

void **setAbsoluteTolerance**(double atol)

Sets the absolute tolerances for the forward problem.

Same tolerance is used for the backward problem if not specified differently via setAbsoluteToleranceASA.

Parameters
atol – absolute tolerance (non-negative number)

double **getRelativeToleranceFSA**() const

Returns the relative tolerances for the forward sensitivity problem.

Returns
relative tolerances

void **setRelativeToleranceFSA**(double rtol)

Sets the relative tolerances for the forward sensitivity problem.

Parameters
rtol – relative tolerance (non-negative number)

double **getAbsoluteToleranceFSA**() const

Returns the absolute tolerances for the forward sensitivity problem.

Returns
absolute tolerances

void **setAbsoluteToleranceFSA**(double atol)

Sets the absolute tolerances for the forward sensitivity problem.

Parameters
atol – absolute tolerance (non-negative number)

double **getRelativeToleranceB**() const

Returns the relative tolerances for the adjoint sensitivity problem.

Returns
relative tolerances

void **setRelativeToleranceB**(double rtol)

Sets the relative tolerances for the adjoint sensitivity problem.

Parameters
rtol – relative tolerance (non-negative number)

double **getAbsoluteToleranceB**() const

Returns the absolute tolerances for the backward problem for adjoint sensitivity analysis.

Returns
absolute tolerances

void **setAbsoluteToleranceB**(double atol)

Sets the absolute tolerances for the backward problem for adjoint sensitivity analysis.

Parameters
atol – absolute tolerance (non-negative number)

double **getRelativeToleranceQuadratures**() const

Returns the relative tolerance for the quadrature problem.

Returns
relative tolerance

void **setRelativeToleranceQuadratures**(double rtol)

sets the relative tolerance for the quadrature problem

Parameters
rtol – relative tolerance (non-negative number)

double **getAbsoluteToleranceQuadratures**() const

returns the absolute tolerance for the quadrature problem

Returns
absolute tolerance

void **setAbsoluteToleranceQuadratures**(double atol)

sets the absolute tolerance for the quadrature problem

Parameters
atol – absolute tolerance (non-negative number)

double **getSteadyStateToleranceFactor**() const

returns the steady state simulation tolerance factor.

Steady state simulation tolerances are the product of the simulation tolerances and this factor, unless manually set with `set(Absolute/Relative)ToleranceSteadyState()`.

Returns
steady state simulation tolerance factor

void **setSteadyStateToleranceFactor**(double factor)

set the steady state simulation tolerance factor.

Steady state simulation tolerances are the product of the simulation tolerances and this factor, unless manually set with `set(Absolute/Relative)ToleranceSteadyState()`.

Parameters
factor – tolerance factor (non-negative number)

double **getRelativeToleranceSteadyState**() const

returns the relative tolerance for the steady state problem

Returns
relative tolerance

void **setRelativeToleranceSteadyState**(double rtol)

sets the relative tolerance for the steady state problem

Parameters
rtol – relative tolerance (non-negative number)

double **getAbsoluteToleranceSteadyState**() const

returns the absolute tolerance for the steady state problem

Returns
absolute tolerance

void **setAbsoluteToleranceSteadyState**(double atol)

sets the absolute tolerance for the steady state problem

Parameters
atol – absolute tolerance (non-negative number)

double **getSteadyStateSensiToleranceFactor**() const

returns the steady state sensitivity simulation tolerance factor.

Steady state sensitivity simulation tolerances are the product of the sensitivity simulation tolerances and this factor, unless manually set with `set(Absolute/Relative)ToleranceSteadyStateSensi()`.

Returns
steady state simulation tolerance factor

void **setSteadyStateSensiToleranceFactor**(double factor)

set the steady state sensitivity simulation tolerance factor.

Steady state sensitivity simulation tolerances are the product of the sensitivity simulation tolerances and this factor, unless manually set with `set(Absolute/Relative)ToleranceSteadyStateSensi()`.

Parameters
factor – tolerance factor (non-negative number)

double **getRelativeToleranceSteadyStateSensi**() const

returns the relative tolerance for the sensitivities of the steady state problem

Returns
relative tolerance

void **setRelativeToleranceSteadyStateSensi**(double rtol)

sets the relative tolerance for the sensitivities of the steady state problem

Parameters
rtol – relative tolerance (non-negative number)

double **getAbsoluteToleranceSteadyStateSensi**() const

returns the absolute tolerance for the sensitivities of the steady state problem

Returns
absolute tolerance

void **setAbsoluteToleranceSteadyStateSensi**(double atol)

sets the absolute tolerance for the sensitivities of the steady state problem

Parameters
atol – absolute tolerance (non-negative number)

long int **getMaxSteps**() const

returns the maximum number of solver steps for the forward problem

Returns
maximum number of solver steps

void **setMaxSteps**(long int maxsteps)

sets the maximum number of solver steps for the forward problem

Parameters
maxsteps – maximum number of solver steps (positive number)

double **getMaxTime**() const

Returns the maximum time allowed for integration.

Returns
Time in seconds

void **setMaxTime**(double maxtime)

Set the maximum CPU time allowed for integration.

Parameters
maxtime – Time in seconds. Zero means infinite time.

void **startTimer**() const

Start timer for tracking integration time.

bool **timeExceeded**(int interval = 1) const

Check whether maximum integration time was exceeded.

Parameters
interval – Only check the time every `interval` ths call to avoid potentially relatively expensive syscalls

Returns
True if the maximum integration time was exceeded, false otherwise.

long int **getMaxStepsBackwardProblem**() const

returns the maximum number of solver steps for the backward problem

Returns
maximum number of solver steps

void **setMaxStepsBackwardProblem**(long int maxsteps)

sets the maximum number of solver steps for the backward problem

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Note: default behaviour (100 times the value for the forward problem) can be restored by passing maxsteps=0

Parameters
maxsteps – maximum number of solver steps (non-negative number)

LinearMultistepMethod **getLinearMultistepMethod**() const

returns the linear system multistep method

Returns
linear system multistep method

void **setLinearMultistepMethod**(*LinearMultistepMethod* lmm)

sets the linear system multistep method

Parameters
lmm – linear system multistep method

NonlinearSolverIteration **getNonlinearSolverIteration**() const

returns the nonlinear system solution method

Returns

void **setNonlinearSolverIteration**(*NonlinearSolverIteration* iter)

sets the nonlinear system solution method

Parameters
iter – nonlinear system solution method

InterpolationType **getInterpolationType**() const

getInterpolationType

Returns

void **setInterpolationType**(*InterpolationType* interpType)

sets the interpolation of the forward solution that is used for the backwards problem

Parameters
interpType – interpolation type

int **getStateOrdering**() const

Gets KLU / SuperLUMT state ordering mode.

Returns
State-ordering as integer according to *SUNLinSolKLU::StateOrdering* or SUNLinSolSuperLUMT::StateOrdering (which differ).

void **setStateOrdering**(int ordering)

Sets KLU / SuperLUMT state ordering mode.

This only applies when linsol is set to LinearSolver::KLU or LinearSolver::SuperLUMT. Mind the difference between *SUNLinSolKLU::StateOrdering* and SUNLinSolSuperLUMT::StateOrdering.

Parameters
ordering – state ordering

bool **getStabilityLimitFlag**() const

returns stability limit detection mode

Returns
stldet can be false (deactivated) or true (activated)

void **setStabilityLimitFlag**(bool stldet)

set stability limit detection mode

Parameters
stldet – can be false (deactivated) or true (activated)

LinearSolver **getLinearSolver**() const

getLinearSolver

Returns

void **setLinearSolver**(*LinearSolver* linsol)

setLinearSolver

Parameters
linsol –

InternalSensitivityMethod **getInternalSensitivityMethod**() const

returns the internal sensitivity method

Returns
internal sensitivity method

void **setInternalSensitivityMethod**(*InternalSensitivityMethod* ism)

sets the internal sensitivity method

Parameters
ism – internal sensitivity method

RDataReporting **getReturnDataReportingMode**() const

returns the *ReturnData* reporting mode

Returns
ReturnData reporting mode

void **setReturnDataReportingMode**(*RDataReporting* rdrm)

sets the *ReturnData* reporting mode

Parameters
rdrm – *ReturnData* reporting mode

void **writeSolution**(*realtype* *t, *AmiVector* &x, *AmiVector* &dx, *AmiVectorArray* &sx, *AmiVector* &xQ) const

write solution from forward simulation

Parameters

- **t** – time
- **x** – state
- **dx** – derivative state
- **sx** – state sensitivity
- **xQ** – quadrature

void **writeSolutionB**(*realtype* *t, *AmiVector* &xB, *AmiVector* &dxB, *AmiVector* &xQB, int which) const

write solution from backward simulation

Parameters

- **t** – time

- **xB** – adjoint state
- **dxB** – adjoint derivative state
- **xQB** – adjoint quadrature
- **which** – index of adjoint problem

AmiVector const &**getState**(*realtype* t) const

Access state solution at time t.

Parameters
t – time

Returns
x or interpolated solution dky

AmiVector const &**getDerivativeState**(*realtype* t) const

Access derivative state solution at time t.

Parameters
t – time

Returns
dx or interpolated solution dky

AmiVectorArray const &**getStateSensitivity**(*realtype* t) const

Access state sensitivity solution at time t.

Parameters
t – time

Returns
(interpolated) solution sx

AmiVector const &**getAdjointState**(int which, *realtype* t) const

Access adjoint solution at time t.

Parameters

- **which** – adjoint problem index
- **t** – time

Returns
(interpolated) solution xB

AmiVector const &**getAdjointDerivativeState**(int which, *realtype* t) const

Access adjoint derivative solution at time t.

Parameters

- **which** – adjoint problem index
- **t** – time

Returns
(interpolated) solution dxB

AmiVector const &**getAdjointQuadrature**(int which, *realtype* t) const

Access adjoint quadrature solution at time t.

Parameters

- **which** – adjoint problem index

- **t** – time

Returns
(interpolated) solution xQB

AmiVector const &**getQuadrature**(*realtype* t) const

Access quadrature solution at time t.

Parameters
t – time

Returns
(interpolated) solution xQ

virtual void **reInit**(*realtype* t0, *AmiVector* const &yy0, *AmiVector* const &yp0) const = 0

Reinitializes the states in the solver after an event occurrence.

Parameters

- **t0** – reinitialization timepoint
- **yy0** – initial state variables
- **yp0** – initial derivative state variables (DAE only)

virtual void **sensReInit**(*AmiVectorArray* const &yyS0, *AmiVectorArray* const &ypS0) const = 0

Reinitializes the state sensitivities in the solver after an event occurrence.

Parameters

- **yyS0** – new state sensitivity
- **ypS0** – new derivative state sensitivities (DAE only)

virtual void **sensToggleOff**() const = 0

Switches off computation of state sensitivities without deallocating the memory for sensitivities.

virtual void **reInitB**(int which, *realtype* tB0, *AmiVector* const &yyB0, *AmiVector* const &ypB0) const = 0

Reinitializes the adjoint states after an event occurrence.

Parameters

- **which** – identifier of the backwards problem
- **tB0** – reinitialization timepoint
- **yyB0** – new adjoint state
- **ypB0** – new adjoint derivative state

virtual void **quadReInitB**(int which, *AmiVector* const &yQB0) const = 0

Reinitialize the adjoint states after an event occurrence.

Parameters

- **which** – identifier of the backwards problem
- **yQB0** – new adjoint quadrature state

realtype **gett**() const

current solver timepoint

Returns
t

realtype **getCpuTime**() const

Reads out the CPU time needed for forward solve.

Returns
cpu_time

realtype **getCpuTimeB**() const

Reads out the CPU time needed for backward solve.

Returns
cpu_timeB

int **nx**() const

number of states with which the solver was initialized

Returns
x.getLength()

int **nplist**() const

number of parameters with which the solver was initialized

Returns
sx.getLength()

int **nquad**() const

number of quadratures with which the solver was initialized

Returns
xQB.getLength()

inline bool **computingFSA**() const

check if FSA is being computed

Returns
flag

inline bool **computingASA**() const

check if ASA is being computed

Returns
flag

void **resetDiagnosis**() const

Resets vectors containing diagnosis information.

void **storeDiagnosis**() const

Stores diagnosis information from solver memory block for forward problem.

void **storeDiagnosisB**(int which) const

Stores diagnosis information from solver memory block for backward problem.

Parameters
which – identifier of the backwards problem

inline std::vector<int> const &**getNumSteps**() const

Accessor ns.

Returns
ns

inline std::vector<int> const &**getNumStepsB**() const

Accessor nsB.

Returns
nsB

inline std::vector<int> const &**getNumRhsEvals**() const

Accessor nrhs.

Returns
nrhs

inline std::vector<int> const &**getNumRhsEvalsB**() const

Accessor nrhsB.

Returns
nrhsB

inline std::vector<int> const &**getNumErrTestFails**() const

Accessor netf.

Returns
netf

inline std::vector<int> const &**getNumErrTestFailsB**() const

Accessor netfB.

Returns
netfB

inline std::vector<int> const &**getNumNonlinSolvConvFails**() const

Accessor nnlscf.

Returns
nnlscf

inline std::vector<int> const &**getNumNonlinSolvConvFailsB**() const

Accessor nnlscfB.

Returns
nnlscfB

inline std::vector<int> const &**getLastOrder**() const

Accessor order.

Returns
order

inline bool **getNewtonStepSteadyStateCheck**() const

Returns how convergence checks for steadystate computation are performed. If activated, convergence checks are limited to every 25 steps in the simulation solver to limit performance impact.

Returns
boolean flag indicating newton step (true) or the right hand side (false)

inline bool **getSensiSteadyStateCheck**() const

Returns how convergence checks for steadystate computation are performed.

Returns
boolean flag indicating state and sensitivity equations (true) or only state variables (false).

inline void **setNewtonStepSteadyStateCheck**(bool flag)

Sets how convergence checks for steadystate computation are performed.

Parameters
flag – boolean flag to pick newton step (true) or the right hand side (false, default)

inline void **setSensiSteadyStateCheck**(bool flag)

Sets for which variables convergence checks for steadystate computation are performed.

Parameters
flag – boolean flag to pick state and sensitivity equations (true, default) or only state variables (false).

void **setMaxNonlinIters**(int max_nonlin_iters)

Set the maximum number of nonlinear solver iterations permitted per step.

Parameters
max_nonlin_iters – maximum number of nonlinear solver iterations

int **getMaxNonlinIters**() const

Get the maximum number of nonlinear solver iterations permitted per step.

Returns
maximum number of nonlinear solver iterations

void **setMaxConvFails**(int max_conv_fails)

Set the maximum number of nonlinear solver convergence failures permitted per step.

Parameters
max_conv_fails – maximum number of nonlinear solver convergence

int **getMaxConvFails**() const

Get the maximum number of nonlinear solver convergence failures permitted per step.

Returns
maximum number of nonlinear solver convergence

void **setConstraints**(std::vector<*realtype*> const &constraints)

Set constraints on the model state.

See https://sundials.readthedocs.io/en/latest/cvode/Usage/index.html#c.CVodeSetConstraints.

Parameters
constraints –

inline std::vector<*realtype*> **getConstraints**() const

Get constraints on the model state.

Returns
constraints

void **setMaxStepSize**(*realtype* max_step_size)

Set the maximum step size.

Parameters
max_step_size – maximum step size. `0.0` means no limit.

realtype **getMaxStepSize**() const

Get the maximum step size.

Returns
maximum step size

Public Members

Logger ***logger** = nullptr

logger

Protected Functions

virtual void **setStopTime**(*realtype* tstop) const = 0

Sets a timepoint at which the simulation will be stopped.

Parameters
tstop – timepoint until which simulation should be performed

virtual int **solve**(*realtype* tout, int itask) const = 0

Solves the forward problem until a predefined timepoint.

Parameters

- **tout** – timepoint until which simulation should be performed
- **itask** – task identifier, can be CV_NORMAL or CV_ONE_STEP

Returns
status flag indicating success of execution

virtual int **solveF**(*realtype* tout, int itask, int *ncheckPtr) const = 0

Solves the forward problem until a predefined timepoint (adjoint only)

Parameters

- **tout** – timepoint until which simulation should be performed
- **itask** – task identifier, can be CV_NORMAL or CV_ONE_STEP
- **ncheckPtr** – pointer to a number that counts the internal checkpoints

Returns
status flag indicating success of execution

virtual void **reInitPostProcessF**(*realtype* tnext) const = 0

reInitPostProcessF postprocessing of the solver memory after a discontinuity in the forward problem

Parameters
tnext – next timepoint (defines integration direction)

virtual void **reInitPostProcessB**(*realtype* tnext) const = 0

reInitPostProcessB postprocessing of the solver memory after a discontinuity in the backward problem

Parameters
tnext – next timepoint (defines integration direction)

virtual void **getSens**() const = 0

extracts the state sensitivity at the current timepoint from solver memory and writes it to the sx member variable

virtual void **getB**(int which) const = 0

extracts the adjoint state at the current timepoint from solver memory and writes it to the xB member variable

Parameters
which – index of the backwards problem

virtual void **getQuadB**(int which) const = 0

extracts the adjoint quadrature state at the current timepoint from solver memory and writes it to the xQB member variable

Parameters
which – index of the backwards problem

virtual void **getQuad**(*realtype* &t) const = 0

extracts the quadrature at the current timepoint from solver memory and writes it to the xQ member variable

Parameters
t – timepoint for quadrature extraction

virtual void **init**(*realtype* t0, *AmiVector* const &x0, *AmiVector* const &dx0) const = 0

Initializes the states at the specified initial timepoint.

Parameters

- **t0** – initial timepoint
- **x0** – initial states
- **dx0** – initial derivative states

virtual void **initSteadystate**(*realtype* t0, *AmiVector* const &x0, *AmiVector* const &dx0) const = 0

Initializes the states at the specified initial timepoint.

Parameters

- **t0** – initial timepoint
- **x0** – initial states
- **dx0** – initial derivative states

virtual void **sensInit1**(*AmiVectorArray* const &sx0, *AmiVectorArray* const &sdx0) const = 0

Initializes the forward sensitivities.

Parameters

- **sx0** – initial states sensitivities
- **sdx0** – initial derivative states sensitivities

virtual void **binit**(int which, *realtype* tf, *AmiVector* const &xB0, *AmiVector* const &dxB0) const = 0

Initialize the adjoint states at the specified final timepoint.

Parameters

- **which** – identifier of the backwards problem
- **tf** – final timepoint
- **xB0** – initial adjoint state
- **dxB0** – initial adjoint derivative state

virtual void **qbinit**(int which, *AmiVector* const &xQB0) const = 0

Initialize the quadrature states at the specified final timepoint.

Parameters

- **which** – identifier of the backwards problem

- **xQB0** – initial adjoint quadrature state

virtual void **rootInit**(int ne) const = 0

Initializes the rootfinding for events.

Parameters
ne – number of different events

void **initializeNonLinearSolverSens**(*Model* const *model) const

Initialize non-linear solver for sensitivities.

Parameters
model – *Model* instance

virtual void **setDenseJacFn**() const = 0

Set the dense Jacobian function.

virtual void **setSparseJacFn**() const = 0

sets the sparse Jacobian function

virtual void **setBandJacFn**() const = 0

sets the banded Jacobian function

virtual void **setJacTimesVecFn**() const = 0

sets the Jacobian vector multiplication function

virtual void **setDenseJacFnB**(int which) const = 0

sets the dense Jacobian function

Parameters
which – identifier of the backwards problem

virtual void **setSparseJacFnB**(int which) const = 0

sets the sparse Jacobian function

Parameters
which – identifier of the backwards problem

virtual void **setBandJacFnB**(int which) const = 0

sets the banded Jacobian function

Parameters
which – identifier of the backwards problem

virtual void **setJacTimesVecFnB**(int which) const = 0

sets the Jacobian vector multiplication function

Parameters
which – identifier of the backwards problem

virtual void **setSparseJacFn_ss**() const = 0

sets the sparse Jacobian function for backward steady state case

virtual void **allocateSolver**() const = 0

Create specifies solver method and initializes solver memory for the forward problem.

virtual void **setSStolerances**(double rtol, double atol) const = 0

sets scalar relative and absolute tolerances for the forward problem

Parameters

- **rtol** – relative tolerances
- **atol** – absolute tolerances

virtual void **setSensSStolerances**(double rtol, double const *atol) const = 0

activates sets scalar relative and absolute tolerances for the sensitivity variables

Parameters

- **rtol** – relative tolerances
- **atol** – array of absolute tolerances for every sensitivity variable

virtual void **setSensErrCon**(bool error_corr) const = 0

SetSensErrCon specifies whether error control is also enforced for sensitivities for the forward problem

Parameters
error_corr – activation flag

virtual void **setQuadErrConB**(int which, bool flag) const = 0

Specifies whether error control is also enforced for the backward quadrature problem.

Parameters

- **which** – identifier of the backwards problem
- **flag** – activation flag

virtual void **setQuadErrCon**(bool flag) const = 0

Specifies whether error control is also enforced for the forward quadrature problem.

Parameters
flag – activation flag

virtual void **setErrHandlerFn**() const = 0

Attaches the error handler function (errMsgIdAndTxt) to the solver.

virtual void **setUserData**() const = 0

Attaches the user data to the forward problem.

virtual void **setUserDataB**(int which) const = 0

attaches the user data to the backward problem

Parameters
which – identifier of the backwards problem

virtual void **setMaxNumSteps**(long int mxsteps) const = 0

specifies the maximum number of steps for the forward problem

---

Note: in contrast to the SUNDIALS method, this sets the overall maximum, not the maximum between output times.

Parameters
mxsteps – number of steps

virtual void **setMaxNumStepsB**(int which, long int mxstepsB) const = 0

specifies the maximum number of steps for the forward problem

---

Note: in contrast to the SUNDIALS method, this sets the overall maximum, not the maximum between output times.

Parameters

- **which** – identifier of the backwards problem
- **mxstepsB** – number of steps

virtual void **setStabLimDet**(int stldet) const = 0

activates stability limit detection for the forward problem

Parameters

stldet – flag for stability limit detection (TRUE or FALSE)

virtual void **setStabLimDetB**(int which, int stldet) const = 0

activates stability limit detection for the backward problem

Parameters

- **which** – identifier of the backwards problem
- **stldet** – flag for stability limit detection (TRUE or FALSE)

virtual void **setId**(*Model* const *model) const = 0

specify algebraic/differential components (DAE only)

Parameters

model – model specification

virtual void **setSuppressAlg**(bool flag) const = 0

deactivates error control for algebraic components (DAE only)

Parameters

flag – deactivation flag

virtual void **setSensParams**(*realtype* const *p, *realtype* const *pbar, int const *plist) const = 0

specifies the scaling and indexes for sensitivity computation

Parameters

- **p** – parameters
- **pbar** – parameter scaling constants
- **plist** – parameter index list

virtual void **getDky**(*realtype* t, int k) const = 0

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order

virtual void **getDkyB**(*realtype* t, int k, int which) const = 0

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order
- **which** – index of backward problem

virtual void **getSensDky**(*realtype* t, int k) const = 0

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order

virtual void **getQuadDkyB**(*realtype* t, int k, int which) const = 0

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order
- **which** – index of backward problem

virtual void **getQuadDky**(*realtype* t, int k) const = 0

interpolates the (derivative of the) solution at the requested timepoint

Parameters

- **t** – timepoint
- **k** – derivative order

virtual void **adjInit**() const = 0

initializes the adjoint problem

virtual void **quadInit**(*AmiVector* const &xQ0) const = 0

initializes the quadratures

Parameters

xQ0 – vector with initial values for xQ

virtual void **allocateSolverB**(int *which) const = 0

Specifies solver method and initializes solver memory for the backward problem.

Parameters

which – identifier of the backwards problem

virtual void **setSStolerancesB**(int which, *realtype* relTolB, *realtype* absTolB) const = 0

sets relative and absolute tolerances for the backward problem

Parameters

- **which** – identifier of the backwards problem
- **relTolB** – relative tolerances
- **absTolB** – absolute tolerances

virtual void **quadSStolerancesB**(int which, *realtype* reltolQB, *realtype* abstolQB) const = 0

sets relative and absolute tolerances for the quadrature backward problem

Parameters

- **which** – identifier of the backwards problem
- **reltolQB** – relative tolerances
- **abstolQB** – absolute tolerances

virtual void **quadSStolerances**(*realtype* reltolQB, *realtype* abstolQB) const = 0

sets relative and absolute tolerances for the quadrature problem

Parameters

- **reltolQB** – relative tolerances
- **abstolQB** – absolute tolerances

virtual void **getNumSteps**(void const *ami_mem, long int *numsteps) const = 0

reports the number of solver steps

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **numsteps** – output array

virtual void **getNumRhsEvals**(void const *ami_mem, long int *numrhsevals) const = 0

reports the number of right hand evaluations

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **numrhsevals** – output array

virtual void **getNumErrTestFails**(void const *ami_mem, long int *numerrtestfails) const = 0

reports the number of local error test failures

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **numerrtestfails** – output array

virtual void **getNumNonlinSolvConvFails**(void const *ami_mem, long int *numnonlinsolvconvfails) const = 0

reports the number of nonlinear convergence failures

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **numnonlinsolvconvfails** – output array

virtual void **getLastOrder**(void const *ami_mem, int *order) const = 0

Reports the order of the integration method during the last internal step.

Parameters

- **ami_mem** – pointer to the solver memory instance (can be from forward or backward problem)
- **order** – output array

void **initializeLinearSolver**(*Model* const *model) const

Initializes and sets the linear solver for the forward problem.

Parameters
model – pointer to the model object

void **initializeNonLinearSolver**() const

Sets the non-linear solver.

virtual void **setLinearSolver**() const = 0

Sets the linear solver for the forward problem.

virtual void **setLinearSolverB**(int which) const = 0

Sets the linear solver for the backward problem.

Parameters
which – index of the backward problem

virtual void **setNonLinearSolver**() const = 0

Set the non-linear solver for the forward problem.

virtual void **setNonLinearSolverB**(int which) const = 0

Set the non-linear solver for the backward problem.

Parameters
which – index of the backward problem

virtual void **setNonLinearSolverSens**() const = 0

Set the non-linear solver for sensitivities.

void **initializeLinearSolverB**(*Model* const *model, int which) const

Initializes the linear solver for the backward problem.

Parameters

- **model** – pointer to the model object
- **which** – index of the backward problem

void **initializeNonLinearSolverB**(int which) const

Initializes the non-linear solver for the backward problem.

Parameters
which – index of the backward problem

virtual *Model* const ***getModel**() const = 0

Accessor function to the model stored in the user data

Returns
user data model

bool **getInitDone**() const

checks whether memory for the forward problem has been allocated

Returns
proxy for solverMemory->(cv|ida)_MallocDone

bool **getSensInitDone**() const

checks whether memory for forward sensitivities has been allocated

Returns
proxy for solverMemory->(cv|ida)_SensMallocDone

bool **getAdjInitDone**() const

checks whether memory for forward interpolation has been allocated

Returns
proxy for solverMemory->(cv|ida)_adjMallocDone

bool **getInitDoneB**(int which) const

checks whether memory for the backward problem has been allocated

Parameters
which – adjoint problem index

Returns
proxy for solverMemoryB->(cv|ida)_MallocDone

bool **getQuadInitDoneB**(int which) const

checks whether memory for backward quadratures has been allocated

Parameters
which – adjoint problem index

Returns
proxy for solverMemoryB->(cv|ida)_QuadMallocDone

bool **getQuadInitDone**() const

checks whether memory for quadratures has been allocated

Returns
proxy for solverMemory->(cv|ida)_QuadMallocDone

virtual void **diag**() const = 0

attaches a diagonal linear solver to the forward problem

virtual void **diagB**(int which) const = 0

attaches a diagonal linear solver to the backward problem

Parameters
which – identifier of the backwards problem

void **resetMutableMemory**(int nx, int nplist, int nquad) const

resets solverMemory and solverMemoryB

Parameters

- **nx** – new number of state variables
- **nplist** – new number of sensitivity parameters
- **nquad** – new number of quadratures (only differs from nplist for higher order sensitivity computation)

virtual void ***getAdjBmem**(void *ami_mem, int which) const = 0

Retrieves the solver memory instance for the backward problem.

Parameters

- **which** – identifier of the backwards problem

- **ami_mem** – pointer to the forward solver memory instance

Returns
A (void *) pointer to the CVODES memory allocated for the backward problem.

void **applyTolerances**() const

updates solver tolerances according to the currently specified member variables

void **applyTolerancesFSA**() const

updates FSA solver tolerances according to the currently specified member variables

void **applyTolerancesASA**(int which) const

updates ASA solver tolerances according to the currently specified member variables

Parameters
which – identifier of the backwards problem

void **applyQuadTolerancesASA**(int which) const

updates ASA quadrature solver tolerances according to the currently specified member variables

Parameters
which – identifier of the backwards problem

void **applyQuadTolerances**() const

updates quadrature solver tolerances according to the currently specified member variables

void **applySensitivityTolerances**() const

updates all sensitivity solver tolerances according to the currently specified member variables

virtual void **apply_constraints**() const

Apply the constraints to the solver.

void **setInitDone**() const

sets that memory for the forward problem has been allocated

void **setSensInitDone**() const

sets that memory for forward sensitivities has been allocated

void **setSensInitOff**() const

sets that memory for forward sensitivities has not been allocated

void **setAdjInitDone**() const

sets that memory for forward interpolation has been allocated

void **setInitDoneB**(int which) const

sets that memory for the backward problem has been allocated

Parameters
which – adjoint problem index

void **setQuadInitDoneB**(int which) const

sets that memory for backward quadratures has been allocated

Parameters
which – adjoint problem index

void **setQuadInitDone**() const

sets that memory for quadratures has been allocated

void **checkSensitivityMethod**(*SensitivityMethod* const sensi_meth, bool preequilibration) const

Sets sensitivity method (for simulation or preequilibration)

Parameters

- **sensi_meth** – new value for sensi_meth[_preeq]
- **preequilibration** – flag indicating preequilibration or simulation

virtual void **apply_max_nonlin_iters**() const = 0

Apply the maximum number of nonlinear solver iterations permitted per step.

virtual void **apply_max_conv_fails**() const = 0

Apply the maximum number of nonlinear solver convergence failures permitted per step.

virtual void **apply_max_step_size**() const = 0

Apply the allowed maximum stepsize to the solver.

Protected Attributes

mutable std::unique_ptr<void, *free_solver_ptr*> **solver_memory_**

pointer to solver memory block

mutable std::vector<std::unique_ptr<void, *free_solver_ptr*>> **solver_memory_B_**

pointer to solver memory block

mutable *user_data_type* **user_data**

Sundials user_data

InternalSensitivityMethod **ism_** = {*InternalSensitivityMethod*::*simultaneous*}

internal sensitivity method flag used to select the sensitivity solution method. Only applies for Forward Sensitivities.

LinearMultistepMethod **lmm_** = {*LinearMultistepMethod*::*BDF*}

specifies the linear multistep method.

NonlinearSolverIteration **iter_** = {*NonlinearSolverIteration*::*newton*}

specifies the type of nonlinear solver iteration

InterpolationType **interp_type_** = {*InterpolationType*::*polynomial*}

interpolation type for the forward problem solution which is then used for the backwards problem.

long int **maxsteps_** = {10000}

maximum number of allowed integration steps

std::chrono::duration<double, std::ratio<1>> **maxtime_** = {0}

Maximum CPU-time for integration in seconds

mutable *CpuTimer* **simulation_timer_**

Time at which solver timer was started

mutable std::unique_ptr<*SUNLinSolWrapper*> **linear_solver_**
: linear solver for the forward problem

mutable std::unique_ptr<*SUNLinSolWrapper*> **linear_solver_B_**
: linear solver for the backward problem

mutable std::unique_ptr<*SUNNonLinSolWrapper*> **non_linear_solver_**
: non-linear solver for the forward problem

mutable std::unique_ptr<*SUNNonLinSolWrapper*> **non_linear_solver_B_**
: non-linear solver for the backward problem

mutable std::unique_ptr<*SUNNonLinSolWrapper*> **non_linear_solver_sens_**
: non-linear solver for the sensitivities

mutable bool **solver_was_called_F_** = {false}
: flag indicating whether the forward solver has been called

mutable bool **solver_was_called_B_** = {false}
: flag indicating whether the backward solver has been called

mutable *AmiVector* **x_** = {0}
: state (dimension: nx_solver)

mutable *AmiVector* **dky_** = {0}
: state interface variable (dimension: nx_solver)

mutable *AmiVector* **dx_** = {0}
: state derivative dummy (dimension: nx_solver)

mutable *AmiVectorArray* **sx_** = {0, 0}
: state sensitivities interface variable (dimension: nx_solver x nplist)

mutable *AmiVectorArray* **sdx_** = {0, 0}
: state derivative sensitivities dummy (dimension: nx_solver x nplist)

mutable *AmiVector* **xB_** = {0}
: adjoint state interface variable (dimension: nx_solver)

mutable *AmiVector* **dxB_** = {0}
: adjoint derivative dummy variable (dimension: nx_solver)

mutable *AmiVector* **xQB_** = {0}
: adjoint quadrature interface variable (dimension: nJ x nplist)

mutable *AmiVector* **xQ_** = {0}

forward quadrature interface variable (dimension: nx_solver)

mutable *realtype* **t_** = {std::nan("")}

integration time of the forward problem

mutable bool **force_reinit_postprocess_F_** = {false}

flag to force reInitPostProcessF before next call to solve

mutable bool **force_reinit_postprocess_B_** = {false}

flag to force reInitPostProcessB before next call to solveB

mutable bool **sens_initialized_** = {false}

flag indicating whether sensInit1 was called

mutable *AmiVector* **constraints_**

Vector of constraints on the solution

Friends

template<class **Archive**>
friend void **serialize**(*Archive* &ar, *Solver* &s, unsigned int version)

Serialize *Solver* (see boost::serialization::serialize)

Parameters

- **ar** – Archive to serialize to
- **s** – Data to serialize
- **version** – Version number

friend bool **operator==**(*Solver* const &a, *Solver* const &b)

Check equality of data members excluding solver memory.

Parameters

- **a** –
- **b** –

Returns

Class SteadystateProblem

- Defined in file_include_amici_steadystateproblem.h

Class Documentation

class **SteadystateProblem**

The *SteadystateProblem* class solves a steady-state problem using Newton's method and falls back to integration on failure.

Public Functions

explicit **SteadystateProblem**(*Solver* const &solver, *Model* const &model)

constructor

Parameters

- **solver** – *Solver* instance
- **model** – *Model* instance

void **workSteadyStateProblem**(*Solver* const &solver, *Model* &model, int it)

Handles steady state computation in the forward case: tries to determine the steady state of the ODE system and computes steady state sensitivities if requested.

Parameters

- **solver** – pointer to the solver object
- **model** – pointer to the model object
- **it** – integer with the index of the current time step

void **workSteadyStateBackwardProblem**(*Solver* const &solver, *Model* &model, *BackwardProblem* const *bwd)

Integrates over the adjoint state backward in time by solving a linear system of equations, which gives the analytical solution. Computes the gradient via adjoint steady state sensitivities

Parameters

- **solver** – pointer to the solver object
- **model** – pointer to the model object
- **bwd** – backward problem

inline *SimulationState* const &**getFinalSimulationState**() const

Returns the stored *SimulationState*.

Returns
stored *SimulationState*

inline *AmiVector* const &**getEquilibrationQuadratures**() const

Returns the quadratures from pre- or postequilibration.

Returns
xQB Vector with quadratures

inline *AmiVector* const &**getState**() const

Returns state at steadystate.

Returns
x

inline *AmiVectorArray* const &**getStateSensitivity**() const

Returns state sensitivity at steadystate.

Returns
sx

inline std::vector<*realtype*> const &**getDJydx**() const

Accessor for dJydx.

Returns
dJydx

inline double **getCPUTime**() const

Accessor for run_time of the forward problem.

Returns
run_time

inline double **getCPUTimeB**() const

Accessor for run_time of the backward problem.

Returns
run_time

inline std::vector<*SteadyStateStatus*> const &**getSteadyStateStatus**() const

Accessor for steady_state_status.

Returns
steady_state_status

inline *realtype* **getSteadyStateTime**() const

Get model time at which steadystate was found through simulation.

Returns
t

inline *realtype* **getResidualNorm**() const

Accessor for wrms.

Returns
wrms

inline std::vector<int> const &**getNumSteps**() const

Accessor for numsteps.

Returns
numsteps

inline int **getNumStepsB**() const

Accessor for numstepsB.

Returns
numstepsB

void **getAdjointUpdates**(*Model* &model, *ExpData* const &edata)

computes adjoint updates dJydx according to provided model and expdata

Parameters

- **model** – *Model* instance
- **edata** – experimental data

inline *AmiVector* const &**getAdjointState**() const

Return the adjoint state.

Returns
xB adjoint state

inline *AmiVector* const &**getAdjointQuadrature**() const

Accessor for xQB.

Returns
xQB

inline bool **hasQuadrature**() const

Accessor for hasQuadrature_.

Returns
hasQuadrature_

bool **checkSteadyStateSuccess**() const

computes adjoint updates dJydx according to provided model and expdata

Returns
convergence of steady state solver

Class SUNLinSolBand

- Defined in file_include_amici_sundials_linsol_wrapper.h

Inheritance Relationships

Base Type

- `public amici::SUNLinSolWrapper` (*Class SUNLinSolWrapper*)

Class Documentation

class **SUNLinSolBand** : public amici::*SUNLinSolWrapper*

SUNDIALS band direct solver.

Public Functions

SUNLinSolBand(N_Vector x, SUNMatrix A)

Create solver using existing matrix A without taking ownership of A.

Parameters

- **x** – A template for cloning vectors needed within the solver.
- **A** – square matrix

SUNLinSolBand(*AmiVector* const &x, int ubw, int lbw)

Create new band solver and matrix A.

Parameters

- **x** – A template for cloning vectors needed within the solver.
- **ubw** – upper bandwidth of band matrix A
- **lbw** – lower bandwidth of band matrix A

virtual SUNMatrix **getMatrix**() const override

Get the matrix A (matrix solvers only).

Returns

A

Class SUNLinSolDense

- Defined in file_include_amici_sundials_linsol_wrapper.h

Inheritance Relationships

Base Type

- `public amici::SUNLinSolWrapper` (*Class SUNLinSolWrapper*)

Class Documentation

class **SUNLinSolDense** : public amici::*SUNLinSolWrapper*

SUNDIALS dense direct solver.

Public Functions

explicit **SUNLinSolDense**(*AmiVector* const &x)

Create dense solver.

Parameters

x – A template for cloning vectors needed within the solver.

virtual SUNMatrix **getMatrix**() const override

Get the matrix A (matrix solvers only).

Returns

A

Class SUNLinSolKLU

- Defined in file_include_amici_sundials_linsol_wrapper.h

Inheritance Relationships

Base Type

- `public amici::SUNLinSolWrapper` (*Class SUNLinSolWrapper*)

Class Documentation

class **SUNLinSolKLU** : public amici::*SUNLinSolWrapper*

SUNDIALS KLU sparse direct solver.

Public Types

enum class **StateOrdering**

KLU state reordering (different from SuperLUMT ordering!)

Values:

enumerator **AMD**

enumerator **COLAMD**

enumerator **natural**

Public Functions

SUNLinSolKLU(N_Vector x, SUNMatrix A)

Create KLU solver with given matrix.

Parameters

- **x** – A template for cloning vectors needed within the solver.
- **A** – sparse matrix

SUNLinSolKLU(*AmiVector* const &x, int nnz, int sparsetype, *StateOrdering* ordering)

Create KLU solver and matrix to operate on.

Parameters

- **x** – A template for cloning vectors needed within the solver.
- **nnz** – Number of non-zeros in matrix A
- **sparsetype** – Sparse matrix type (CSC_MAT, CSR_MAT)
- **ordering** –

virtual SUNMatrix **getMatrix**() const override

Get the matrix A (matrix solvers only).

Returns
A

void **reInit**(int nnz, int reinit_type)

Reinitializes memory and flags for a new factorization (symbolic and numeric) to be conducted at the next solver setup call.

For more details see sunlinsol/sunlinsol_klu.h

Parameters

- **nnz** – Number of non-zeros
- **reinit_type** – SUNKLU_REINIT_FULL or SUNKLU_REINIT_PARTIAL

void **setOrdering**(*StateOrdering* ordering)

Sets the ordering used by KLU for reducing fill in the linear solve.

Parameters
ordering –

Class SUNLinSolPCG

- Defined in file_include_amici_sundials_linsol_wrapper.h

Inheritance Relationships

Base Type

- public amici::SUNLinSolWrapper (*Class SUNLinSolWrapper*)

Class Documentation

class **SUNLinSolPCG** : public amici::*SUNLinSolWrapper*

SUNDIALS scaled preconditioned CG (Conjugate Gradient method) (PCG) solver.

Public Functions

SUNLinSolPCG(N_Vector y, int pretype, int maxl)

Create PCG solver.

Parameters

- **y** –
- **pretype** – Preconditioner type (PREC_NONE, PREC_LEFT, PREC_RIGHT, PREC_BOTH)
- **maxl** – Maximum number of solver iterations

int **setATimes**(void *A_data, ATimesFn ATimes)

Sets the function pointer for ATimes (see sundials/sundials_linearsolver.h).

Parameters

- **A_data** –
- **ATimes** –

Returns

int **setPreconditioner**(void *P_data, PSetupFn Pset, PSolveFn Psol)

Sets function pointers for PSetup and PSolve routines inside of iterative linear solver objects (see sundials/sundials_linearsolver.h).

Parameters

- **P_data** –
- **Pset** –
- **Psol** –

Returns

int **setScalingVectors**(N_Vector s, N_Vector nul)

Sets pointers to left/right scaling vectors for the linear system solve (see sundials/sundials_linearsolver.h).

Parameters

- **s** –
- **nul** –

Returns

int **getNumIters**() const

Returns the number of linear iterations performed in the last 'Solve' call.

Returns
Number of iterations

realtype **getResNorm**() const

Returns the final residual norm from the last 'Solve' call.

Returns
residual norm

N_Vector **getResid**() const

Get preconditioned initial residual (see sundials/sundials_linearsolver.h).

Returns

Class SUNLinSolSPBCGS

- Defined in file_include_amici_sundials_linsol_wrapper.h

Inheritance Relationships

Base Type

- `public amici::SUNLinSolWrapper` (*Class SUNLinSolWrapper*)

Class Documentation

class **SUNLinSolSPBCGS** : public amici::*SUNLinSolWrapper*

SUNDIALS scaled preconditioned Bi-CGStab (Bi-Conjugate Gradient Stable method) (SPBCGS) solver.

Public Functions

explicit **SUNLinSolSPBCGS**(N_Vector x, int pretype = PREC_NONE, int maxl = SUNSPBCGS_MAXL_DEFAULT)

SUNLinSolSPBCGS.

Parameters

- **x** – A template for cloning vectors needed within the solver.
- **pretype** – Preconditioner type (PREC_NONE, PREC_LEFT, PREC_RIGHT, PREC_BOTH)
- **maxl** – Maximum number of solver iterations

explicit **SUNLinSolSPBCGS**(*AmiVector* const &x, int pretype = PREC_NONE, int maxl = SUNSPBCGS_MAXL_DEFAULT)

SUNLinSolSPBCGS.

Parameters

- **x** – A template for cloning vectors needed within the solver.
- **pretype** – Preconditioner type (PREC_NONE, PREC_LEFT, PREC_RIGHT, PREC_BOTH)
- **maxl** – Maximum number of solver iterations

int **setATimes**(void *A_data, ATimesFn ATimes)

Sets the function pointer for ATimes (see sundials/sundials_linearsolver.h).

Parameters

- **A_data** –
- **ATimes** –

Returns

int **setPreconditioner**(void *P_data, PSetupFn Pset, PSolveFn Psol)

Sets function pointers for PSetup and PSolve routines inside of iterative linear solver objects (see sundials/sundials_linearsolver.h).

Parameters

- **P_data** –
- **Pset** –
- **Psol** –

Returns

int **setScalingVectors**(N_Vector s, N_Vector nul)

Sets pointers to left/right scaling vectors for the linear system solve (see sundials/sundials_linearsolver.h).

Parameters

- **s** –
- **nul** –

Returns

int **getNumIters**() const

Returns the number of linear iterations performed in the last 'Solve' call.

Returns
Number of iterations

realtype **getResNorm**() const

Returns the final residual norm from the last 'Solve' call.

Returns
residual norm

N_Vector **getResid**() const

Get preconditioned initial residual (see sundials/sundials_linearsolver.h).

Returns

Class SUNLinSolSPFGMR

- Defined in file_include_amici_sundials_linsol_wrapper.h

Inheritance Relationships

Base Type

- public amici::SUNLinSolWrapper (*Class SUNLinSolWrapper*)

Class Documentation

class **SUNLinSolSPFGMR** : public amici::*SUNLinSolWrapper*

SUNDIALS scaled preconditioned FGMRES (Flexible Generalized Minimal Residual method) (SPFGMR) solver.

Public Functions

SUNLinSolSPFGMR(*AmiVector* const &x, int pretype, int maxl)

SUNLinSolSPFGMR.

Parameters

- **x** – A template for cloning vectors needed within the solver.
- **pretype** – Preconditioner type (PREC_NONE, PREC_LEFT, PREC_RIGHT, PREC_BOTH)
- **maxl** – Maximum number of solver iterations

int **setATimes**(void *A_data, ATimesFn ATimes)

Sets the function pointer for ATimes (see sundials/sundials_linearsolver.h).

Parameters

- **A_data** –
- **ATimes** –

Returns

int **setPreconditioner**(void *P_data, PSetupFn Pset, PSolveFn Psol)

Sets function pointers for PSetup and PSolve routines inside of iterative linear solver objects (see sundials/sundials_linearsolver.h).

Parameters

- **P_data** –
- **Pset** –
- **Psol** –

Returns

int **setScalingVectors**(N_Vector s, N_Vector nul)

Sets pointers to left/right scaling vectors for the linear system solve (see sundials/sundials_linearsolver.h).

Parameters

- **s** –
- **nul** –

Returns

int **getNumIters**() const

Returns the number of linear iterations performed in the last 'Solve' call.

Returns

Number of iterations

realtype **getResNorm**() const

Returns the final residual norm from the last 'Solve' call.

Returns
residual norm

N_Vector **getResid**() const

Get preconditioned initial residual (see sundials/sundials_linearsolver.h).

Returns

Class SUNLinSolSPGMR

- Defined in file_include_amici_sundials_linsol_wrapper.h

Inheritance Relationships

Base Type

- `public amici::SUNLinSolWrapper` (*Class SUNLinSolWrapper*)

Class Documentation

class **SUNLinSolSPGMR** : public amici::*SUNLinSolWrapper*

SUNDIALS scaled preconditioned GMRES (Generalized Minimal Residual method) solver (SPGMR).

Public Functions

explicit **SUNLinSolSPGMR**(*AmiVector* const &x, int pretype = PREC_NONE, int maxl = SUNSPGMR_MAXL_DEFAULT)

Create SPGMR solver.

Parameters

- **x** – A template for cloning vectors needed within the solver.
- **pretype** – Preconditioner type (PREC_NONE, PREC_LEFT, PREC_RIGHT, PREC_BOTH)
- **maxl** – Maximum number of solver iterations

int **setATimes**(void *A_data, ATimesFn ATimes)

Sets the function pointer for ATimes (see sundials/sundials_linearsolver.h).

Parameters

- **A_data** –
- **ATimes** –

Returns

int **setPreconditioner**(void *P_data, PSetupFn Pset, PSolveFn Psol)

Sets function pointers for PSetup and PSolve routines inside of iterative linear solver objects (see sundials/sundials_linearsolver.h).

Parameters

- **P_data** –
- **Pset** –
- **Psol** –

Returns

int **setScalingVectors**(N_Vector s, N_Vector nul)

Sets pointers to left/right scaling vectors for the linear system solve (see sundials/sundials_linearsolver.h).

Parameters

- **s** –
- **nul** –

Returns

int **getNumIters**() const

Returns the number of linear iterations performed in the last 'Solve' call.

Returns
Number of iterations

realtype **getResNorm**() const

Returns the final residual norm from the last 'Solve' call.

Returns
residual norm

N_Vector **getResid**() const

Get preconditioned initial residual (see sundials/sundials_linearsolver.h).

Returns

Class SUNLinSolSPTFQMR

- Defined in file_include_amici_sundials_linsol_wrapper.h

Inheritance Relationships

Base Type

- public amici::SUNLinSolWrapper (*Class SUNLinSolWrapper*)

Class Documentation

class **SUNLinSolSPTFQMR** : public amici::*SUNLinSolWrapper*

SUNDIALS scaled preconditioned TFQMR (Transpose-Free Quasi-Minimal Residual method) (SPTFQMR) solver.

Public Functions

explicit **SUNLinSolSPTFQMR**(N_Vector x, int pretype = PREC_NONE, int maxl = SUNSPTFQMR_MAXL_DEFAULT)

Create SPTFQMR solver.

Parameters

- **x** – A template for cloning vectors needed within the solver.
- **pretype** – Preconditioner type (PREC_NONE, PREC_LEFT, PREC_RIGHT, PREC_BOTH)
- **maxl** – Maximum number of solver iterations

explicit **SUNLinSolSPTFQMR**(*AmiVector* const &x, int pretype = PREC_NONE, int maxl = SUNSPTFQMR_MAXL_DEFAULT)

Create SPTFQMR solver.

Parameters

- **x** – A template for cloning vectors needed within the solver.
- **pretype** – Preconditioner type (PREC_NONE, PREC_LEFT, PREC_RIGHT, PREC_BOTH)
- **maxl** – Maximum number of solver iterations

int **setATimes**(void *A_data, ATimesFn ATimes)

Sets the function pointer for ATimes (see sundials/sundials_linearsolver.h).

Parameters

- **A_data** –
- **ATimes** –

Returns

int **setPreconditioner**(void *P_data, PSetupFn Pset, PSolveFn Psol)

Sets function pointers for PSetup and PSolve routines inside of iterative linear solver objects (see sundials/sundials_linearsolver.h).

Parameters

- **P_data** –
- **Pset** –
- **Psol** –

Returns

int **setScalingVectors**(N_Vector s, N_Vector nul)

Sets pointers to left/right scaling vectors for the linear system solve (see sundials/sundials_linearsolver.h).

Parameters

- **s** –
- **nul** –

Returns

int **getNumIters**() const

Returns the number of linear iterations performed in the last 'Solve' call.

Returns

Number of iterations

realtype **getResNorm**() const

Returns the final residual norm from the last 'Solve' call.

Returns

residual norm

N_Vector **getResid**() const

Get preconditioned initial residual (see sundials/sundials_linearsolver.h).

Returns

Class SUNLinSolWrapper

- Defined in file_include_amici_sundials_linsol_wrapper.h

Inheritance Relationships

Derived Types

- public amici::SUNLinSolBand (*Class SUNLinSolBand*)
- public amici::SUNLinSolDense (*Class SUNLinSolDense*)
- public amici::SUNLinSolKLU (*Class SUNLinSolKLU*)
- public amici::SUNLinSolPCG (*Class SUNLinSolPCG*)
- public amici::SUNLinSolSPBCGS (*Class SUNLinSolSPBCGS*)
- public amici::SUNLinSolSPFGMR (*Class SUNLinSolSPFGMR*)
- public amici::SUNLinSolSPGMR (*Class SUNLinSolSPGMR*)
- public amici::SUNLinSolSPTFQMR (*Class SUNLinSolSPTFQMR*)

Class Documentation

class **SUNLinSolWrapper**

A RAII wrapper for SUNLinearSolver structs.

For details on member functions see documentation in sunlinsol/sundials_linearsolver.h.

Subclassed by *amici::SUNLinSolBand*, *amici::SUNLinSolDense*, *amici::SUNLinSolKLU*, *amici::SUNLinSolPCG*, *amici::SUNLinSolSPBCGS*, *amici::SUNLinSolSPFGMR*, *amici::SUNLinSolSPGMR*, *amici::SUNLinSolSPTFQMR*

Public Functions

SUNLinSolWrapper() = default

explicit **SUNLinSolWrapper**(SUNLinearSolver linsol)

Wrap existing SUNLinearSolver.

Parameters
linsol –

virtual **~SUNLinSolWrapper**()

SUNLinSolWrapper(*SUNLinSolWrapper* const &other) = delete

Copy constructor.

Parameters
other –

SUNLinSolWrapper(*SUNLinSolWrapper* &&other) noexcept

Move constructor.

Parameters
other –

SUNLinSolWrapper &**operator=**(*SUNLinSolWrapper* const &other) = delete

Copy assignment.

Parameters
other –

Returns

SUNLinSolWrapper &**operator=**(*SUNLinSolWrapper* &&other) noexcept

Move assignment.

Parameters
other –

Returns

SUNLinearSolver **get**() const

Returns the wrapped SUNLinSol.

Returns
SUNLinearSolver

SUNLinearSolver_Type **getType**() const

Returns an identifier for the linear solver type.

Returns

void **setup**(SUNMatrix A) const

Performs any linear solver setup needed, based on an updated system matrix A.

Parameters
A –

void **setup**(*SUNMatrixWrapper* const &A) const

Performs any linear solver setup needed, based on an updated system matrix A.

Parameters
A –

int **Solve**(SUNMatrix A, N_Vector x, N_Vector b, *realtype* tol) const

Solves a linear system A*x = b.

Parameters

- **A** –
- **x** – A template for cloning vectors needed within the solver.
- **b** –
- **tol** – Tolerance (weighted 2-norm), iterative solvers only

Returns
error flag

long int **getLastFlag**() const

Returns the last error flag encountered within the linear solver.

Returns
error flag

int **space**(long int *lenrwLS, long int *leniwLS) const

Returns the integer and real workspace sizes for the linear solver.

Parameters

- **lenrwLS** – output argument for size of real workspace
- **leniwLS** – output argument for size of integer workspace

Returns
workspace size

virtual SUNMatrix **getMatrix**() const

Get the matrix A (matrix solvers only).

Returns
A

Protected Functions

int **initialize**()

Performs linear solver initialization (assumes that all solver-specific options have been set).

Returns
error code

Protected Attributes

SUNLinearSolver **solver_** = {nullptr}

Wrapped solver

Class SUNMatrixWrapper

- Defined in file_include_amici_sundials_matrix_wrapper.h

Class Documentation

class **SUNMatrixWrapper**

A RAII wrapper for SUNMatrix structs.

This can create dense, sparse, or banded matrices using the respective constructor.

Public Functions

SUNMatrixWrapper() = default

SUNMatrixWrapper(sunindextype M, sunindextype N, sunindextype NNZ, int sparsetype)

Create sparse matrix. See SUNSparseMatrix in sunmatrix_sparse.h.

Parameters

- **M** – Number of rows
- **N** – Number of columns
- **NNZ** – Number of nonzeros
- **sparsetype** – Sparse type

SUNMatrixWrapper(sunindextype M, sunindextype N)

Create dense matrix. See SUNDenseMatrix in sunmatrix_dense.h.

Parameters

- **M** – Number of rows
- **N** – Number of columns

SUNMatrixWrapper(sunindextype M, sunindextype ubw, sunindextype lbw)

Create banded matrix. See SUNBandMatrix in sunmatrix_band.h.

Parameters

- **M** – Number of rows and columns
- **ubw** – Upper bandwidth
- **lbw** – Lower bandwidth

SUNMatrixWrapper(*SUNMatrixWrapper* const &A, *realtype* droptol, int sparsetype)

Create sparse matrix from dense or banded matrix. See SUNSparseFromDenseMatrix and SUNSparseFromBandMatrix in sunmatrix_sparse.h.

Parameters

- **A** – Wrapper for dense matrix
- **droptol** – tolerance for dropping entries
- **sparsetype** – Sparse type

explicit **SUNMatrixWrapper**(SUNMatrix mat)

Wrap existing SUNMatrix.

Parameters

mat –

~SUNMatrixWrapper()

inline **operator SUNMatrix**()

Conversion function.

SUNMatrixWrapper(*SUNMatrixWrapper* const &other)

Copy constructor.

Parameters

other –

SUNMatrixWrapper(*SUNMatrixWrapper* &&other)

Move constructor.

Parameters

other –

SUNMatrixWrapper &**operator=**(*SUNMatrixWrapper* const &other)

Copy assignment.

Parameters

other –

Returns

SUNMatrixWrapper &**operator=**(*SUNMatrixWrapper* &&other)

Move assignment.

Parameters

other –

Returns

void **reallocate**(sunindextype nnz)

Reallocate space for sparse matrix according to specified nnz.

Parameters
nnz – new number of nonzero entries

void **realloc**()

Reallocate space for sparse matrix to used space according to last entry in indexptrs.

SUNMatrix **get**() const

Get the wrapped SUNMatrix.

Note: Even though the returned matrix_ pointer is const qualified, matrix_->content will not be const. This is a shortcoming in the underlying C library, which we cannot address and it is not intended that any of those values are modified externally. If matrix_->content is manipulated, cpp:meth:SUNMatrixWrapper:`refresh` needs to be called.

Returns
raw SunMatrix object

inline sunindextype **rows**() const

Get the number of rows.

Returns
number of rows

inline sunindextype **columns**() const

Get the number of columns.

Returns
number of columns

sunindextype **num_nonzeros**() const

Get the number of specified non-zero elements (sparse matrices only)

Note: value will be 0 before indexptrs are set.

Returns
number of nonzero entries

sunindextype **num_indexptrs**() const

Get the number of indexptrs that can be specified (sparse matrices only)

Returns
number of indexptrs

sunindextype **capacity**() const

Get the number of allocated data elements.

Returns
number of allocated entries

realtype ***data()**

Get raw data of a sparse matrix.

Returns
pointer to first data entry

realtype const ***data() const**

Get const raw data of a sparse matrix.

Returns
pointer to first data entry

inline *realtype* **get_data**(sunindextype idx) const

Get data of a sparse matrix.

Parameters
idx – data index

Returns
idx-th data entry

inline *realtype* **get_data**(sunindextype irow, sunindextype icol) const

Get data entry for a dense matrix.

Parameters

- **irow** – row
- **icol** – col

Returns
A(irow,icol)

inline void **set_data**(sunindextype idx, *realtype* data)

Set data entry for a sparse matrix.

Parameters

- **idx** – data index
- **data** – data for idx-th entry

inline void **set_data**(sunindextype irow, sunindextype icol, *realtype* data)

Set data entry for a dense matrix.

Parameters

- **irow** – row
- **icol** – col
- **data** – data for idx-th entry

inline sunindextype **get_indexval**(sunindextype idx) const

Get the index value of a sparse matrix.

Parameters
idx – data index

Returns
row (CSC) or column (CSR) for idx-th data entry

inline void **set_indexval**(sunindextype idx, sunindextype val)

Set the index value of a sparse matrix.

Parameters

- **idx** – data index
- **val** – row (CSC) or column (CSR) for idx-th data entry

inline void **set_indexvals**(gsl::span<sunindextype const> const vals)

Set the index values of a sparse matrix.

Parameters

vals – rows (CSC) or columns (CSR) for data entries

inline sunindextype **get_indexptr**(sunindextype ptr_idx) const

Get the index pointer of a sparse matrix.

Parameters

ptr_idx – pointer index

Returns

index where the ptr_idx-th column (CSC) or row (CSR) starts

inline void **set_indexptr**(sunindextype ptr_idx, sunindextype ptr)

Set the index pointer of a sparse matrix.

Parameters

- **ptr_idx** – pointer index
- **ptr** – data-index where the ptr_idx-th column (CSC) or row (CSR) starts

inline void **set_indexptrs**(gsl::span<sunindextype const> const ptrs)

Set the index pointers of a sparse matrix.

Parameters

ptrs – starting data-indices where the columns (CSC) or rows (CSR) start

int **sparsetype**() const

Get the type of sparse matrix.

Returns

matrix type

void **scale**(*realtype* a)

multiply with a scalar (in-place)

Parameters

a – scalar value to multiply matrix

void **multiply**(N_Vector c, *const_N_Vector* b, *realtype* alpha = 1.0) const

N_Vector interface for multiply.

Parameters

- **c** – output vector, may already contain values
- **b** – multiplication vector
- **alpha** – scalar coefficient for matrix

inline void **multiply**(*AmiVector* &c, *AmiVector* const &b, *realtype* alpha = 1.0) const

AmiVector interface for multiply.

Parameters

- **c** – output vector, may already contain values
- **b** – multiplication vector
- **alpha** – scalar coefficient for matrix

void **multiply**(gsl::span<*realtype*> c, gsl::span<*realtype* const> b, *realtype* const alpha = 1.0) const

Perform matrix vector multiplication c += alpha * A*b.

Parameters

- **c** – output vector, may already contain values
- **b** – multiplication vector
- **alpha** – scalar coefficient

void **multiply**(N_Vector c, *const_N_Vector* b, gsl::span<int const> cols, bool transpose) const

Perform reordered matrix vector multiplication c += A[:,cols]*b.

Parameters

- **c** – output vector, may already contain values
- **b** – multiplication vector
- **cols** – int vector for column reordering
- **transpose** – bool transpose A before multiplication

void **multiply**(gsl::span<*realtype*> c, gsl::span<*realtype* const> b, gsl::span<int const> cols, bool transpose) const

Perform reordered matrix vector multiplication c += A[:,cols]*b.

Parameters

- **c** – output vector, may already contain values
- **b** – multiplication vector
- **cols** – int vector for column reordering
- **transpose** – bool transpose A before multiplication

void **sparse_multiply**(*SUNMatrixWrapper* &C, *SUNMatrixWrapper* const &B) const

Perform matrix matrix multiplication C = A * B for sparse A, B, C.

Note: will overwrite existing data, indexptrs, indexvals for C, but will use preallocated space for these vars

Parameters

- **C** – output matrix,
- **B** – multiplication matrix

void **sparse_add**(*SUNMatrixWrapper* const &A, *realtype* alpha, *SUNMatrixWrapper* const &B, *realtype* beta)

Perform sparse matrix matrix addition C = alpha * A + beta * B.

Note: will overwrite existing data, indexptrs, indexvals for C, but will use preallocated space for these vars

Parameters

- **A** – addition matrix
- **alpha** – scalar A
- **B** – addition matrix
- **beta** – scalar B

void **sparse_sum**(std::vector<*SUNMatrixWrapper*> const &mats)

Perform matrix-matrix addition A = sum(mats(0)...mats(len(mats)))

Note: will overwrite existing data, indexptrs, indexvals for A, but will use preallocated space for these vars

Parameters

mats – vector of sparse matrices

sunindextype **scatter**(sunindextype const k, *realtype* const beta, sunindextype *w, gsl::span<*realtype*> x, sunindextype const mark, *SUNMatrixWrapper* *C, sunindextype nnz) const

Compute x = x + beta * A(:,k), where x is a dense vector and A(:,k) is sparse, and update the sparsity pattern for C(:,j) if applicable.

This function currently has two purposes:

- perform parts of sparse matrix-matrix multiplication C(:,j)=A(:,k)*B(k,j) enabled by passing beta=B(k,j), x=C(:,j), C=C, w=sparsity of C(:,j) from B(k,0...j-1), nnz=nnz(C(:,0...j-1)
- add the k-th column of the sparse matrix A multiplied by beta to the dense vector x. enabled by passing beta=*, x=x, C=nullptr, w=nullptr, nnz=*

Parameters

- **k** – column index
- **beta** – scaling factor
- **w** – index workspace, (w[i]<mark) indicates non-zeroness of C(i,j) (dimension: m), if this is a nullptr, sparsity pattern of C will not be updated (if applicable).
- **x** – dense output vector (dimension: m)
- **mark** – marker for w to indicate nonzero pattern
- **C** – sparse output matrix, if this is a nullptr, sparsity pattern of C will not be updated
- **nnz** – number of nonzeros that were already written to C

Returns

updated number of nonzeros in C

void **transpose**(*SUNMatrixWrapper* &C, *realtype* const alpha, sunindextype blocksize) const

Compute transpose A' of sparse matrix A and writes it to the matrix C = alpha * A'.

Parameters

- **C** – output matrix (sparse or dense)
- **alpha** – scalar multiplier
- **blocksize** – blocksize for transposition. For full matrix transpose set to ncols/nrows

void **to_dense**(*SUNMatrixWrapper* &D) const

Writes a sparse matrix A to a dense matrix D.

Parameters

D – dense output matrix

void **to_diag**(N_Vector v) const

Writes the diagonal of sparse matrix A to a dense vector v.

Parameters

v – dense outut vector

void **zero**()

Set to 0.0, for sparse matrices also resets indexptr/indexvals.

inline SUNMatrix_ID **matrix_id**() const

Get matrix id.

Returns

SUNMatrix_ID

void **refresh**()

Update internal cache, needs to be called after external manipulation of matrix_->content.

Class SUNNonLinSolFixedPoint

- Defined in file_include_amici_sundials_linsol_wrapper.h

Inheritance Relationships

Base Type

- `public amici::SUNNonLinSolWrapper` (*Class SUNNonLinSolWrapper*)

Class Documentation

class **SUNNonLinSolFixedPoint** : public amici::*SUNNonLinSolWrapper*

SUNDIALS Fixed point non-linear solver to solve G(y) = y.

Public Functions

explicit **SUNNonLinSolFixedPoint**(*const_N_Vector* x, int m = 0)

Create fixed-point solver.

Parameters

- **x** – template for cloning vectors needed within the solver.
- **m** – number of acceleration vectors to use

SUNNonLinSolFixedPoint(int count, *const_N_Vector* x, int m = 0)

Create fixed-point solver for use with sensitivity analysis.

Parameters

- **count** – Number of vectors in the nonlinear solve. When integrating a system containing Ns sensitivities the value of count is:
  - Ns+1 if using a simultaneous corrector approach.
  - Ns if using a staggered corrector approach.
- **x** – template for cloning vectors needed within the solver.
- **m** – number of acceleration vectors to use

int **getSysFn**(SUNNonlinSolSysFn *SysFn) const

Get function to evaluate the fixed point function G(y) = y.

Parameters
SysFn –

Returns

Class SUNNonLinSolNewton

- Defined in file_include_amici_sundials_linsol_wrapper.h

Inheritance Relationships

Base Type

- `public amici::SUNNonLinSolWrapper` (*Class SUNNonLinSolWrapper*)

Class Documentation

class **SUNNonLinSolNewton** : public amici::*SUNNonLinSolWrapper*

SUNDIALS Newton non-linear solver to solve F (y) = 0.

Public Functions

explicit **SUNNonLinSolNewton**(N_Vector x)

Create Newton solver.

Parameters
x – A template for cloning vectors needed within the solver.

SUNNonLinSolNewton(int count, N_Vector x)

Create Newton solver for enabled sensitivity analysis.

Parameters

- **count** – Number of vectors in the nonlinear solve. When integrating a system containing Ns sensitivities the value of count is:
  - Ns+1 if using a simultaneous corrector approach.
  - Ns if using a staggered corrector approach.
- **x** – A template for cloning vectors needed within the solver.

int **getSysFn**(SUNNonlinSolSysFn *SysFn) const

Get function to evaluate the nonlinear residual function F(y) = 0.

Parameters
SysFn –

Returns

Class SUNNonLinSolWrapper

- Defined in file_include_amici_sundials_linsol_wrapper.h

Inheritance Relationships

Derived Types

- `public amici::SUNNonLinSolFixedPoint` (*Class SUNNonLinSolFixedPoint*)
- `public amici::SUNNonLinSolNewton` (*Class SUNNonLinSolNewton*)

Class Documentation

class **SUNNonLinSolWrapper**

A RAII wrapper for SUNNonLinearSolver structs which solve the nonlinear system F (y) = 0 or G(y) = y.

Subclassed by *amici::SUNNonLinSolFixedPoint*, *amici::SUNNonLinSolNewton*

Public Functions

explicit **SUNNonLinSolWrapper**(SUNNonlinearSolver sol)

SUNNonLinSolWrapper from existing SUNNonlinearSolver.

Parameters
sol –

virtual **~SUNNonLinSolWrapper**()

SUNNonLinSolWrapper(*SUNNonLinSolWrapper* const &other) = delete

Copy constructor.

Parameters
other –

SUNNonLinSolWrapper(*SUNNonLinSolWrapper* &&other) noexcept

Move constructor.

Parameters
other –

SUNNonLinSolWrapper &**operator=**(*SUNNonLinSolWrapper* const &other) = delete

Copy assignment.

Parameters
other –

Returns

SUNNonLinSolWrapper &**operator=**(*SUNNonLinSolWrapper* &&other) noexcept

Move assignment.

Parameters
other –

Returns

SUNNonlinearSolver **get**() const

Get the wrapped SUNNonlinearSolver.

Returns
SUNNonlinearSolver

SUNNonlinearSolver_Type **getType**() const

Get type ID of the solver.

Returns

int **setup**(N_Vector y, void *mem)

Setup solver.

Parameters

- **y** – the initial iteration passed to the nonlinear solver.
- **mem** – the sundials integrator memory structure.

Returns

int **Solve**(N_Vector y0, N_Vector y, N_Vector w, *realtype* tol, bool callLSetup, void *mem)

Solve the nonlinear system F (y) = 0 or G(y) = y.

Parameters

- **y0** – the initial iterate for the nonlinear solve. This must remain unchanged throughout the solution process.
- **y** – the solution to the nonlinear system
- **w** – the solution error weight vector used for computing weighted error norms.
- **tol** – the requested solution tolerance in the weighted root-mean- squared norm.
- **callLSetup** – a flag indicating that the integrator recommends for the linear solver setup function to be called.
- **mem** – the sundials integrator memory structure.

Returns

int **setSysFn**(SUNNonlinSolSysFn SysFn)

Set function to evaluate the nonlinear residual function F(y) = 0 or the fixed point function G(y) = y.

Parameters
SysFn –

Returns

int **setLSetupFn**(SUNNonlinSolLSetupFn SetupFn)

Set linear solver setup function.

Parameters
SetupFn –

Returns

int **setLSolveFn**(SUNNonlinSolLSolveFn SolveFn)

Set linear solver solve function.

Parameters
SolveFn –

Returns

int **setConvTestFn**(SUNNonlinSolConvTestFn CTestFn, void *ctest_data)

Set function to test for convergence.

Parameters

- **CTestFn** –
- **ctest_data** –

Returns

int **setMaxIters**(int maxiters)

Set maximum number of non-linear iterations.

Parameters
maxiters –

Returns

long int **getNumIters**() const

getNumIters

Returns

int **getCurIter**() const

getCurIter

Returns

long int **getNumConvFails**() const

getNumConvFails

Returns

Protected Functions

void **initialize**()

initialize

Protected Attributes

SUNNonlinearSolver **solver** = nullptr

the wrapper solver

Enums

Enum BLASLayout

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**BLASLayout**

BLAS Matrix Layout, affects dgemm and gemv calls

Values:

enumerator **rowMajor**

enumerator **colMajor**

Enum BLASTranspose

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**BLASTranspose**

BLAS Matrix Transposition, affects dgemm and gemv calls

Values:

enumerator **noTrans**

enumerator **trans**

enumerator **conjTrans**

Enum Constraint

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**Constraint**

Constraints on state variables

Values:

enumerator **none**

enumerator **non_negative**

enumerator **non_positive**

enumerator **positive**

enumerator **negative**

Enum FixedParameterContext

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**FixedParameterContext**

fixedParameter to be used in condition context

Values:

enumerator **simulation**

enumerator **preequilibration**

enumerator **presimulation**

Enum InternalSensitivityMethod

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**InternalSensitivityMethod**

CVODES/IDAS forward sensitivity computation method

Values:

enumerator **simultaneous**

enumerator **staggered**

enumerator **staggered1**

Enum InterpolationType

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**InterpolationType**

CVODES/IDAS state interpolation for adjoint sensitivity analysis

Values:

enumerator **hermite**

enumerator **polynomial**

Enum LinearMultistepMethod

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**LinearMultistepMethod**

CVODES/IDAS linear multistep method

Values:

enumerator **adams**

enumerator **BDF**

Enum LinearSolver

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**LinearSolver**

linear solvers for CVODES/IDAS

Values:

enumerator **dense**

enumerator **band**

enumerator **LAPACKDense**

enumerator **LAPACKBand**

enumerator **diag**

enumerator **SPGMR**

enumerator **SPBCG**

enumerator **SPTFQMR**

enumerator **KLU**

enumerator **SuperLUMT**

Enum LogSeverity

- Defined in file_include_amici_logging.h

Enum Documentation

enum class amici::**LogSeverity**

Severity levels for logging.

Values:

enumerator **error**

enumerator **warning**

enumerator **debug**

Enum ModelQuantity

- Defined in file_include_amici_model.h

Enum Documentation

enum class amici::**ModelQuantity**

Describes the various model quantities.

Values:

enumerator **J**

enumerator **JB**

enumerator **Jv**

enumerator **JvB**

enumerator **JDiag**

enumerator **sx**

enumerator **sy**

enumerator **sz**

enumerator **srz**

enumerator **ssigmay**

enumerator **ssigmaz**

enumerator **xdot**

enumerator **sxdot**

enumerator **xBdot**

enumerator **x0_rdata**

enumerator **x0**

enumerator **x_rdata**

enumerator **x**

enumerator **dwdw**

enumerator **dwdx**

enumerator **dwdp**

enumerator **y**

enumerator **dydp**

enumerator **dydx**

enumerator **w**

enumerator **root**

enumerator **qBdot**

enumerator **qBdot_ss**

enumerator **xBdot_ss**

enumerator **JSparseB_ss**

enumerator **deltax**

enumerator **deltasx**

enumerator **deltaxB**

enumerator **k**

enumerator **p**

enumerator **ts**

enumerator **dJydy**

enumerator **dJydy_matlab**

enumerator **deltaqB**

enumerator **dsigmaydp**

enumerator **dsigmaydy**

enumerator **dsigmazdp**

enumerator **dJydsigma**

enumerator **dJydx**

enumerator **dzdx**

enumerator **dzdp**

enumerator **dJrzdsigma**

enumerator **dJrzdz**

enumerator **dJrzdx**

enumerator **dJzdsigma**

enumerator **dJzdz**

enumerator **dJzdx**

enumerator **drzdp**

enumerator **drzdx**

Enum NewtonDampingFactorMode

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**NewtonDampingFactorMode**

Damping factor flag for the Newton method

Values:

enumerator **off**

enumerator **on**

Enum NonlinearSolverIteration

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**NonlinearSolverIteration**

CVODES/IDAS Nonlinear Iteration method

Values:

enumerator **functional**

enumerator **fixedpoint**

deprecated

enumerator **newton**

Enum ObservableScaling

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**ObservableScaling**

modes for observable scaling

Values:

enumerator **lin**

enumerator **log**

enumerator **log10**

Enum ParameterScaling

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::ParameterScaling
modes for parameter transformations

Values:

enumerator none

enumerator ln

enumerator log10

Enum RDataReporting

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::RDataReporting

Values:

enumerator full

enumerator residuals

enumerator likelihood

Enum SecondOrderMode

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::SecondOrderMode
modes for second order sensitivity analysis

Values:

enumerator none

enumerator full

enumerator directional

Enum SensitivityMethod

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**SensitivityMethod**

methods for sensitivity computation

Values:

enumerator **none**

Don't compute sensitivities.

enumerator **forward**

Forward sensitivity analysis.

enumerator **adjoint**

Adjoint sensitivity analysis.

Enum SensitivityOrder

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**SensitivityOrder**

orders of sensitivity analysis

Values:

enumerator **none**

Don't compute sensitivities.

enumerator **first**

First-order sensitivities.

enumerator **second**

Second-order sensitivities.

Enum SplineBoundaryCondition

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**SplineBoundaryCondition**

boundary conditions for splines

Values:

enumerator **given**

enumerator **zeroDerivative**

enumerator **natural**

enumerator **naturalZeroDerivative**

enumerator **periodic**

Enum SplineExtrapolation

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**SplineExtrapolation**

extrapolation methods for splines

Values:

enumerator **noExtrapolation**

enumerator **constant**

enumerator **linear**

enumerator **polynomial**

enumerator **periodic**

Enum SteadyStateComputationMode

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**SteadyStateComputationMode**

Steady-state computation mode in steadyStateProblem

Values:

enumerator **newtonOnly**

enumerator **integrationOnly**

enumerator **integrateIfNewtonFails**

Enum SteadyStateContext

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::**SteadyStateContext**

Context for which the sensitivity flag should be computed

Values:

enumerator **newtonSensi**

enumerator **sensiStorage**

enumerator **solverCreation**

Enum SteadyStateSensitivityMode

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::SteadyStateSensitivityMode

Sensitivity computation mode in steadyStateProblem

Values:

enumerator **newtonOnly**

enumerator **integrationOnly**

enumerator **integrateIfNewtonFails**

Enum SteadyStateStatus

- Defined in file_include_amici_defines.h

Enum Documentation

enum class amici::SteadyStateStatus

State in which the steady state computation finished

Values:

enumerator **failed_too_long_simulation**

enumerator **failed_damping**

enumerator **failed_factorization**

enumerator **failed_convergence**

enumerator **failed**

enumerator **not_run**

enumerator **success**

Functions

Template Function amici::addSlice(gsl::span<T const> const, gsl::span<T>)

- Defined in file_include_amici_misc.h

Function Documentation

template<class **T**>
void `amici::addSlice`(gsl::span<*T* const> const slice, gsl::span<*T*> buffer)

local helper function to add the computed slice to provided buffer (span)

Parameters

- **slice** – computed value
- **buffer** – buffer to which values are to be added

Template Function amici::addSlice(std::vector<T> const&, gsl::span<T>)

- Defined in file_include_amici_misc.h

Function Documentation

template<class **T**>
void `amici::addSlice`(std::vector<*T*> const &s, gsl::span<*T*> b)

local helper function to add the computed slice to provided buffer (vector/span)

Parameters

- **s** – computed value
- **b** – buffer to which values are to be written

Function amici::amici_daxpy

- Defined in file_include_amici_cblas.h

Function Documentation

void `amici::amici_daxpy`(int n, double alpha, double const *x, int incx, double *y, int incy)

Compute y = a*x + y.

Parameters

- **n** – number of elements in y
- **alpha** – scalar coefficient of x
- **x** – vector of length n*incx
- **incx** – x stride
- **y** – vector of length n*incy

- **incy** – y stride

Function amici::amici_dgemm

- Defined in file_include_amici_cblas.h

Function Documentation

void amici::**amici_dgemm**(*BLASLayout* layout, *BLASTranspose* TransA, *BLASTranspose* TransB, int M, int N, int K, double alpha, double const *A, int lda, double const *B, int ldb, double beta, double *C, int ldc)

CBLAS matrix matrix multiplication (dgemm)

This routines computes $C = alpha * A * B + beta * C$ with A: [MxK] B:[KxN] C:[MxN]

Parameters

- **layout** – memory layout.
- **TransA** – flag indicating whether A should be transposed before multiplication
- **TransB** – flag indicating whether B should be transposed before multiplication
- **M** – number of rows in A/C
- **N** – number of columns in B/C
- **K** – number of rows in B, number of columns in A
- **alpha** – coefficient alpha
- **A** – matrix A
- **lda** – leading dimension of A (>=M or >=K)
- **B** – matrix B
- **ldb** – leading dimension of B (>=K or >=N)
- **beta** – coefficient beta
- **C** – matrix C
- **ldc** – leading dimension of C (>=M or >= N)

Function amici::amici_dgemv

- Defined in file_include_amici_cblas.h

Function Documentation

void amici::**amici_dgemv**(*BLASLayout* layout, *BLASTranspose* TransA, int M, int N, double alpha, double const *A, int lda, double const *X, int incX, double beta, double *Y, int incY)

CBLAS matrix vector multiplication (dgemv).

Computes $y = alpha * A * x + beta * y$ with A: [MxN] x:[Nx1] y:[Mx1]

Parameters

- **layout** – Matrix layout, column major or row major.
- **TransA** – flag indicating whether A should be transposed before multiplication
- **M** – number of rows in A
- **N** – number of columns in A
- **alpha** – coefficient alpha
- **A** – matrix A
- **lda** – leading dimension / stride of A (>=N if row-major, >=M if col-major)
- **X** – vector X
- **incX** – increment for entries of X
- **beta** – coefficient beta
- **Y** – vector Y
- **incY** – increment for entries of Y

Function amici::backtraceString

- Defined in file_include_amici_misc.h

Function Documentation

std::string amici::**backtraceString**(int maxFrames, int const first_frame = 0)

Returns the current backtrace as std::string.

Parameters

- **maxFrames** – Number of frames to include
- **first_frame** – Index of first frame to include

Returns

Backtrace

Template Function amici::checkBufferSize

- Defined in file_include_amici_misc.h

Function Documentation

template<class **T**>
void `amici::checkBufferSize`(gsl::span<*T*> buffer, typename gsl::span<*T*>::index_type expected_size)

local helper to check whether the provided buffer has the expected size

Parameters

- **buffer** – buffer to which values are to be written
- **expected_size** – expected size of the buffer

Function amici::checkSigmaPositivity(std::vector<realtype> const&, char const *)

- Defined in file_include_amici_edata.h

Function Documentation

void `amici::checkSigmaPositivity`(std::vector<*realtype*> const &sigmaVector, char const *vectorName)

checks input vector of sigmas for not strictly positive values

Parameters

- **sigmaVector** – vector input to be checked
- **vectorName** – name of the input

Function amici::checkSigmaPositivity(realtype, char const *)

- Defined in file_include_amici_edata.h

Function Documentation

void `amici::checkSigmaPositivity`(*realtype* sigma, char const *sigmaName)

checks input scalar sigma for not strictly positive value

Parameters

- **sigma** – input to be checked
- **sigmaName** – name of the input

Template Function amici::deserializeFromChar

- Defined in file_include_amici_serialization.h

Function Documentation

template<typename **T**>
T `amici::`**`deserializeFromChar`**`(char const *buffer, int size)`

Deserialize object that has been serialized using serializeToChar.

Parameters

- **`buffer`** – serialized object
- **`size`** – length of buffer

Returns
The deserialized object

Template Function amici::deserializeFromString

- Defined in file_include_amici_serialization.h

Function Documentation

template<typename **T**>
T `amici::`**`deserializeFromString`**`(std::string const &serialized)`

Deserialize object that has been serialized using serializeToString.

Parameters
`serialized` – serialized object

Returns
The deserialized object

Function amici::dotProd

- Defined in file_include_amici_vector.h

Function Documentation

inline *realtype* `amici::`**`dotProd`**`(`*AmiVector* `const &x, `*AmiVector* `const &y)`

Compute dot product of x and y.

Parameters

- **`x`** – vector
- **`y`** – vector

Returns
dot product of x and y

Function amici::getScaledParameter

- Defined in file_include_amici_misc.h

Function Documentation

double `amici::getScaledParameter`(double unscaledParameter, *ParameterScaling* scaling)

Apply parameter scaling according to `scaling`

Parameters

- **`unscaledParameter`** –
- **`scaling`** – parameter scaling

Returns

Scaled parameter

Function amici::getUnscaledParameter

- Defined in file_include_amici_misc.h

Function Documentation

double `amici::getUnscaledParameter`(double scaledParameter, *ParameterScaling* scaling)

Remove parameter scaling according to `scaling`

Parameters

- **`scaledParameter`** – scaled parameter
- **`scaling`** – parameter scaling

Returns

Unscaled parameter

Function amici::hdf5::attributeExists(H5::H5File const&, std::string const&, std::string const&)

- Defined in file_include_amici_hdf5.h

Function Documentation

bool `amici::hdf5::attributeExists`(H5::H5File const &file, std::string const &optionsObject, std::string const &attributeName)

Check whether an attribute with the given name exists on the given dataset.

Parameters

- **`file`** – The HDF5 file object
- **`optionsObject`** – Dataset of which attributes should be checked
- **`attributeName`** – Name of the attribute of interest

Returns
`true` if attribute exists, `false` otherwise

Function amici::hdf5::attributeExists(H5::H5Object const&, std::string const&)

- Defined in file_include_amici_hdf5.h

Function Documentation

bool `amici::hdf5::attributeExists`(H5::H5Object const &object, std::string const &attributeName)

Check whether an attribute with the given name exists on the given object.

Parameters

- **`object`** – An HDF5 object
- **`attributeName`** – Name of the attribute of interest

Returns
`true` if attribute exists, `false` otherwise

Function amici::hdf5::createAndWriteDouble1DDataset

- Defined in file_include_amici_hdf5.h

Function Documentation

void `amici::hdf5::createAndWriteDouble1DDataset`(H5::H5File const &file, std::string const &datasetName, gsl::span<double const> buffer)

Create and write to 1-dimensional native double dataset.

Parameters

- **`file`** – HDF5 file object
- **`datasetName`** – Name of dataset to create
- **`buffer`** – Data to write to dataset

Function amici::hdf5::createAndWriteDouble2DDataset

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**createAndWriteDouble2DDataset**(H5::H5File const &file, std::string const &datasetName, gsl::span<double const> buffer, hsize_t m, hsize_t n)

Create and write to 2-dimensional native double dataset.

Parameters

- **file** – HDF5 file object
- **datasetName** – Name of dataset to create
- **buffer** – Flattened data to write to dataset (assuming row-major)
- **m** – Number of rows in buffer
- **n** – Number of columns buffer

Function amici::hdf5::createAndWriteDouble3DDataset

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**createAndWriteDouble3DDataset**(H5::H5File const &file, std::string const &datasetName, gsl::span<double const> buffer, hsize_t m, hsize_t n, hsize_t o)

Create and write to 3-dimensional native double dataset.

Parameters

- **file** – HDF5 file object
- **datasetName** – Name of dataset to create
- **buffer** – Flattened data to write to dataset (assuming row-major)
- **m** – Length of first dimension in buffer
- **n** – Length of first dimension in buffer
- **o** – Length of first dimension in buffer

Function amici::hdf5::createAndWriteInt1DDataset

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**createAndWriteInt1DDataset**(H5::H5File const &file, std::string const &datasetName, gsl::span<int const> buffer)

Create and write to 1-dimensional native integer dataset.

Parameters

- **file** – HDF5 file object
- **datasetName** – Name of dataset to create
- **buffer** – Data to write to dataset

Function amici::hdf5::createAndWriteInt2DDataset

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**createAndWriteInt2DDataset**(H5::H5File const &file, std::string const &datasetName, gsl::span<int const> buffer, hsize_t m, hsize_t n)

Create and write to 2-dimensional native integer dataset.

Parameters

- **file** – HDF5 file object
- **datasetName** – Name of dataset to create
- **buffer** – Flattened data to write to dataset (assuming row-major)
- **m** – Number of rows in buffer
- **n** – Number of columns buffer

Function amici::hdf5::createGroup

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**createGroup**(const H5::H5File &file, std::string const &groupPath, bool recursively = true)

Create the given group and possibly parents.

Parameters

- **file** – HDF5 file to write to
- **groupPath** – Path to the group to be created
- **recursively** – Create intermediary groups

Function amici::hdf5::createOrOpenForWriting

- Defined in file_include_amici_hdf5.h

Function Documentation

H5::H5File amici::hdf5::**createOrOpenForWriting**(std::string const &hdf5filename)

Open the given file for writing.

Append if exists, create if not.

Parameters
hdf5filename – File to open

Returns
File object

Function amici::hdf5::getDoubleDataset1D

- Defined in file_include_amici_hdf5.h

Function Documentation

std::vector<double> amici::hdf5::**getDoubleDataset1D**(const H5::H5File &file, std::string const &name)

Read 1-dimensional native double dataset from HDF5 file.

Parameters

- **file** – HDF5 file object
- **name** – Name of dataset to read

Returns
Data read

Function amici::hdf5::getDoubleDataset2D

- Defined in file_include_amici_hdf5.h

Function Documentation

std::vector<double> amici::hdf5::**getDoubleDataset2D**(const H5::H5File &file, std::string const &name, hsize_t &m, hsize_t &n)

Read 2-dimensional native double dataset from HDF5 file.

Parameters

- **file** – HDF5 file object
- **name** – Name of dataset to read
- **m** – Number of rows in the dataset
- **n** – Number of columns in the dataset

Returns
Flattened data (row-major)

Function amici::hdf5::getDoubleDataset3D

- Defined in file_include_amici_hdf5.h

Function Documentation

std::vector<double> amici::hdf5::**getDoubleDataset3D**(const H5::H5File &file, std::string const &name, hsize_t &m, hsize_t &n, hsize_t &o)

Read 3-dimensional native double dataset from HDF5 file.

Parameters

- **file** – HDF5 file object
- **name** – Name of dataset to read
- **m** – Length of first dimension in dataset
- **n** – Length of first dimension in dataset
- **o** – Length of first dimension in dataset

Returns
Flattened data (row-major)

Function amici::hdf5::getDoubleScalarAttribute

- Defined in file_include_amici_hdf5.h

Function Documentation

double amici::hdf5::**getDoubleScalarAttribute**(const H5::H5File &file, std::string const &optionsObject, std::string const &attributeName)

Read scalar native double attribute from HDF5 object.

Parameters

- **file** – HDF5 file
- **optionsObject** – Object to read attribute from
- **attributeName** – Name of attribute to read

Returns
Attribute value

Function amici::hdf5::getIntDataset1D

- Defined in file_include_amici_hdf5.h

Function Documentation

std::vector<int> amici::hdf5::**getIntDataset1D**(const H5::H5File &file, std::string const &name)

Read 1-dimensional native integer dataset from HDF5 file.

Parameters

- **file** – HDF5 file object
- **name** – Name of dataset to read

Returns

Data read

Function amici::hdf5::getIntScalarAttribute

- Defined in file_include_amici_hdf5.h

Function Documentation

int amici::hdf5::**getIntScalarAttribute**(const H5::H5File &file, std::string const &optionsObject, std::string const &attributeName)

Read scalar native integer attribute from HDF5 object.

Parameters

- **file** – HDF5 file
- **optionsObject** – Object to read attribute from
- **attributeName** – Name of attribute to read

Returns

Attribute value

Function amici::hdf5::getStringAttribute

- Defined in file_include_amici_hdf5.h

Function Documentation

std::string amici::hdf5::**getStringAttribute**(H5::H5File const &file, std::string const &optionsObject, std::string const &attributeName)

Read string attribute from HDF5 object.

Parameters

- **file** – HDF5 file
- **optionsObject** – Object to read attribute from

- **attributeName** – Name of attribute to read

Returns
Attribute value

Function amici::hdf5::locationExists(std::string const&, std::string const&)

- Defined in file_include_amici_hdf5.h

Function Documentation

bool amici::hdf5::**locationExists**(std::string const &filename, std::string const &location)
Check if the given location (group, link or dataset) exists in the given file.

Parameters

- **filename** – HDF5 filename
- **location** – Location to test for

Returns
`true` if exists, `false` otherwise

Function amici::hdf5::locationExists(H5::H5File const&, std::string const&)

- Defined in file_include_amici_hdf5.h

Function Documentation

bool amici::hdf5::**locationExists**(H5::H5File const &file, std::string const &location)
Check if the given location (group, link or dataset) exists in the given file.

Parameters

- **file** – HDF5 file object
- **location** – Location to test for

Returns
`true` if exists, `false` otherwise

Function amici::hdf5::readModelDataFromHDF5(std::string const&, Model&, std::string const&)

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**readModelDataFromHDF5**(std::string const &hdffile, *Model* &model, std::string const &datasetPath)

Read model data from HDF5 file.

Parameters

- **hdffile** – Name of HDF5 file
- **model** – *Model* to set data on
- **datasetPath** – Path inside the HDF5 file

Function amici::hdf5::readModelDataFromHDF5(H5::H5File const&, Model&, std::string const&)

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**readModelDataFromHDF5**(H5::H5File const &file, *Model* &model, std::string const &datasetPath)

Read model data from HDF5 file.

Parameters

- **file** – HDF5 file handle to read from
- **model** – *Model* to set data on
- **datasetPath** – Path inside the HDF5 file

Function amici::hdf5::readSimulationExpData

- Defined in file_include_amici_hdf5.h

Function Documentation

std::unique_ptr<*ExpData*> amici::hdf5::**readSimulationExpData**(std::string const &hdf5Filename, std::string const &hdf5Root, *Model* const &model)

Read AMICI *ExpData* data from HDF5 file.

Parameters

- **hdf5Filename** – Name of HDF5 file
- **hdf5Root** – Path inside the HDF5 file to object having *ExpData*
- **model** – The model for which data is to be read

Returns

ExpData created from data in the given location

Function amici::hdf5::readSolverSettingsFromHDF5(const H5::H5File&, Solver&, std::string const&)

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**readSolverSettingsFromHDF5**(const H5::H5File &file, *Solver* &solver, std::string const &datasetPath)

Read solver options from HDF5 file.

Parameters

- **file** – HDF5 file to read from
- **solver** – *Solver* to set options on
- **datasetPath** – Path inside the HDF5 file

Function amici::hdf5::readSolverSettingsFromHDF5(std::string const&, Solver&, std::string const&)

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**readSolverSettingsFromHDF5**(std::string const &hdffile, *Solver* &solver, std::string const &datasetPath)

Read solver options from HDF5 file.

Parameters

- **hdffile** – Name of HDF5 file
- **solver** – *Solver* to set options on
- **datasetPath** – Path inside the HDF5 file

Function amici::hdf5::writeReturnData(ReturnData const&, H5::H5File const&, std::string const&)

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**writeReturnData**(*ReturnData* const &rdata, H5::H5File const &file, std::string const &hdf5Location)

Write *ReturnData* to HDF5 file.

Parameters

- **rdata** – Data to write
- **file** – HDF5 file to write to

- **hdf5Location** – Full dataset path inside the HDF5 file (will be created)

Function amici::hdf5::writeReturnData(ReturnData const&, std::string const&, std::string const&)

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**writeReturnData**(*ReturnData* const &rdata, std::string const &hdf5Filename, std::string const &hdf5Location)

Write *ReturnData* to HDF5 file.

Parameters

- **rdata** – Data to write
- **hdf5Filename** – Filename of HDF5 file
- **hdf5Location** – Full dataset path inside the HDF5 file (will be created)

Function amici::hdf5::writeReturnDataDiagnosis

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**writeReturnDataDiagnosis**(*ReturnData* const &rdata, H5::H5File const &file, std::string const &hdf5Location)

Write *ReturnData* diagnosis data to HDF5 file.

Parameters

- **rdata** – Data to write
- **file** – HDF5 file to write to
- **hdf5Location** – Full dataset path inside the HDF5 file (will be created)

Function amici::hdf5::writeSimulationExpData

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**writeSimulationExpData**(*ExpData* const &edata, H5::H5File const &file, std::string const &hdf5Location)

Write AMICI experimental data to HDF5 file.

Parameters

- **edata** – The experimental data which is to be written
- **file** – Name of HDF5 file

- **hdf5Location** – Path inside the HDF5 file to object having *ExpData*

Function amici::hdf5::writeSolverSettingsToHDF5(Solver const&, std::string const&, std::string const&)

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**writeSolverSettingsToHDF5**(*Solver* const &solver, std::string const &hdf5Filename, std::string const &hdf5Location)

Write solver options to HDF5 file.

Parameters

- **hdf5Filename** – Name of HDF5 file to write to
- **solver** – *Solver* to write options from
- **hdf5Location** – Path inside the HDF5 file

Function amici::hdf5::writeSolverSettingsToHDF5(Solver const&, H5::H5File const&, std::string const&)

- Defined in file_include_amici_hdf5.h

Function Documentation

void amici::hdf5::**writeSolverSettingsToHDF5**(*Solver* const &solver, H5::H5File const &file, std::string const &hdf5Location)

Write solver options to HDF5 file.

Parameters

- **file** – File to read from
- **solver** – *Solver* to write options from
- **hdf5Location** – Path inside the HDF5 file

Template Function amici::is_equal

- Defined in file_include_amici_misc.h

Function Documentation

template<class **T**>
bool **amici::is_equal**(*T* const &a, *T* const &b)

Check if two spans are equal, treating NaNs in the same position as equal.

Parameters

- **a** –
- **b** –

Returns

Whether the contents of the two spans are equal.

Function amici::linearSum

- Defined in file_include_amici_vector.h

Function Documentation

inline void **amici::linearSum**(*realtype* a, *AmiVector* const &x, *realtype* b, *AmiVector* const &y, *AmiVector* &z)

Computes z = a*x + b*y.

Parameters

- **a** – coefficient for x
- **x** – a vector
- **b** – coefficient for y
- **y** – another vector with same size as x
- **z** – result vector of same size as x and y

Function amici::N_VGetArrayPointerConst

- Defined in file_include_amici_vector.h

Function Documentation

inline *realtype* const *amici::**N_VGetArrayPointerConst**(*const_N_Vector* x)

Function amici::operator==(ExpData const&, ExpData const&)

- Defined in file_include_amici_edata.h

Function Documentation

inline bool amici::**operator==**(*ExpData* const &lhs, *ExpData* const &rhs)

Equality operator.

Parameters

- **lhs** – some object
- **rhs** – another object

Returns

`true`, if both arguments are equal; `false` otherwise.

Function amici::operator==(Model const&, Model const&)

- Defined in file_include_amici_model.h

Function Documentation

bool amici::**operator==**(*Model* const &a, *Model* const &b)

Parameters

- **a** – First model instance
- **b** – Second model instance

Returns

Equality

Function amici::operator==(ModelDimensions const&, ModelDimensions const&)

- Defined in file_include_amici_model.h

Function Documentation

bool amici::**operator==**(*ModelDimensions* const &a, *ModelDimensions* const &b)

Function amici::operator==(ModelState const&, ModelState const&)

- Defined in file_include_amici_model_state.h

Function Documentation

inline bool amici::**operator==**(*ModelState* const &a, *ModelState* const &b)

Function amici::operator==(SimulationParameters const&, SimulationParameters const&)

- Defined in file_include_amici_simulation_parameters.h

Function Documentation

bool amici::**operator==**(*SimulationParameters* const &a, *SimulationParameters* const &b)

Function amici::operator==(Solver const&, Solver const&)

- Defined in file_include_amici_solver.h

Function Documentation

bool amici::**operator==**(*Solver* const &a, *Solver* const &b)

Parameters

- **a** –
- **b** –

Returns

Function amici::printfToString

- Defined in file_include_amici_misc.h

Function Documentation

std::string amici::**printfToString**(char const *fmt, va_list ap)

Format printf-style arguments to std::string.

Parameters

- **fmt** – Format string
- **ap** – Argument list pointer

Returns

Formatted String

Function amici::regexErrorToString

- Defined in file_include_amici_misc.h

Function Documentation

std::string amici::**regexErrorToString**(std::regex_constants::error_type err_type)

Convert std::regex_constants::error_type to string.

Parameters
err_type – error type

Returns
Error type as string

Function amici::runAmiciSimulation

- Defined in file_include_amici_amici.h

Function Documentation

std::unique_ptr<*ReturnData*> amici::**runAmiciSimulation**(*Solver* &solver, *ExpData* const *edata, *Model* &model, bool rethrow = false)

Core integration routine. Initializes the solver and runs the forward and backward problem.

Parameters

- **solver** – *Solver* instance
- **edata** – pointer to experimental data object
- **model** – model specification object
- **rethrow** – rethrow integration exceptions?

Returns
rdata pointer to return data object

Function amici::runAmiciSimulations

- Defined in file_include_amici_amici.h

Function Documentation

std::vector<std::unique_ptr<*ReturnData*>> amici::**runAmiciSimulations**(*Solver* const &solver, std::vector<*ExpData**> const &edatas, *Model* const &model, bool failfast, int num_threads)

Same as runAmiciSimulation, but for multiple *ExpData* instances. When compiled with OpenMP support, this function runs multi-threaded.

Parameters

- **solver** – *Solver* instance
- **edatas** – experimental data objects
- **model** – model specification object
- **failfast** – flag to allow early termination
- **num_threads** – number of threads for parallel execution

Returns
vector of pointers to return data objects

Function amici::scaleParameters

- Defined in file_include_amici_misc.h

Function Documentation

void amici::**scaleParameters**(gsl::span<*realtype* const> bufferUnscaled, gsl::span<*ParameterScaling* const> pscale, gsl::span<*realtype*> bufferScaled)

Apply parameter scaling according to `scaling`

Parameters

- **bufferUnscaled** –
- **pscale** – parameter scaling
- **bufferScaled** – destination

Template Function amici::serializeToChar

- Defined in file_include_amici_serialization.h

Function Documentation

template<typename **T**>
char *amici::**serializeToChar**(*T* const &data, int *size)

Serialize object to char array.

Parameters

- **data** – input object
- **size** – maximum char length

Returns
The object serialized as char

Template Function amici::serializeToStdVec

- Defined in file_include_amici_serialization.h

Function Documentation

template<typename **T**>
std::vector<char> `amici::`**`serializeToStdVec`**(*T* const &data)

Serialize object to std::vector<char>

Parameters
`data` – input object

Returns
The object serialized as std::vector<char>

Template Function amici::serializeToString

- Defined in file_include_amici_serialization.h

Function Documentation

template<typename **T**>
std::string `amici::`**`serializeToString`**(*T* const &data)

Serialize object to string.

Parameters
`data` – input object

Returns
The object serialized as string

Function amici::simulation_status_to_str

- Defined in file_include_amici_amici.h

Function Documentation

std::string `amici::`**`simulation_status_to_str`**(int status)

Get the string representation of the given simulation status code (see *ReturnData::status*).

Parameters
`status` – Status code

Returns
Name of the variable representing this status code.

Template Function amici::slice(std::vector<T>&, int, unsigned)

- Defined in file_include_amici_misc.h

Function Documentation

template<class **T**>
gsl::span<*T*> `amici::slice`(std::vector<*T*> &data, int index, unsigned size)

creates a slice from existing data

Parameters

- **data** – to be sliced
- **index** – slice index
- **size** – slice size

Returns
span of the slice

Template Function amici::slice(std::vector<T> const&, int, unsigned)

- Defined in file_include_amici_misc.h

Function Documentation

template<class **T**>
gsl::span<*T* const> `amici::slice`(std::vector<*T*> const &data, int index, unsigned size)

creates a constant slice from existing constant data

Parameters

- **data** – to be sliced
- **index** – slice index
- **size** – slice size

Returns
span of the slice

Function amici::unravel_index(size_t, size_t)

- Defined in file_include_amici_misc.h

Function Documentation

auto amici::**unravel_index**(size_t flat_idx, size_t num_cols) -> std::pair<size_t, size_t>

Convert a flat index to a pair of row/column indices, assuming row-major order.

Parameters

- **flat_idx** – flat index
- **num_cols** – number of columns of referred to matrix

Returns

row index, column index

Function amici::unravel_index(sunindextype, SUNMatrix)

- Defined in file_include_amici_sundials_matrix_wrapper.h

Function Documentation

auto amici::**unravel_index**(sunindextype i, SUNMatrix m) -> std::pair<sunindextype, sunindextype>

Convert a flat index to a pair of row/column indices.

Parameters

- **i** – flat index
- **m** – referred to matrix

Returns

row index, column index

Function amici::unscaleParameters

- Defined in file_include_amici_misc.h

Function Documentation

void amici::**unscaleParameters**(gsl::span<*realtype* const> bufferScaled, gsl::span<*ParameterScaling* const> pscale, gsl::span<*realtype*> bufferUnscaled)

Remove parameter scaling according to the parameter scaling in pscale.

All vectors must be of same length.

Parameters

- **bufferScaled** – scaled parameters
- **pscale** – parameter scaling
- **bufferUnscaled** – unscaled parameters are written to the array

Function amici::wrapErrHandlerFn

- Defined in file_include_amici_solver.h

Function Documentation

void amici::**wrapErrHandlerFn**(int error_code, char const *module, char const *function, char *msg, void *eh_data)

Extracts diagnosis information from solver memory block and passes them to the specified output function.

Parameters

- **error_code** – error identifier
- **module** – name of the module in which the error occurred
- **function** – name of the function in which the error occurred
- **msg** – error message
- **eh_data** – *amici::Solver* as void*

Template Function amici::writeSlice(gsl::span<T const> const, gsl::span<T>)

- Defined in file_include_amici_misc.h

Function Documentation

template<class **T**>
void amici::**writeSlice**(gsl::span<*T* const> const slice, gsl::span<*T*> buffer)

local helper function to write computed slice to provided buffer (span)

Parameters

- **slice** – computed value
- **buffer** – buffer to which values are to be written

Template Function amici::writeSlice(std::vector<T> const&, std::vector<T>&)

- Defined in file_include_amici_misc.h

Function Documentation

template<class **T**>
void amici::**writeSlice**(std::vector<*T*> const &s, std::vector<*T*> &b)

local helper function to write computed slice to provided buffer (vector)

Parameters

- **s** – computed value
- **b** – buffer to which values are to be written

Template Function amici::writeSlice(std::vector<T> const&, gsl::span<T>)

- Defined in file_include_amici_misc.h

Function Documentation

template<class **T**>
void `amici::`**`writeSlice`**(std::vector<*T*> const &s, gsl::span<*T*> b)

local helper function to write computed slice to provided buffer (vector/span)

Parameters

- **`s`** – computed value
- **`b`** – buffer to which values are to be written

Function amici::writeSlice(AmiVector const&, gsl::span<realtype>)

- Defined in file_include_amici_misc.h

Function Documentation

void `amici::`**`writeSlice`**(*AmiVector* const &s, gsl::span<*realtype*> b)

local helper function to write computed slice to provided buffer (AmiVector/span)

Parameters

- **`s`** – computed value
- **`b`** – buffer to which values are to be written

Template Function boost::serialization::archiveVector

- Defined in file_include_amici_serialization.h

Function Documentation

template<class **Archive**, typename **T**>
void `boost::serialization::`**`archiveVector`**(*Archive* &ar, *T* **p, int size)

Serialize a raw array to a boost archive.

Parameters

- **`ar`** – archive
- **`p`** – Pointer to array
- **`size`** – Size of p

Template Function boost::serialization::serialize(Archive&, amici::Model&, unsigned int)

- Defined in file_include_amici_model.h

Function Documentation

template<class **Archive**>
void `boost::serialization::`**`serialize`**(*Archive* &ar, amici::*Model* &m, unsigned int version)

Template Function boost::serialization::serialize(Archive&, amici::ReturnData&, unsigned int)

- Defined in file_include_amici_rdata.h

Function Documentation

template<class **Archive**>
void `boost::serialization::`**`serialize`**(*Archive* &ar, amici::*ReturnData* &r, unsigned int version)

Template Function boost::serialization::serialize(Archive&, amici::Solver&, unsigned int)

- Defined in file_include_amici_solver.h

Function Documentation

template<class **Archive**>
void `boost::serialization::`**`serialize`**(*Archive* &ar, amici::*Solver* &s, unsigned int version)

Template Function boost::serialization::serialize(Archive&, amici::CVodeSolver&, unsigned int)

- Defined in file_include_amici_solver_cvodes.h

Function Documentation

template<class **Archive**>
void `boost::serialization::`**`serialize`**(*Archive* &ar, amici::*CVodeSolver* &s, unsigned int version)

Template Function boost::serialization::serialize(Archive&, amici::IDASolver&, unsigned int)

- Defined in file_include_amici_solver_idas.h

Function Documentation

template<class **Archive**>
void `boost::serialization::`**`serialize`**(*Archive* &ar, amici::*IDASolver* &s, unsigned int version)

Template Function boost::serialization::serialize(Archive&, amici::AmiVector&, unsigned int)

- Defined in file_include_amici_vector.h

Function Documentation

template<class **Archive**>
void `boost::serialization::`**`serialize`**(*Archive* &ar, amici::*AmiVector* &s, unsigned int version)

Function gsl::make_span(SUNMatrix)

- Defined in file_include_amici_sundials_matrix_wrapper.h

Function Documentation

inline span<realtype> `gsl::`**`make_span`**(SUNMatrix m)

Create span from SUNMatrix.

Parameters
m – SUNMatrix

Returns
Created span

Function gsl::make_span(N_Vector)

- Defined in file_include_amici_vector.h

Function Documentation

inline span<realtype> `gsl::`**`make_span`**(N_Vector nv)

Create span from N_Vector.

Parameters
nv –

Returns

Function gsl::make_span(amici::AmiVector const&)

- Defined in file_include_amici_vector.h

Function Documentation

inline span<realtype const> gsl::**make_span**(amici::*AmiVector* const &av)

Create span from N_Vector.

Parameters

nv –

Variables

Variable amici::AMICI_CONV_FAILURE

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_CONV_FAILURE** = -4

Variable amici::AMICI_DAMPING_FACTOR_ERROR

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_DAMPING_FACTOR_ERROR** = -86

Variable amici::AMICI_DATA_RETURN

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_DATA_RETURN** = 1

Variable amici::AMICI_ERR_FAILURE

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_ERR_FAILURE** = -3

Variable amici::AMICI_ERROR

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_ERROR** = -99

Variable amici::AMICI_FIRST_RHSFUNC_ERR

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_FIRST_RHSFUNC_ERR** = -9

Variable amici::AMICI_ILL_INPUT

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_ILL_INPUT** = -22

Variable amici::AMICI_LSETUP_FAIL

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_LSETUP_FAIL** = -6

Variable amici::AMICI_MAX_TIME_EXCEEDED

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_MAX_TIME_EXCEEDED** = -1000

Variable amici::AMICI_NO_STEADY_STATE

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_NO_STEADY_STATE** = -81

Variable amici::AMICI_NORMAL

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_NORMAL** = 1

Variable amici::AMICI_NOT_IMPLEMENTED

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_NOT_IMPLEMENTED** = -999

Variable amici::AMICI_NOT_RUN

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_NOT_RUN** = -1001

Variable amici::AMICI_ONE_STEP

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_ONE_STEP** = 2

Variable amici::AMICI_ONEOUTPUT

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_ONEOUTPUT** = 5

Variable amici::AMICI_PREEQUILIBRATE

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_PREEQUILIBRATE** = -1

Variable amici::AMICI_RECOVERABLE_ERROR

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::AMICI_RECOVERABLE_ERROR = 1

Variable amici::AMICI_RHSFUNC_FAIL

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::AMICI_RHSFUNC_FAIL = -8

Variable amici::AMICI_ROOT_RETURN

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::AMICI_ROOT_RETURN = 2

Variable amici::AMICI_SINGULAR_JACOBIAN

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::AMICI_SINGULAR_JACOBIAN = -809

Variable amici::AMICI_SUCCESS

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::AMICI_SUCCESS = 0

Variable amici::AMICI_TOO_MUCH_ACC

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_TOO_MUCH_ACC** = -2

Variable amici::AMICI_TOO_MUCH_WORK

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_TOO_MUCH_WORK** = -1

Variable amici::AMICI_UNRECOVERABLE_ERROR

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr int amici::**AMICI_UNRECOVERABLE_ERROR** = -10

Variable amici::model_quantity_to_str

- Defined in file_include_amici_model.h

Variable Documentation

std::map<*ModelQuantity*, std::string> const amici::**model_quantity_to_str**

Variable amici::pi

- Defined in file_include_amici_defines.h

Variable Documentation

constexpr double **amici::pi** = 3.14159265358979323846

Defines

Define _USE_MATH_DEFINES

- Defined in file_include_amici_defines.h

Define Documentation

_USE_MATH_DEFINES

Define AMICI_H5_RESTORE_ERROR_HANDLER

- Defined in file_include_amici_hdf5.h

Define Documentation

AMICI_H5_RESTORE_ERROR_HANDLER

Define AMICI_H5_SAVE_ERROR_HANDLER

- Defined in file_include_amici_hdf5.h

Define Documentation

AMICI_H5_SAVE_ERROR_HANDLER

Define AMICI_VERSION

- Defined in file_include_amici_version.in.h

Define Documentation

AMICI_VERSION

Define M_1_PI

- Defined in file_include_amici_defines.h

Define Documentation

M_1_PI

Define M_2_PI

- Defined in file_include_amici_defines.h

Define Documentation

M_2_PI

Define M_2_SQRTPI

- Defined in file_include_amici_defines.h

Define Documentation

M_2_SQRTPI

Define M_E

- Defined in file_include_amici_defines.h

Define Documentation

M_E

Define M_LN10

- Defined in file_include_amici_defines.h

Define Documentation

M_LN10

Define M_LN2

- Defined in file_include_amici_defines.h

Define Documentation

M_LN2

Define M_LOG10E

- Defined in file_include_amici_defines.h

Define Documentation

M_LOG10E

Define M_LOG2E

- Defined in file_include_amici_defines.h

Define Documentation

M_LOG2E

Define M_PI

- Defined in file_include_amici_defines.h

Define Documentation

```
M_PI
```

Define M_PI_2

- Defined in file_include_amici_defines.h

Define Documentation

```
M_PI_2
```

Define M_PI_4

- Defined in file_include_amici_defines.h

Define Documentation

```
M_PI_4
```

Define M_SQRT1_2

- Defined in file_include_amici_defines.h

Define Documentation

```
M_SQRT1_2
```

Define M_SQRT2

- Defined in file_include_amici_defines.h

Define Documentation

```
M_SQRT2
```

Typedefs

Typedef amici::const_N_Vector

- Defined in file_include_amici_vector.h

Typedef Documentation

using amici::**const_N_Vector** = std::add_const_t<typename std::remove_pointer_t<N_Vector>>*

Since const N_Vector is not what we want

Typedef amici::realtype

- Defined in file_include_amici_defines.h

Typedef Documentation

using amici::**realtype** = double

defines variable type for simulation variables (determines numerical accuracy)

CHAPTER

TWELVE

MATLAB INTERFACE

12.1 Installing the AMICI MATLAB toolbox

To use AMICI from MATLAB, start MATLAB and add the `AMICI/matlab` directory to the MATLAB path. To add all toolbox directories to the MATLAB path, execute the matlab script:

```
installAMICI.m
```

To store the installation for further MATLAB session, the path can be saved via:

```
savepath
```

For the compilation of `.mex` files, MATLAB needs to be configured with a working C++ compiler. The C++ compiler needs to be installed and configured via:

```
mex -setup c++
```

For a list of supported compilers we refer to the respective MathWorks documentation.

12.2 Using AMICI's MATLAB interface

In the following we will give a detailed overview how to specify models in MATLAB and how to call the generated simulation files.

Note: The MATLAB interface requires the MathWorks Symbolic Math Toolbox for model import (but not for model simulation).

The Symbolic Math Toolbox requirement can be circumvented by performing model import using the Python interface. The resulting code can then be used from Matlab (see *Compiling a Python-generated model*).

Warning: Due to changes in the Symbolic Math Toolbox, the last MATLAB release with working AMICI model import is R2017b (see https://github.com/AMICI-dev/AMICI/issues/307).

12.2.1 Specifying models in Matlab

This guide will guide the user on how to specify models in MATLAB. For example implementations see the examples in the `matlab/examples` directory.

Header

The model definition needs to be defined as a function which returns a `struct` with all symbolic definitions and options.

```
function [model] = example_model_syms()
```

Options

Set the options by specifying the respective field of the model struct

```
model.(fieldname) = value
```

The options specify default options for simulation, parametrisation and compilation. All of these options are optional.

field	description	default
.param	default parametrisation 'log'/'log10'/'lin'	'lin'
.debug	flag to compile with debug symbols	false
.forward	flag to activate forward sensitivities	true
.adjoint	flag to activate adjoint sensitivities	true

When set to `false`, the fields `forward` and `adjoint` will speed up the time required to compile the model but also disable the respective sensitivity computation.

States

Create the respective symbolic variables. The name of the symbolic variable can be chosen arbitrarily.

```
syms state1 state2 state3
```

Create the state vector containing all states:

```
model.sym.x = [ state1 state2 state3 ];
```

Parameters

Create the respective symbolic variables. The name of the symbolic variable can be chosen arbitrarily. Sensitivities will be derived for all *parameters*.

```
syms param1 param2 param3 param4 param5 param6
```

Create the parameters vector

```
model.sym.p = [ param1 param2 param3 param4 param5 param6 ];
```

Constants

Create the respective symbolic variables. The name of the symbolic variable can be chosen arbitrarily. Sensitivities with respect to *constants* will not be derived.

```
syms const1 const2
```

Create the constants vector

```
model.sym.k = [ const1 const2 ];
```

Differential equations

For time-dependent differential equations you can specify a symbolic variable for time. This **needs** to be denoted by `t`.

```
syms t
```

Specify the right hand side of the differential equation `f` or `xdot`

```
model.sym.xdot(1) = [ const1 - param1*state1 ];
model.sym.xdot(2) = [ +param2*state1 + dirac(t-param3) - const2*state2 ];
model.sym.xdot(3) = [ param4*state2 ];
```

or

```
model.sym.f(1) = [ const1 - param1*state1 ];
model.sym.f(2) = [ +param2*state1 + dirac(t-param3) - const2*state2 ];
model.sym.f(3) = [ param4*state2 ];
```

The specification of `f` or `xdot` may depend on states, parameters and constants.

For DAEs also specify the mass matrix.

```
model.sym.M = [1, 0, 0;...
               0, 1, 0;...
               0, 0, 0];
```

The specification of `M` may depend on parameters and constants.

For ODEs the integrator will solve the equation $\dot{x} = f$ and for DAEs the equations $M \cdot \dot{x} = f$. AMICI will decide whether to use CVODES (for ODEs) or IDAS (for DAEs) based on whether the mass matrix is defined or not.

In the definition of the differential equation you can use certain symbolic functions. For a full list of available functions see `src/symbolic_functions.cpp`.

Dirac functions can be used to cause a jump in the respective states at the specified time-point. This is typically used to model injections, or other external stimuli. Spline functions can be used to model time/state dependent response with unknown time/state dependence.

Initial Conditions

Specify the initial conditions. These may depend on parameters on constants and must have the same size as `x`.

```
model.sym.x0 = [ param4, 0, 0 ];
```

Observables

Specify the observables. These may depend on parameters and constants.

```
model.sym.y(1) = state1 + state2;
model.sym.y(2) = state3 - state2;
```

In the definition of the observable you can use certain symbolic functions. For a full list of available functions see `src/symbolic_functions.cpp`. Dirac functions in observables will have no effect.

Events

Specifying events is optional. Events are specified in terms of a trigger function, a bolus function and an output function. The roots of the trigger function defines the occurrences of the event. The bolus function defines the change in the state on event occurrences. The output function defines the expression which is evaluated and reported by the simulation routine on every event occurrence. The user can create events by constructing a vector of objects of the class *amievent*.

```
model.sym.event(1) = amievent(state1 - state2,0,[]);
```

Events may depend on states, parameters and constants but *not* on observables.

For more details about event support see:

> Fröhlich, F., Theis, F. J., Rädler, J. O., & Hasenauer, J. (2017). Parameter estimation for dynamical systems with discrete events and logical operations. Bioinformatics, 33(7), 1049-1056. doi:10.1093/bioinformatics/btw764.

Standard deviation

Specifying standard deviations is optional. It only has an effect when computing adjoint sensitivities. It allows the user to specify standard deviations of experimental data for observables and events.

Standard deviation for observable data is denoted by `sigma_y`

```
model.sym.sigma_y(1) = param5;
```

Standard deviation for event data is denoted by `sigma_t`

```
model.sym.sigma_t(1) = param6;
```

Both `sigma_y` and `sigma_t` can either be a scalar or of the same dimension as the observables / events function. They can depend on time and parameters but must not depend on the states or observables. The values provided in `sigma_y` and `sigma_t` will only be used if the value in `D.Sigma_Y` or `D.Sigma_T` in the user-provided data struct is `NaN`. See simulation for details.

Objective Function

By default, AMICI assumes a normal noise model and uses the corresponding negative log-likelihood

$$J = 1/2 * sum(((y_i(t) - my_ti)/sigma_{y_i})^2 + log(2 * pi * sigma_y^2)$$

as objective function. A user provided objective function can be specified in

```
model.sym.Jy
```

As reference see the default specification of `this.sym.Jy` in `amimodel.makeSyms`.

12.2.2 SBML

AMICI can also import SBML models using the command `SBML2AMICI`. This will generate a model specification as described above, which may be edited by the user to apply further changes.

12.2.3 Model Compilation

The model can then be compiled by calling `amiwrap.m`:

```
amiwrap(modelname,'example_model_syms',dir,o2flag)
```

Here `modelname` should be a string defining the name of the model, `dir` should be a string containing the path to the directory in which simulation files should be placed and `o2flag` is a flag indicating whether second order sensitivities should also be compiled. The user should make sure that the previously defined function `example_model_syms` is in the user path. Alternatively, the user can also call the function `example_model_syms`

```
[model] = example_model_syms()
```

and subsequently provide the generated struct to `amiwrap(...)`, instead of providing the symbolic function:

```
amiwrap(modelname,model,dir,o2flag)
```

In a similar fashion, the user could also generate multiple models and pass them directly to `amiwrap(...)` without generating respective model definition scripts.

Compiling a Python-generated model

For better performance or to avoid the Symbolic Math Toolbox requirement, it might be desirable to import a model in Python and compile the resulting code into a mex file. For Python model import, consult the respective section of the Python documentation. Once the imported succeeded, there will be a `compileMexFile.m` script inside the newly created model directory which can be invoked to compile the mex file. This mex file and `simulate_*.m` can be used as if fully created by matlab.

Using Python-AMICI model import from Matlab

With recent matlab versions it is possible to use the AMICI python package from within Matlab. This not quite comfortable yet, but it is possible.

Here for proof of concept:

- Install the python package as described in the documentation
- Ensure `pyversion` shows the correct python version (3.6 or 3.7)
- Then, from within the AMICI `matlab/` directory:

```
sbml_importer = py.amici.SbmlImporter('../python/examples/example_steadystate/model_
↪steadystate_scaled.xml')
sbml_importer.sbml2amici('steadystate', 'steadystate_example_from_python')
model = py.steadystate.getModel()
solver = model.getSolver()
model.setTimepoints(linspace(0, 50, 51))
rdata = py.amici.runAmiciSimulation(model, solver)
result = struct(py.dict(rdata.items()))
t = double(py.array.array('d', result.ts))
x = double(py.array.array('d', result.x.flatten()))
x = reshape(x, flip(double(py.array.array('d', result.x.shape))))
plot(t, x)
```

12.2.4 Model simulation

After the call to `amiwrap(...)` two files will be placed in the specified directory. One is a `_modelname_.mex` and the other is `simulate_*modelname*.m`. The mex file should never be called directly. Instead the MATLAB script, which acts as a wrapper around the .mex simulation file should be used.

The `simulate_ _modelname_.m` itself carries extensive documentation on how to call the function, what it returns and what additional options can be specified. In the following we will give a short overview of possible function calls.

Integration

Define a time vector:

```
t = linspace(0,10,100)
```

Generate a parameter vector:

```
theta = ones(6,1);
```

Generate a constants vector:

```
kappa = ones(2,1);
```

Integrate:

```
sol = simulate_modelname(t,theta,kappa,[],options)
```

The integration status will be indicated by the `sol.status` flag. Negative values indicated failed integration. The states will then be available as `sol.x`. The observables will then be available as `sol.y`. The event outputs will then

be available as `sol.z`. If no event occurred there will be an event at the end of the considered interval with the final value of the root function is stored in `sol.rz`.

Alternatively the integration can also be called via

```
[status,t,x,y] = simulate_modelname(t,theta,kappa,[],options)
```

The integration status will be indicated by the flag `status` . Negative values indicated failed integration. The states will then be available as `x`. The observables will then be available as `y`. No event output will be given.

Forward Sensitivities

Set the sensitivity computation to forward sensitivities and integrate:

```
options.sensi = 1;
options.sensi_meth = 'forward';
sol = simulate_modelname(t,theta,kappa,[],options)
```

The integration status will be indicated by the `sol.status` flag. Negative values indicate failed integration. The states will be available as `sol.x`, with the derivative with respect to the parameters in `sol.sx`. The observables will be available as `sol.y`, with the derivative with respect to the parameters in `sol.sy`. The event outputs will be available as `sol.z`, with the derivative with respect to the parameters in `sol.sz`. If no event occured there will be an event at the end of the considered interval with the final value of the root function stored in `sol.rz`, with the derivative with respect to the parameters in `sol.srz`.

Alternatively the integration can also be called via

```
[status,t,x,y,sx,sy] = simulate_modelname(t,theta,kappa,[],options)
```

The integration status will be indicated by the status flag. Negative values indicate failed integration. The states will then be available as `x`, with derivative with respect to the parameters in `sx`. The observables will then be available as `y`, with derivative with respect to the parameters in `sy`. No event output will be given.

Adjoint sensitivities

Set the sensitivity computation to adjoint sensitivities:

```
options.sensi = 1;
options.sensi_meth = 'adjoint';
```

Define Experimental Data:

```
D.Y = [NaN(1,2)],ones(length(t)-1,2)];
D.Sigma_Y = [0.1*ones(length(t)-1,2),NaN(1,2)];
D.T = ones(1,1);
D.Sigma_T = NaN;
```

The `NaN` values in `Sigma_Y` and `Sigma_T` will be replaced by the specification in `model.sym.sigma_y` and `model.sym.sigma_t`. Data points with `NaN` value will be completely ignored.

Integrate:

```
sol = simulate_modelname(t,theta,kappa,D,options)
```

The integration status will be indicated by the sol.status flag. Negative values indicate failed integration. The log-likelihood will then be available as `sol.llh` and the derivative with respect to the parameters in `sol.sllh`. Note that for adjoint sensitivities no state, observable and event sensitivities will be available. Yet this approach can be expected to be significantly faster for systems with a large number of parameters.

Steady-state sensitivities

This will compute state sensitivities according to the formula

$$s_k^x = -\left(\frac{\partial f}{\partial x}\right)^{-1} \frac{\partial f}{\partial \theta_k}$$

In the current implementation this formulation does not allow for conservation laws as this would result in a singular Jacobian.

Set the final timepoint as infinity, this will indicate the solver to compute the steadystate:

```
t = Inf;
```

Set the sensitivity computation to steady state sensitivities:

```
options.sensi = 1;
```

Integrate:

```
sol = simulate_modelname(t,theta,kappa,D,options)
```

The states will be available as `sol.x`, with the derivative with respect to the parameters in `sol.sx`. The observables will be available as `sol.y`, with the derivative with respect to the parameters in `sol.sy`. Notice that for steady state sensitivities no event sensitivities will be available. For the accuracy of the computed derivatives it is essential that the system is sufficiently close to a steady state. This can be checked by examining the right hand side of the system at the final time-point via `sol.diagnosis.xdot`.

12.3 FAQ

Q: My model fails to build.

A: Remove the corresponding model directory located in AMICI/models/*yourmodelname* and compile again.

Q: It still does not compile.

A: Remove the directory AMICI/models/`mexext` and compile again.

Q: It still does not compile.

A: Make an issue and we will have a look.

Q: My Python-generated model does not compile from MATLAB.

A: Try building any of the available examples before. If this succeeds, retry building the original model. Some dependencies might not be built correctly when using only the `compileMexFile.m` script.

Q: I get an out of memory error while compiling my model on a Windows machine.

A: This may be due to an old compiler version. See issue #161 for instructions on how to install a new compiler.

Q: How are events interpreted in a DAE context?

A: Currently we only support impulse free events. Also sensitivities have never been tested. Proceed with care and create an issue if any problems arise!

Q: The simulation/sensitivities I get are incorrect.

A: There are some known issues, especially with adjoint sensitivities, events and DAEs. If your particular problem is not featured in the issues list, please add it!

12.4 AMICI Matlab API

AMICI Matlab library functions

12.4.1 Class Hierarchy

12.4.2 File Hierarchy

12.4.3 Full API

Namespaces

Namespace matlab

Contents

Namespaces

Namespace matlab::mixin

Classes and Structs

Class amidata

- Defined in file_matlab_@amidata_amidata.m

Inheritance Relationships

Base Type

- `public handle`

Class Documentation

`amidata : public handle`

AMIDATA provides a data container to pass experimental data to the simulation routine for likelihood computation. when any of the properties are updated, the class automatically checks consistency of dimension and updates related properties and initialises them with NaNs.

Public Functions

`amidata::amidata(matlabtypesubstitute varargin)`

amidata creates an amidata container for experimental data with specified dimensions amidata.

AMIDATA(amidata) creates a copy of the input container

AMIDATA(struct) tries to creates an amidata container from the input struct. the struct should have the following

AMIDATA(nt,ny,nz,ne,nk) constructs an empty data container with in the provided dimensions intialised with NaNs

fields

t [nt,1] Y [nt,ny] Sigma_Y [nt,ny] Z [ne,nz] Sigma_Z [ne,nz] condition [nk,1] conditionPreequilibration [nk,1] if some fields are missing the function will try to initialise them with NaNs with consistent dimensions

param varargin

Public Members

`matlabtypesubstitute nt = 0`

number of timepoints

Default: 0

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute ny = 0`

number of observables

Default: 0

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute nz = 0`

number of event observables

Default: 0

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute ne = 0`

number of events

Default: 0

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute nk = 0`

number of conditions/constants

Default: 0

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute t = double.empty("")`

timepoints of observations

Default: double.empty(“”)

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute Y = double.empty("")`

observations

Default: double.empty(“”)

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute Sigma_Y = double.empty("")`

standard deviation of observations

Default: double.empty(“”)

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute Z = double.empty("")`

event observations

Default: double.empty(“”)

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute Sigma_Z = double.empty("")`

standard deviation of event observations

Default: double.empty(“”)

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute condition = double.empty("")`

experimental condition

Default: double.empty(“”)

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute conditionPreequilibration = double.empty("")`

experimental condition for preequilibration

Default: double.empty(“”)

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute reinitializeStates = false`

reinitialize states based on fixed parameters after preeq.?

Default: false

Class amievent

- Defined in file_matlab_@amievent_amievent.m

Class Documentation

class amievent

AMIEVENT defines events which later on will be transformed into appropriate C code.

Public Functions

amievent::amievent(matlabtypesubstitute trigger, matlabtypesubstitute bolus, matlabtypesubstitute z)

amievent constructs an amievent object from the provided input.

param trigger
trigger function, the event will be triggered on at all roots of this function

param bolus
the bolus that will be added to all states on every occurence of the event

param z
the event output that will be reported on every occurence of the event

mlhsInnerSubst<::amievent > amievent::setHflag(matlabtypesubstitute hflag)

setHflag sets the hflag property.

param hflag
value for the hflag property, type double

retval this
updated event definition object

Public Members

::symbolic trigger = sym.empty("")

the trigger function activates the event on every zero crossing

---

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** sym.empty("")

::symbolic bolus = sym.empty("")

the bolus function defines the change in states that is applied on every event occurence

---

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** sym.empty("")

`::symbolic z = sym.empty("")`

output function for the event

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** sym.empty("")

`matlabtypesubstitute hflag = logical.empty("")`

flag indicating that a heaviside function is present, this helps to speed up symbolic computations

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** logical.empty("")

Class amifun

- Defined in file_matlab_@amifun_amifun.m

Class Documentation

`class amifun`

AMIFUN defines functions which later on will be transformed into appropriate C code.

Public Functions

`amifun::amifun(matlabtypesubstitute funstr, matlabtypesubstitute model)`

amievent constructs an amifun object from the provided input.

param funstr
name of the requested function

param model
amimodel object which carries all symbolic definitions to construct the function

`noret::substitute amifun::writeCcode_sensi(::amimodel model, ::fileid fid)`

writeCcode_sensi is a wrapper for writeCcode which loops over parameters and reduces overhead by check nonzero values

param model
model defintion object

param fid
file id in which the final expression is written

retval fid
void

`noret::substitute amifun::writeCcode(::amimodel model, ::fileid fid)`

writeCcode is a wrapper for gccode which initialises data and reduces overhead by check nonzero values

param model
model defintion object

param fid
file id in which the final expression is written

retval fid
void

`noret::substitute amifun::writeMcode(::amimodel model)`

writeMcode generates matlab evaluable code for specific model functions

param model
model defintion object

retval model
void

`mlhsInnerSubst<::amifun > amifun::gccode(::amimodel model, ::fileid fid)`

gccode transforms symbolic expressions into c code and writes the respective expression into a specified file

param model
model definition object

param fid
file id in which the expression should be written

retval this
function definition object

`mlhsInnerSubst<::amifun > amifun::getDeps(::amimodel model)`

getDeps populates the sensiflag for the requested function

param model
model definition object

retval this
updated function definition object

`mlhsInnerSubst<::amifun > amifun::getArgs(::amimodel model)`

getFArgs populates the fargstr property with the argument string of the respective model function (if applicable). model functions are not wrapped versions of functions which have a model specific name and for which the call is solver specific.

param model
model definition object

retval this
updated function definition object

`mlhsInnerSubst<::amifun > amifun::getNVecs()`

getfunargs populates the nvecs property with the names of the N_Vector elements which are required in the execution of the function (if applicable). the information is directly extracted from the argument string

retval this
updated function definition object

`mlhsInnerSubst<::amifun > amifun::getCVar()`

getCVar populates the cvar property

retval this
updated function definition object

`mlhsInnerSubst<::amifun > amifun::getSensiFlag()`

getSensiFlag populates the sensiflag property

retval this
updated function definition object

`mlhsSubst< mlhsInnerSubst<::amifun >,mlhsInnerSubst<::amimodel > > amifun::getSyms(::amimodel model)`

getSyms computes the symbolic expression for the requested function

param model
model definition object

retval this
updated function definition object

retval model
updated model definition object

Public Members

`::symbolic sym = sym("[]")`

symbolic definition struct

Default: sym("[]")

`::symbolic sym_noopt = sym("[]")`

symbolic definition which was not optimized (no dependencies on w)

Default: sym("[]")

`::symbolic strsym = sym("[]")`

short symbolic string which can be used for the reuse of precomputed values

Default: sym("[]")

`::symbolic strsym_old = sym("[]")`

short symbolic string which can be used for the reuse of old values

Default: sym("[]")

`::char funstr = char.empty("")`

name of the model

Default: char.empty("")

`::char cvar = char.empty("")`

name of the c variable

Default: char.empty("")

`::char argstr = char.empty("")`

argument string (solver specific)

Default: char.empty("")

`::cell deps = cell.empty("")`

dependencies on other functions

Default: cell.empty("")

`matlabtypesubstitute nvecs = cell.empty("")`

nvec dependencies

Default: cell.empty("")

`matlabtypesubstitute sensiflag = logical.empty("")`

indicates whether the function is a sensitivity or derivative with respect to parameters

Default: logical.empty("")

Class amimodel

- Defined in file_matlab_@amimodel_amimodel.m

Inheritance Relationships

Base Type

- `public handle`

Class Documentation

`amimodel : public handle`

AMIMODEL carries all model definitions including functions and events.

Public Functions

`amimodel::amimodel(::string symfun, ::string modelname)`

amimodel initializes the model object based on the provided symfun and modelname

param symfun
this is the string to the function which generates the modelstruct. You can also directly pass the struct here

param modelname
name of the model

`noret::substitute amimodel::updateRHS(matlabtypesubstitute xdot)`

updateRHS updates the private fun property .fun.xdot.sym (right hand side of the differential equation)

param xdot
new right hand side of the differential equation

retval xdot
void

`noret::substitute amimodel::updateModelName(matlabtypesubstitute modelname)`

updateModelName updates the modelname

param modelname
new modelname

retval modelname
void

`noret::substitute amimodel::updateWrapPath(matlabtypesubstitute wrap_path)`

updateModelName updates the modelname

param wrap_path
new wrap_path

retval wrap_path
void

`noret::substitute amimodel::parseModel()`

parseModel parses the model definition and computes all necessary symbolic expressions.

retval void

`noret::substitute amimodel::generateC()`

generateC generates the c files which will be used in the compilation.

retval void

noret::substitute amimodel::generateRebuildM()

generateRebuildM generates a Matlab script for recompilation of this model

retval void

noret::substitute amimodel::compileC()

compileC compiles the mex simulation file

retval void

noret::substitute amimodel::generateM(::amimodel amimodelo2)

generateM generates the matlab wrapper for the compiled C files.

param amimodelo2
this struct must contain all necessary symbolic definitions for second order sensivities

retval amimodelo2
void

noret::substitute amimodel::getFun(::struct HTable, ::string funstr)

getFun generates symbolic expressions for the requested function.

param HTable
struct with hashes of symbolic definition from the previous compilation

param funstr
function for which symbolic expressions should be computed

retval funstr
void

noret::substitute amimodel::makeEvents()

makeEvents extracts discontiniuties from the model right hand side and converts them into events

retval void

noret::substitute amimodel::makeSyms()

makeSyms extracts symbolic definition from the user provided model and checks them for consistency

retval void

mlhsInnerSubst<::bool > amimodel::checkDeps(::struct HTable, ::cell deps)

checkDeps checks the dependencies of functions and populates sym fields if necessary

param HTable
struct with reference hashes of functions in its fields

param deps
cell array with containing a list of dependencies

retval cflag
boolean indicating whether any of the dependencies have changed with respect to the hashes stored in HTable

`mlhsInnerSubst<::struct > amimodel::loadOldHashes()`

loadOldHashes loads information from a previous compilation of the model.

retval HTable
struct with hashes of symbolic definition from the previous compilation

`mlhsInnerSubst< matlabtypesubstitute > amimodel::augmento2()`

augmento2 augments the system equation to also include equations for sensitivity equation. This will enable us to compute second order sensitivities in a forward-adjoint or forward-forward apporach later on.

retval this
augmented system which contains symbolic definition of the original system and its sensitivities

`mlhsInnerSubst<::amimodel > amimodel::augmento2vec()`

augmento2 augments the system equation to also include equations for sensitivity equation. This will enable us to compute second order sensitivities in a forward-adjoint or forward-forward apporach later on.

retval modelo2vec
augmented system which contains symbolic definition of the original system and its sensitivities

Public Members

`::struct sym = struct.empty("")`

symbolic definition struct

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** struct.empty("")

`::struct fun = struct.empty("")`

struct which stores information for which functions c code needs to be generated

---

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** struct.empty("")

`::amievent event = amievent.empty("")`

struct which stores information for which functions c code needs to be generated

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** amievent.empty("")

`::string modelname = char.empty("")`

name of the model

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** char.empty("")

`::struct HTable = struct.empty("")`

struct that contains hash values for the symbolic model definitions

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** struct.empty("")

`::bool debug = false`

flag indicating whether debugging symbols should be compiled

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** false

`::bool adjoint = true`

flag indicating whether adjoint sensitivities should be enabled

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** true

::bool forward = true

flag indicating whether forward sensitivities should be enabled

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** true

::double t0 = 0

default initial time

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** 0

::string wtype = char.empty("")

type of wrapper (cvodes/idas)

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** char.empty("")

::int nx = double.empty("")

number of states

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::int nxtrue = double.empty("")

number of original states for second order sensitivities

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::int ny = double.empty("")

number of observables

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::int nytrue = double.empty("")

number of original observables for second order sensitivities

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::int np = double.empty("")

number of parameters

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::int nk = double.empty("")

number of constants

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::int ng = double.empty("")

number of objective functions

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

`::int nevent = double.empty("")`

number of events

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

`::int nz = double.empty("")`

number of event outputs

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

`::int nztrue = double.empty("")`

number of original event outputs for second order sensitivities

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

`::*int id = double.empty("")`

flag for DAEs

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::int ubw = double.empty("")

upper Jacobian bandwidth

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::int lbw = double.empty("")

lower Jacobian bandwidth

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::int nnz = double.empty("")

number of nonzero entries in Jacobian

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::*int sparseidx = double.empty("")

dataindexes of sparse Jacobian

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::*int rowvals = double.empty("")

rowindexes of sparse Jacobian

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::*int colptrs = double.empty("")

columnindexes of sparse Jacobian

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::*int sparseidxB = double.empty("")

dataindexes of sparse Jacobian

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::*int rowvalsB = double.empty("")

rowindexes of sparse Jacobian

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::*int colptrsB = double.empty("")

columnindexes of sparse Jacobian

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** double.empty("")

::*cell funs = cell.empty("")

cell array of functions to be compiled

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** cell.empty("")

`::*cell mfuns = cell.empty("")`

cell array of matlab functions to be compiled

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** cell.empty("")

`::string coptim = "-O3"`

optimisation flag for compilation

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** "-O3"

`::string param = "lin"`

default parametrisation

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** "lin"

`matlabtypesubstitute wrap_path = char.empty("")`

path to wrapper

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** char.empty("")

`matlabtypesubstitute recompile = false`

flag to enforce recompilation of the model

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** false

`matlabtypesubstitute cfun = struct.empty("")`

storage for flags determining recompilation of individual functions

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** struct.empty(“”)

`matlabtypesubstitute o2flag = 0`

flag which identifies augmented models 0 indicates no augmentation 1 indicates augmentation by first order sensitivities (yields second order sensitivities) 2 indicates augmentation by one linear combination of first order sensitivities (yields hessian-vector product)

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** 0

`matlabtypesubstitute z2event = double.empty("")`

vector that maps outputs to events

Default: double.empty(“”)

`matlabtypesubstitute splineflag = false`

flag indicating whether the model contains spline functions

Default: false

`matlabtypesubstitute minflag = false`

flag indicating whether the model contains min functions

Default: false

`matlabtypesubstitute maxflag = false`

flag indicating whether the model contains max functions

Default: false

`::int nw = 0`

number of derived variables w, w is used for code optimization to reduce the number of frequently occuring expressions

Default: 0

`::int ndwdx = 0`

number of derivatives of derived variables w, dwdx

Default: 0

`::int ndwdp = 0`

number of derivatives of derived variables w, dwdp

Default: 0

Public Static Functions

`noret::substitute amimodel::compileAndLinkModel(matlabtypesubstitute modelname, matlabtypesubstitute modelSourceFolder, matlabtypesubstitute coptim, matlabtypesubstitute debug, matlabtypesubstitute funs, matlabtypesubstitute cfun)`

compileAndLinkModel compiles the mex simulation file. It does not check if the model files have changed since generating C++ code or whether all files are still present. Use only if you know what you are doing. The safer alternative is rerunning *amiwrap()*.

param modelname
name of the model as specified for *amiwrap()*

param modelSourceFolder
path to model source directory

param coptim
optimization flags

param debug
enable debugging

param funs
array with names of the model functions, will be guessed from source files if left empty

param cfun
struct indicating which files should be recompiled

retval cfun
void

`noret::substitute amimodel::generateMatlabWrapper(matlabtypesubstitute nx, matlabtypesubstitute ny, matlabtypesubstitute np, matlabtypesubstitute nk, matlabtypesubstitute nz, matlabtypesubstitute o2flag, ::amimodel amimodelo2, matlabtypesubstitute wrapperFilename, matlabtypesubstitute modelname, matlabtypesubstitute pscale, matlabtypesubstitute forward, matlabtypesubstitute adjoint)`

generateMatlabWrapper generates the matlab wrapper for the compiled C files.

param nx
number of states

param ny
number of observables

param np
number of parameters

param nk
number of fixed parameters

param nz
number of events

param o2flag
o2flag

param amimodelo2
this struct must contain all necessary symbolic definitions for second order sensivities

param wrapperFilename
output filename

param modelname
name of the model

param pscale
default parameter scaling

param forward
has forward sensitivity equations

param adjoint
has adjoint sensitivity equations

retval adjoint
void

Class amioption

- Defined in file_matlab_@amioption_amioption.m

Inheritance Relationships

Base Type

- `public matlab::mixin::CustomDisplay`

Class Documentation

amioption : public matlab::mixin::CustomDisplay

AMIOPTION provides an option container to pass simulation parameters to the simulation routine.

Public Functions

amioption::amioption(matlabtypesubstitute varargin)

amioptions Construct a new amioptions object OPTS = *amioption()* creates a set of options with each option set to its default value.

OPTS = *amioption(PARAM, VAL, ...)* creates a set of options with the named parameters altered with the specified values.

OPTS = *amioption(OLDOPTS, PARAM, VAL, ...)* creates a copy of OLDOPTS with the named parameters altered with the specified value

Note: to see the parameters, check the documentation page for amioption

param varargin
input to construct amioption object, see function function description

Public Members

matlabtypesubstitute atol = 1e-16

absolute integration tolerace

Default: 1e-16

matlabtypesubstitute rtol = 1e-8

relative integration tolerace

Default: 1e-8

matlabtypesubstitute maxsteps = 1e4

maximum number of integration steps

Default: 1e4

matlabtypesubstitute quad_atol = 1e-12

absolute quadrature tolerace

Default: 1e-12

matlabtypesubstitute quad_rtol = 1e-8

relative quadrature tolerace

Default: 1e-8

`matlabtypesubstitute maxstepsB = 0`

maximum number of integration steps

Default: 0

`matlabtypesubstitute ss_atol = 1e-16`

absolute steady state tolerace

Default: 1e-16

`matlabtypesubstitute ss_rtol = 1e-8`

relative steady state tolerace

Default: 1e-8

`matlabtypesubstitute sens_ind = double.empty("")`

index of parameters for which the sensitivities are computed

Default: double.empty(“”)

`matlabtypesubstitute tstart = 0`

starting time of the simulation

Default: 0

`matlabtypesubstitute lmm = 2`

linear multistep method.

Default: 2

`matlabtypesubstitute iter = 2`

iteration method for linear multistep.

Default: 2

`matlabtypesubstitute linsol = 9`

linear solver

Default: 9

`matlabtypesubstitute stldet = true`

stability detection flag

Default: true

`matlabtypesubstitute interpType = 1`

interpolation type

Default: 1

`matlabtypesubstitute ism = 1`

forward sensitivity mode

Default: 1

matlabtypesubstitute sensi_meth = 1

sensitivity method

Default: 1

Note: This property has custom functionality when its value is changed.

matlabtypesubstitute sensi_meth_preeq = 1

sensitivity method for preequilibration

Default: 1

matlabtypesubstitute sensi = 0

sensitivity order

Default: 0

Note: This property has custom functionality when its value is changed.

matlabtypesubstitute nmaxevent = 10

number of reported events

Default: 10

matlabtypesubstitute ordering = 0

reordering of states

Default: 0

matlabtypesubstitute ss = 0

steady state sensitivity flag

Default: 0

matlabtypesubstitute x0 = double.empty("")

custom initial state

Default: double.empty(“”)

matlabtypesubstitute sx0 = double.empty("")

custom initial sensitivity

Default: double.empty(“”)

matlabtypesubstitute newton_maxsteps = 40

newton solver: maximum newton steps

Default: 40

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute z2event = double.empty("")`

mapping of event ouputs to events

Default: double.empty(“”)

`matlabtypesubstitute pscale = "[]"`

parameter scaling Single value or vector matching sens_ind. Valid options are “log”,”log10” and “lin” for log, log10 or unscaled parameters p. Use [] for default as specified in the model (fallback: `lin`).

Default: “[]”

Note: This property has custom functionality when its value is changed.

`matlabtypesubstitute steadyStateSensitivityMode = 0`

Mode for for computing sensitivities ({0: Newton}, 1: Simulation)

Default: 0

Public Static Functions

`mlhsInnerSubst< matlabtypesubstitute > amioption::getIntegerPScale(matlabtypesubstitute pscaleString)`

pscaleInt converts a parameter scaling string into the corresponding integer representation

param pscaleString
parameter scaling string

retval pscaleString
int

Class amised

- Defined in file_matlab_@amised_amised.m

Inheritance Relationships

Base Type

- `public handle`

Class Documentation

amised : public handle

AMISED is a container for SED-ML objects.

Public Functions

amised::amised(matlabtypesubstitute sedname)

amised reads in an SEDML document using the JAVA binding of of libSEDML

param sedname
name/path of the SEDML document

Public Members

matlabtypesubstitute model = struct("'event',[],'sym',[]")

amimodel from the specified model

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** struct(“‘event’,[],’sym’,[]”)

matlabtypesubstitute modelname = {""}

cell array of model identifiers

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** {“”}

matlabtypesubstitute sedml = struct.empty("")

stores the struct tree from the xml definition

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** struct.empty(“”)

`matlabtypesubstitute outputcount = "[]"`

count the number of outputs per model

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** "[]"

`matlabtypesubstitute varidx = "[]"`

indexes for dataGenerators

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** "[]"

`matlabtypesubstitute varsym = sym("[]")`

symbolic expressions for variables

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** sym("[]")

`matlabtypesubstitute datasym = sym("[]")`

symbolic expressions for data

Note: This property has non-standard access specifiers: `SetAccess = Private, GetAccess = Public`

Note: Matlab documentation of property attributes. **Default:** sym("[]")

Class optsym

- Defined in file_matlab_@optsym_optsym.m

Inheritance Relationships

Base Type

- `public sym`

Class Documentation

optsym : public sym

OPTSYM is an auxiliary class to gain access to the private symbolic property `s` which is necessary to be able to call symobj::optimize on it.

Public Functions

optsym::optsym(::sym symbol)

optsym converts the symbolic object into a optsym object

param symbol
symbolic object

mlhsInnerSubst<::sym > optsym::getoptimized()

getoptimized calls symobj::optimize on the optsym object

retval out
optimized symbolic object

Functions

Function am_and

- Defined in file_matlab_symbolic_am_and.m

Function Documentation

mlhsInnerSubst< matlabtypesubstitute > am_and(::sym a, ::sym b)

am_and is the amici implementation of the symbolic and function

param a
first input parameter

param b
second input parameter

retval fun
logical value, negative for false, positive for true

Function am_eq

- Defined in file_matlab_symbolic_am_eq.m

Function Documentation

`mlhsInnerSubst< matlabtypesubstitute > am_eq(matlabtypesubstitute varargin)`

am_eq is currently a placeholder that simply produces an error message

param varargin
elements for chain of equalities

retval fun
logical value, negative for false, positive for true

Function am_ge

- Defined in file_matlab_symbolic_am_ge.m

Function Documentation

`mlhsInnerSubst< matlabtypesubstitute > am_ge(::sym varargin)`

am_ge is the amici implementation of the n-ary mathml greaterorequal function this is an n-ary function, for more than 2 input parameters it will check whether and(varargin{1} >= varargin{2},varargin{2} >= varargin{3},...)

param varargin
chain of input parameters

retval fun
a >= b logical value, negative for false, positive for true

Function am_gt

- Defined in file_matlab_symbolic_am_gt.m

Function Documentation

`mlhsInnerSubst< matlabtypesubstitute > am_gt(::sym varargin)`

am_gt is the amici implementation of the n-ary mathml greaterthan function this is an n-ary function, for more than 2 input parameters it will check whether and(varargin{1} > varargin{2},varargin{2} > varargin{3},...)

param varargin
chain of input parameters

retval fun
a > b logical value, negative for false, positive for true

Function am_if

- Defined in file_matlab_symbolic_am_if.m

Function Documentation

`mlhsInnerSubst< matlabtypesubstitute > am_if(::sym condition, ::sym truepart, ::sym falsepart)`

am_if is the amici implementation of the symbolic if function

param condition
logical value

param truepart
value if condition is true

param falsepart
value if condition is false

retval fun
if condition is true truepart, else falsepart

Function am_le

- Defined in file_matlab_symbolic_am_le.m

Function Documentation

`mlhsInnerSubst< matlabtypesubstitute > am_le(::sym varargin)`

am_le is the amici implementation of the n-ary mathml lessorequal function this is an n-ary function, for more than 2 input parameters it will check whether and(varargin{1} <= varargin{2},varargin{2} <= varargin{3},...)

param varargin
chain of input parameters

retval fun
a <= b logical value, negative for false, positive for true

Function am_lt

- Defined in file_matlab_symbolic_am_lt.m

Function Documentation

mlhsInnerSubst< matlabtypesubstitute > am_lt(::sym varargin)

am_lt is the amici implementation of the n-ary mathml lessthan function this is an n-ary function, for more than 2 input parameters it will check whether and(varargin{1} < varargin{2},varargin{2} < varargin{3},...)

param varargin
chain of input parameters

retval fun
a < b logical value, negative for false, positive for true

Function am_max

- Defined in file_matlab_symbolic_am_max.m

Function Documentation

mlhsInnerSubst< matlabtypesubstitute > am_max(::sym a, ::sym b)

am_max is the amici implementation of the symbolic max function

param a
first input parameter

param b
second input parameter

retval fun
maximum of a and b

Function am_min

- Defined in file_matlab_symbolic_am_min.m

Function Documentation

mlhsInnerSubst< matlabtypesubstitute > am_min(::sym a, ::sym b)

am_min is the amici implementation of the symbolic min function

param a
first input parameter

param b
second input parameter

retval fun
minimum of a and b

Function am_or

- Defined in file_matlab_symbolic_am_or.m

Function Documentation

`mlhsInnerSubst< matlabtypesubstitute > am_or(::sym a, ::sym b)`

am_or is the amici implementation of the symbolic or function

param a
first input parameter

param b
second input parameter

retval fun
logical value, negative for false, positive for true

Function am_piecewise

- Defined in file_matlab_symbolic_am_piecewise.m

Function Documentation

`mlhsInnerSubst< matlabtypesubstitute > am_piecewise(matlabtypesubstitute piece, matlabtypesubstitute condition, matlabtypesubstitute default)`

am_piecewise is the amici implementation of the mathml piecewise function

param piece
value if condition is true

param condition
logical value

param default
value if condition is false

retval fun
return value, piece if condition is true, default if not

Function am_spline

- Defined in file_matlab_symbolic_am_spline.m

Function Documentation

`mlhsInnerSubst< matlabtypesubstitute > am_spline(matlabtypesubstitute varargin)`

Function am_spline_pos

- Defined in file_matlab_symbolic_am_spline_pos.m

Function Documentation

`mlhsInnerSubst< matlabtypesubstitute > am_spline_pos(matlabtypesubstitute varargin)`

Function am_stepfun

- Defined in file_matlab_symbolic_am_stepfun.m

Function Documentation

`mlhsInnerSubst< matlabtypesubstitute > am_stepfun(::sym t, matlabtypesubstitute tstart, matlabtypesubstitute vstart, matlabtypesubstitute tend, matlabtypesubstitute vend)`

am_stepfun is the amici implementation of the step function

param t
input variable

param tstart
input variable value at which the step starts

param vstart
value during the step

param tend
input variable value at which the step end

param vend
value after the step

retval fun
0 before tstart, vstart between tstart and tend and vend after tend

Function am_xor

- Defined in file_matlab_symbolic_am_xor.m

Function Documentation

mlhsInnerSubst< matlabtypesubstitute > am_xor(::sym a, ::sym b)

am_xor is the amici implementation of the symbolic exclusive or function

param a
first input parameter

param b
second input parameter

retval fun
logical value, negative for false, positive for true

Function AMICI2D2D

- Defined in file_matlab_AMICI2D2D.m

Function Documentation

noret::substitute AMICI2D2D(matlabtypesubstitute filename, matlabtypesubstitute modelname)

Function amiwrap

- Defined in file_matlab_amiwrap.m

Function Documentation

noret::substitute amiwrap(matlabtypesubstitute varargin)

AMIWRAP generates c++ mex files for the simulation of systems of differential equations via CVODES and IDAS.

param varargin

```
amiwrap ( modelname, symfun, tdir, o2flag )
```

Required Parameters for varargin:

- modelname specifies the name of the model which will be later used for the naming of the simulation file
- symfun specifies a function which executes model definition
- tdir target directory where the simulation file should be placed **Default:** $AMICIDIR/models/modelname

- o2flag boolean whether second order sensitivities should be enabled **Default:** false

retval o2flag
void

Function installAMICI

- Defined in file_matlab_installAMICI.m

Function Documentation

`noret::substitute installAMICI()`

Function SBML2AMICI

- Defined in file_matlab_SBML2AMICI.m

Function Documentation

`noret::substitute SBML2AMICI(matlabtypesubstitute filename, matlabtypesubstitute modelname)`

SBML2AMICI generates AMICI model definition files from SBML.

param filename
name of the SBML file (withouth extension)

param modelname
name of the model, this will define the name of the output file (default: input filename)

retval modelname
void

12.5 AMICI developer's guide

This document contains information for AMICI developers, not too relevant to regular users.

12.5.1 Branches / releases

AMICI roughly follows the GitFlow. All new contributions are merged into `develop`. These changes are regularly merged into `master` as new releases. For release versioning we are trying to follow semantic versioning. New releases are created on GitHub and are automatically deployed to Zenodo for archiving and to obtain a digital object identifier (DOI) to make them citable. Furthermore, our CI pipeline will automatically create and deploy a new release on PyPI.

We try to keep a clean git history. Therefore, feature pull requests are squash-merged to `develop`. Merging of release branches to master is done via merge commits.

12.5.2 When starting to work on some issue

When starting to work on some Github issue, please assign yourself to let other developers know that you are working on it to avoid duplicate work. If the respective issue is not completely clear, it is generally a good idea to ask for clarification before starting to work on it.

If you want to work on something new, please create a Github issue first.

12.5.3 Code contributions

When making code contributions, please follow our style guide and the process described below:

- Check if you agree to release your contribution under the conditions provided in `LICENSE`. By opening a pull requests you confirm us that you do agree.
- Start a new branch from `develop` (on your fork, or at the main repository if you have access)
- Implement your changes
- Submit a pull request to the `develop` branch
- Ensure all tests pass
- When adding new functionality, please also provide test cases (see `tests/cpp/`, `python/tests/`, and documentation/CI.md)
- Write meaningful commit messages
- Run all tests to ensure nothing was broken (more details)
  - Run `scripts/buildAll.sh && scripts/run-cpp-tests.sh`.
  - If you made changes to the Matlab or C++ code and have a Matlab license, please also run `tests/cpp/wrapTestModels.m` and `tests/testModels.m`
  - If you made changes to the Python or C++ code, run `make python-tests` in `build`
- When all tests are passing and you think your code is ready to merge, request a code review (see also our code review guideline)
- Wait for feedback. If you do not receive feedback to your pull request within a week, please give us a friendly reminder.

Style/compatibility guide

General

- All files and functions should come with file-level and function-level documentation.
- All new functionality should be covered by unit or integration tests. Runtime of those tests should be kept as short as possible.

Python

- In terms of Python compatibility, we follow numpy's NEP 29.
- For the Python code we want to follow PEP8. Although this is not the case for all existing code, any new contributions should do so. We use black for code formatting.

  To run black as pre-commit hook, install the pre-commit package (e.g. `pip install pre-commit`), and enable AMICI-hooks by running `pre-commit install` from within the AMICI directory.
- We use Python type hints for all functions (but not for class attributes, since they are not supported by the current Python doxygen filter). In Python code, type hints should be used instead of doxygen `@type`.

  For function docstrings, follow this format:

```
"""One-line description.

Possible a more detailed description

Arguments:
    Argument1: This needs to start on the same line, otherwise the current
        doxygen filter will fail.

    Returns:
        Return value

    Raises:
        SomeError in case of some error.
"""
```

C++

- We use C++17
- We want to maintain compatibility with g++, clang, and the Intel C++ compiler
- For code formatting, we use `clang-format` and `cmake-format`. They can be invoked by `make clang-format cmake-format` from the CMake build directory.

Matlab

To be defined

12.5.4 Further topics

AMICI documentation

This file describes how the AMICI documentation is organized and compiled.

Building documentation

Multi-interface documentation

AMICI documentation hosted at Read the Docs (RTD) is generated using Sphinx and related packages. The legacy GitHub Pages URL https://amici-dev.github.io/AMICI/ is set up as a redirect to RTD.

The main configuration file is `documentation/conf.py` and the documentation is generated using `tox -e doc`. The documentation is written to `documentation/_build/`.

The documentation comprises:

- reStructuredText / Markdown files from `documentation/`
- Python API documentation of native Python modules
- Python API documentation of Python generated via SWIG (doxygen-style comments translated to docstrings by SWIG)
- C++ API documentation (doxygen -> exhale -> breathe -> sphinx)
- Matlab API documentation (mtocpp -> doxygen -> exhale -> breathe -> sphinx)

Doxygen-only (legacy)

(Parts of the) AMICI documentation can also be directly created using doxygen directly. It combines Markdown files from the root directory, from `documentation/` and in-source documentation from the C++ and Matlab source files.

The documentation is generated by running

```
scripts/run-doxygen.sh
```

The resulting HTML and PDF documentation will be created in `doc/`. `scripts/run-doxygen.sh` also checks for any missing in-source documentation.

Doxygen configuration

The main doxygen configuration file is located in `matlab/mtoc/config/Doxyfile.template`. Edit this file for inclusion or exclusion of additional files.

Matlab documentation

Matlab documentation is processed by mtoc++. This is configured in `matlab/mtoc/config`.

Writing documentation

Out-of-source documentation

Out-of-source documentation files should be written in reStructuredText if intended for Read the Docs or in Markdown if intended for rendering on GitHub. Files to be included in the Sphinx/RTD documentation live in `documentation/`. Graphics for documentation are kept in `documentation/gfx/`.

When using Markdown

- Note that there are some incompatibilities of GitHub Markdown and Doxygen Markdown. Ideally documentation should be written in a format compatible with both. This affects for example images links which currently cause trouble in Doxygen.
- Where possible, relative links are preferred over absolute links. However, they should work with both Github and Doxygen and ideally with local files for offline use.
- Please stick to the limit of 80 characters per line for readability of raw Markdown files where possible.

  However, note that some Markdown interpreters can handle line breaks within links and headings, whereas others cannot. Here, compatibility is preferred over linebreaks.
- Avoid trailing whitespace

Maintaining the list of publications

We want to maintain a list of publications / projects using AMICI. This is located at `documentation/references.md`. This file is created by `documentation/recreate_reference_list.py` based on the bibtex file `documentation/amici_refs.bib`.

After any changes to `documentation/amici_refs.bib`, please run

```
documentation/recreate_reference_list.py
```

(requires biblib)

Code review guide

A guide for reviewing code and having your code reviewed by others.

Everyone

- Don't be too protective of your code
- Accept that, to a large extent, coding decisions are a matter of personal preference
- Don't get personal
- Ask for clarification
- Avoid strong language
- Try to understand your counterpart's perspective
- Clarify how strong you feel about each discussion point

Reviewing code

- If there are no objective advantages, don't force your style on others
- Ask questions instead of making demands
- Assume the author gave his best
- Mind the scope (many things are nice to have, but might be out of scope of the current change - open a new issue)
- The goal is "good enough", not "perfect"
- Be constructive
- You do not always have to request changes

Having your code reviewed

- Don't take it personal - the review is on the code, not on you
- Code reviews take time, appreciate the reviewer's comments
- Assume the reviewer did his best (but might still be wrong)
- Keep code changes small (e.g. separate wide reformatting from actual code changes to facility review)
- If the reviewer does not understand your code, probably many others won't either

Checklist

- [ ] Adherence to project-specific style guide
- [ ] The code is self-explanatory
- [ ] The code is concise / expressive
- [ ] Meaningful identifiers are used
- [ ] Corner-cases are covered, cases not covered fail loudly
- [ ] The code can be expected to scale well (enough)
- [ ] The code is well documented (e.g., input, operation, output), but without trivial comments
- [ ] The code is SOLID
- [ ] New code is added in the most meaningful place (i.e. matches the current architecture)
- [ ] No magic numbers
- [ ] No hard-coded values that should be user inputs
- [ ] No dead code left
- [ ] The changes make sense
- [ ] The changes are not obviously degrading performance
- [ ] There is no duplicated code
- [ ] The API is convenient
- [ ] Code block length and complexity is adequate
- [ ] Spelling okay

- [ ] The code is tested

Continuous integration (CI) and tests

AMICI uses a continuous integration pipeline running via https://github.com/features/actions. This includes the following steps:

- Checking existence and format of documentation
- Static code analysis (http://cppcheck.sourceforge.net/)
- Unit and integration tests
- Memory leak detection

More details are provided in the sections below.

The CI scripts and tests can be found in `tests/` and `scripts/`. Some of the tests are integrated with CMake, see `make help` in the build directory.

C++ unit and integration tests

To run C++ tests, build AMICI with `make` or `scripts/buildAll.sh`, then run `scripts/run-cpp-tests.sh`.

Python unit and integration tests

To run Python tests, run `../scripts/run-python-tests.sh` from anywhere (assumes build directory is `build/`) or run `make python-tests` in your build directory.

SBML Test Suite

We test Python-AMICI SBML support using the test cases from the semantic SBML Test Suite. When making changes to the model import functions, make sure to run these tests.

To run the SBML Test Suite test cases, the easiest way is:

1. Running `scripts/installAmiciSource.sh` which creates a virtual Python environment and performs a development installation of AMICI from the current repository. (This needs to be run only once or after AMICI model generation or C++ changes).
2. Running `scripts/run-SBMLTestsuite.sh`. This will download the test cases if necessary and run them all. A subset of test cases can be selected with an optional argument (e.g. `scripts/run-SBMLTestsuite.sh 1, 3-6,8`, to run cases 1, 3, 4, 5, 6 and 8).

   Once the test cases are available locally, for debugging it might be easier to directly use `pytest` with `tests/testSBMLSuite.py`.

Matlab tests (not included in CI pipeline)

To execute the Matlab test suite, run `tests/testModels.m`.

Model simulation integration tests

Many of our integration tests are model simulations. The simulation results obtained from the Python and C++ are compared to results saved in an HDF5 file (`tests/cpp/expectedResults.h5`). Settings and data for the test simulations are also specified in this file.

Note: The C++ code for the models is included in the repository under `models/`. This code is to be updated whenever `amici::Model` changes.

Regenerating C++ code of the test models

Regeneration of the model code has to be done whenever `amici::Model` or the Matlab model import routines change.

This is done with

```
tests/cpp/wrapTestModels.m
```

Note: This is currently only possible from Matlab < R2018a. This should change as soon as 1) all second-order sensitivity code is ported to C++/Python, 2) a non-SBML import exists for Python and 3) support for events has been added for Python.

Regenerating expected results

To update test results, run `make test` in the build directory, replace `tests/cpp/expectedResults.h5` by `tests/cpp/writeResults.h5.bak` [ONLY DO THIS AFTER TRIPLE CHECKING CORRECTNESS OF RESULTS] Before replacing the test results, confirm that only expected datasets have changed, e.g. using

```
h5diff -v --relative 1e-8 tests/cpp/expectedResults.h5 tests/cpp/writeResults.h5.bak |␣
↪less
```

Adding/Updating tests

To add new tests add a new corresponding python script (see, e.g., `./tests/generateTestConfig/example_dirac.py`) and add it to and run `tests/generateTestConfigurationForExamples.sh`. Then regenerate the expected test results (see above).

Debugging AMICI

This document contains some information on how to debug any issues in AMICI, in particular for C++ Python extensions.

Caveman debugging / printf-debugging

The simplest approach may often be adding some print-statements to the code, as this does not require any special tools.

Note that after each change of the C++ files, the AMICI extension *as well as the model extension* (if any model functions are called), need to be recompiled. The simplest and safest approach would be re-installation of the amici package and re-import of the model. As this can be very time-consuming, the following shortcut is possible, assuming you are using a development installation (`pip install -e ...`):

```
# rebuild the amici base extension, from within the amici root directory
# (note that this only recompiles the amici source files, NOT third-party
# dependencies such as sundials):
cd python/sdist/
python setup.py build_ext --build-lib .

# rebuild the model, from within the model package directory:
python setup.py build_ext --force --build-lib .
```

Note: Be careful when working interactively, Python may not pick up any changes in already imported modules. The safest is to start a new Python process after any changes.

Using a proper debugger

Debugging with with [gdb](https://www.sourceware.org/gdb/) is most convenient with a minimal reproducible example that is directly invoked from gdb. For example:

```
# start gdb
gdb --args python -m pytest ../tests/test_sbml_import.py::test_nosensi

# inside gdb, set a meaningful breakpoint and launch:
break amici::runAmiciSimulation
run
# ... (see one of the many gdb tutorials)
```

Alternative, gdb can attach to a running process by passing the `--pid` argument.

For many users, it may be more convenient to use gdb via some graphical user interface as provided by various C++ IDEs.

Note: For better debugging experience, but at the cost of runtime performance, consider building the amici and model extension with environment variable `ENABLE_AMICI_DEBUGGING=TRUE`. This will include debugging symbols and disable compiler optimizations.

12.6 Handling of Discontinuities

This document provides guidance and rationale on the implementation of events in AMICI. Events include any discontinuities in the right hand side of the differential equation. There are three types of discontinuities:

- **Solution Jump Discontinuities** can be created by SBML events or delta functions in the right hand side.
- **Right-Hand-Side Jump Discontinuities** result in removable discontinuities in the solution and can be created by Piecewise, Heaviside functions and other logical operators in the right hand side.
- **Right-Hand-Side Removable Discontinuities** do not lead to discontinuities in the solution, but may lead to discontinuous higher order temporal derivatives and can be created by functions such as max or min in the right hand side.

12.6.1 Mathematical Considerations

A detailed mathematical description of the required sensitivity formulas is provided in

- Fröhlich, F., Theis, F. J., Rädler, J. O., & Hasenauer, J. (2017). Parameter estimation for dynamical systems with discrete events and logical operations. Bioinformatics, 33(7), 1049-1056. doi:10.1093/bioinformatics/btw764.

12.6.2 Algorithmic Considerations

Solution Jump Discontinuities

SUNDIALS by itself does not support solution jump discontinuities. We implement support by accessing private SUNDIALS API in `amici::Solver::resetState()`, `amici::Solver::reInitPostProcess()` and *amici::Solver::reInitPostProcessB()*. These functions reset interval variables to initial values to simulate a fresh integration start, but keep/update the solution history, which is important for adjoint solutions.

Right-Hand-Side Jump Discontinuities

In principle these discontinuities do not need any special treatment, but empirically, the solver may overstep or completely ignore the discontinuity, leading to poor solution quality. This is particularly problematic when step size is large and changes in step size, which can be caused by parameter changes, inclusion of forward sensitivities or during backward solves, may alter solutions in unexpected ways. Accordingly, finite difference approximations, forward sensitivities as well as adjoint sensitivities will yield poor derivative approximations.

To address these issues, we use the built-in rootfinding functionality in SUNDIALS, which pauses the solver at the locations of discontinuities and avoids overstepping or ignoring of discontinuities.

Another difficulty comes with the evaluation of Heaviside functions. After or during processing of discontinuities, Heaviside functions need to be evaluated at the left and right hand limit of discontinuities. This is challenging as the solver may slightly over- or understep the discontinuity timepoint by a small epsilon and limits have to be correctly computed in both forward and backward passes.

To address this issue, AMICI uses a vector of Heaviside helper variables h that keeps track of the values of the Heaviside functions that have the respective root function as argument. These will be automatically updated during events and take either 0 or 1 values as appropriate pre/post event limits.

In order to fully support SBML events and Piecewise functions, AMICI uses the SUNDIALS functionality to only track zero crossings from negative to positive. Accordingly, two root functions are necessary to keep track of Heaviside functions and two Heaviside function helper variables will be created, where one corresponds to the value of *Heaviside(...)* and one to the value of *1-Heaviside(...)*. To ensure that Heaviside functions are correctly evaluated at the beginning of the simulation, Heaviside functions are implement as unit steps that evaluate to *1* at *0*. The arguments

of Heaviside functions are normalized such that respective properties of Piecewise functions are conserved for the first Heaviside function variable. Accordingly, the value of of the second helper variable is incorrect when simulation starts when the respective Heaviside function evaluates to zero at initialization and should generally not be used.

Right-Hand-Side Removable Discontinuities

Removable discontinuities do not require any special treatment. Numerically, this may be advantageous, but is currently not implemented.

CHAPTER

THIRTEEN

INDICES AND TABLES

- genindex
- modindex
- search

PYTHON MODULE INDEX

a

INDEX

Symbols

A

B

C

D

E

F

G

H

I

J

K

L

M

N

O

P

R

S

T

U

V

W

X

Y

Z