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# What's New

Morpheus 2 is a major release that improves modeling flexibility, usability, and allowing extensibility.

## **Open source**

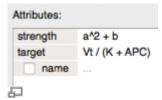
- Morpheus 2 is now open source.
  - Source code is available in the Git repository.
  - Released under a permissive BSD license
- Morpheus 2 is an extensible framework
  - Modeling and analysis tools can be customized or added as plugins
  - A stable C++ API has been developed for plugin development
    - Simple integration of XML and implementation
    - Automated symbol dependency tracking and scheduling

## **Simulator**

#### **Modeling**

#### • Expressions everywhere

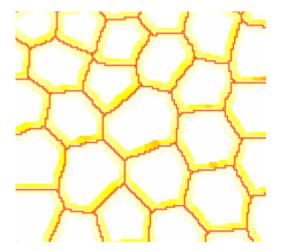
- In addition to numerical values, plugin can now take mathematical expressions as inputs
- Greatly improves modeling flexibility by coupling of submodels



Parameters can given as math expressions, interpreted at run-time.

#### MembraneProperties

- Variables with spatial resolution, mapped to cell membrane
- Uses circular (2D) or spherical (3D) approximation of cell shape
- Allows spatially resolved registration of (neighboring) cell properties
- Enables reaction-diffusion of properties on membrane

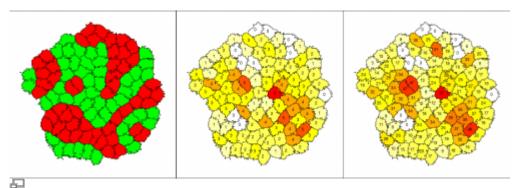


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MembraneProperties provide a scalar field mapped to the cell membrane on which reaction-diffusion systems can be simulated.

#### Reporters

- All Reporters, plugins that generate statistics and mappings, have been revised and generalized.
- NeighborhoodReporter provides statistics (e.g.sum, mean) on properties of the cell's directly adjacent microenvironment
- CellReporter provides statistics on properties of the cellular environment such as including the concentration of MembraneProperties and Fields.



NeighborhoodReporter counts the number of neighbors of the other cell type. Left: colors show two cell types. Middle: colors and labels show number of non-identical neighboring cells. Right: colors and labels show length of interface to non-identical neighboring cells

- A number of **new plugins** introduce new modeling features, including
  - AddCell: add CPM cells during simulation based on a condition and a location specified by a probability density function.
  - ChangeCelltype: change the cell type of a cell based on a condition.
  - Protrusion: actin-inspired feedback model that control shape and motility of CPM cells, as proposed by Niculescu et al., 2015.



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The new Protrusion plugin models positive feedback of active membrane regions, inspired by actin dynamics.

#### **Performance**

## • Performance optimization

- Automatic scheduling has been revised to optimize computational performance.
- Performance measurements and plugin profiling

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- Information on execution time (wall time, CPU time) and peak memory usage
- Execution times (wall time) are listed per plugin

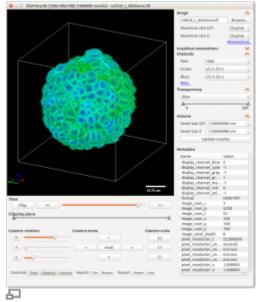
```
Time Schedule Performance Table
                  5731.61[ms]
                                   Gnuplotter [APC,g] -> []
      20.44% -
                                   CPM [Vt] -> [cell.center]
                                   CellReporter [report field] [cell.center,g] -> [g_l]
CellDivision [CDK1,c,cell.volume] -> [Vt,c,cell.center,d]
       3.86% =
                   305.52[ms]
       1.25% =
                     98.86[ms]
       0.71% =
                                    Diffusion [g] -> [g]
                     55.88[ms]
       0.668 =
                     52.53[ms]
                                    System [APC] -> [g]
                                 | Logger [dist] -> []
| System [K,g_l,n,\alpha1,\alpha2,\alpha3,\beta1,\beta2,\beta3] -> [APC,CDK1,Plk1]
       0.48% =
                     37.87[ms]
                      4.52[ms]
       0.06% -
                                 | Event [reset timeout] [CDK1] -> [c]
    Simulation finished ---
             - 0s 120ms
- 7s 909ms
Init Time
Wall Time
CPU Time
              = 5s 021ms (4 threads)
Memory peak = 29.1328 Mb
```

A performance profile is generated after each simulation.

#### **Analysis**

#### TIFFPlotter

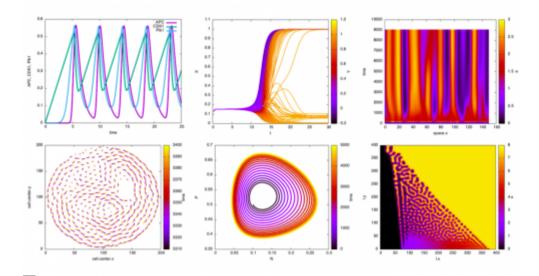
 Now writes OME-TIFF headers (Open Microscopy Environment) to facilitate visualization of 3D-5D image data with external such as Fiji or BioView3D.



Morpheus' TIFFPlotter exports time-lapse multichannel TIFF stacks with OME-TIFF header can be easily visualized with external tools such as BioView3D.

#### Logger

- The completely revised Logger plugin provides generic tool for data export.
- Data export: Periodically writes any combination of variables (Globals, Properties, Fields, etc.) to file in CSV or Matrix format.
- Plotting: Logger also provides a versatile interface for generating data visualizations including time plots, phase diagrams, cell trajectory plot, spacetime plot, profile plots, surface plots etc.



The new Logger plugin provides a versatile interface for data export and data visualization.

## MorpheusML

## Scoping

- Lexical scoping was introduced: symbols are only valid on the scope in which they are declared.
- Improves intuitive character and consistency of model description language
- Allows multiple usages of symbols, setting global defaults, etc.

#### Globals

- New Globals section for global constants, variables and Fields
- Scalar field previously PDE/Layer are moved into Globals/Fields

#### MorpheusML 2.0

- Restructured MorpheusML markup language
- Allows better future integration with other formats such as SBML
- Fixboard can partially convert Morpheus 1.x models into new format.

#### GUI

#### Documentation

- Doxygen-generated in-app docs appear in HTML (using QtWebKit)
- Docs are both context-sensitive and can be searched (using QtHelp framework)
- Docs can include latex-based maths (displayed using MathJax)

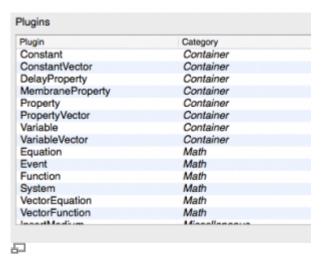
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The new in-app documentation is context-sensitive, browsable, features Latex equations and XML examples.

## • Panel with addable plugins

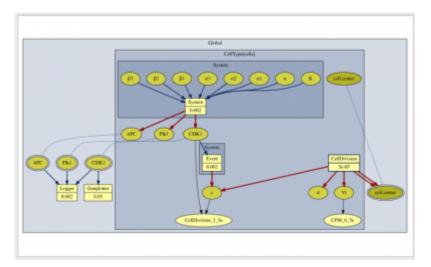
New context-sensitive overview of addable plugins shows what plugins can be added



Plugins can now be added using a new panel that shows what can be added at the selected position.

#### Generate symbol graph

Shows interdependencies between symbols and scopes

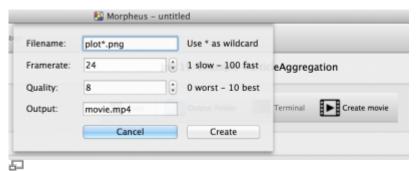




Symbol graphs show how Morpheus interprets the model. This can be used for model testing and tracing bugs.

#### Generate movies

- Images can be generatedfrom image sequences within GUI
- Also generates multiple movies from ParamSweep
- Requires ffmpeg or avconv (download from here)



Create movies from images.

## ImageTable

 Generate visual tables of ParamSweep results including images or movies (viewable in HTML5-enabled web browsers)





The new ImageTable feature gives a quick overview of the results of a parameter sweep from a web browser.

# Version 1.2.1

## Changes

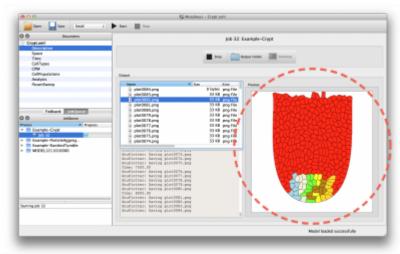
- SBML support is built-in for Ubuntu 14.04+ as libSBML was removed from repositories.
- Fixed rare GUI crashes on Mac OSX when moving model elements.

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## Version 1.2

The changes in this version focus on improving modeling flexibility, but also include several improvements in automatic scheduling as well as a new preview panel in the user interface. Download version 1.2 here.

#### Major changes



New panel to preview images and text files in result browser.

- New **preview panel** in GUI in the result browser for images and plain text files.
- New ChildID option for Proliferation. This supports the representation of asymmetric cell divisions by providing a symbolic handle to treat daughter cells differently after cell division.
  - See new example Crypt.xml
- New ChangeCellType plugin to conditionally **change the cell type** of a cell. By default, cell properties are copied, but may be overridden using Triggers.
  - See new example Crypt.xml
- New VectorRule to manipulate PropertyVector, either in x,y,z or phi,theta,radius (spherical coordinates). This facilitates **vector computations** to e.g. control directed cell motility.
  - See new example RunAndTumble.xml
- New FlipCells plugin to represent **cell motility** in CA-like models. This plugin enables the conditional switching of positions with a random neighboring site.
  - See new example ParticleAggregation.xml
- New PopulationReporter to collect **population-level statistics** on cell Properties. This allows individual cell behavior to depend on population-level properties, or to collect population statistics to log and plot.
  - See new examples ParticleAggregation.xml and Crypt.xml
- New StopCondition to terminate a simulation upon a Condition before reaching StopTime. This can significantly improve efficiency in e.g. parameter explorations or sensitivity analysis.
  - See new example ParticleAggregation.xml

- New trigger option for Event. This provides a choice to **trigger events** (1) whenever the condition changes from false to true (as in SBML) or (2) whenever the condition is true.
- Several fixes and many improvements to automatic scheduling.
  - Analysis tools are now scheduled according to input symbols if interval=0

#### Minor changes

- New InitCA plugin to populate CA-like models.
  - See examples ParticleAggregation.xml, LateralSignaling.xml, GameOfLife.xml and FrenchFlag.xml
- Fix InitRectangle on hexagonal lattices.
- Support for \$\alpha\$-synchronous simulation.
- Fixed issue with Delay properties.
- HistogramLogger now supports logarithmic binning and plotting

## **Acknowledgments**

Many of these new features are the result of requests from users. In particular, we thank *Maria Herberg* (Medical Faculty, TU Dresden), *Angelo Torelli* (Mannheim University of Applied Sciences) and *Ovidiu Pârvu* (Brunel University) for useful suggestions.

## Version 1.1.1

#### Minor changes

- Fix issue in Windows with SBML import feature.
- Fix issue in GUI with displaying newly created elements.
- Updated version for math expression parser (muparser).

# **Version 1.1**

#### **Major changes**

- Added **SBML Import** feature that converts SBML-based models into equivalent intracellular models of differential equations in Morpheus description language. An example model is added.
- Added DelayProperty that returns assigned values after a specified time lag which enables the simulation of **delay differential equations**. An example model is added.

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• A distinction is made between **Equations and Rules** whereby the latter are equations within a System. Unlike Equations, Rules may have recurrency and be part algebraic loops.

- **Events** are now triggered whenever the condition change from false to true, for SBML compatibility.
- Sequential processes are now **scheduled** only as often as their input symbol can change. This avoids redundant processing and optimizes computational performance.

## Minor changes

- Fixed issues with file dialogs and output folder button under Windows.
- Fixed libfreetype problems with Gnuplot.app under Mac OSX.
- Reduced verbosity in standard output (model.xml.out).
- Moved Examples menu to toolbar menu.
- · Various minor fixes.

From:

https://imc.zih.tu-dresden.de/wiki/morpheus/ - Morpheus

Permanent link:

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