

# 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 cellbased 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.

000		Morpheus - CellCycle yml	
Open Save local	Start Stop		
O Documents	Element	Name/Symbol Value	1
CellCycle.xml		cells	Expression:
Description	Property	APC = 0	$\alpha_1 = 81 + CDK1 + (APCAn) / (KAn + APCAn)$
Space	Property	Plk1 = 0	ar probar (area, , (area, )
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CellTypes	▼ System		
CellPopulations	Constant	n = 8	
Analysis	Constant	K = 0.5	
ParamSweep	Constant	α1 = 0.1	
	Constant	α2 = 3.0	
	Constant	α3 = 3.0	
	Constant	β1 = 3.0	
	Constant	$\beta 2 = 1.0$	
	Constant	β3 = 1.0	Symbol Description
	▼ DiffEgn	$dCDK1 / dt = \alpha 1 - \beta 1 * CDK$	
	Expression		CDK1
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Example-CellCycle			Documentation:
🔽 Job 3817			
🔽 Job 3816			Expression to be evaluated during run-time.
Job 3815			
Job 3814			Operators:
🔽 Job 3813			+, -, ^, /, ^, =, >=, !=, ==, <, >
Job 3812			Functions:
Job 3811			if([condition], [then], [else]), and, or, xor, sin, cos, tan, asin,
Job 3810			acos, atan, sinh, cosh, tanh, asinh, acosh, atanh, log2,
🔽 Job 3807			log10, In, exp, pow, sqrt, sign, rint, abs, min, max, sum,
<b>V</b> Job 3806			avg, mod
Job 3805	T I		
			Random number generators:
			rand_uni([min], [max])
			rand gamma([shape], [scale])
			rand_bool()
			-
			Model loaded successfully

Morpheus' graphical user interface

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

## MorpheusML

MorpheusML is a SBML-like language for

## 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 multithreaded 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.



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.

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.



### Modeling and simulation

#### Differential equations



## Cell-based modeling

images. Interactions are speci-

for Linux, Mac OSX and Windows that Cells can be represented as consists of two stand-alone programs: a point-like objects or with explicit C++-based simulator and a Qt-based 2D or 3D cell shapes, e.g. imgraphical user interface. ported from TIFF microscopy

Morpheus is a self-contained application

Software

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 multistack images.



fied between individual discrete cells. Cell motility and biophysical 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.

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**.



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