Morpheus: a user-friendly modeling environment for multiscale multicellular systems biology

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Introduction

Morpheus is a modeling environment for the **simulation and integration** of cell-based models with ordinary differential equations and reaction-diffusion systems (Starruß et al., *Bioinformatics*, 2014).

It allows **rapid model development** of multi-scale models in biological terms and mathematical expressions rather than programming code.

Its **graphical user interface** supports the entire workflow from model construction and simulation to visualization, archiving and batch processing.
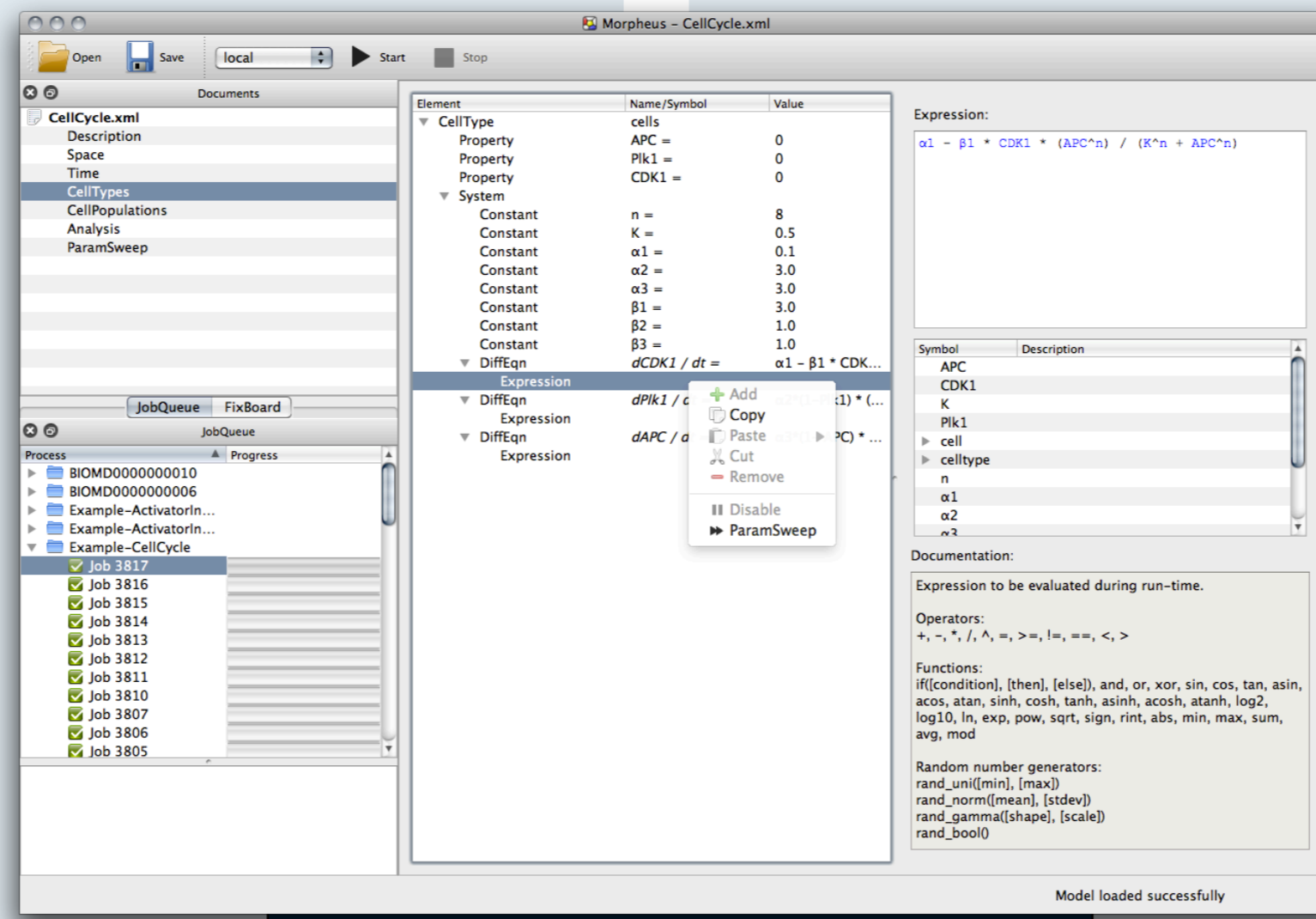
Morpheus' graphical user interface

Usability

✦ **Modeling without programming**
Morpheus separates modeling from programming by MorpheusML: a novel domain-specific SBML-like mark-up language for multicellular systems biology.

✦ **Automated model integration**
It automates model integration linking models of cellular, intra-cellular and extra-cellular dynamics.

✦ **Graphical work-flow tools**
The graphical interface provides tools for rapid model development, simulation, batch processing and archiving.

Graphical user interface

✦ **Model editor**
Rapid model development with add/remove, copy/paste, disable/enable model elements.
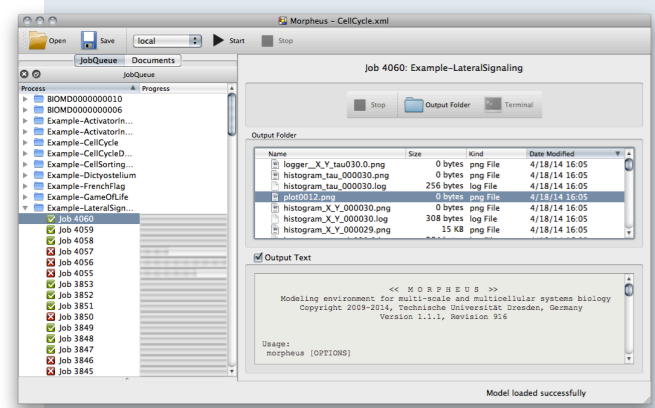
✦ **Job scheduler**
Scheduling of multi-threaded and parallel simulations, on both local and remote computing resources.

✦ **Simulation archive**
Browsable archive of simulation models with results, allows old models to be restored.

✦ **High performance computing**
Support for high performance computing with batch systems like LSF and SLURM. Syncing results back to local computer via sftp.
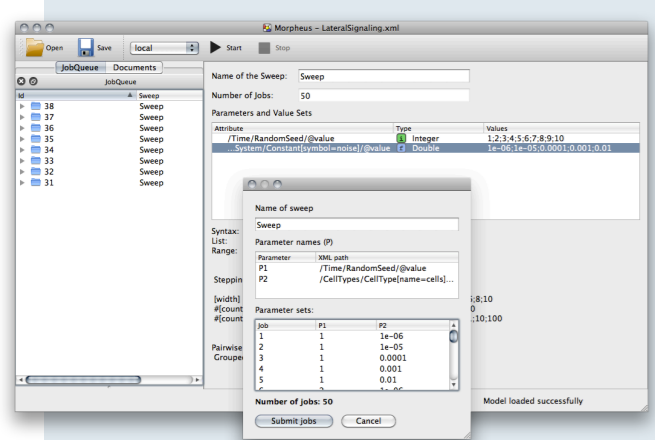
✦ **Batch processing**
Parameter exploration by creating sequences of simulations with different parameter sets.

Examples, documentation and downloads for **Linux**, **Mac OSX** and **Windows** at:
http://imc.zih.tu-dresden.de/wiki/morpheus
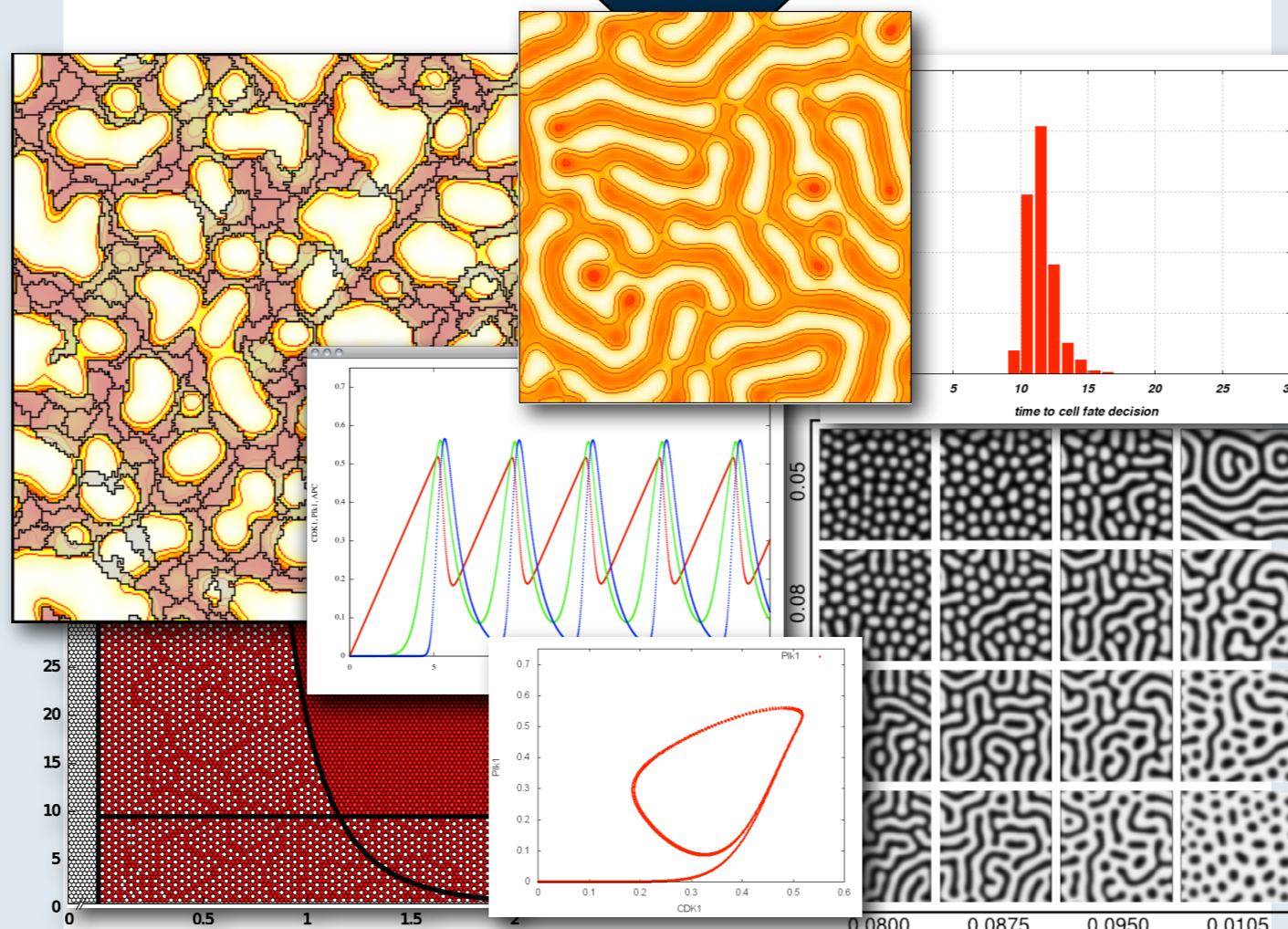
Simulation, visualization and analysis

Key references
✦ J. Starruß, W. de Back, L. Brusch and A. Deutsch (2014). Morpheus: a user-friendly modeling environment for multiscale and multicellular systems biology. **Bioinformatics**, btt772.
✦ A. Köhn-Luque, W. de Back, et al. (2013) Dynamics of VEGF Matrix-Retention in Vascular Network Patterning. **Physical Biology**, 10:066007.
✦ W. de Back, R. Zimm, L. Brusch (2013) Transdifferentiation of Pancreatic Cells by Loss of Contact-mediated Signaling. **BMC Systems Biology**, 7:77.
✦ W. de Back, J. X. Zhou, L. Brusch (2012) On the Role of Lateral Stabilization during Early Patterning in the Pancreas. **J. R. Soc. Interface** 10(79):20120766.

MorpheusML

MorpheusML is a SBML-like language for multicellular systems biology. The markup language **separates modeling from programming** and enables users to describe computational models in **biological and mathematical terminology** rather than programming code.

Mathematical expressions (functions, differential equations and events) are specified in familiar **infix notation**.

MorpheusML enables **model integration** by automatically resolving dependencies between symbolic identifiers to determine e.g. the order in which model components must be updated.
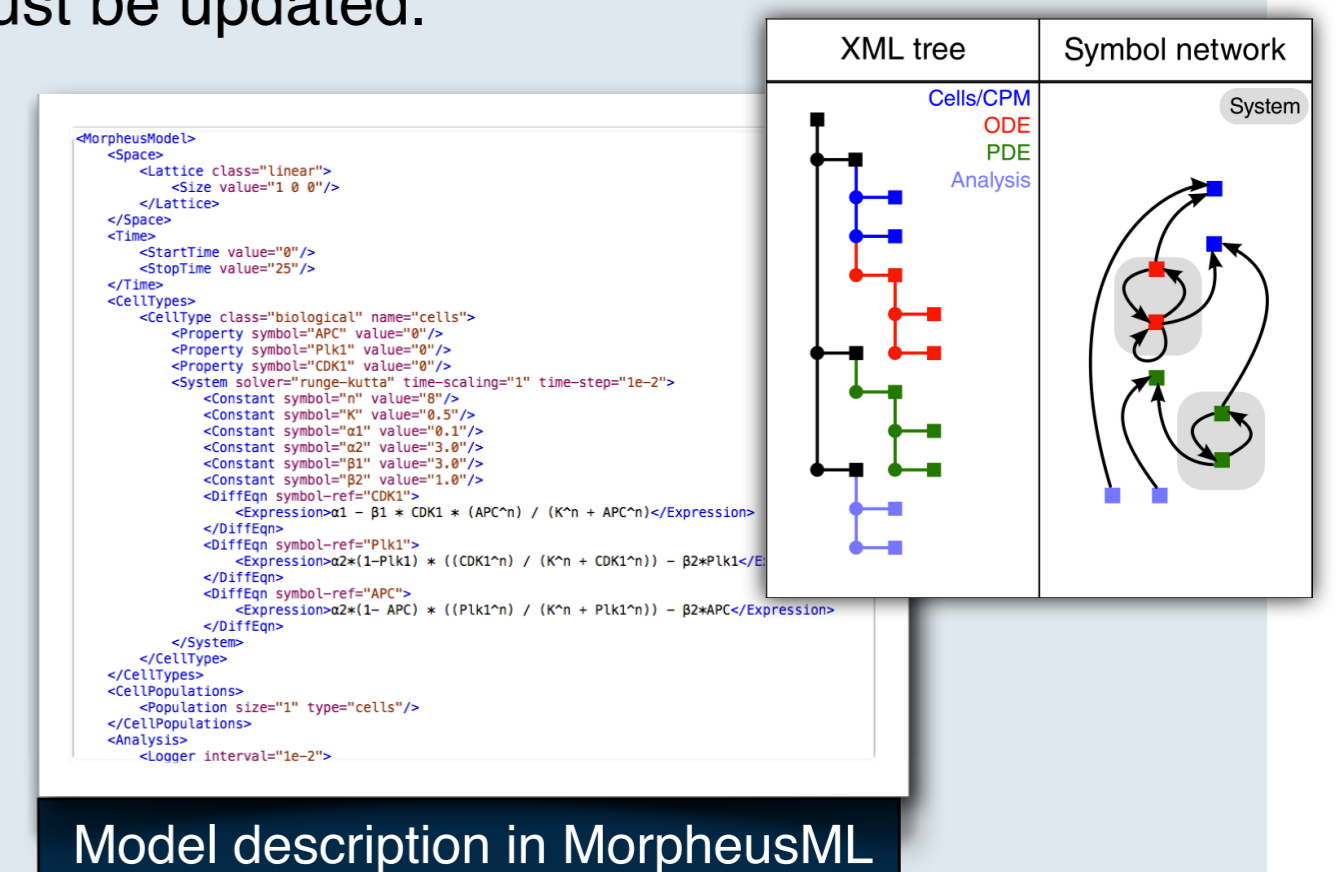
Model description in MorpheusML

Modeling and simulation

✦ **Differential equations**
Systems of ordinary, stochastic and delay differential equations can represent **temporal dynamics** such as gene regulation, metabolism or signaling and can be imported from **SBML models** available in repositories such as the BioModels database.

✦ **Reaction-diffusion**
Reaction-diffusion systems can be used to model e.g. the **spatial distribution of morphogens** and binding/unbinding to extracellular matrix components. The spatial domain may be imported from multi-stack images.
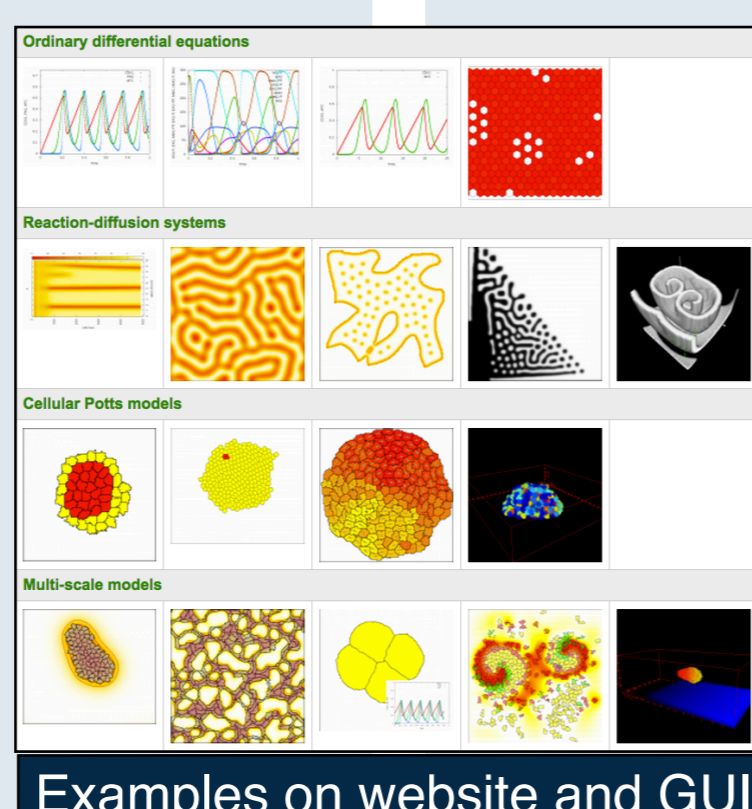
Examples on website and GUI

✦ **Cell-based modeling**
Cells can be represented as point-like objects or with explicit 2D or 3D cell shapes, e.g. imported from TIFF **microscopy images**. Interactions are specified between individual discrete cells. **Cell motility and bio-physical constraints** may be added using the cellular Potts model (CPM) framework.

✦ **Multiscale multicellular models**
To study **feedbacks** between various levels of biological organization, models can be constructed that couple cellular dynamics with intra- and/or extracellular dynamics.

Software

Morpheus is a self-contained application for **Linux, Mac OSX and Windows** that consists of two stand-alone programs: a **C++**-based simulator and a **Qt**-based graphical user interface.

It uses **muparser** to evaluate math expressions, **eigen** for matrix operations, **openMP** for parallel computing, **libTIFF** for import/export of 3D images, **SQLite** for archiving, and **gnuplot** as data visualization back-end.

Morpheus features a **plug-in architecture** that allows extensions to be written in C++. This transforms the current binary application into a flexible framework following the planned **open-source release**.