

Morpheus
modeling environment for
multicellular systems biology

Walter de Back

Institute for Medical Informatics and Biometry
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TU Dresden



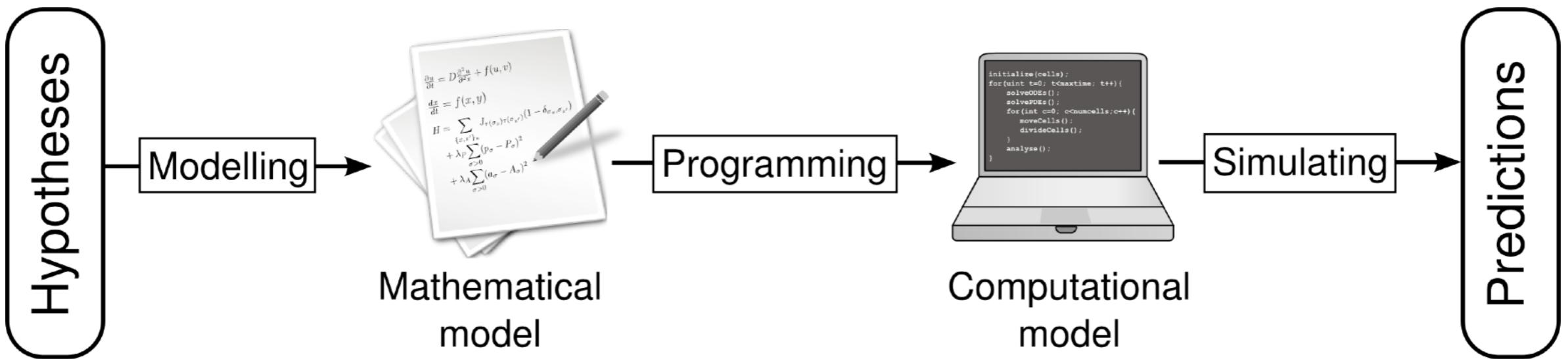
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Jörn Starruß
Center for Information Services
and High Performance Computing
TU Dresden



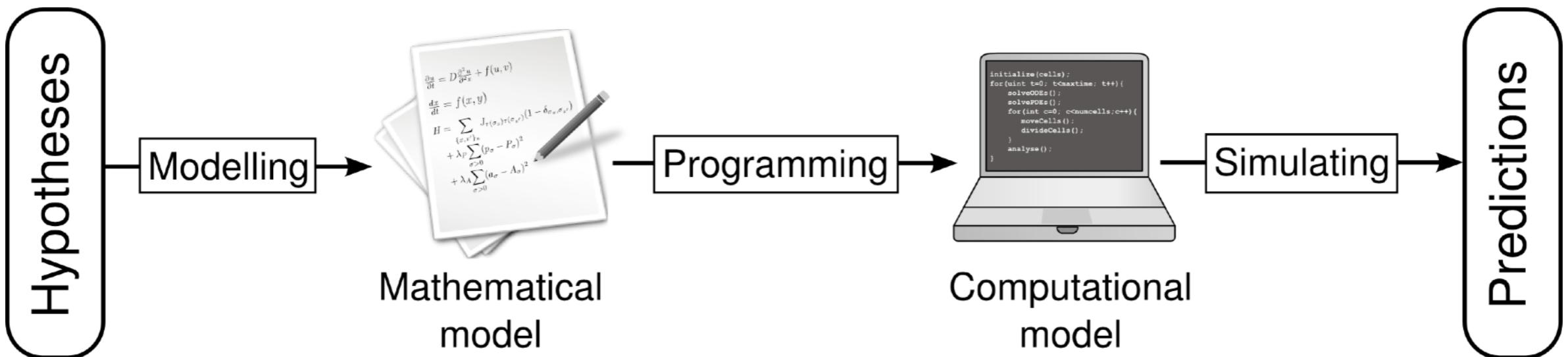
Computational modeling

Common workflow



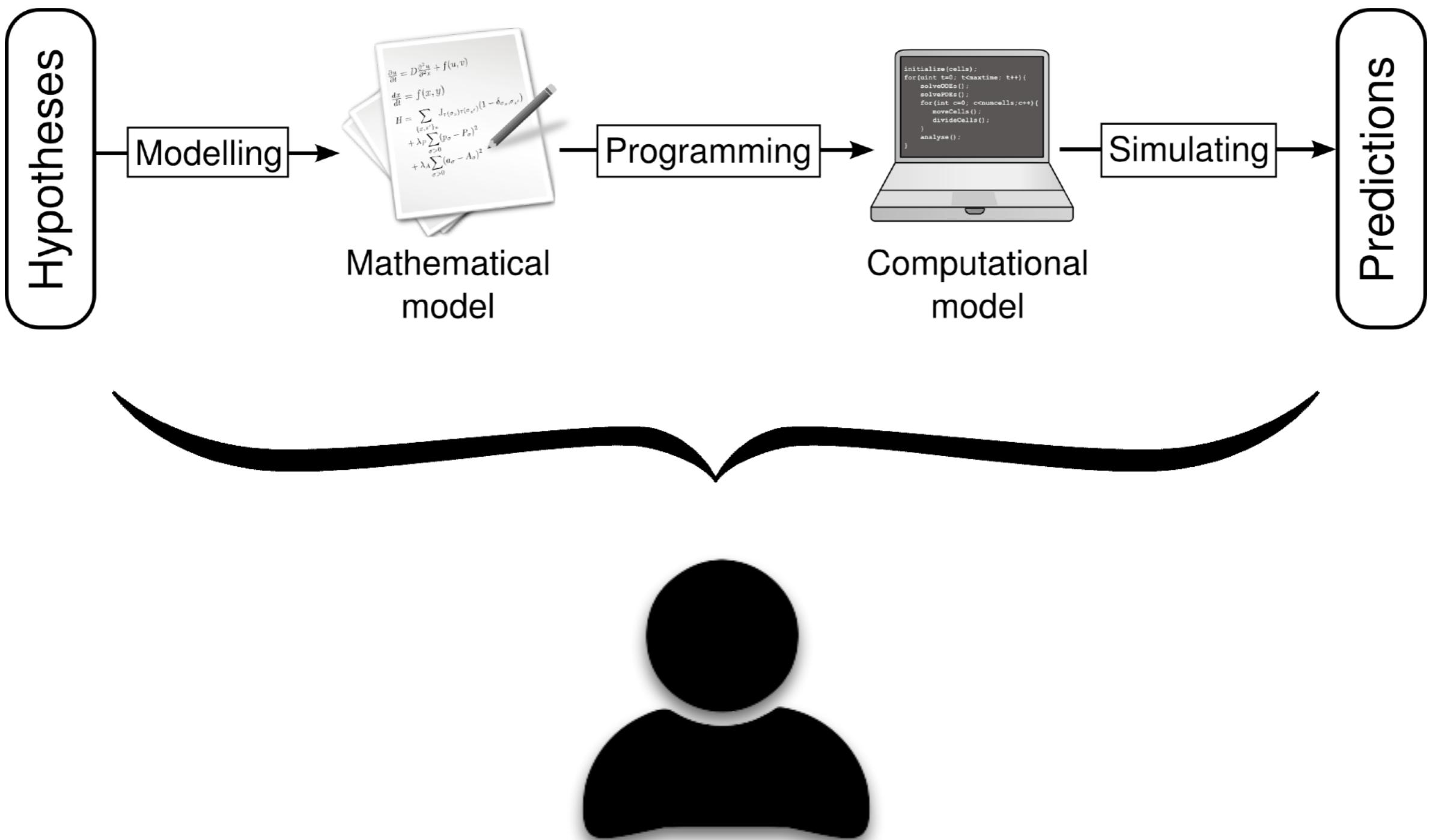
Computational modeling

Common workflow



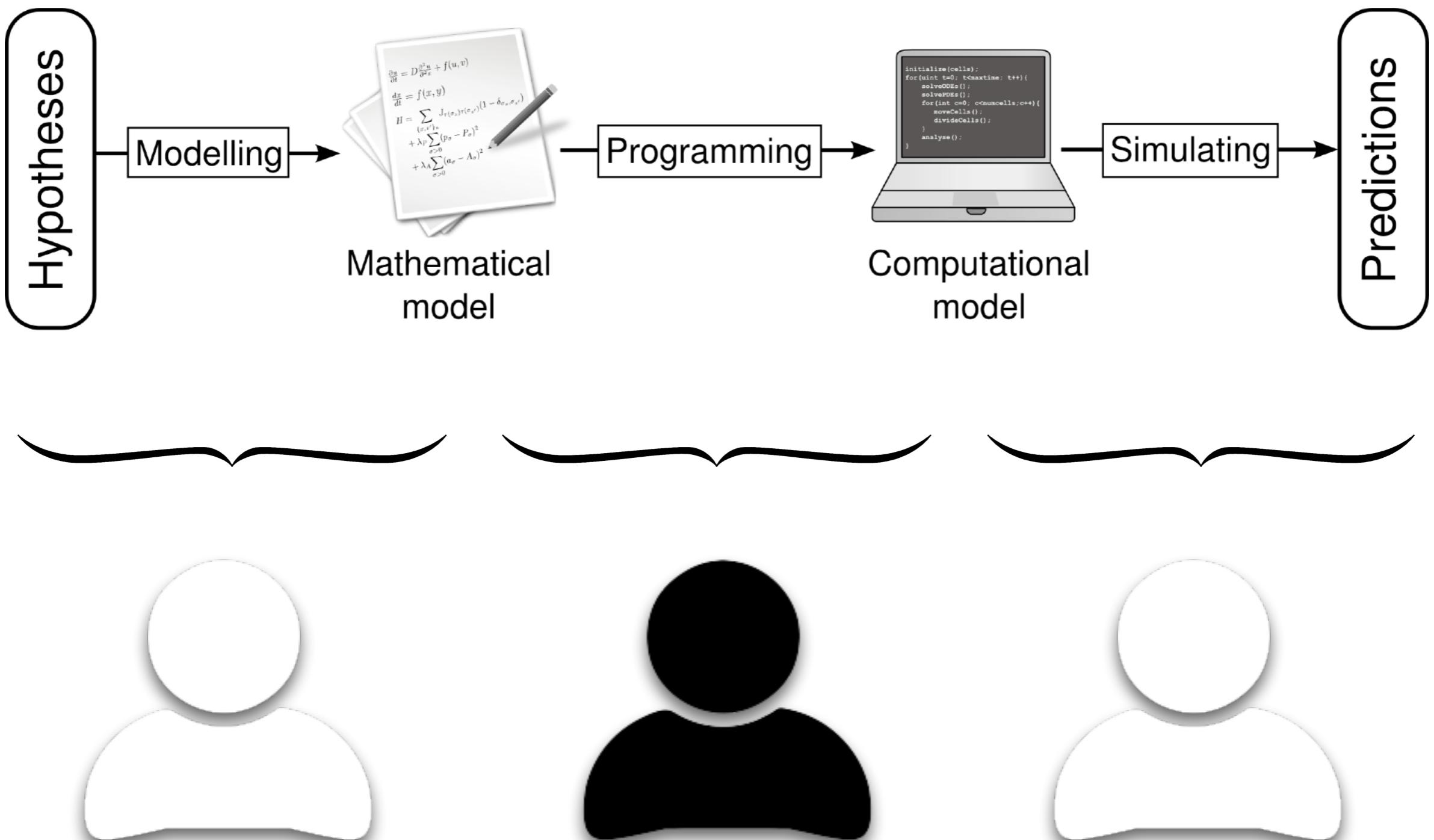
Computational modeling

Common workflow



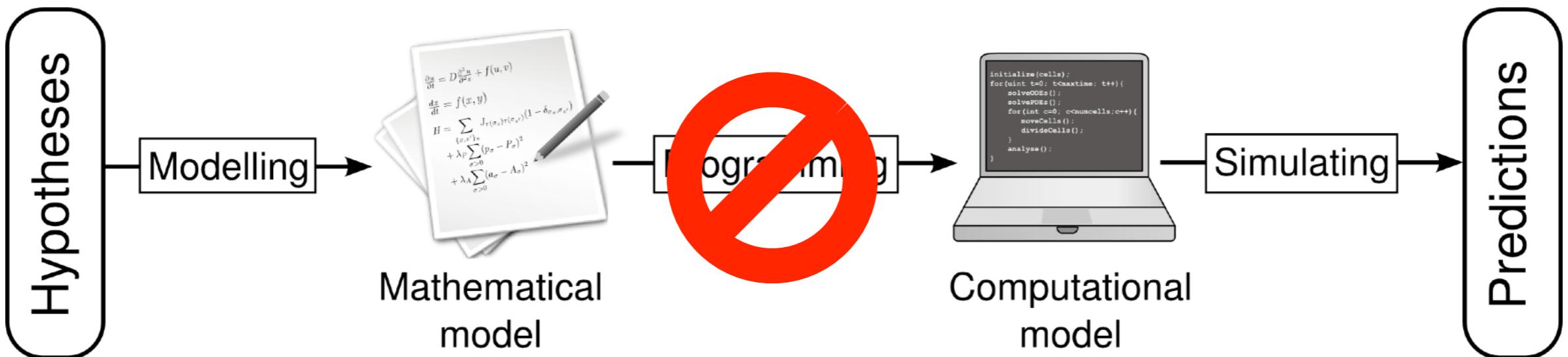
Computational modeling

Separation of modeling and programming



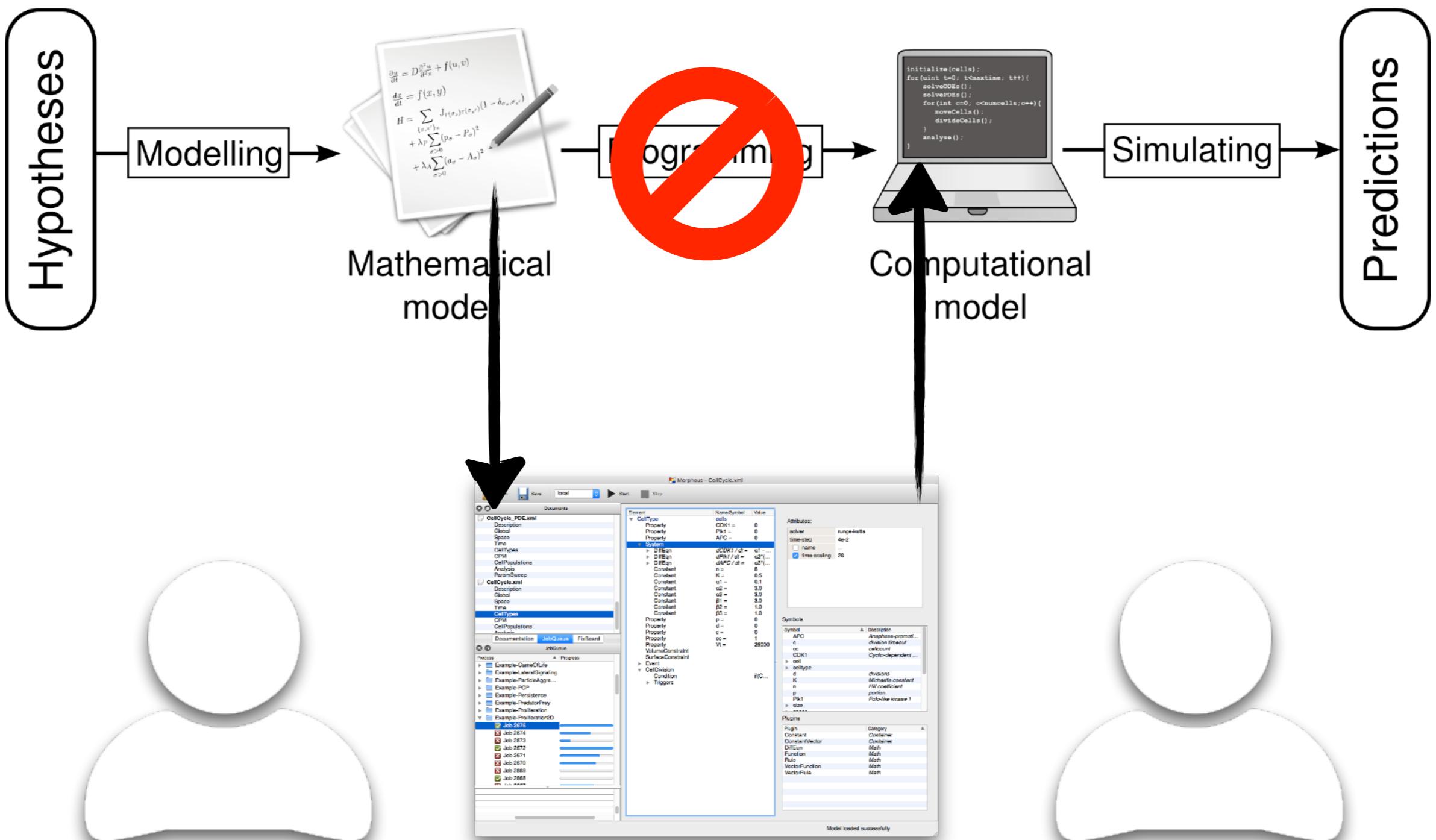
Computational modeling

Without the need for programming



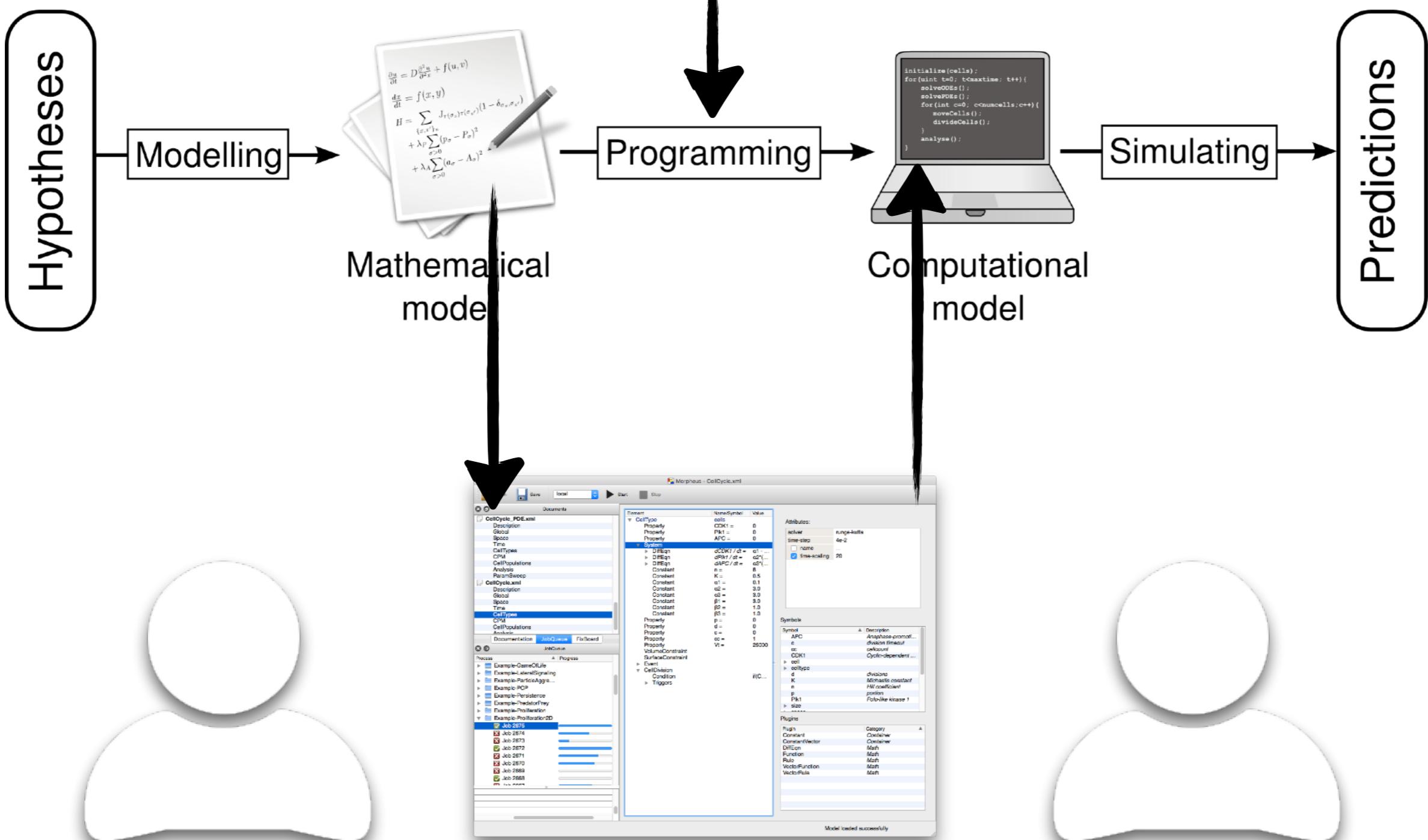
Computational modeling

Without the need for programming



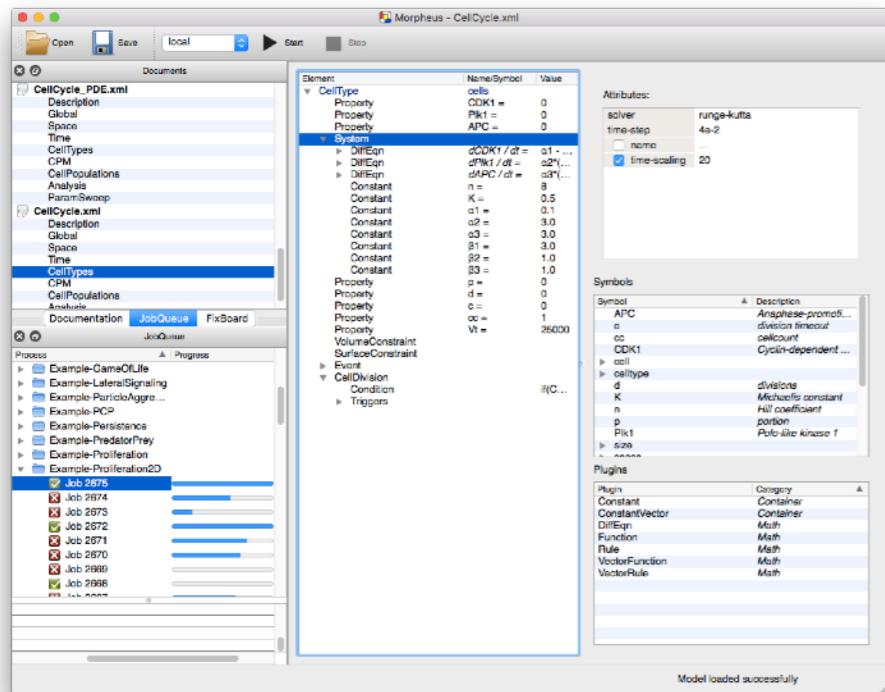
Extensibility

Open-source framework

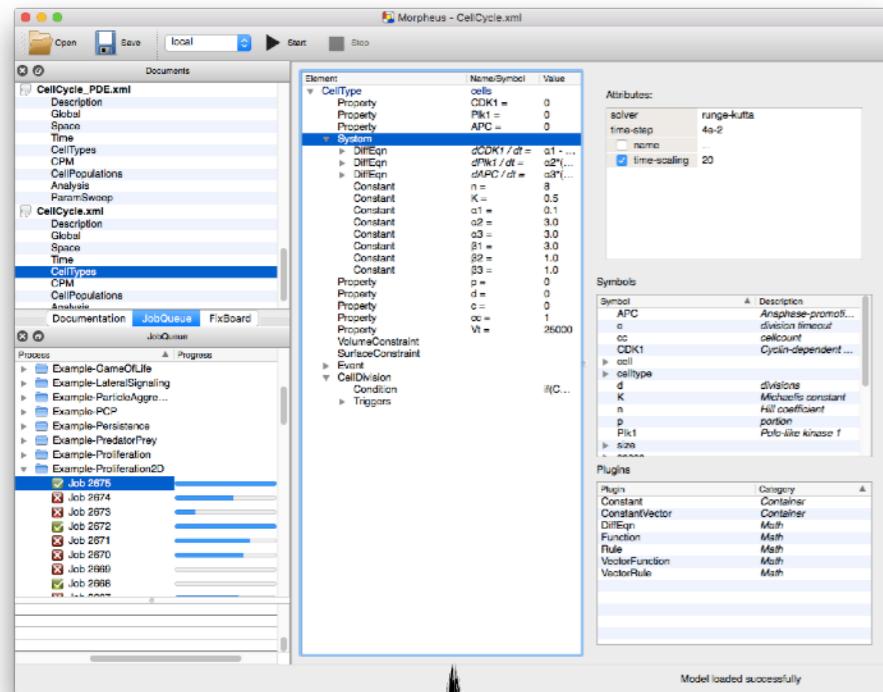


Automation and model integration

Convert mathematical models into simulations

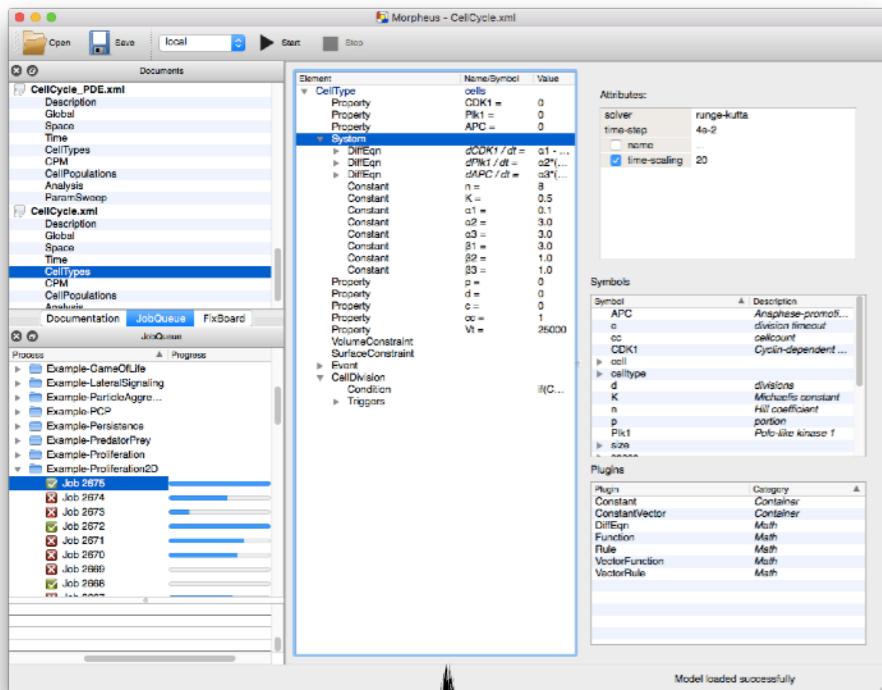


Convert mathematical models into simulations

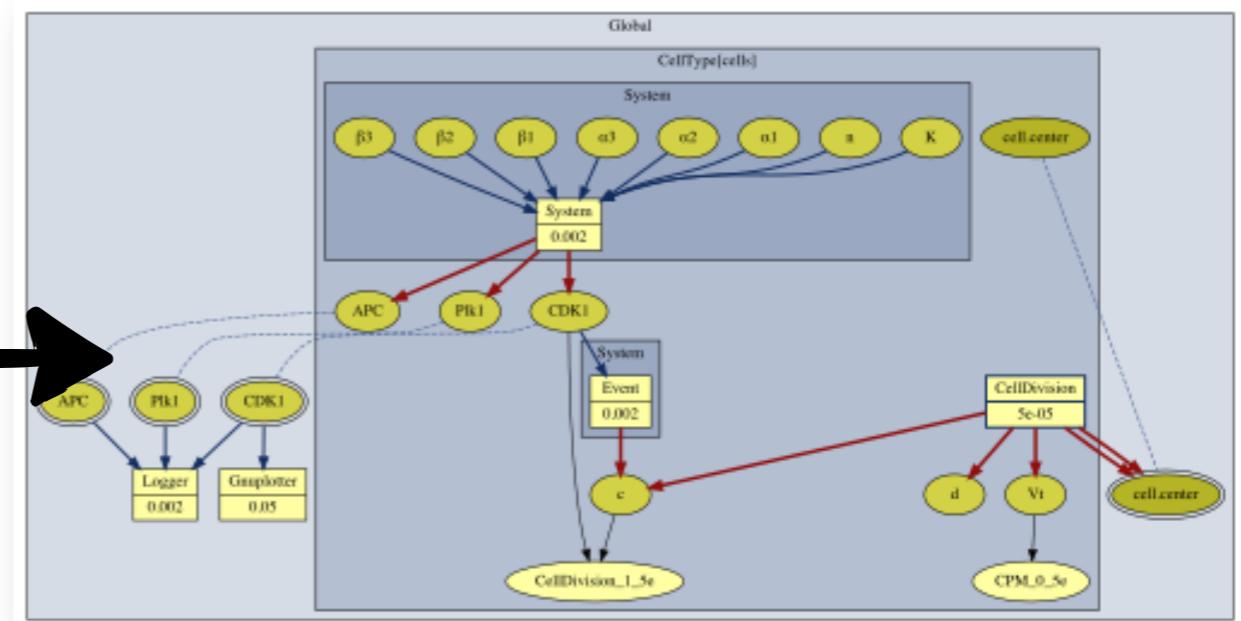


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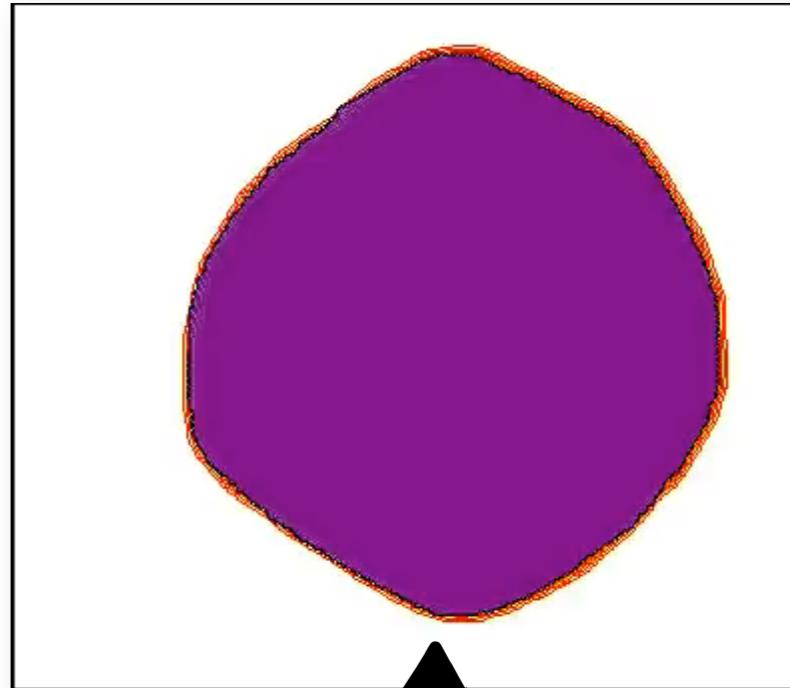
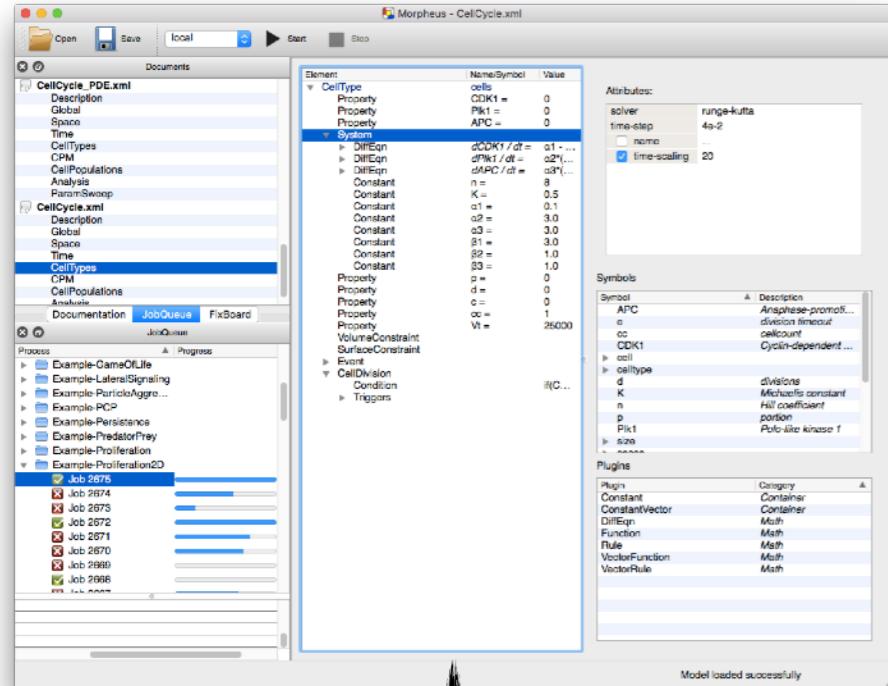
Convert mathematical models into simulations



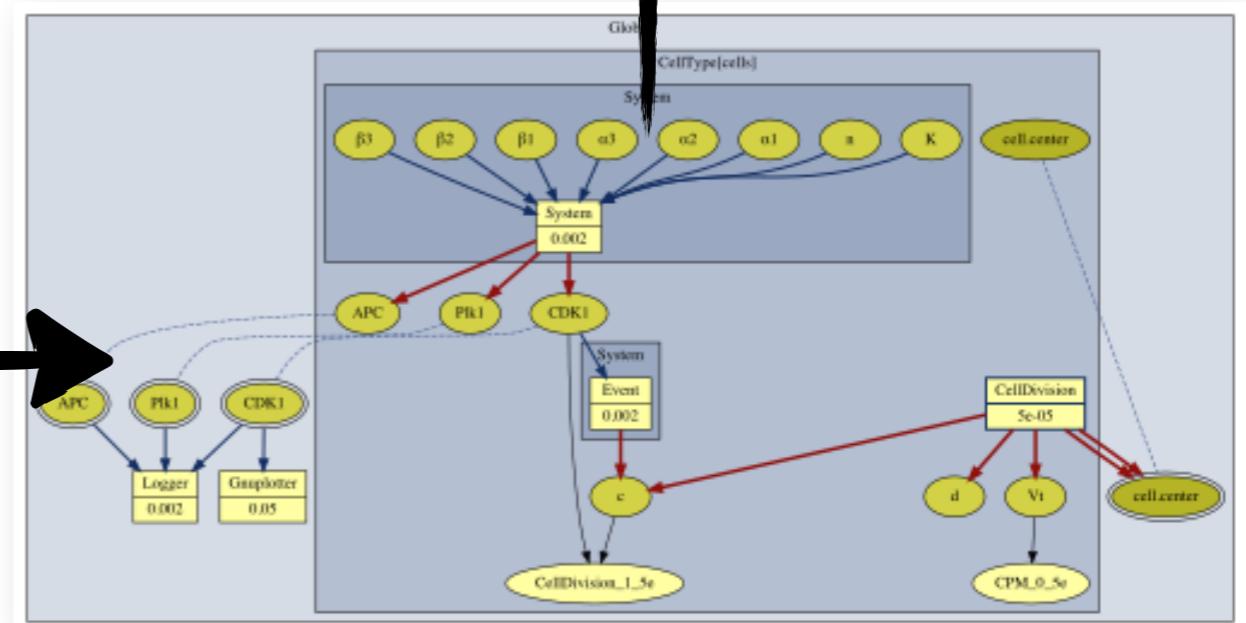
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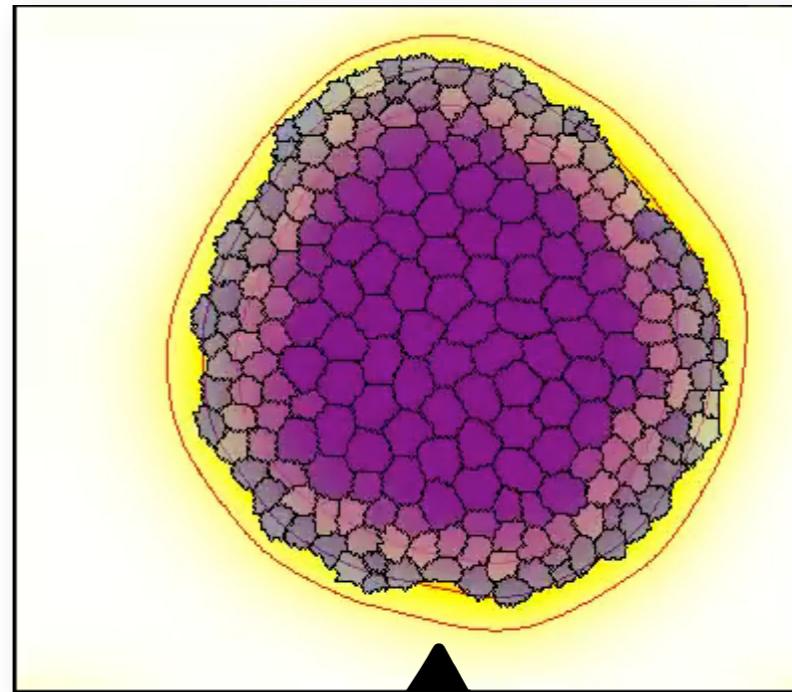
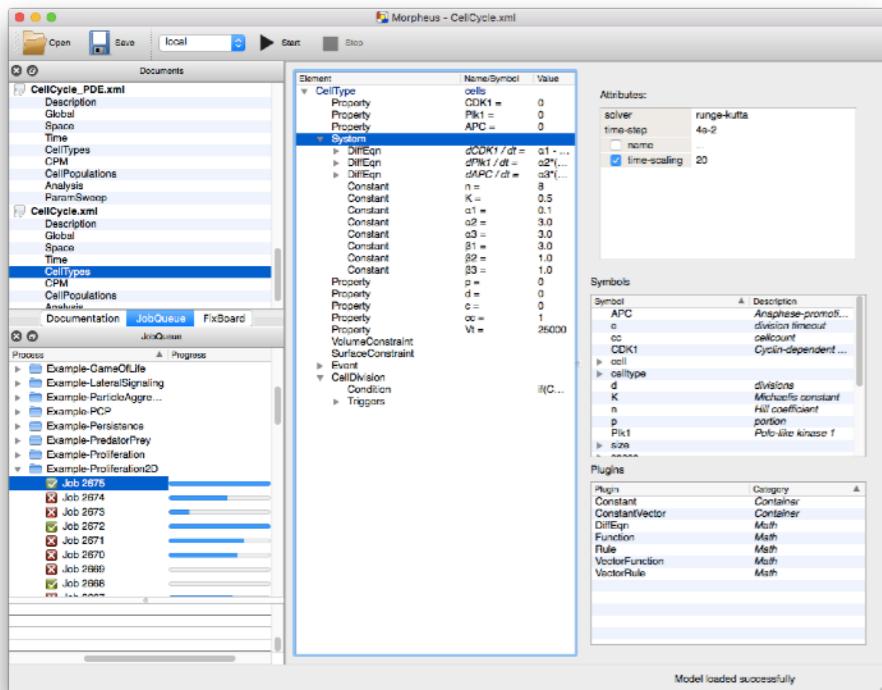
Convert mathematical models into simulations



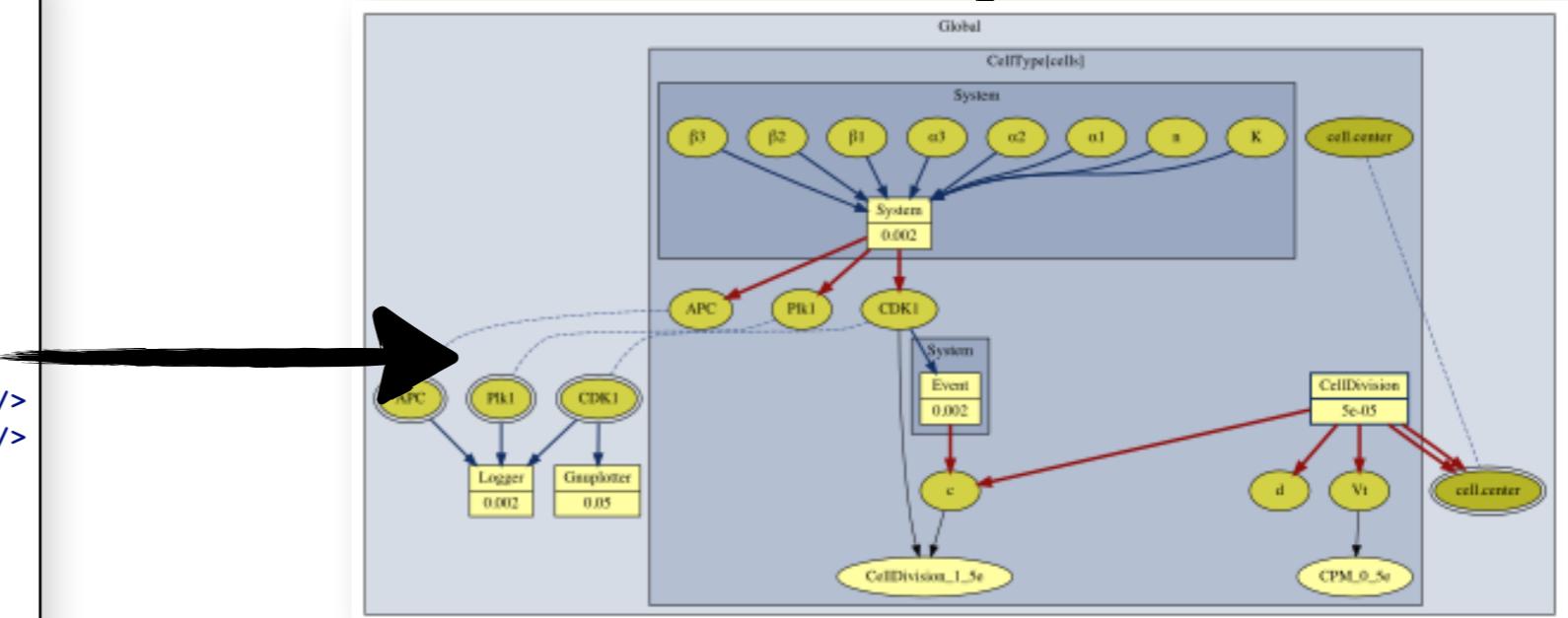
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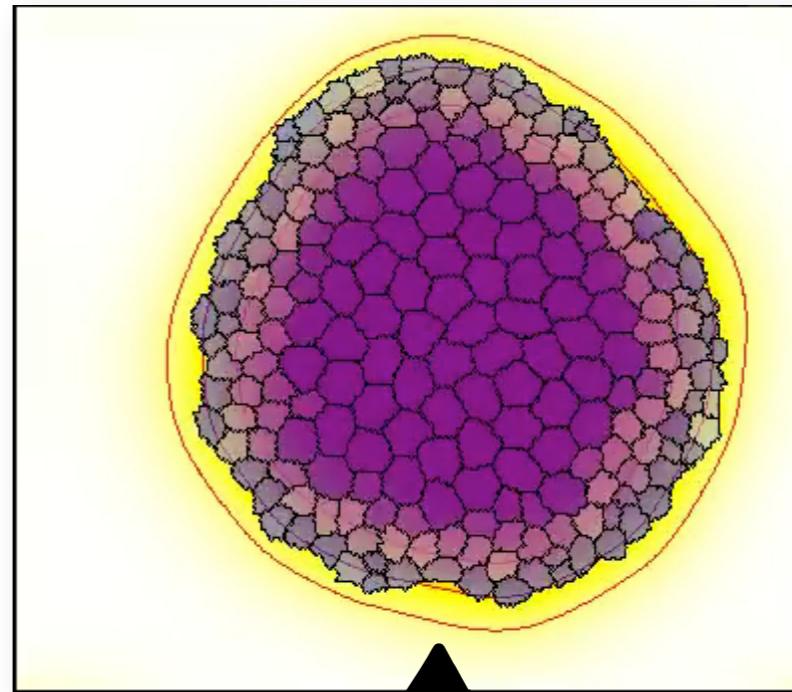
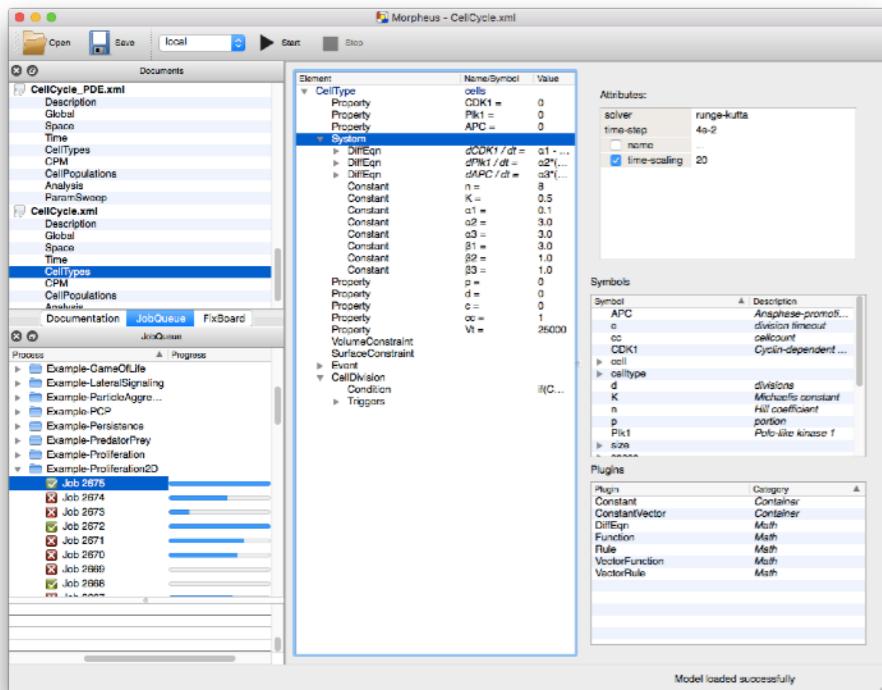
Convert mathematical models into simulations



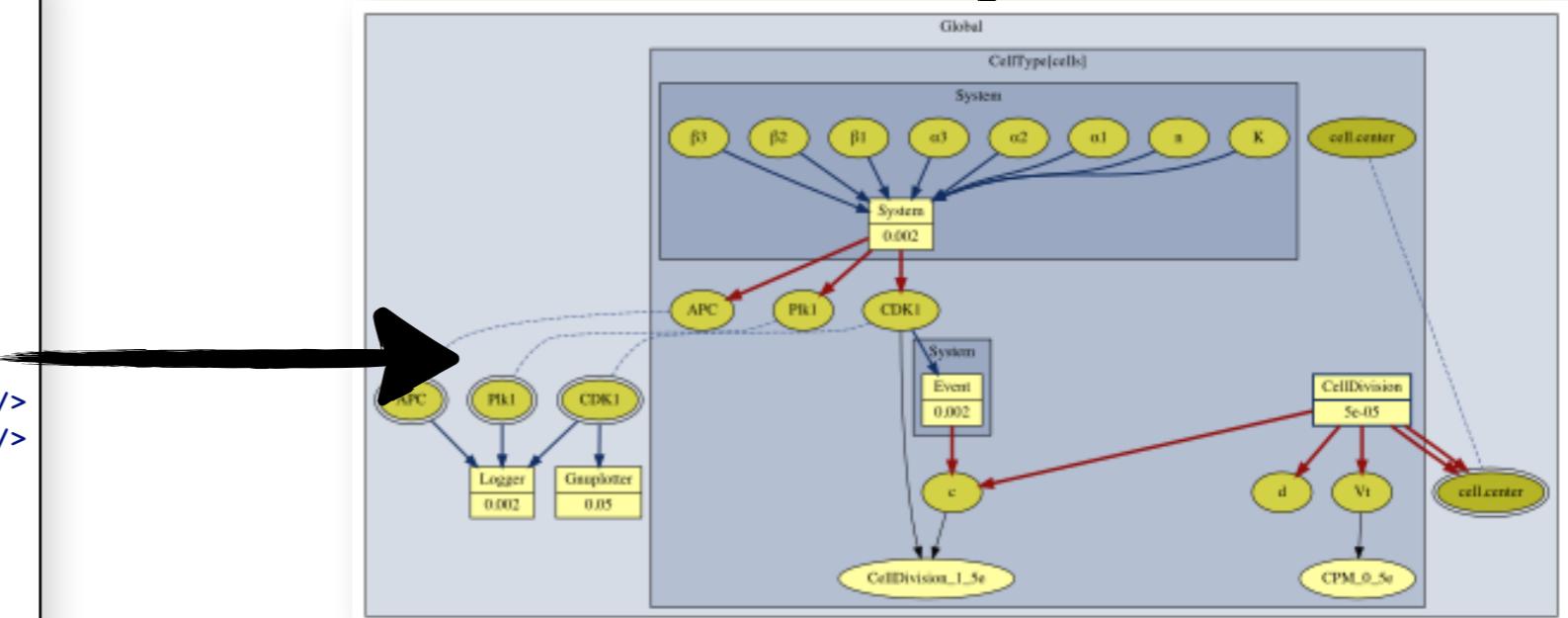
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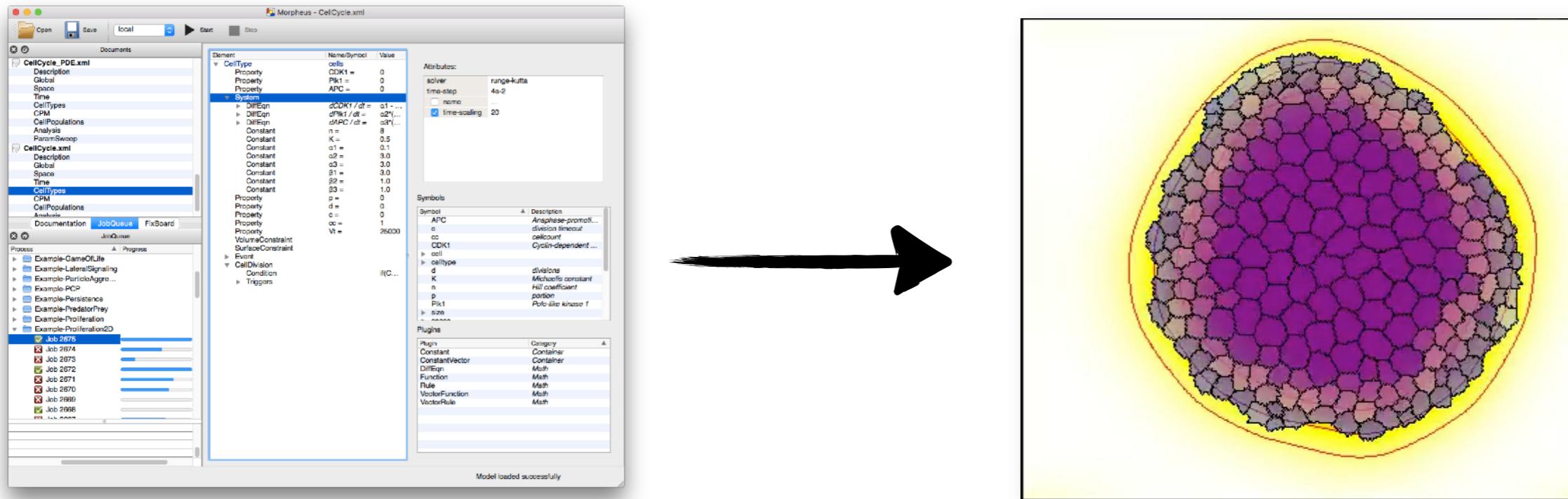
Convert mathematical models into simulations



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Convert mathematical models into simulations



Advantages

Automation and model integration

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- Improves usability

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- Widens audience

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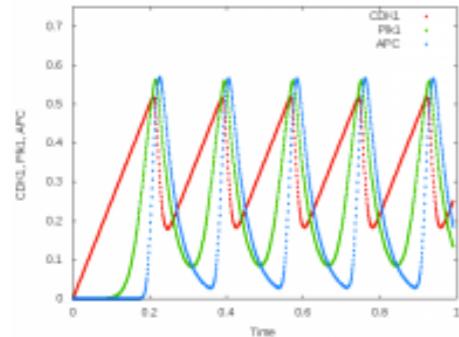
All depends on
the separation of
model and code

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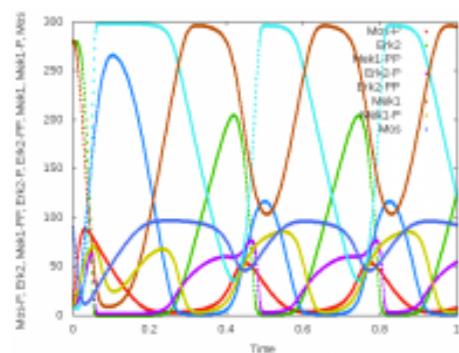
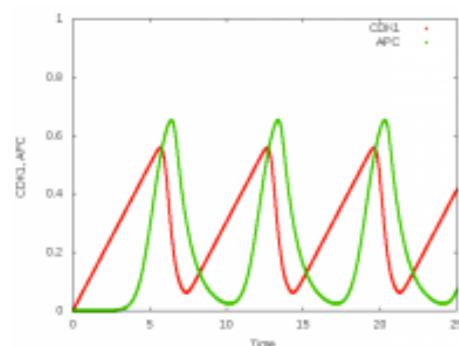
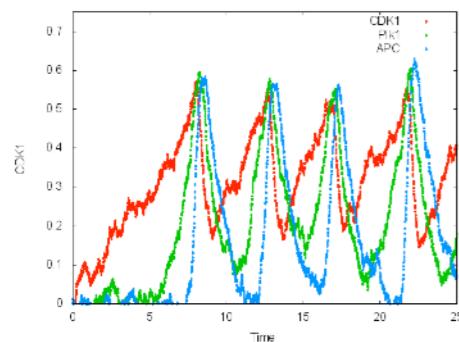
Modeling features

Differential equations

Gene regulatory and signaling networks

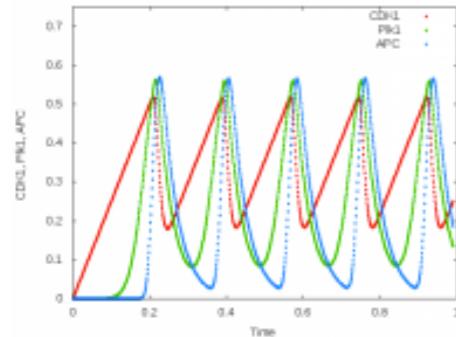


Ordinary differential equations
Euler, Heun, Runge-Kutta

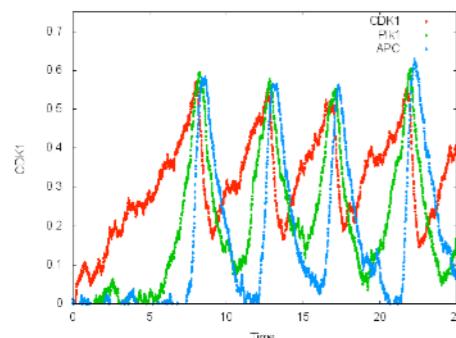


Differential equations

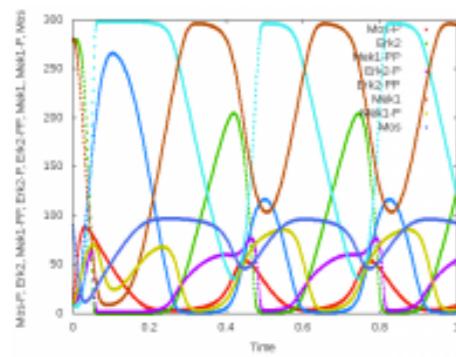
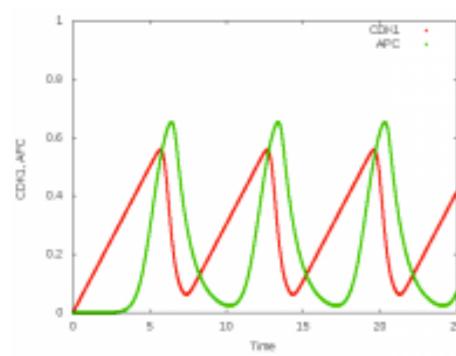
Gene regulatory and signaling networks



Ordinary differential equations
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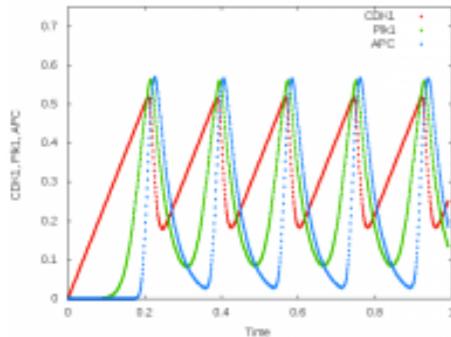


Stochastic differential equations
Heun-Maruyama

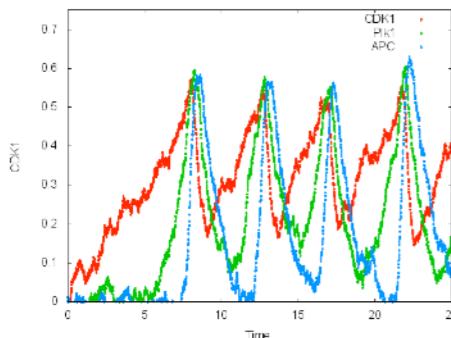


Differential equations

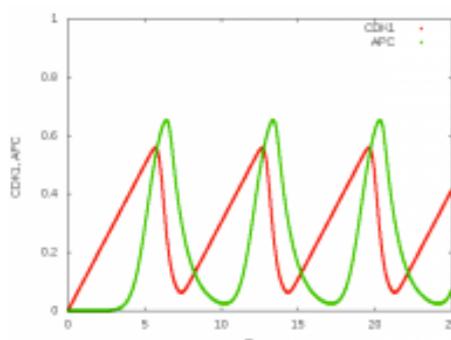
Gene regulatory and signaling networks



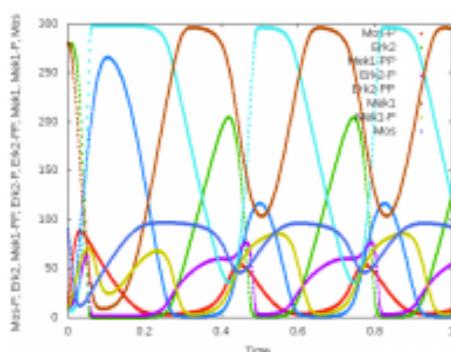
Ordinary differential equations
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Stochastic differential equations
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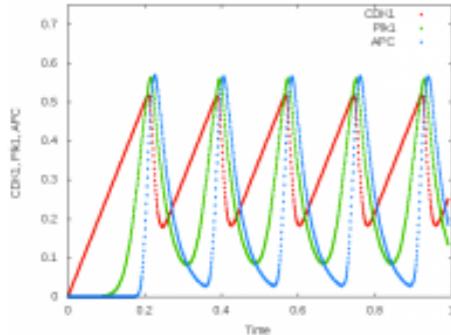


Delay differential equations
with constant delays

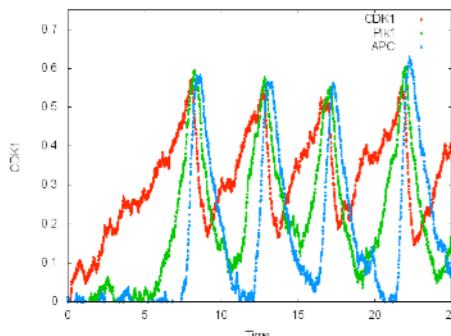


Differential equations

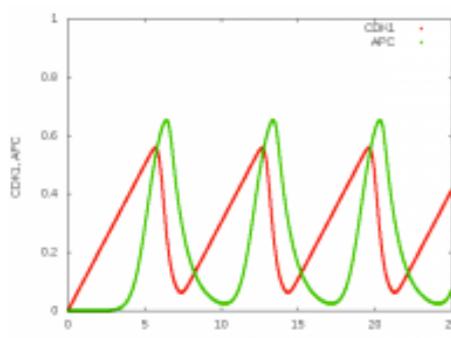
Gene regulatory and signaling networks



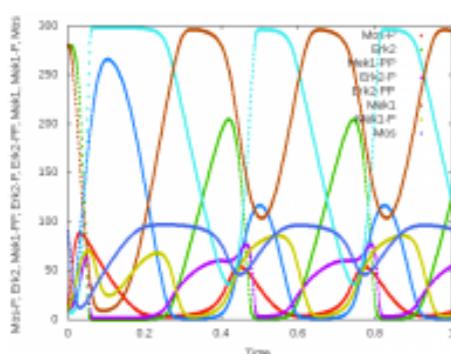
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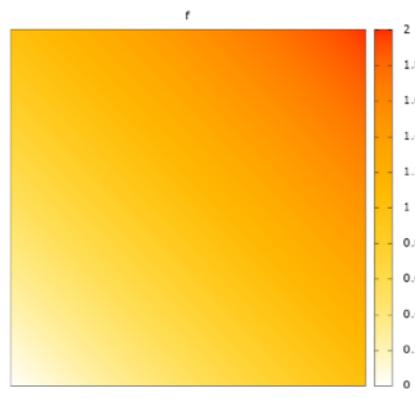
Delay differential equations
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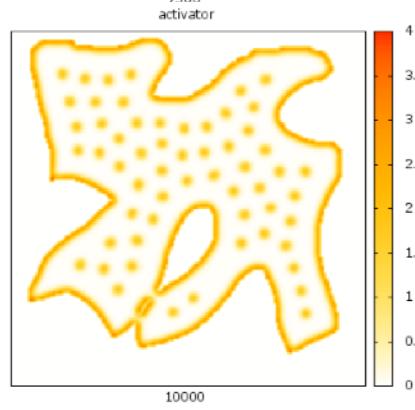
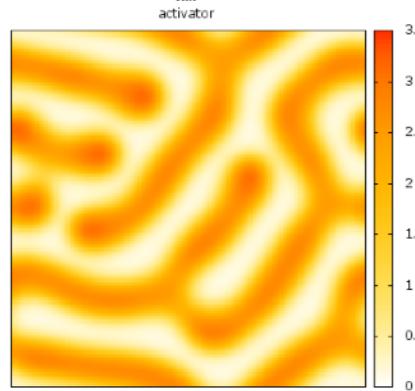
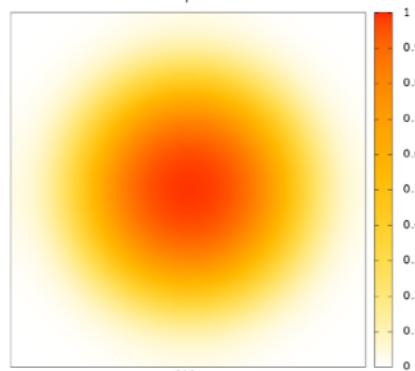
Import models in SBML format
e.g. from BioModels database

Reaction-diffusion systems

Morphogen gradients and intercellular signaling

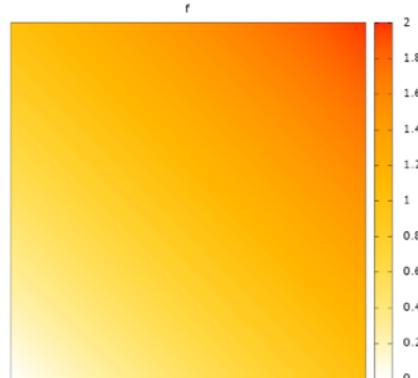


Static gradients
Scalar fields

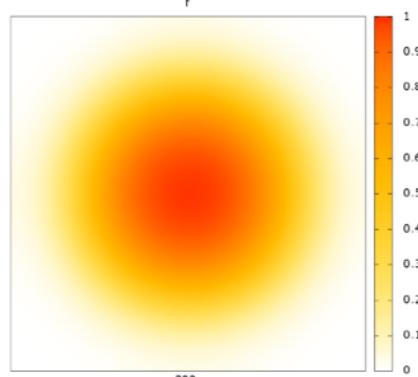


Reaction-diffusion systems

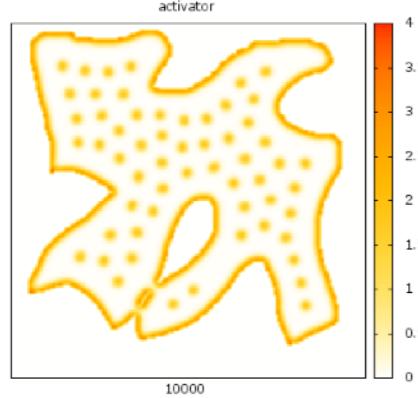
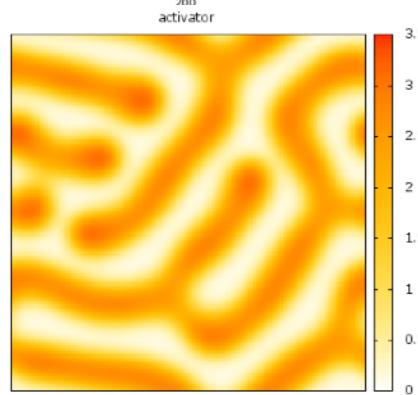
Morphogen gradients and intercellular signaling



Static gradients
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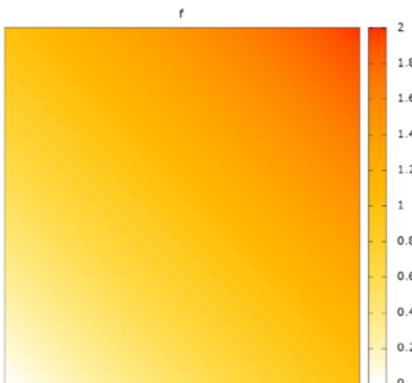


Diffusion
Finite volume method

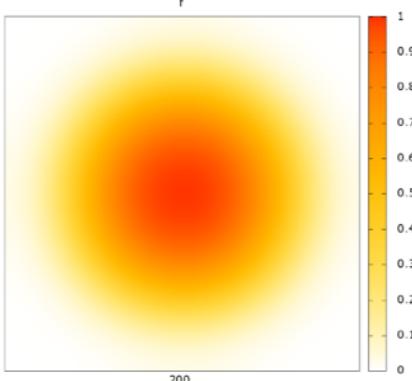


Reaction-diffusion systems

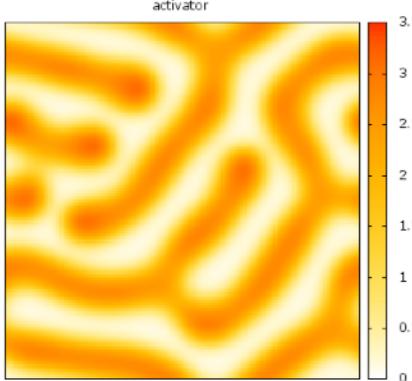
Morphogen gradients and intercellular signaling



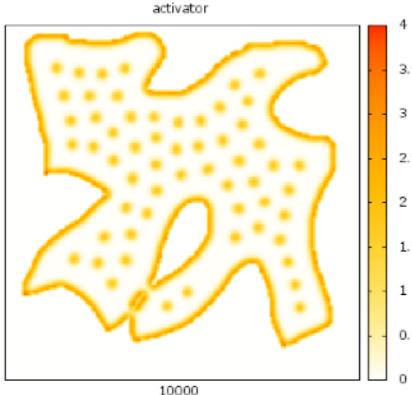
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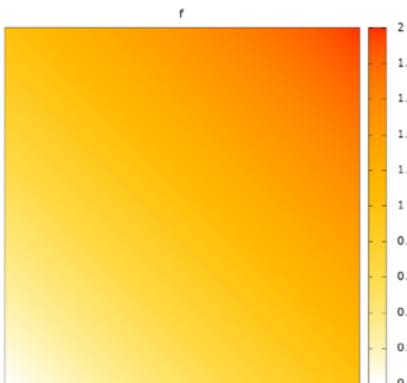


Reaction-diffusion systems
Operator-splitting method

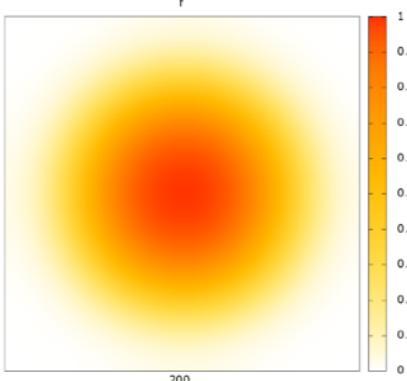


Reaction-diffusion systems

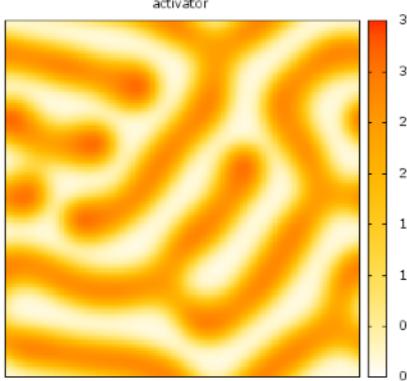
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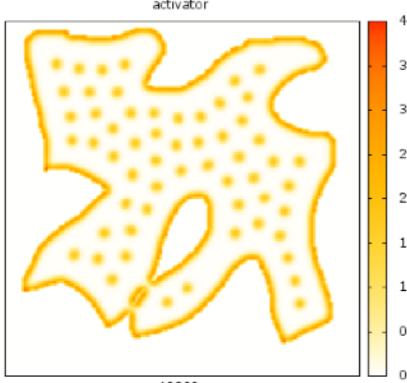
Static gradients
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Diffusion
Finite volume method



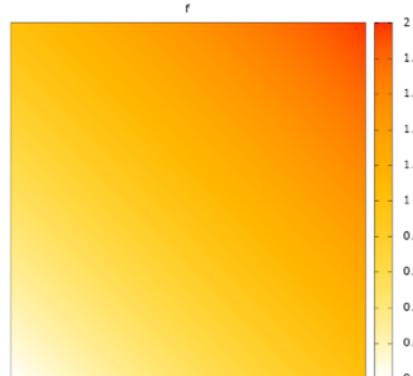
Reaction-diffusion systems
Operator-splitting method



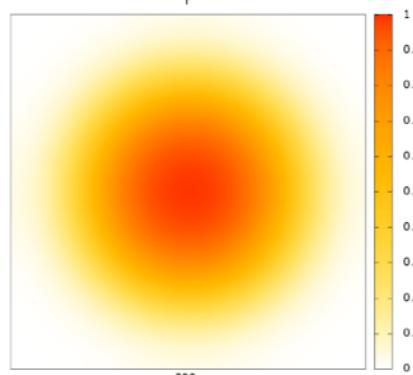
Import domains from images
TIFF format

Reaction-diffusion systems

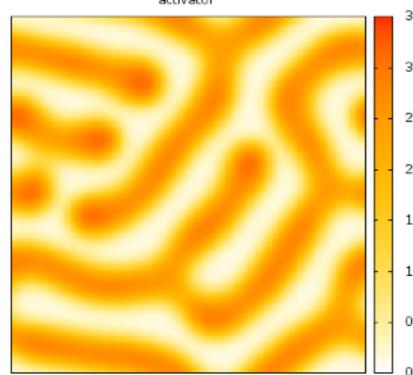
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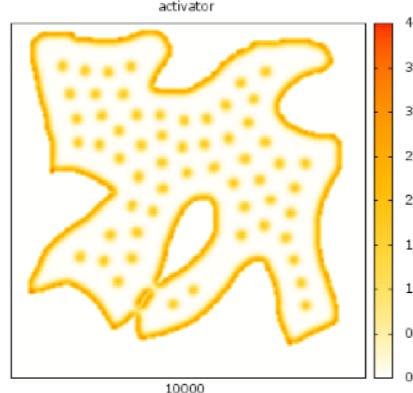
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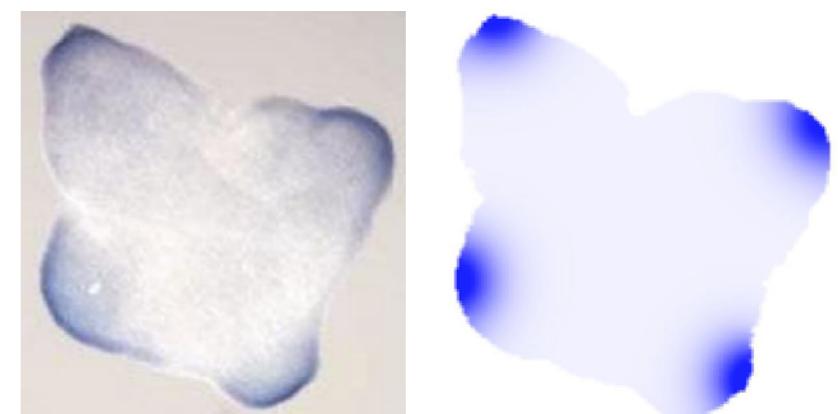
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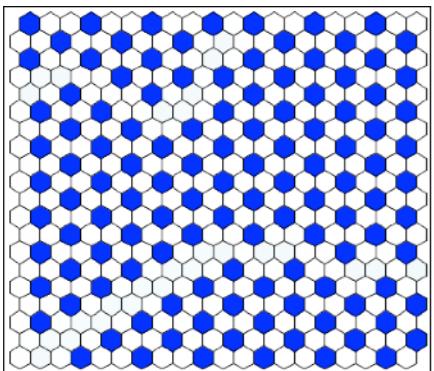
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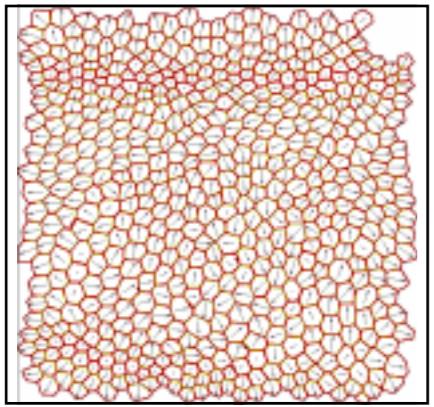
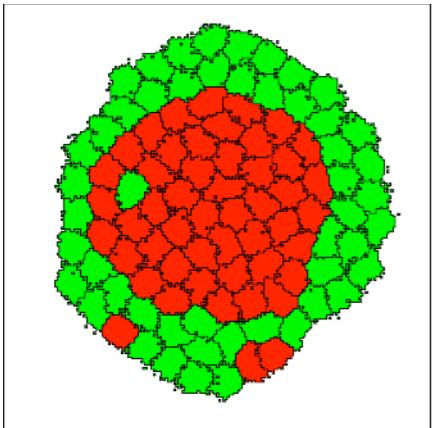
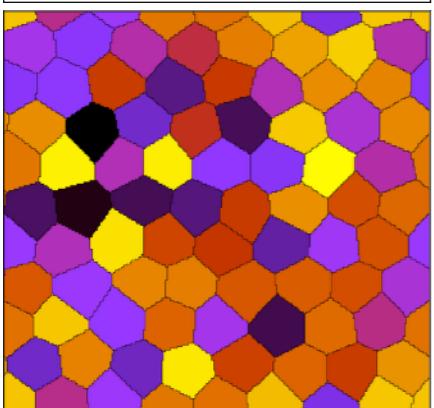
Brusch et al., *Curr Top Dev Biol*, 2014

Cell-based models

Cell shape, motility and surface mechanics

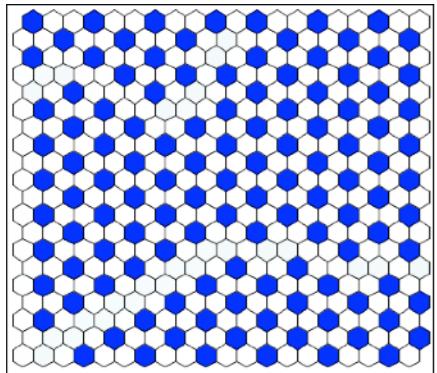


Discrete lattice
regular cell shape

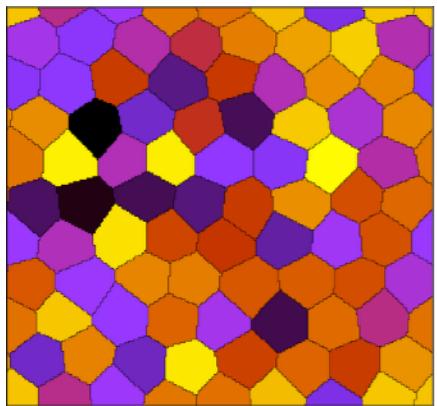


Cell-based models

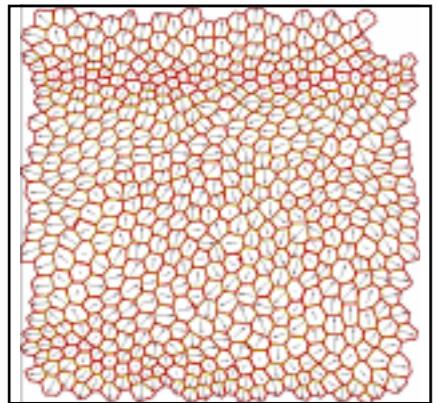
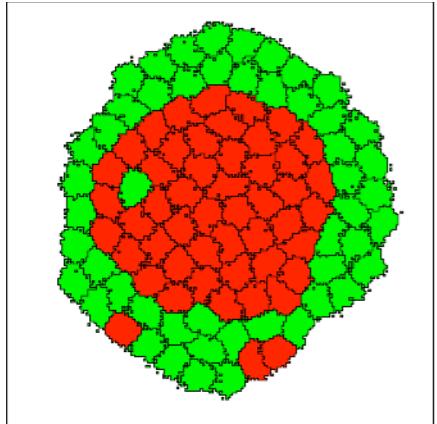
Cell shape, motility and surface mechanics



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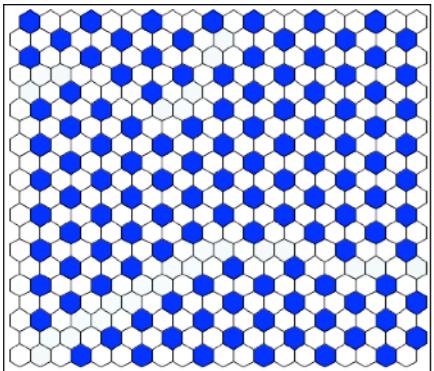


Voronoi tessellations
irregular cell shape

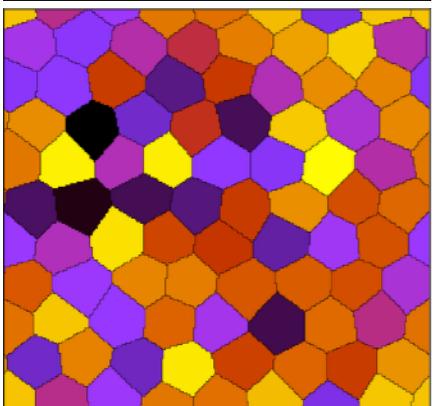


Cell-based models

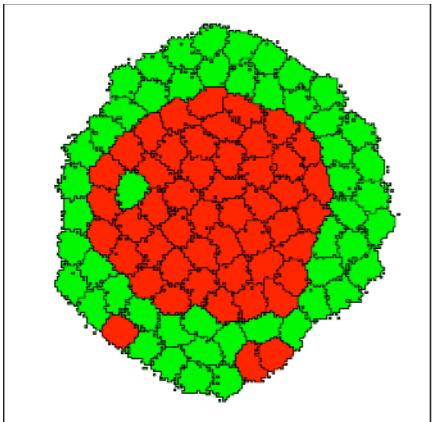
Cell shape, motility and surface mechanics



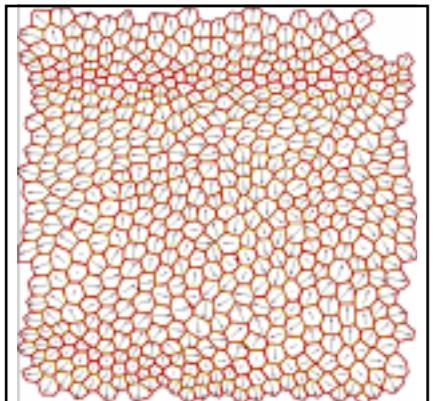
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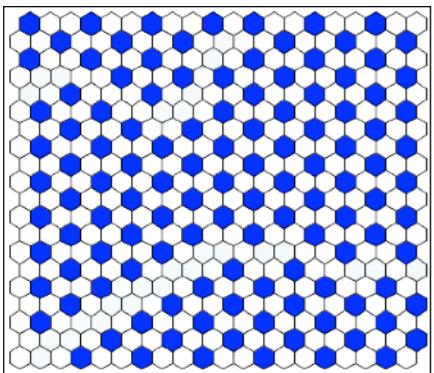


Cellular Potts model
cell shape and motility

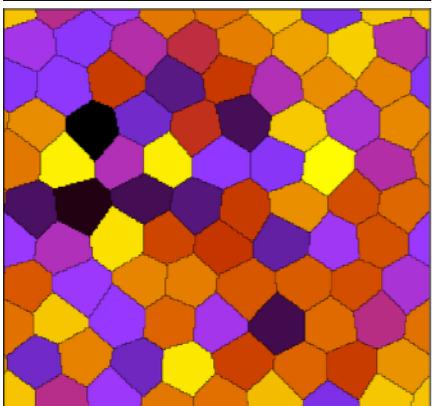


Cell-based models

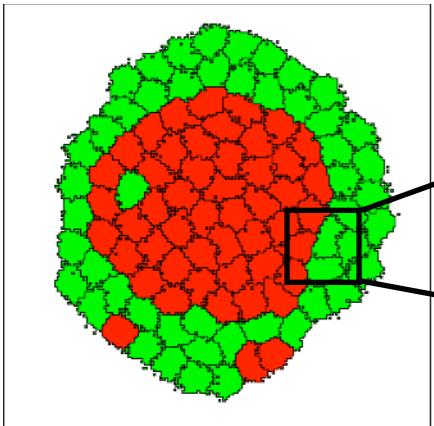
Cell shape, motility and surface mechanics



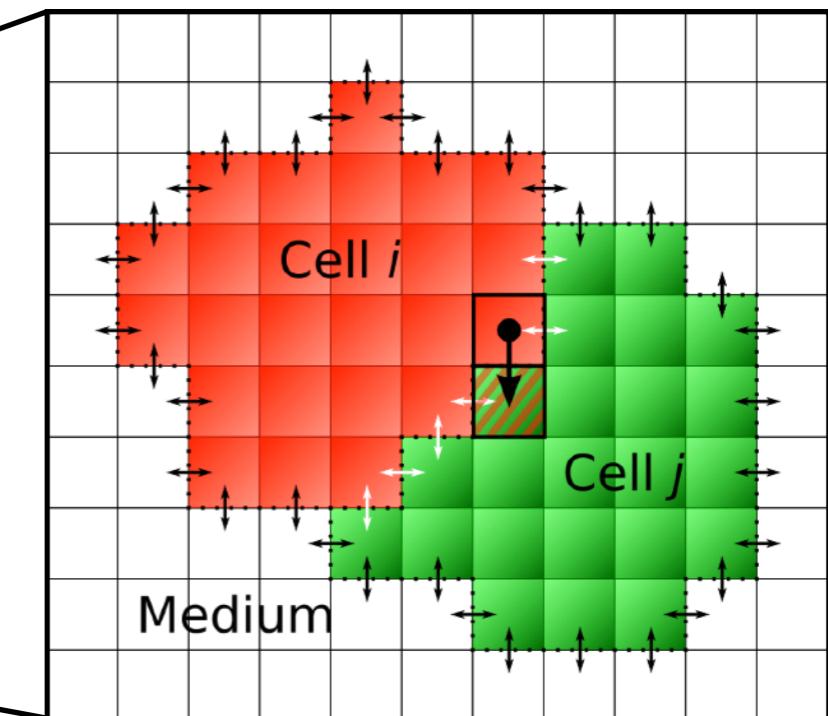
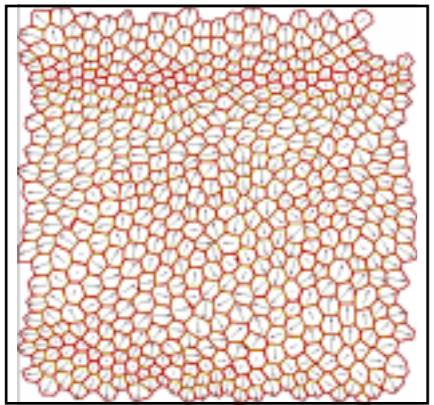
Discrete lattice
regular cell shape



Voronoi tessellations
irregular cell shape



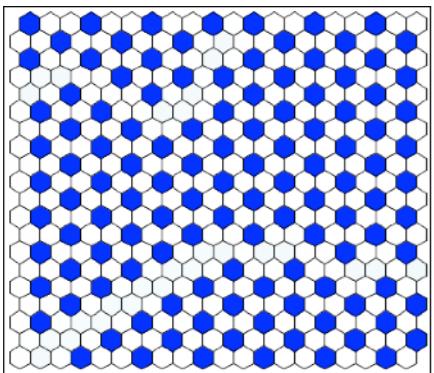
Cellular Potts model
cell shape and motility



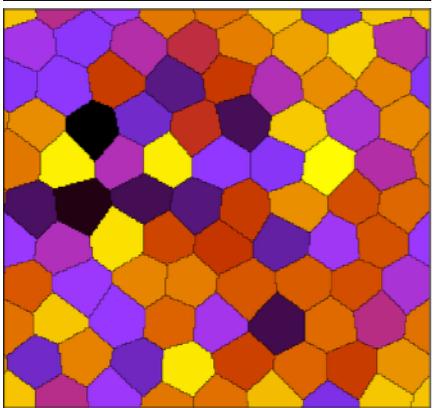
Graner and Glazier, PRL, 1992

Cell-based models

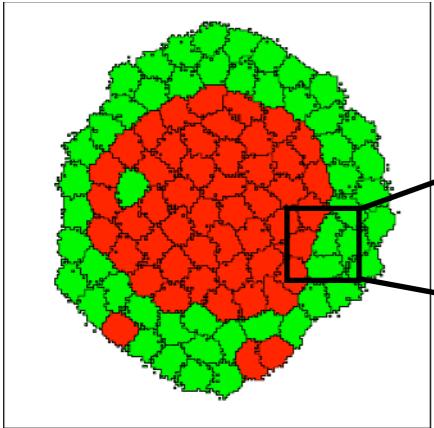
Cell shape, motility and surface mechanics



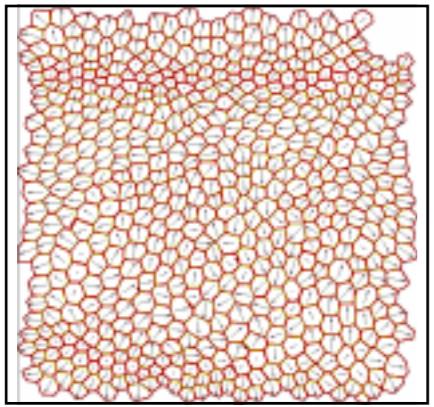
Discrete lattice
regular cell shape



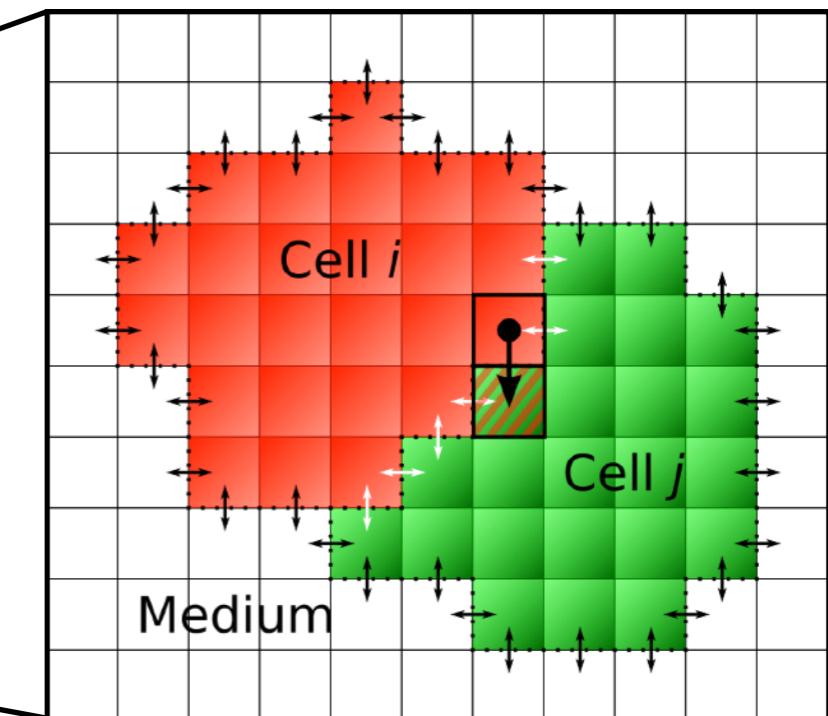
Voronoi tessellations
irregular cell shape



Cellular Potts model
cell shape and motility



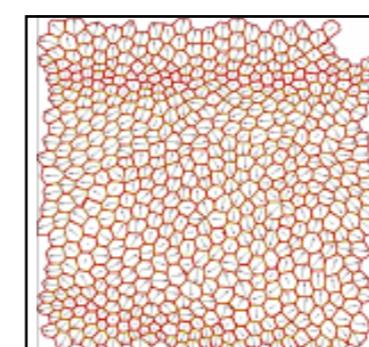
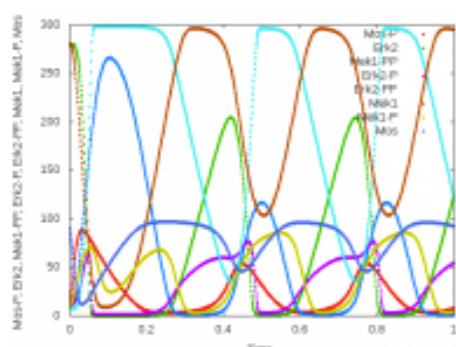
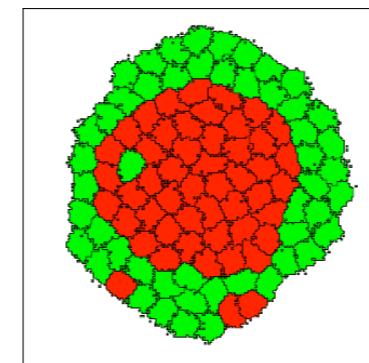
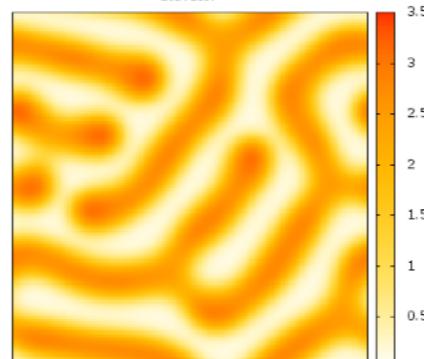
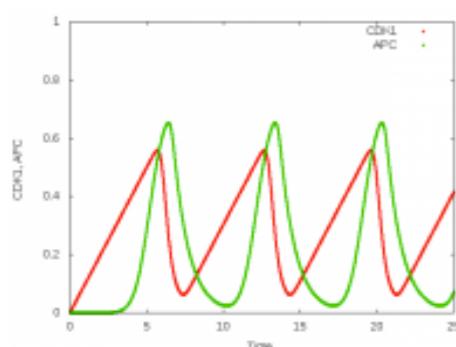
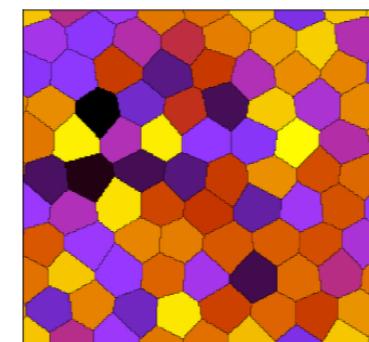
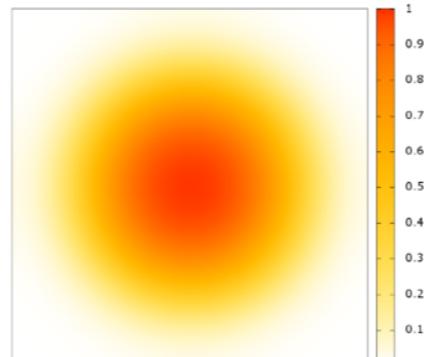
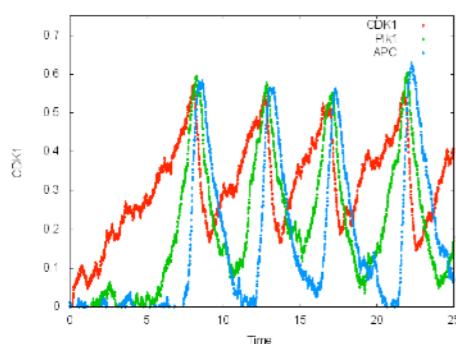
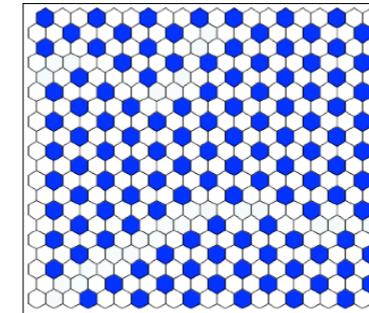
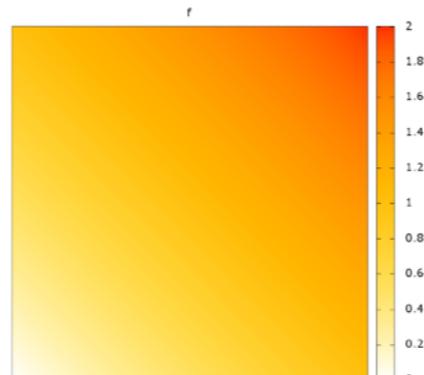
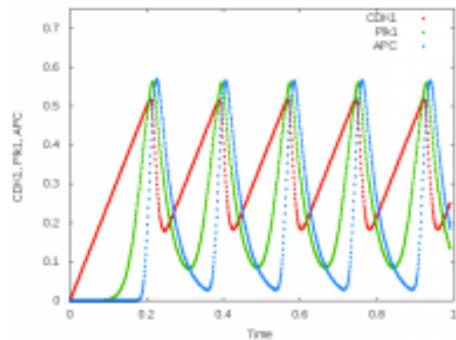
Import microscopy images
realistic cell shape



Graner and Glazier, PRL, 1992

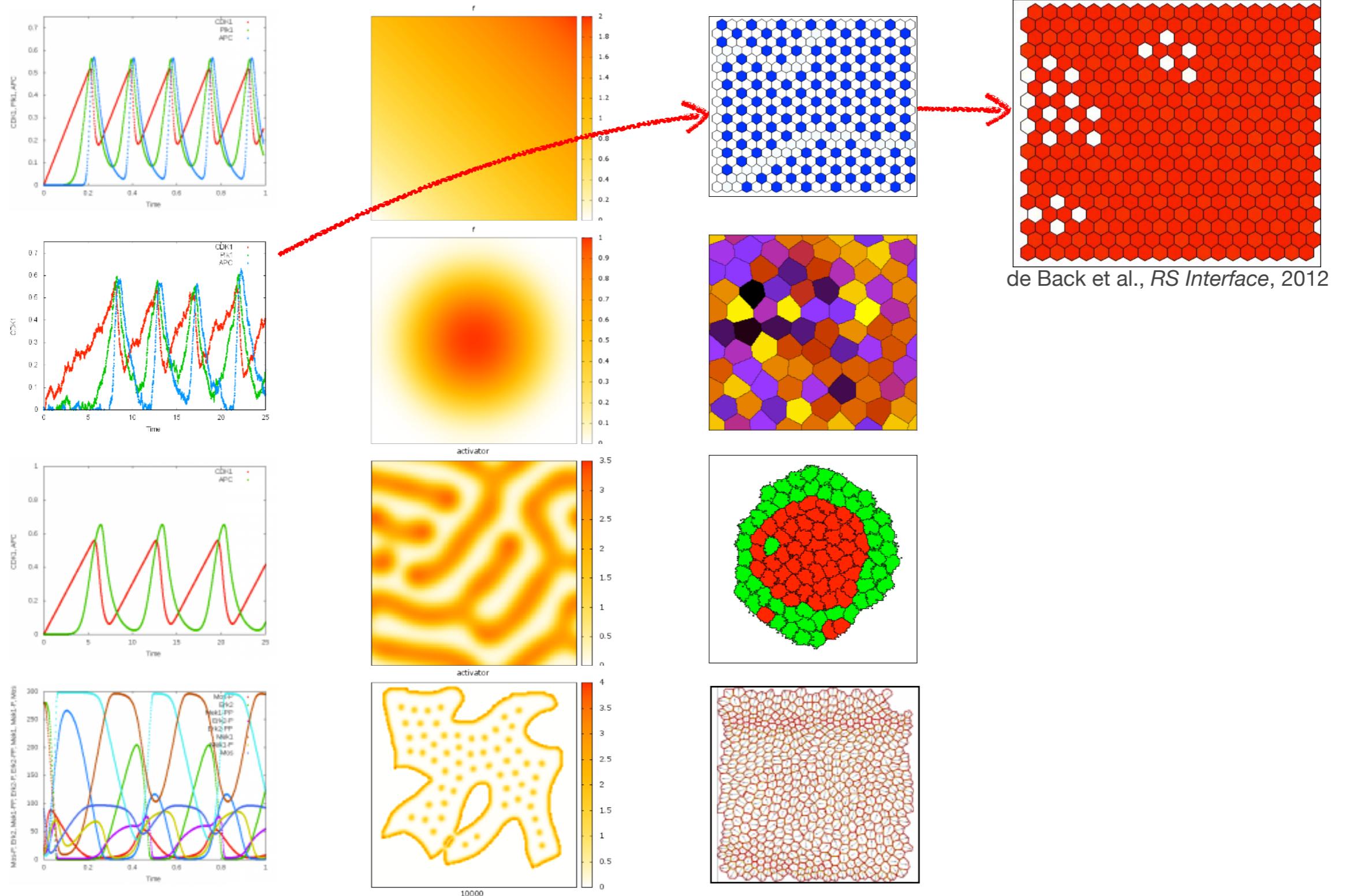
Multi-scale models

Coupling model formalisms



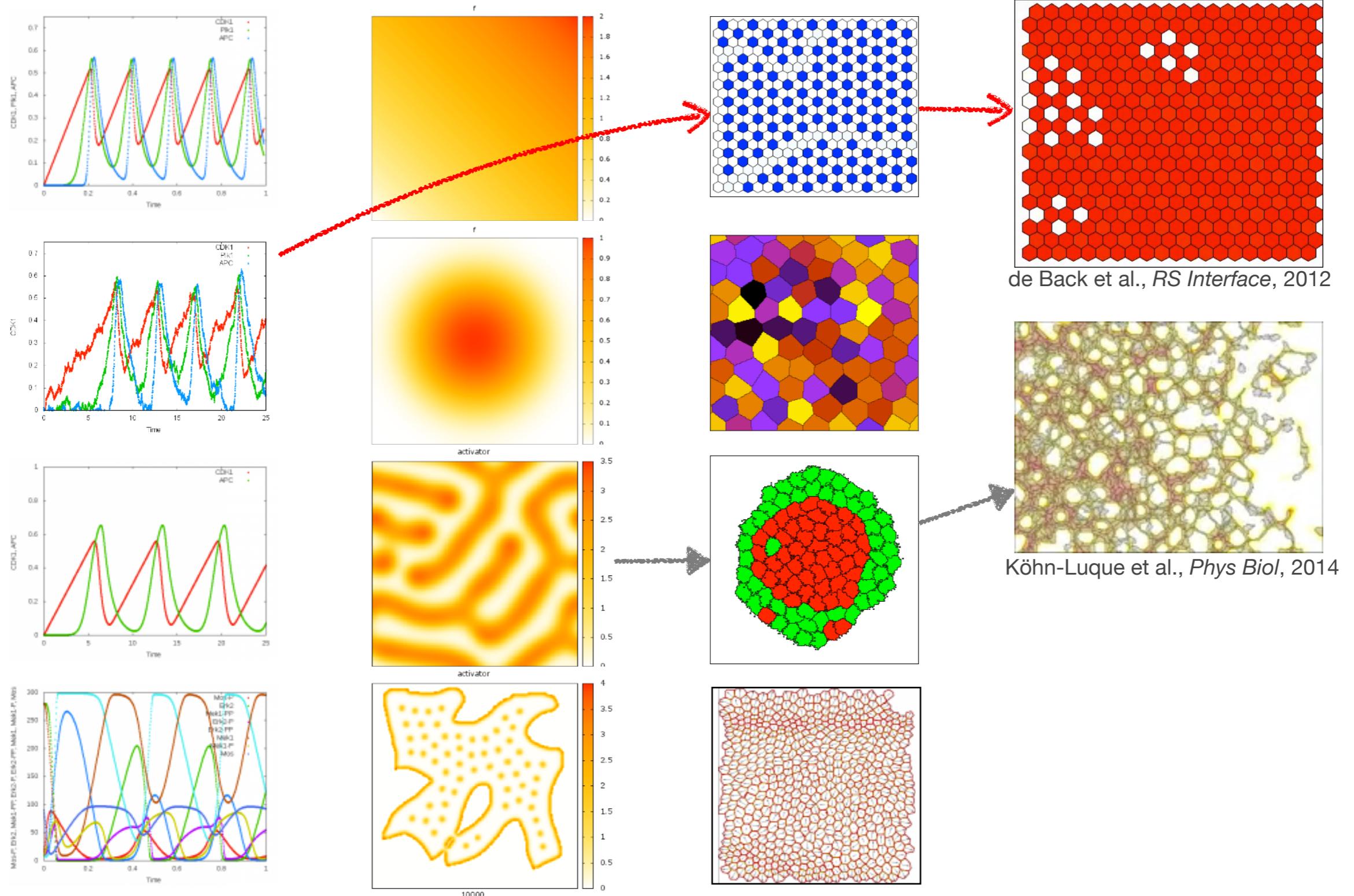
Multi-scale models

Coupling model formalisms



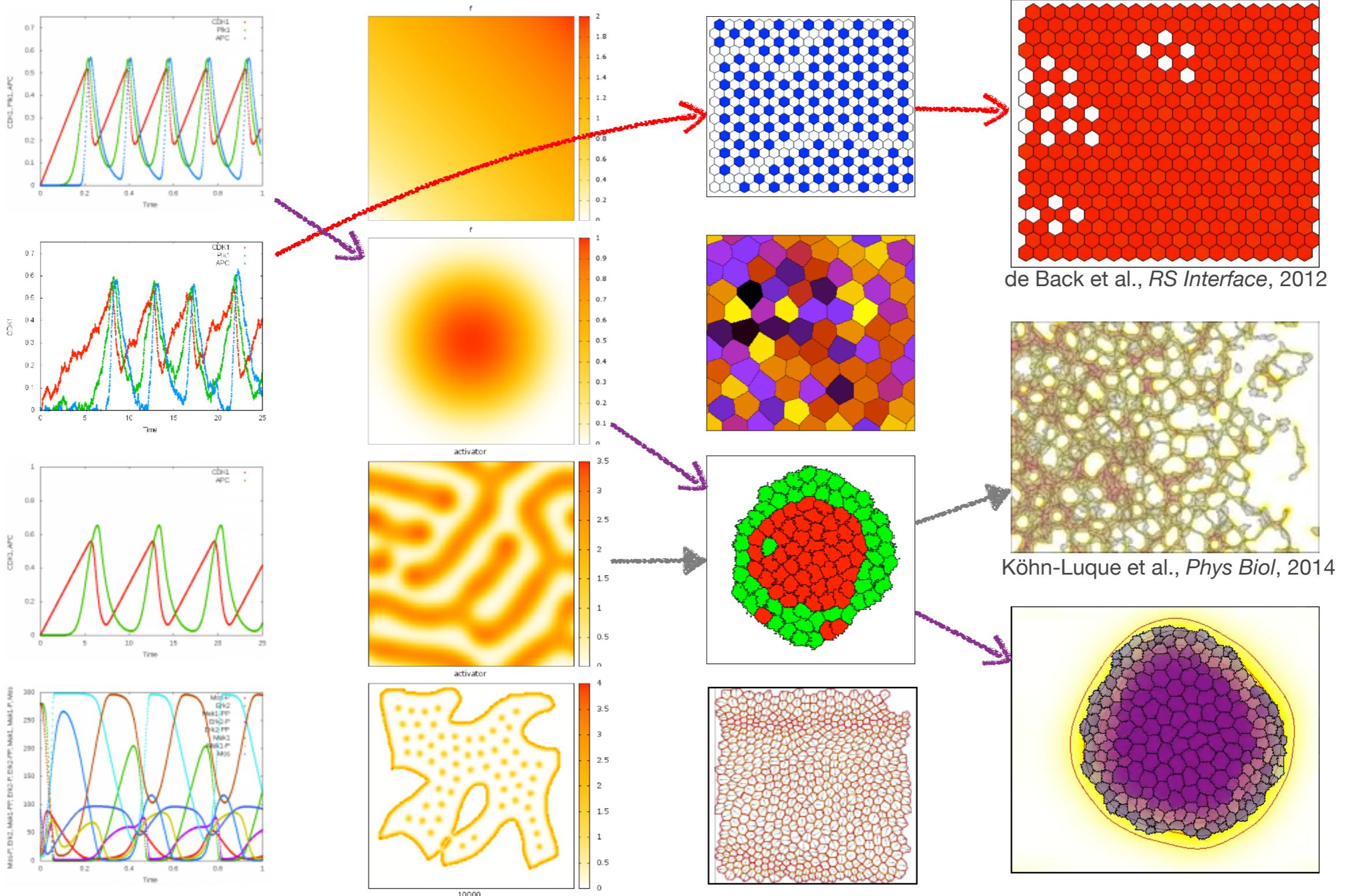
Multi-scale models

Coupling model formalisms



Multi-scale models

Coupling model formalisms



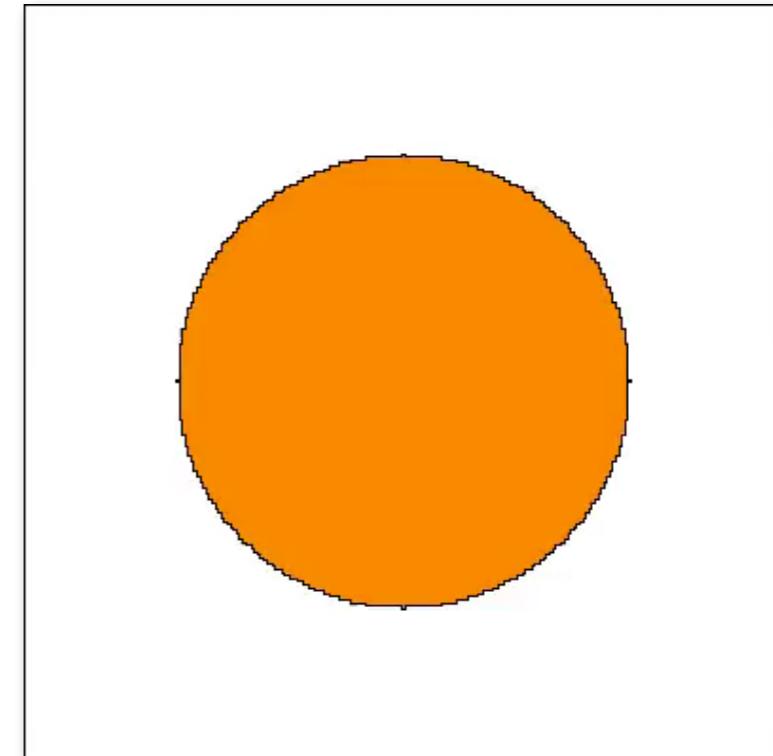
Multi-scale models

Cell cycle example

- Intracellular ODE model
for cell cycle dynamics



- Cell-based Potts model
cell surface mechanics
and cell division



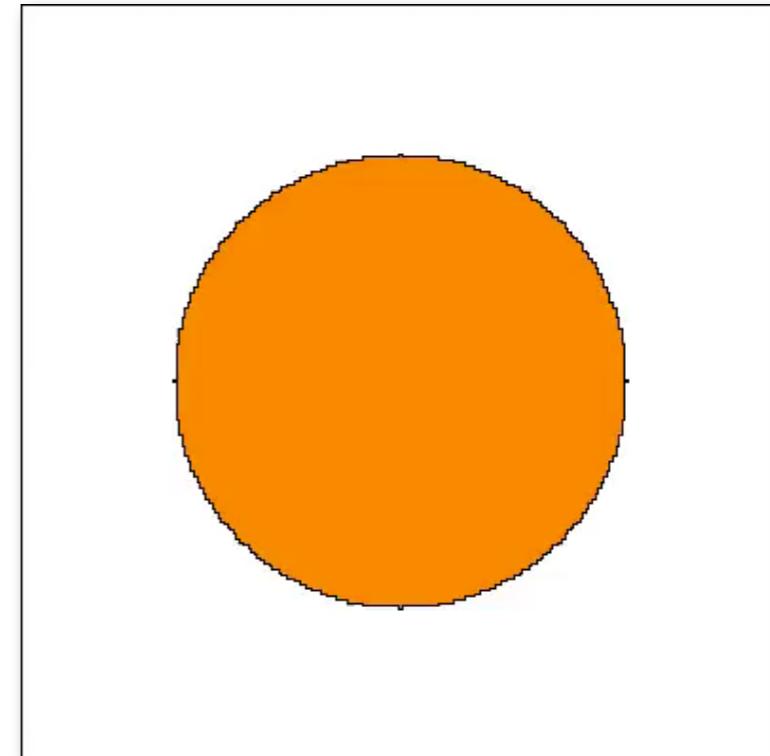
Multi-scale models

Cell cycle example

- Intracellular ODE model
for cell cycle dynamics



- Cell-based Potts model
cell surface mechanics
and cell division



Multi-scale models

Cell cycle example

Element	Name/Symbol	Value
▼ CellType	cells	
Property	Vt =	25000
Property	CDK1 =	0
Property	Plk1 =	0
Property	APC =	0

Cell-specific variables

Multi-scale models

Cell cycle example

Element	Name/Symbol	Value	
▼ CellType	cells		
Property	Vt =	25000	
Property	CDK1 =	0	Cell-specific variables
Property	Plk1 =	0	
Property	APC =	0	
▼ System			
► DiffEqn	$dCDK1 / dt =$	$a1 - \beta1 * CDK1 * (APC^n / (K^n + APC^n))$	
► DiffEqn	$dPlk1 / dt =$	$a2*(1-Plk1) * ((CDK1^n) / (K^n + CDK1^n)) - \beta2*Plk1$	
► DiffEqn	$dAPC / dt =$	$a3*(1- APC) * ((Plk1^n) / (K^n + Plk1^n)) - \beta3*APC$	
Constant	n =	8	
Constant	K =	0.5	Intracellular ODE model for cell cycle
Constant	a1 =	0.1	
Constant	a2 =	3.0	
Constant	a3 =	3.0	
Constant	$\beta1 =$	3.0	
Constant	$\beta2 =$	1.0	
Constant	$\beta3 =$	1.0	

Multi-scale models

Cell cycle example

Element	Name/Symbol	Value	
CellType	cells		
Property	Vt =	25000	
Property	CDK1 =	0	Cell-specific variables
Property	Plk1 =	0	
Property	APC =	0	
System			
DiffEqn	$dCDK1 / dt =$	$a1 - \beta1 * CDK1 * (APC^n / (K^n + APC^n))$	
DiffEqn	$dPlk1 / dt =$	$a2 * (1-Plk1) * ((CDK1^n) / (K^n + CDK1^n)) - \beta2 * Plk1$	
DiffEqn	$dAPC / dt =$	$a3 * (1- APC) * ((Plk1^n) / (K^n + Plk1^n)) - \beta3 * APC$	
Constant	n =	8	
Constant	K =	0.5	Intracellular ODE model for cell cycle
Constant	a1 =	0.1	
Constant	a2 =	3.0	
Constant	a3 =	3.0	
Constant	$\beta1 =$	3.0	
Constant	$\beta2 =$	1.0	
Constant	$\beta3 =$	1.0	
VolumeConstraint			
SurfaceConstraint			
CellDivision			
Condition		$CDK1 > 0.5$	Cell shape and division
Triggers			
Rule	Vt =	$Vt/2$	
Rule	CDK1 =	$CDK1 + rand_norm(0,0.01)$	

Multi-scale models

Cell cycle example

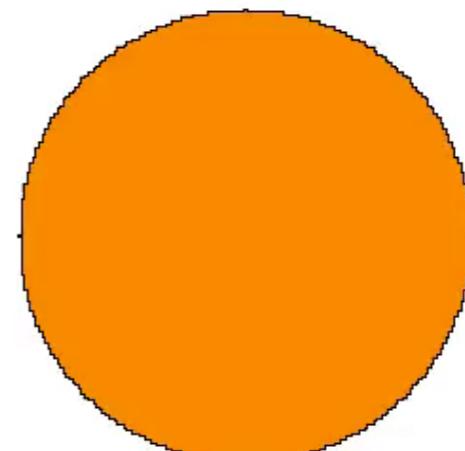
Element	Name/Symbol	Value	
CellType	cells		
Property	Vt =	25000	
Property	CDK1 =	0	Cell-specific variables
Property	Plk1 =	0	
Property	APC =	0	
System			
DiffEqn	dCDK1 / dt =	$a1 - \beta1 * CDK1 * (APC^n / (K^n + APC^n))$	
DiffEqn	dPlk1 / dt =	$a2 * (1 - Plk1) * ((CDK1^n) / (K^n + CDK1^n)) - \beta2 * Plk1$	
DiffEqn	dAPC / dt =	$a3 * (1 - APC) * ((Plk1^n) / (K^n + Plk1^n)) - \beta3 * APC$	
Constant	n =	8	Intracellular ODE model for cell cycle
Constant	K =	0.5	
Constant	a1 =	0.1	
Constant	a2 =	3.0	
Constant	a3 =	3.0	
Constant	β1 =	3.0	
Constant	β2 =	1.0	
Constant	β3 =	1.0	
VolumeConstraint			
SurfaceConstraint			
CellDivision			
Condition			
Triggers			
Rule	Vt =	Vt/2	
Rule	CDK1 =	CDK1 + rand_norm(0,0.01)	Cell shape and division

Multi-scale models

Cell cycle example

Element	Name/Symbol	Value
▼ CellType	cells	
Property	Vt =	25000
Property	CDK1 =	0
Property	Plk1 =	0
Property	APC =	0
▼ System		
► DiffEqn	$dCDK1 / dt =$	$a1 - \beta1 * CDK1$
► DiffEqn	$dPlk1 / dt =$	$a2*(1-Plk1) * ((C - K) / n)$
► DiffEqn	$dAPC / dt =$	$a3*(1- APC) * ((C - K) / n)$
Constant	n =	8
Constant	K =	0.5
Constant	a1 =	0.1
Constant	a2 =	3.0
Constant	a3 =	3.0
Constant	$\beta1 =$	3.0
Constant	$\beta2 =$	1.0
Constant	$\beta3 =$	1.0
VolumeConstraint		
SurfaceConstraint		
▼ CellDivision		
Condition		
▼ Triggers		
► Rule	Vt =	$Vt/2$
► Rule	CDK1 =	$CDK1 + rand_no$

Intracellular ODE

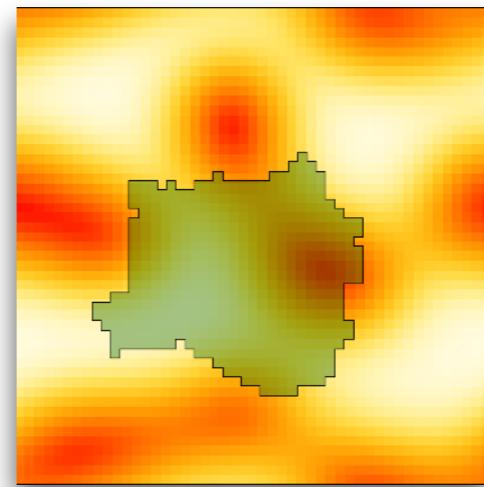


Multi-scale models

Mapping between different spatial contexts

CellReporter

Collect data within cellular domain

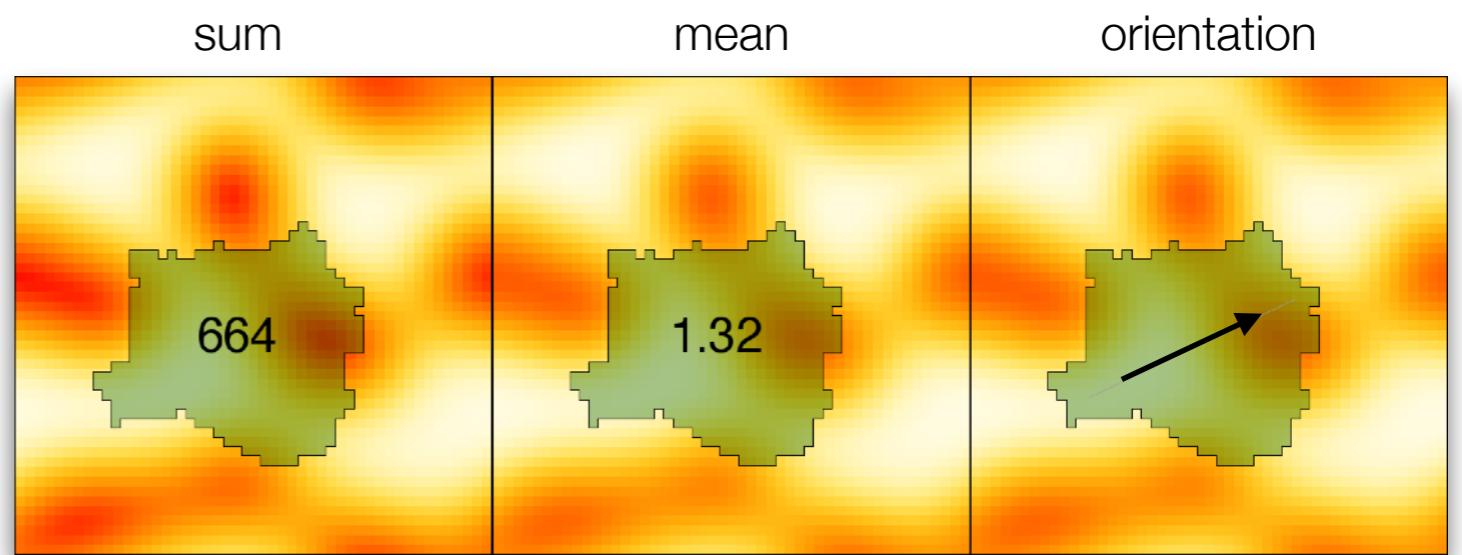


Multi-scale models

Mapping between different spatial contexts

CellReporter

Collect data within cellular domain

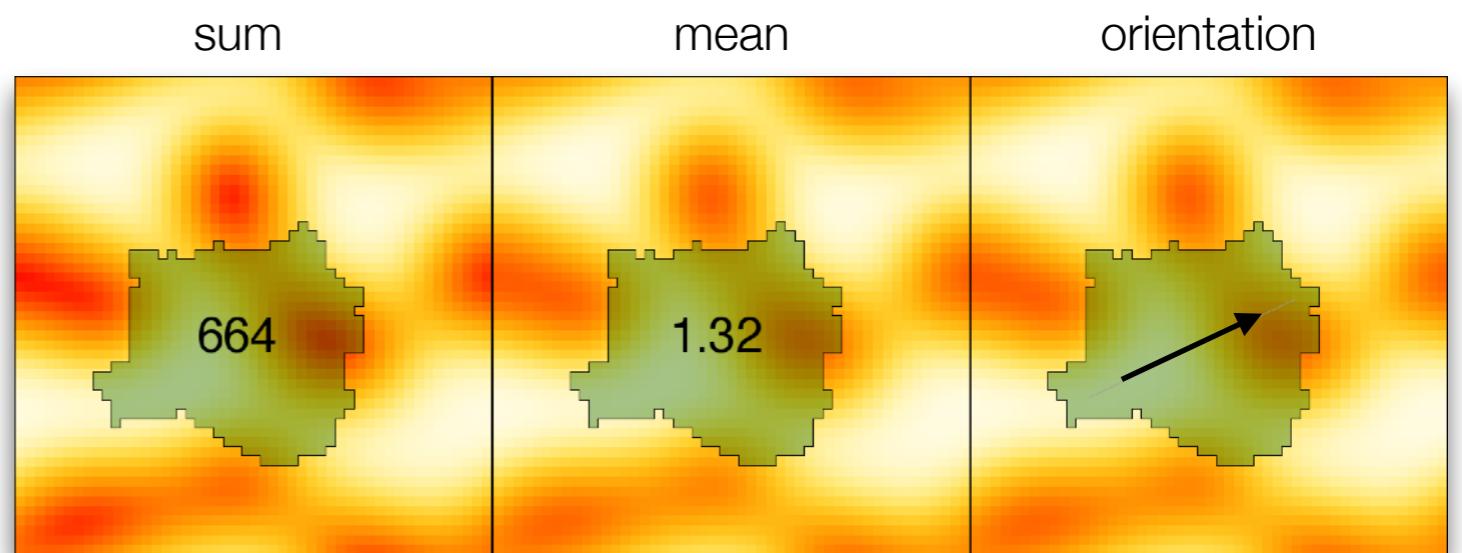


Multi-scale models

Mapping between different spatial contexts

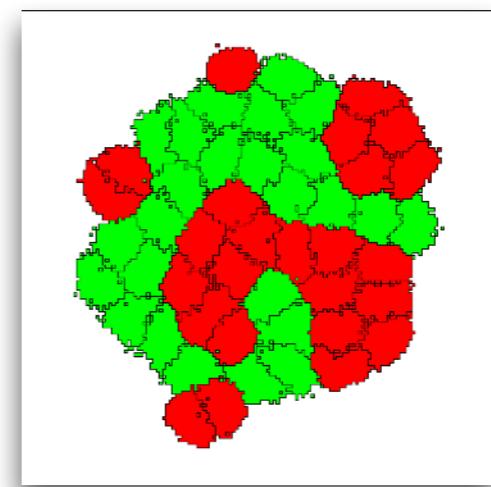
CellReporter

Collect data within cellular domain



NeighborhoodReporter

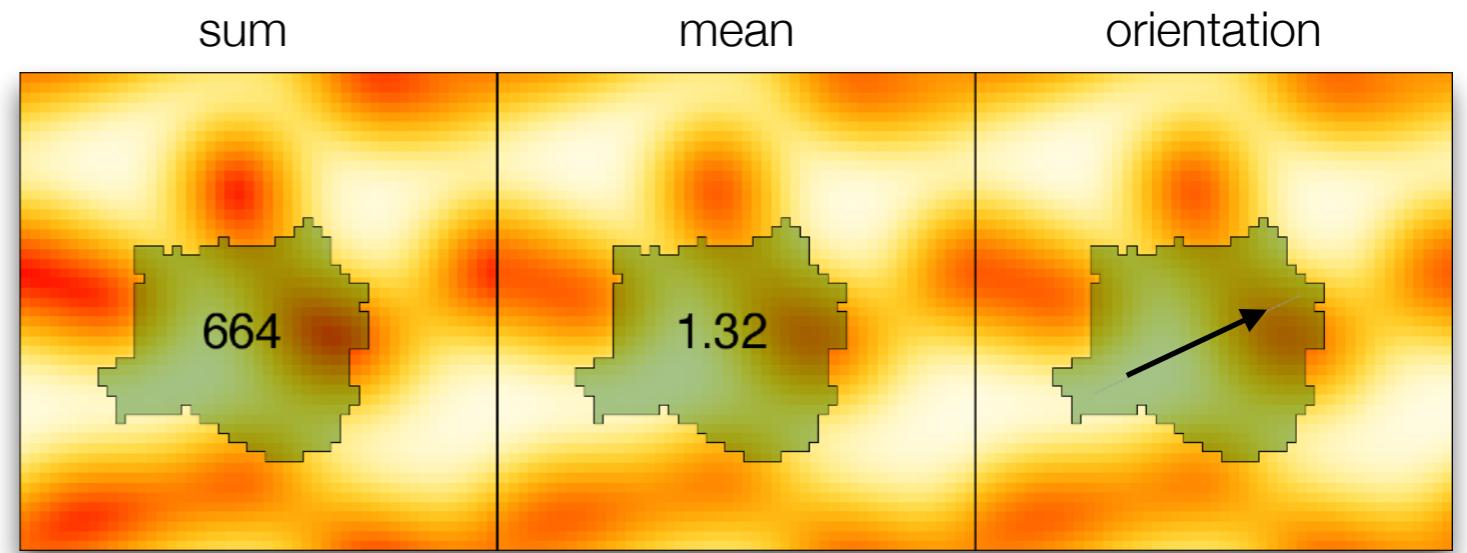
Collect data about
cell's microenvironment



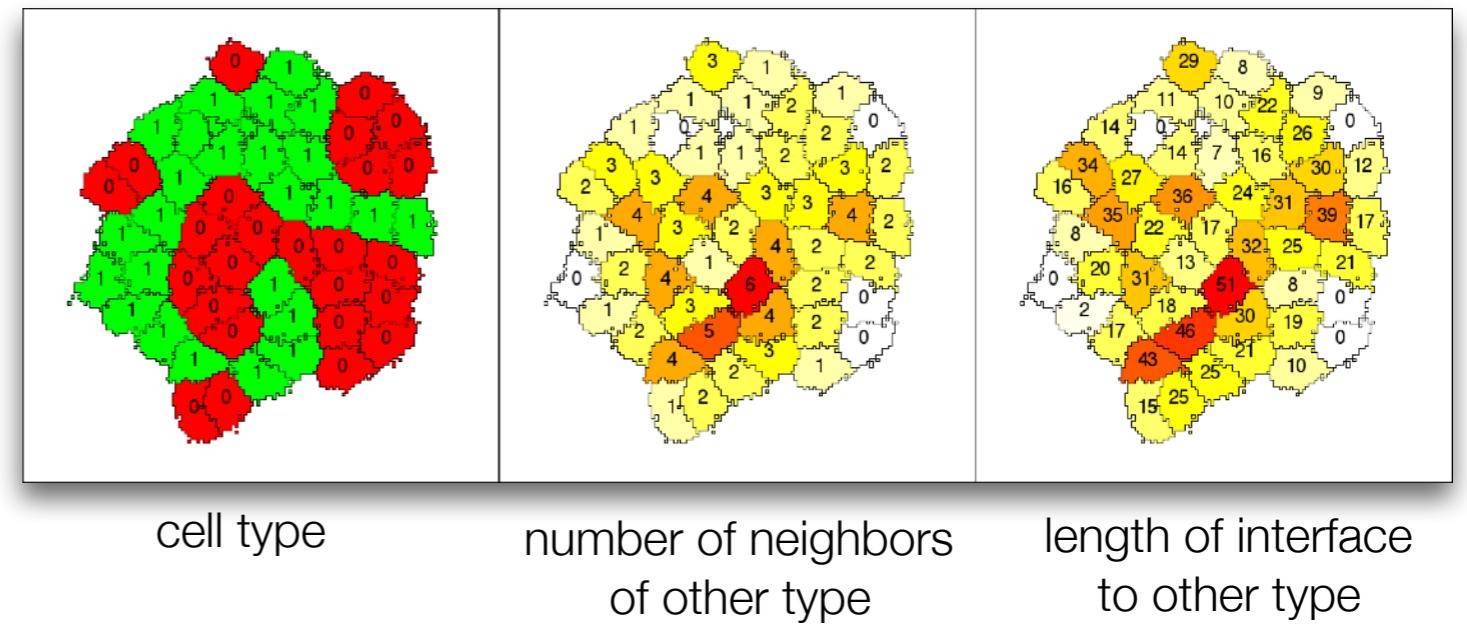
Multi-scale models

Mapping between different spatial contexts

CellReporter
Collect data within cellular domain

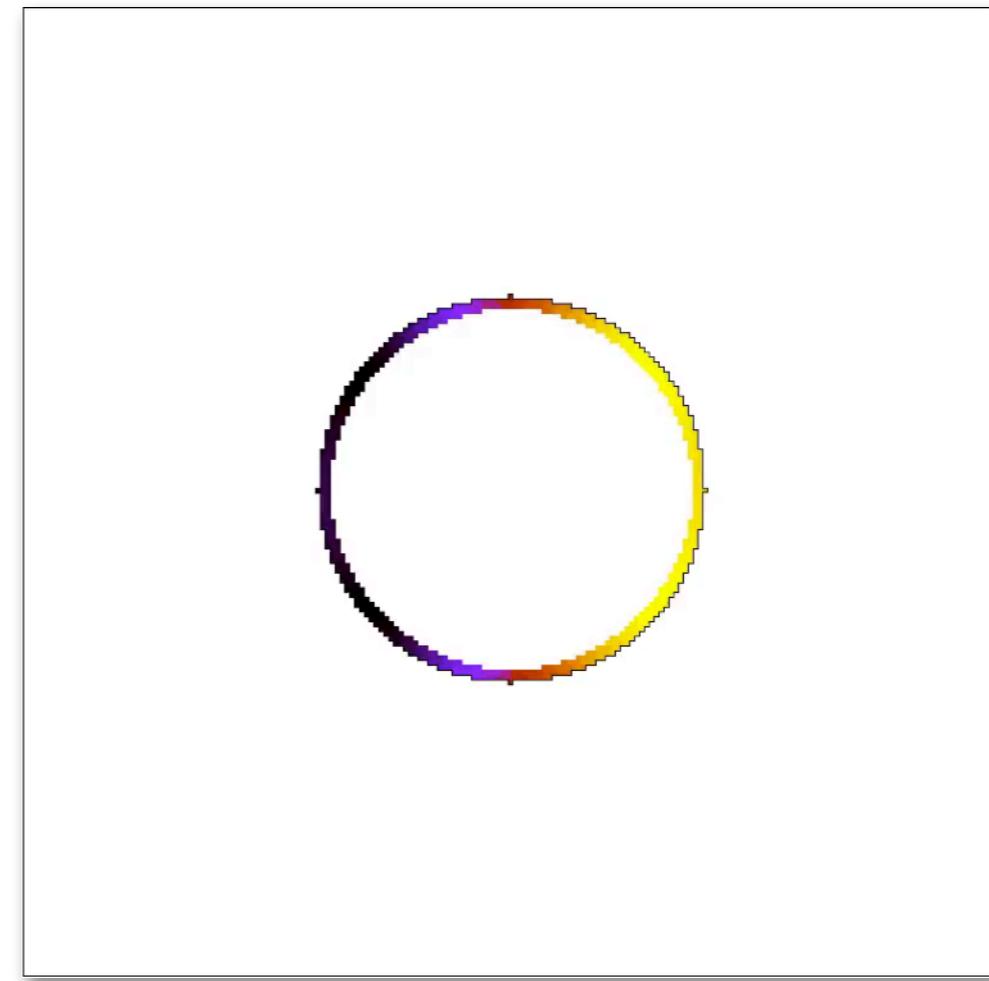


NeighborhoodReporter
Collect data about
cell's microenvironment



Multi-scale models

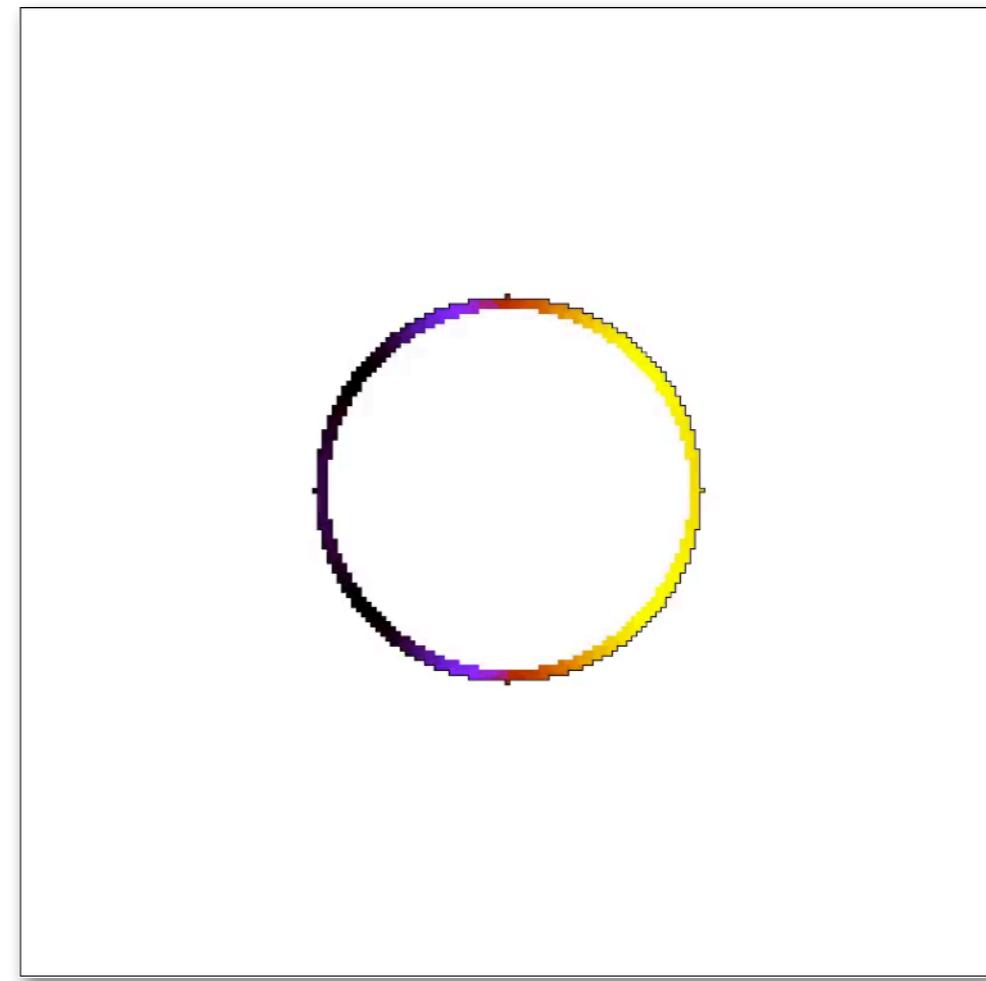
Mapping data to cell membranes



Multi-scale models

Mapping data to cell membranes

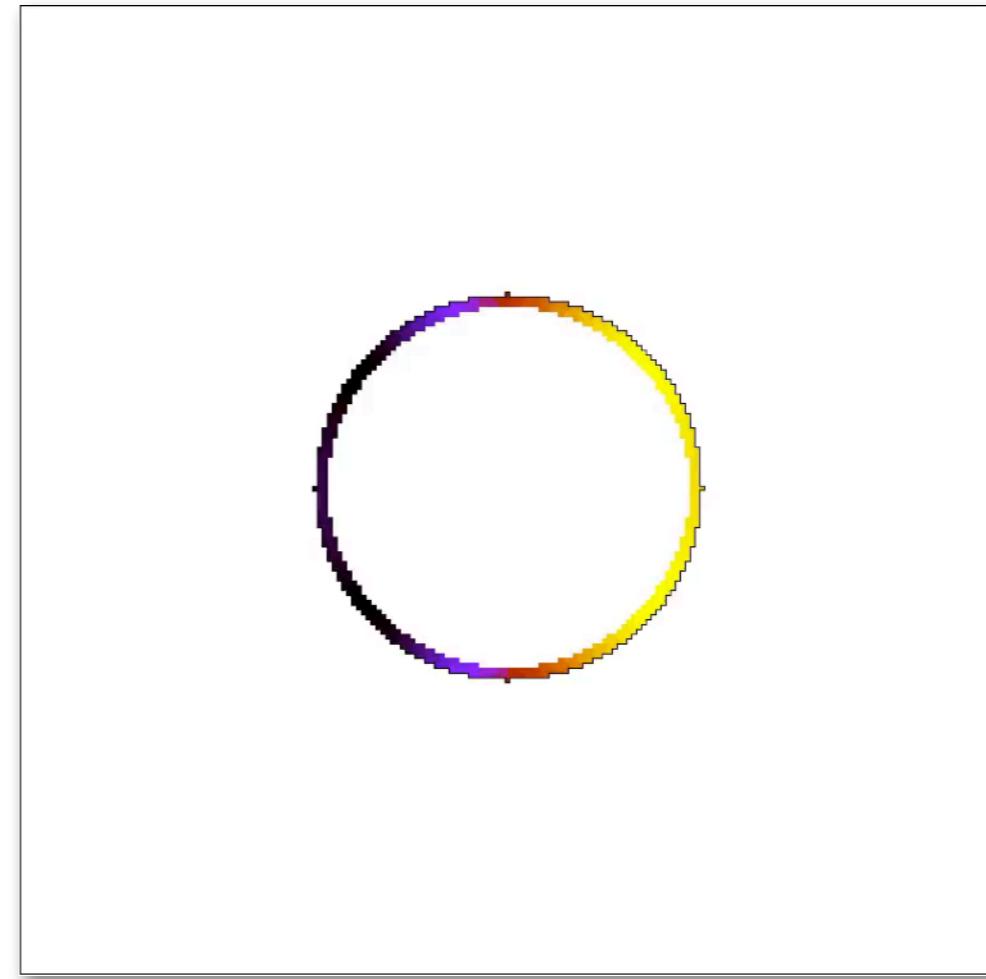
MembraneProperties



Multi-scale models

Mapping data to cell membranes

MembraneProperties

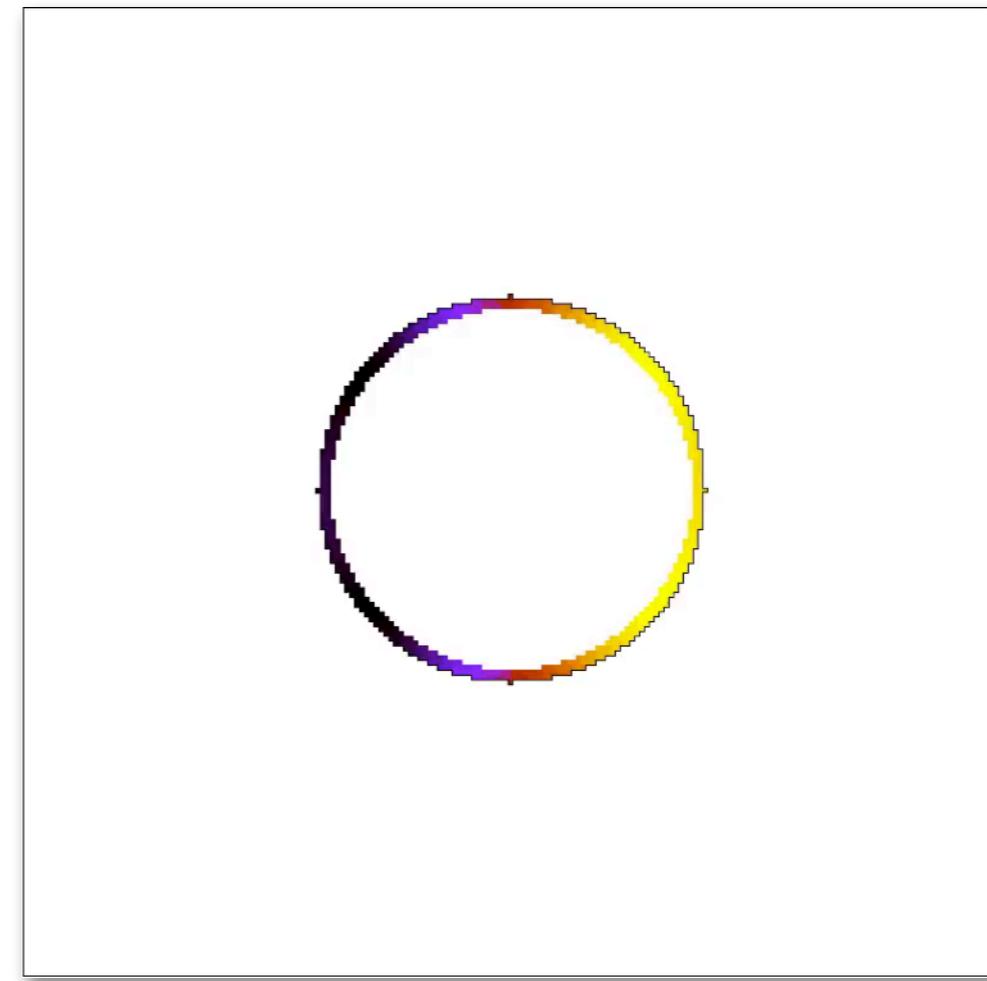


Multi-scale models

Mapping data to cell membranes

MembraneProperties

- Scalar field on cell membrane

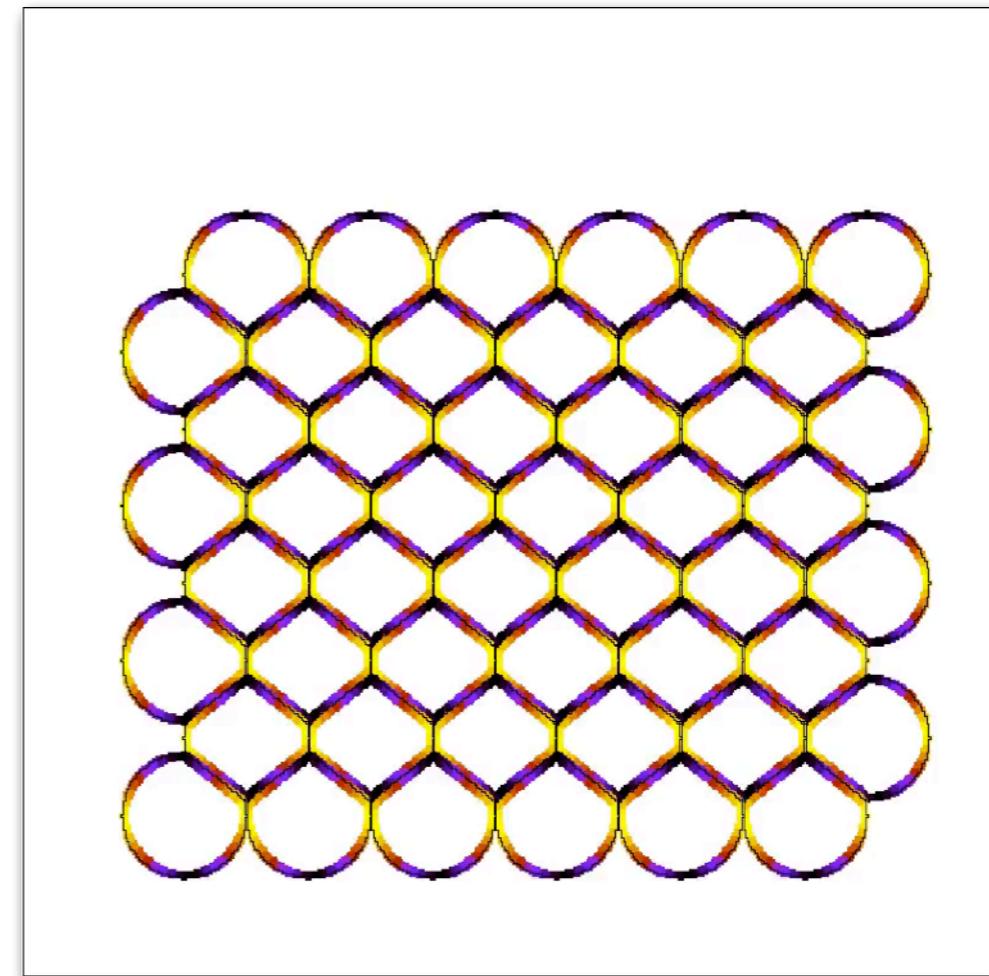


Multi-scale models

Mapping data to cell membranes

MembraneProperties

- Scalar field on cell membrane
- Couple to biomechanical properties



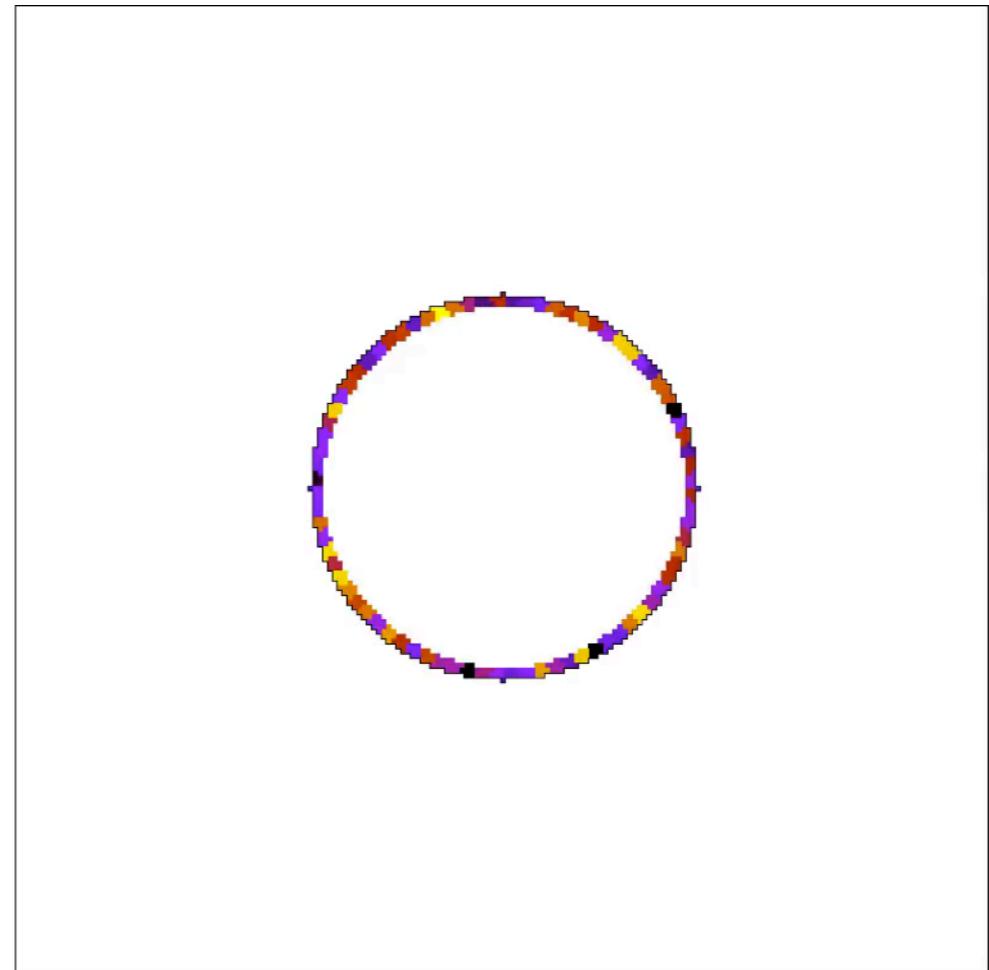
Ouchi et al., ??, 2006

Multi-scale models

Mapping data to cell membranes

MembraneProperties

- Scalar field on cell membrane
- + System
- Reaction-diffusion on membrane

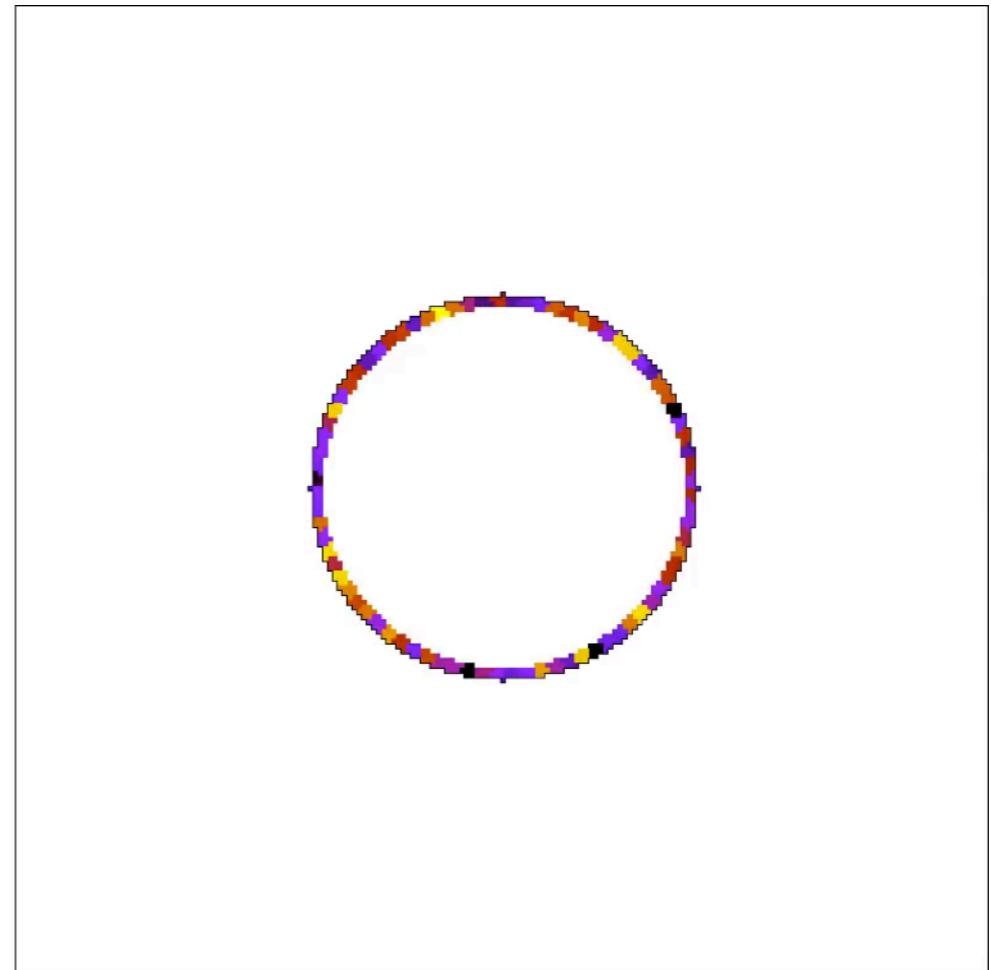


Multi-scale models

Mapping data to cell membranes

MembraneProperties

- Scalar field on cell membrane
- + System
- Reaction-diffusion on membrane

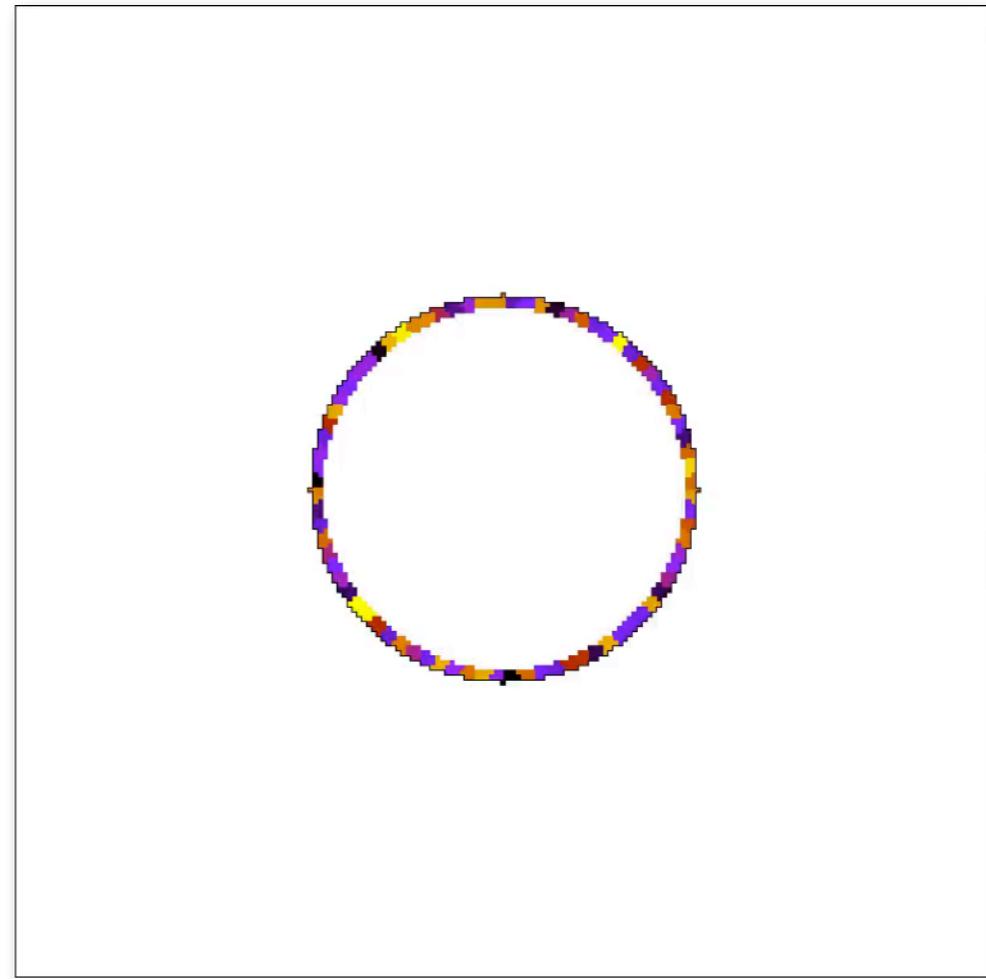


Multi-scale models

Mapping data to cell membranes

MembraneProperties

- Scalar field on cell membrane
- + System
- Reaction-diffusion on membrane

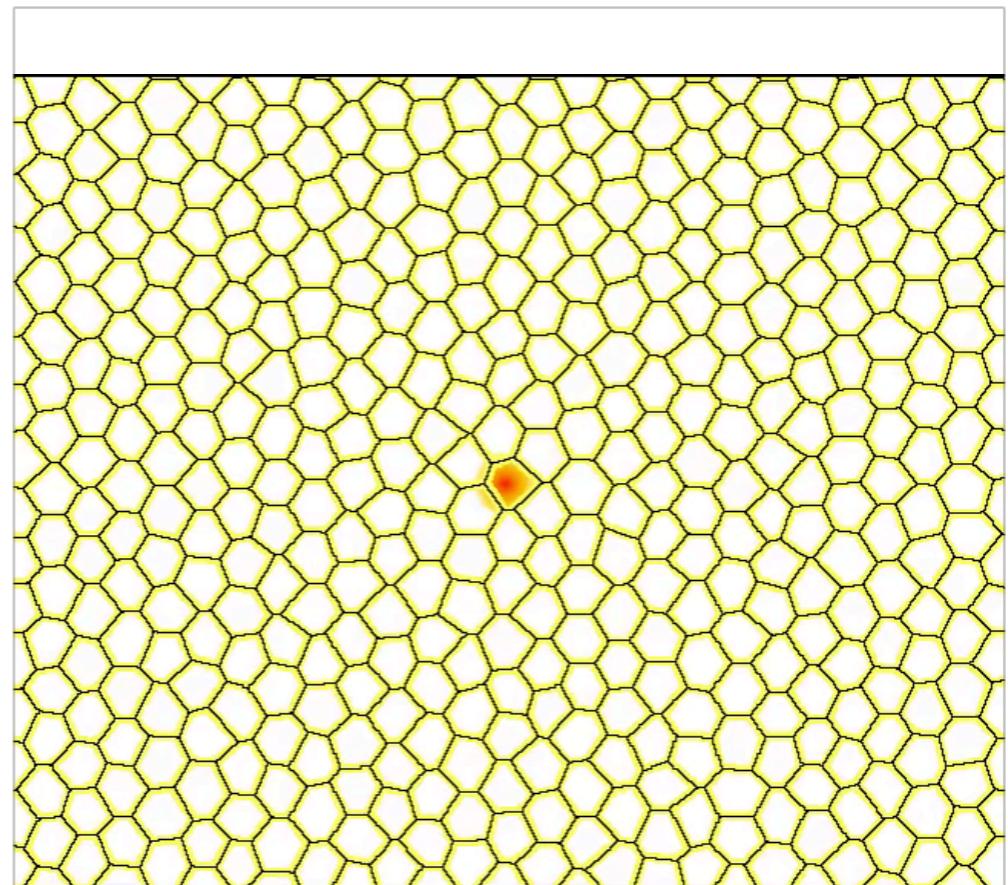


Multi-scale models

Mapping data to cell membranes

MembraneProperties

- Scalar field on cell membrane
- + System
 - Reaction-diffusion on membrane
- + NeighborhoodReporter
 - Modeling cell-cell signaling via membrane-bound ligands/receptors



Multi-scale models

Mapping data to cell membranes

MembraneProperties

- Scalar field on cell membrane
- + System
 - Reaction-diffusion on membrane
- + NeighborhoodReporter
 - Modeling cell-cell signaling via membrane-bound ligands/receptors

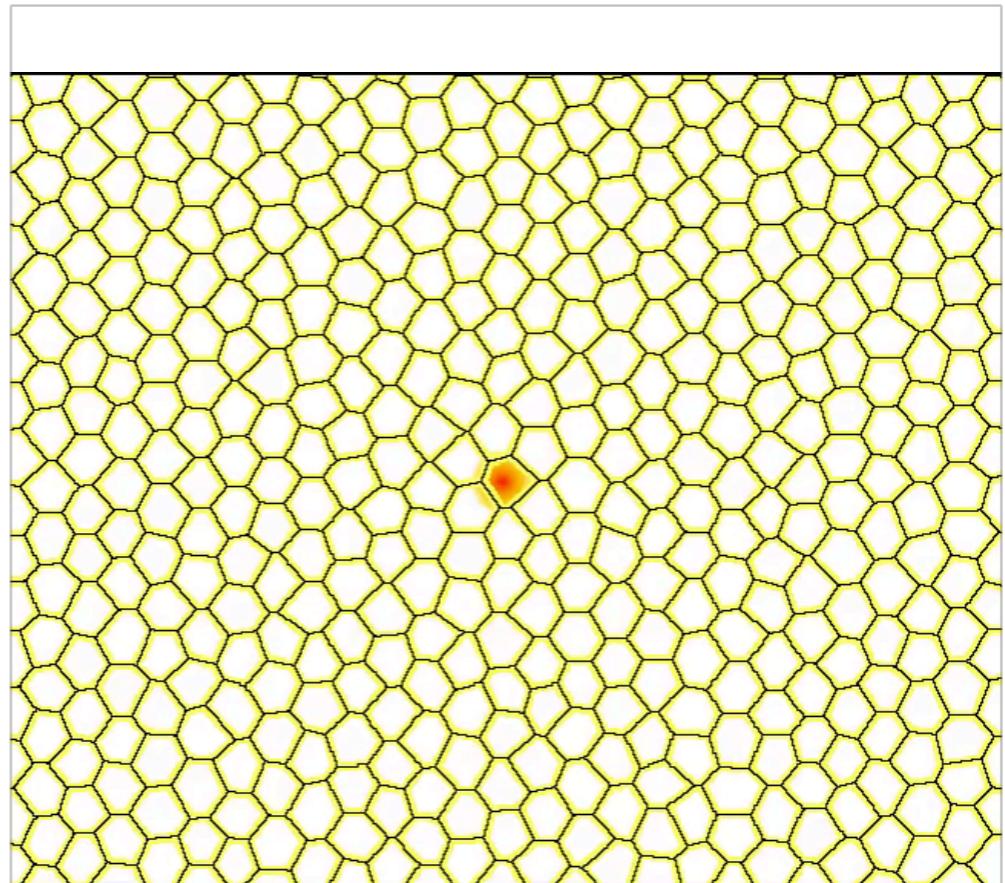
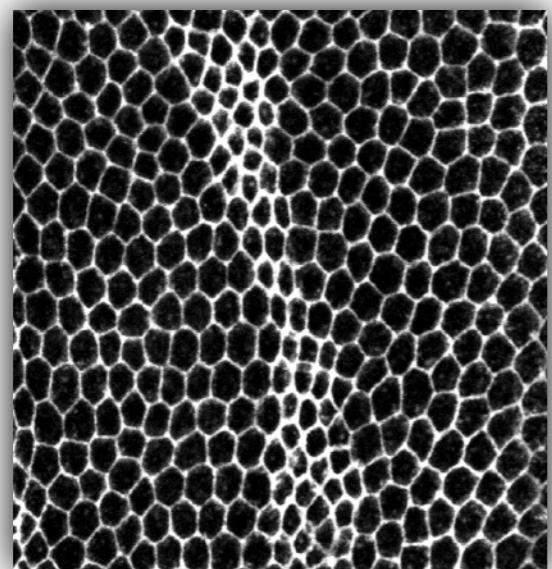
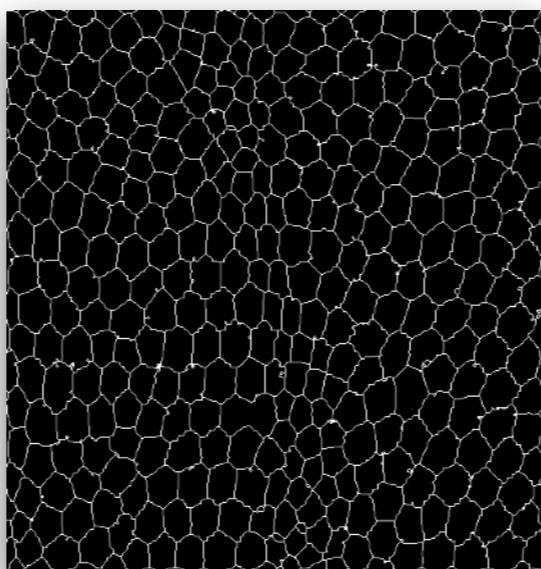


Image-based modeling

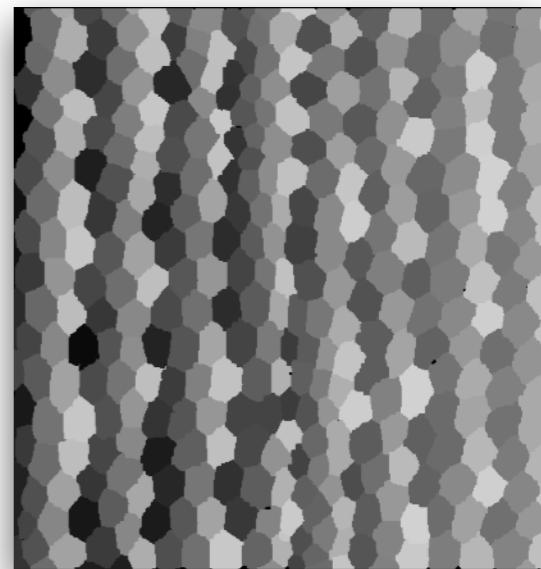
Simulation based on microscopy data



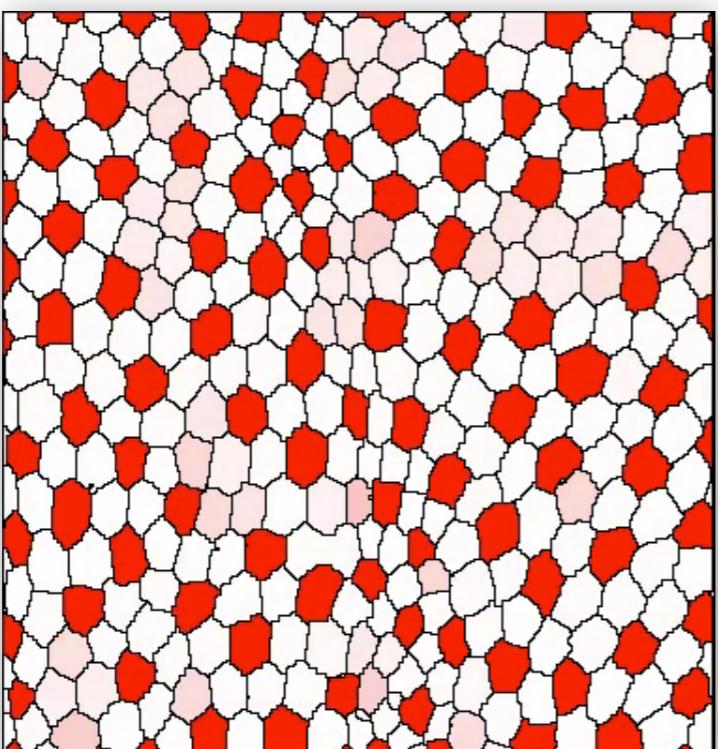
Skeletonize
→



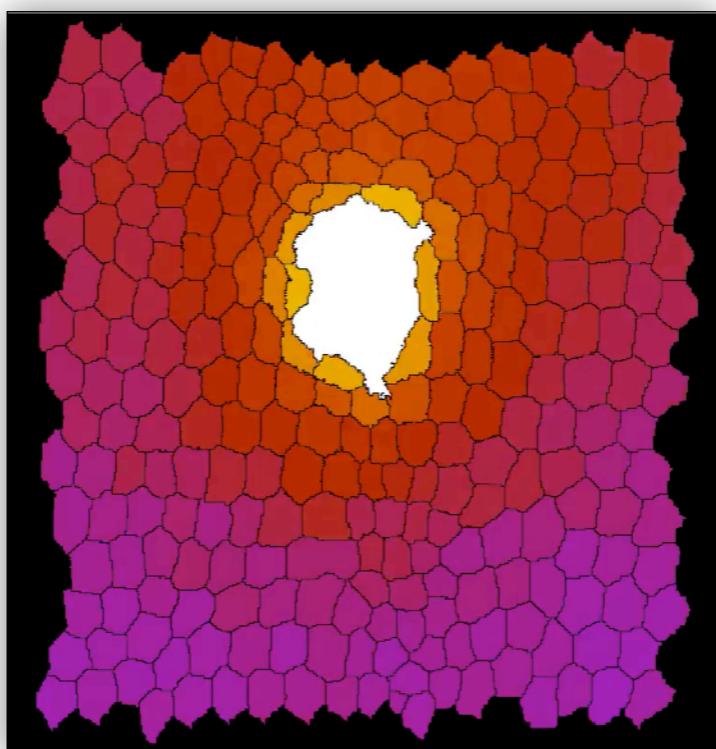
Label cells
→



Eaton lab, MPI-CBG



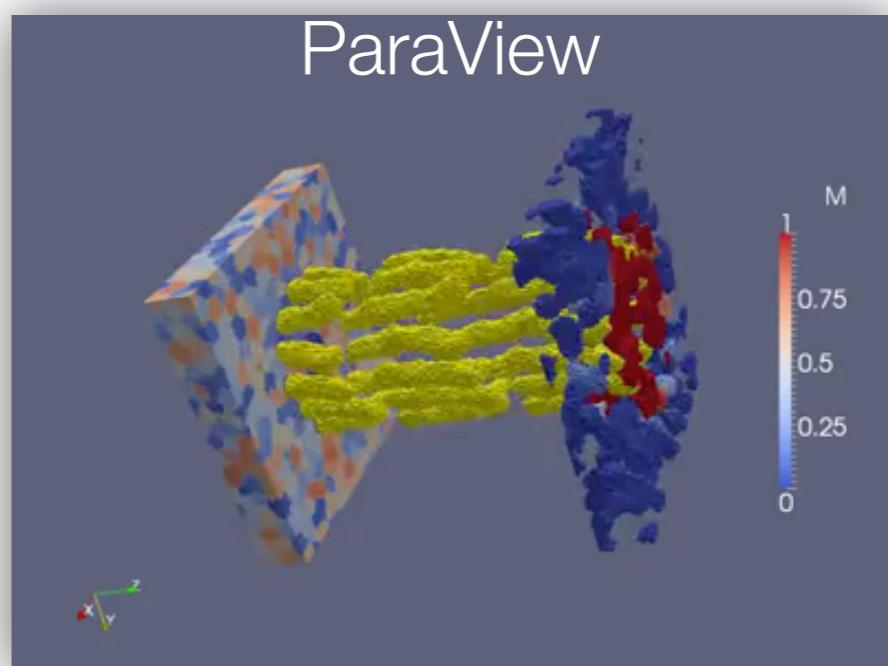
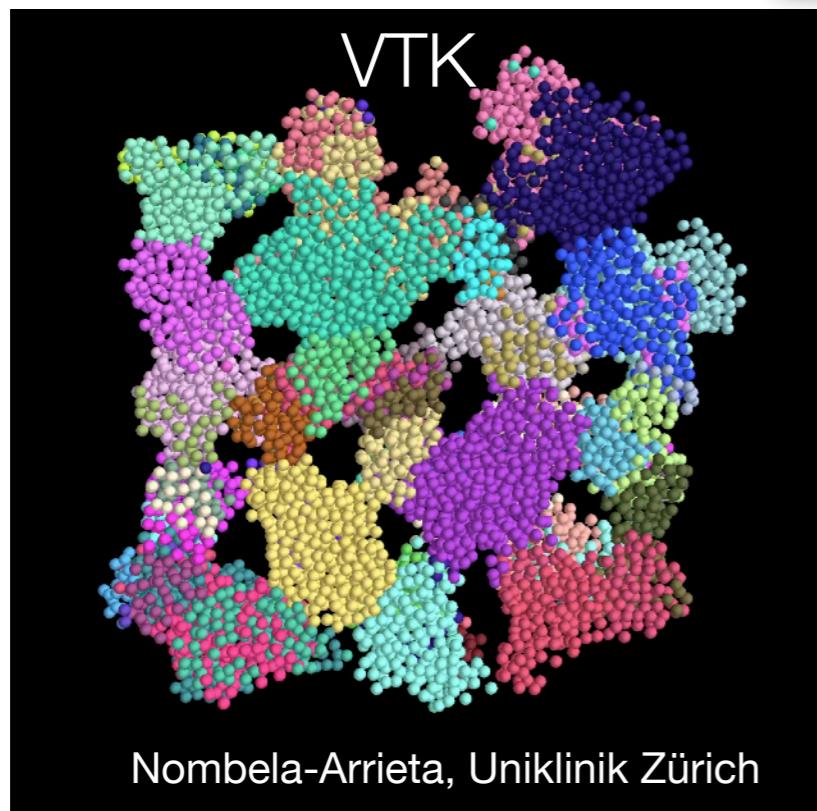
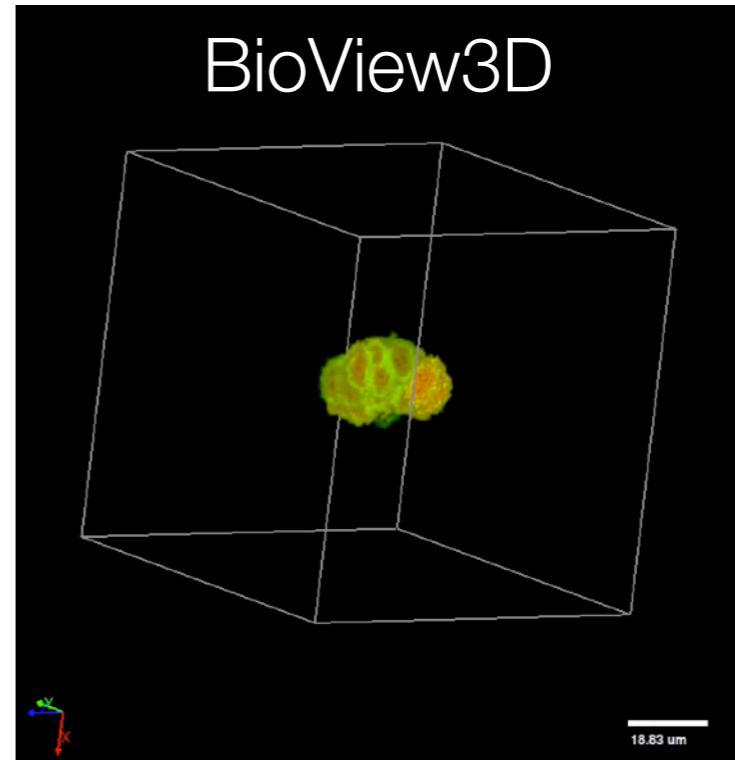
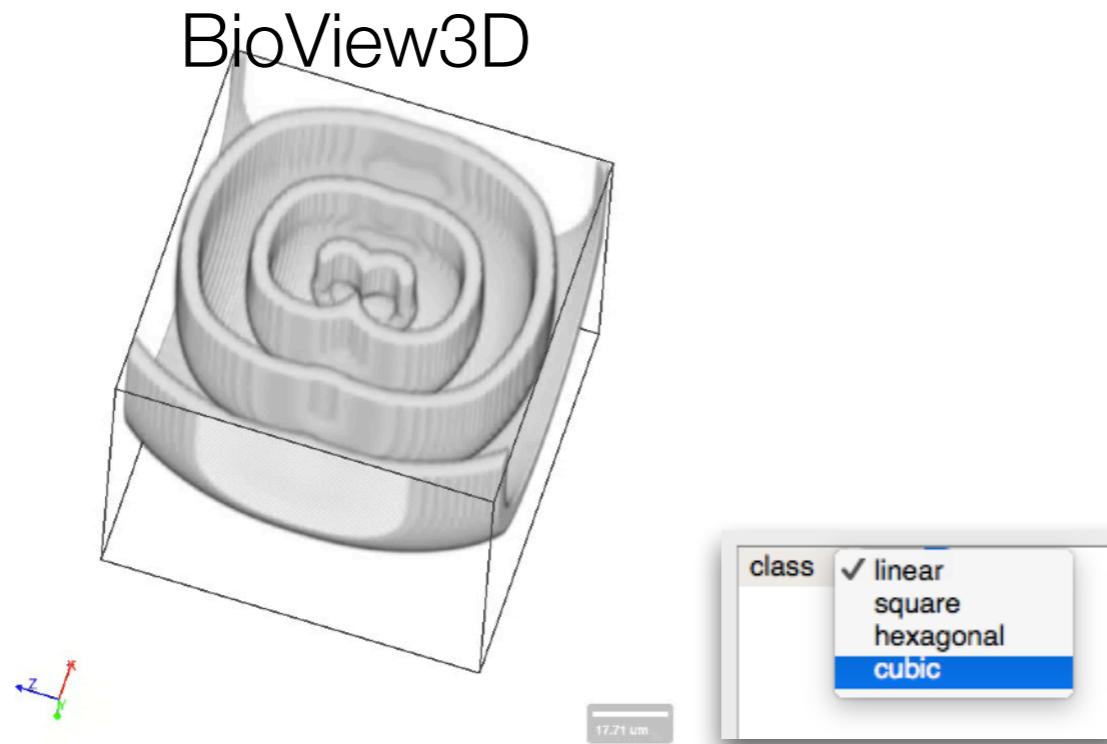
Cell-cell communication



Laser ablation

3D simulation

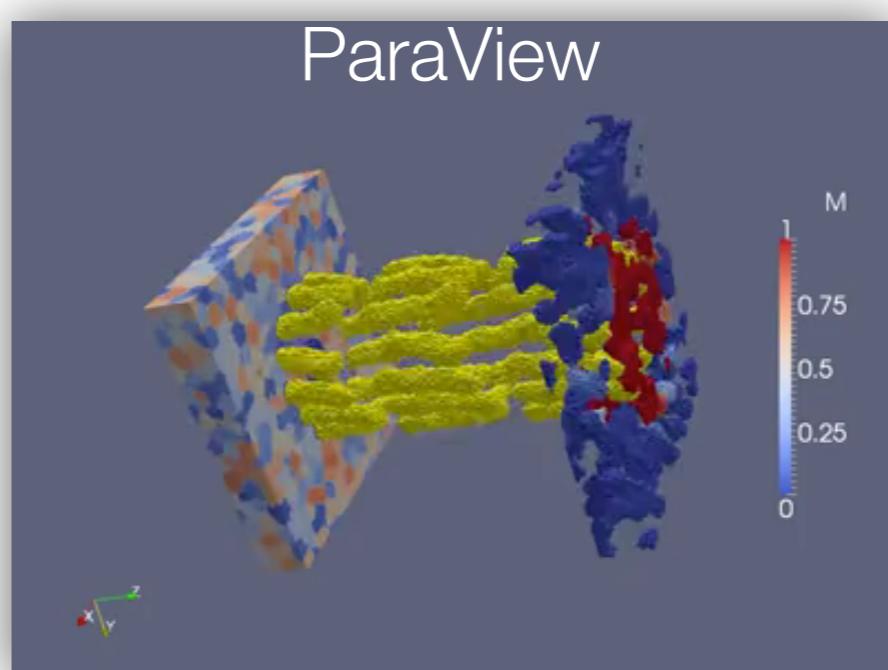
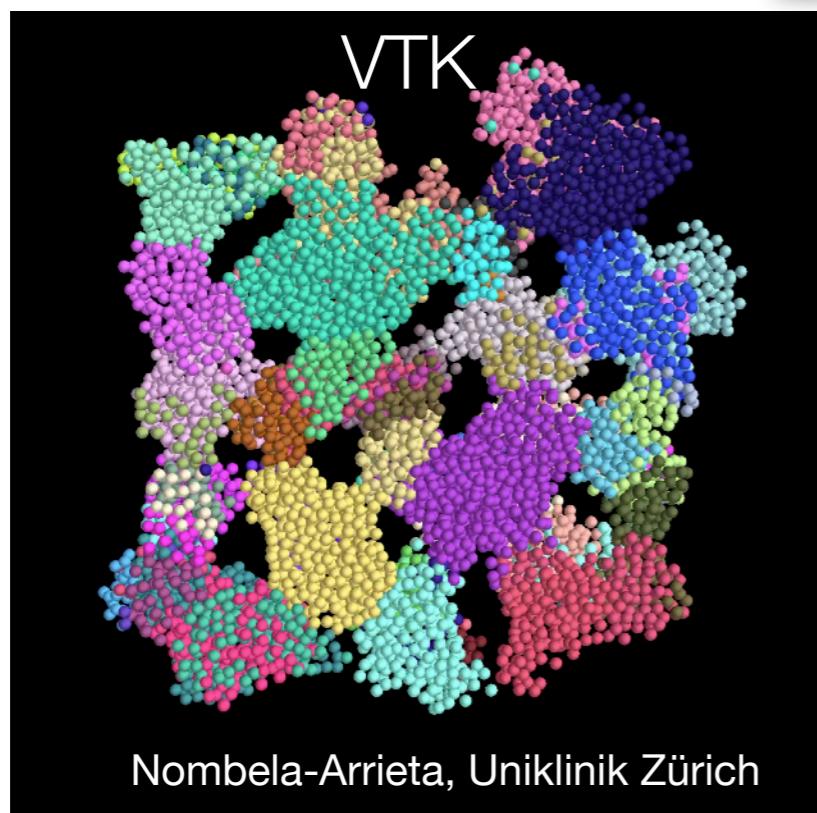
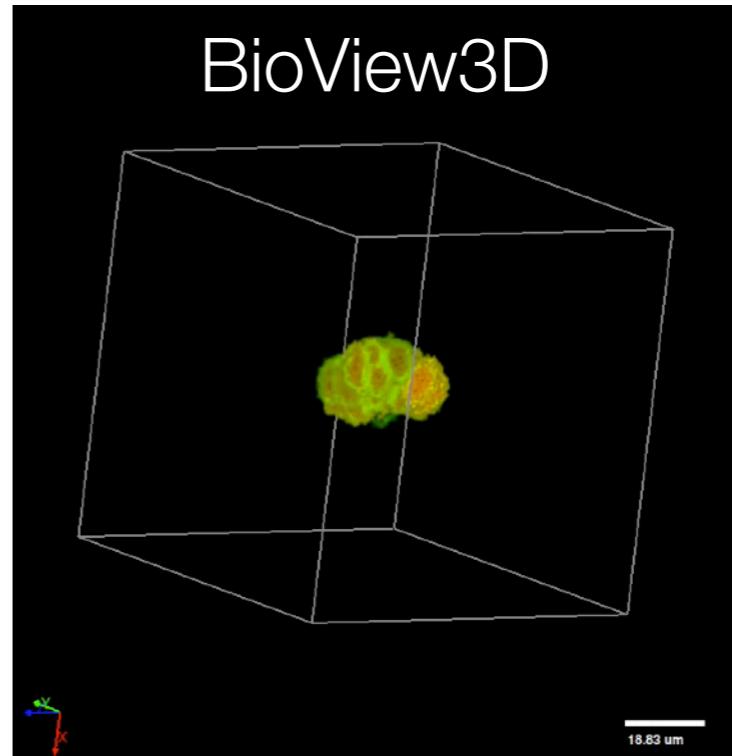
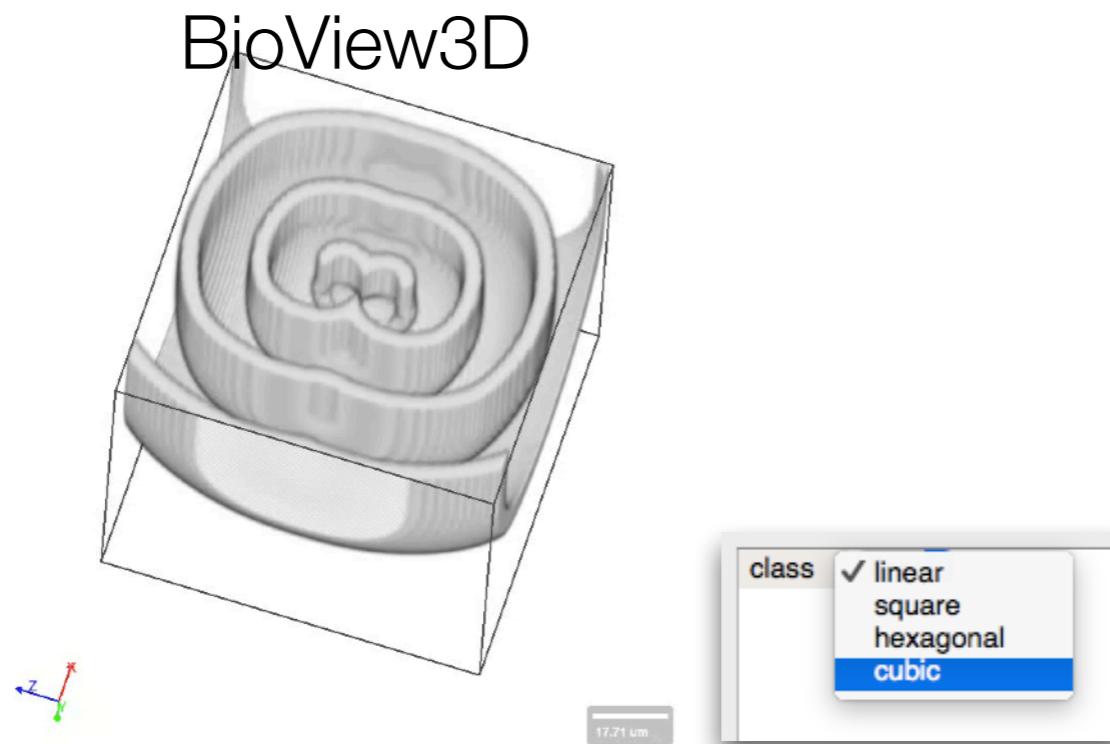
Output as TIFF stacks or VTK files, visualized with external tools



Müller, Brusch and Tanaka, TUD

3D simulation

Output as TIFF stacks or VTK files, visualized with external tools



Müller, Brusch and Tanaka, TUD

Graphical user interface

Morpheus - CellCycle.xml

Open Save local Start Stop

Documents

- CellCycle.xml**
 - Description
 - Global
 - Space
 - Time
 - CellTypes**
 - CPM
 - CellPopulations
 - Analysis
 - ParamSweep
- ActivatorInhibitor_2D.xml**
 - Description
 - Global
 - Space
 - Time
 - Analysis
 - ParamSweep
- CellSorting_2D.xml**
 - Description
 - Global

JobQueue FixBoard

JobQueue

Process Progress

- BIOMD00000000...
- Example-Activat...
- Example-Activat...
- Example-Activat...
- Example-Autocri...
- Example-CellCycle**
 - Job 2761**
 - Job 2760
 - Job 2759
 - Job 2758
 - Job 2757
 - Job 2756
 - Job 2755
 - Job 2686
 - Job 2685

Starting Job 2757
Starting Job 2758
Starting Job 2759
Starting Job 2760

Element

Element	Name/Symbol	V
CellType	cells	
Property	CDK1 =	0
Property	Plk1 =	0
Property	APC =	0
System		
DiffEqn	$dCDK1 / dt =$	
Expression		
DiffEqn	$dPlk1 / dt =$	
DiffEqn	$dAPC / dt =$	
Constant	n =	8
Constant	K =	
Constant	a1 =	
Constant	a2 =	
Constant	a3 =	
Constant	B1 =	
Constant	B2 =	
Constant	B3 =	
Property	p =	0
Property	d =	0
Property	c =	0
Property	cc =	1
VolumeConstraint	Vt =	
SurfaceConstraint		
Event		
Condition		
Rule		
CellDivision		
Condition		
Triggers		
c =	0	

Attributes:

solver	runge-kutta
time-step	4e-2
<input type="checkbox"/> name	...
<input checked="" type="checkbox"/> time-scaling	20

Symbols

Symbol	Description
APC	Anaphase-pr...
c	division timeout
cc	cellcount
CDK1	Cyclin-depen...
cell	
celltype	
d	divisions
K	Michaelis co...
n	Hill coefficient
p	portion
Plk1	Polo-like kin...

Plugins

Plugin	Category
Constant	Container
ConstantVector	Container
DiffEqn	Math
Function	Math
Rule	Math
VectorFunction	Math
VectorRule	Math

Documentation

- Continuous Process Plugins
- Instantaneous Process Plugins
- ModelStructure
- Symbols
- MathExpressions
- Plugins
- Concepts
- ContactLogger

System

MathExpressions

Environment for tightly coupled Rule and DiffEqn. Expressions with a System are synchronously updated and may contain recurrence relations.

- solver:** numerical solver for DiffEqn: Euler (1st order), Heun (aka explicit trapezoid rule, 2nd order) or Runge-Kutta (4th order)
- time-step:** integration step size.
- time-scaling (optional):** scales the dynamics of System to the simulation time. Equivalent to multiplying all DiffEqn in the System with a scalar.

Note: Systems define their own Scope. This implies that values of symbols defined within a System are not accessible outside of the System.

Model loaded successfully

Models

Morpheus - CellCycle.xml

Open Save local Start Stop

Documents

- CellCycle.xml
 - Description
 - Global
 - Space
 - Time
 - CellTypes**
 - CPM
 - CellPopulations
 - Analysis
 - ParamSweep
- ActivatorInhibitor_2D.xml
 - Description
 - Global
 - Space
 - Time
 - Analysis
 - ParamSweep
- CellSorting_2D.xml
 - Description
 - Global

JobQueue FixBoard

JobQueue

Process Progress

- BIOMD00000000...
- Example-Activat...
- Example-Activat...
- Example-Activat...
- Example-Autocri...
- Example-CellCycle
 - Job 2761**
 - Job 2760
 - Job 2759
 - Job 2758
 - Job 2757
 - Job 2756
 - Job 2755
 - Job 2686
 - Job 2685

Starting Job 2757
Starting Job 2758
Starting Job 2759
Starting Job 2760

Element

Element	Name/Symbol	V
CellType	cells	0
Property	CDK1 =	0
Property	Plk1 =	0
Property	APC =	0
System	dCDK1 / dt =	8
DiffEqn	Expression	
DiffEqn	dPlk1 / dt =	
DiffEqn	dAPC / dt =	
Constant	n =	
Constant	K =	
Constant	a1 =	
Constant	a2 =	
Constant	a3 =	
Constant	b1 =	
Constant	b2 =	
Constant	b3 =	
Property	p =	0
Property	d =	0
Property	c =	0
Property	cc =	1
VolumeConstraint	Vt =	
SurfaceConstraint		
Event		
Condition		
Rule		
CellDivision		
Condition		
Triggers		
c =	0	

Attributes:

solver	runge-kutta
time-step	4e-2
<input type="checkbox"/> name	...
<input checked="" type="checkbox"/> time-scaling	20

Symbols

Symbol	Description
APC	Anaphase-pr...
c	division timeout
cc	cellcount
CDK1	Cyclin-depen...
cell	
celltype	
d	divisions
K	Michaelis co...
n	Hill coefficient
p	portion
Plk1	Polo-like kin...

Plugins

Plugin	Category
Constant	Container
ConstantVector	Container
DiffEqn	Math
Function	Math
Rule	Math
VectorFunction	Math
VectorRule	Math

Documentation

- Continuous Process Plugins
- Instantaneous Process Plugins
- ModelStructure
- Symbols
- MathExpressions
- Plugins
- Concepts
- ContactLogger

System

MathExpressions

Environment for tightly coupled Rule and DiffEqn. Expressions with a System are synchronously updated and may contain recurrence relations.

- solver:** numerical solver for DiffEqn: Euler (1st order), Heun (aka explicit trapezoid rule, 2nd order) or Runge-Kutta (4th order)
- time-step:** integration step size.
- time-scaling (optional):** scales the dynamics of System to the simulation time. Equivalent to multiplying all DiffEqn in the System with a scalar.

Note: Systems define their own Scope. This implies that values of symbols defined within a System are not accessible outside of the System.

Model loaded successfully

Models

Editor

Morpheus - CellCycle.xml

Open Save local Start Stop

Documents

- CellCycle.xml
 - Description
 - Global
 - Space
 - Time
 - CellTypes**
 - CPM
 - CellPopulations
 - Analysis
 - ParamSweep
- ActivatorInhibitor_2D.xml
 - Description
 - Global
 - Space
 - Time
 - Analysis
 - ParamSweep
- CellSorting_2D.xml
 - Description
 - Global

JobQueue FixBoard

Process Progress

- BIOMD00000000...
- Example-Activat...
- Example-Activat...
- Example-Activat...
- Example-Autocri...
- Example-CellCycle
 - Job 2761**
 - Job 2760
 - Job 2759
 - Job 2758
 - Job 2757
 - Job 2756
 - Job 2755
 - Job 2686
 - Job 2685

Starting Job 2757
Starting Job 2758
Starting Job 2759
Starting Job 2760

CellType

- Property
- Property
- Property
- System**
 - DiffEqn Expression
 - DiffEqn Constant
 - Property
 - Property
 - Property
 - Property
 - Property
 - VolumeConstraint
 - SurfaceConstraint
 - Event Condition
 - Rule
 - CellDivision Condition
 - Triggers

cells

- CDK1 =
- Plk1 =
- APC =
- dCDK1 / dt =
- dPlk1 / dt =
- dAPC / dt =
- n =
- K =
- a1 =
- a2 =
- a3 =
- b1 =
- b2 =
- b3 =
- p =
- d =
- c =
- cc =
- Vt =
- c =

Attributes:

solver	runge-kutta
time-step	4e-2
<input type="checkbox"/> name	...
<input checked="" type="checkbox"/> time-scaling	20

Symbols

Symbol	Description
APC	Anaphase-pr...
c	division timeout
cc	cellcount
CDK1	Cyclin-depen...
cell	divisions
celltype	
d	Michaelis co...
K	Hill coefficient
n	portion
p	Polo-like kin...
Plk1	

Plugins

Plugin	Category
Constant	Container
ConstantVector	Container
DiffEqn	Math
Function	Math
Rule	Math
VectorFunction	Math
VectorRule	Math

Documentation

- Continuous Process Plugins
- Instantaneous Process Plugins
- ModelStructure
- Symbols
- MathExpressions
- Plugins
- Concepts
- ContactLogger

System

MathExpressions

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Model loaded successfully

Models

Editor

Attributes

System

Documentation

Morpheus - CellCycle.xml

Open Save local Start Stop

Documents

- CellCycle.xml
 - Description
 - Global
 - Space
 - Time
 - CellTypes**
 - CPM
 - CellPopulations
 - Analysis
 - ParamSweep
- ActivatorInhibitor_2D.xml
 - Description
 - Global
 - Space
 - Time
 - Analysis
 - ParamSweep
- CellSorting_2D.xml
 - Description
 - Global

JobQueue FixBoard

JobQueue

Process Progress

- BIOMD00000000...
- Example-Activat...
- Example-Activat...
- Example-Activat...
- Example-Autocri...
- Example-CellCycle
 - Job 2761**
 - Job 2760
 - Job 2759
 - Job 2758
 - Job 2757
 - Job 2756
 - Job 2755
 - Job 2686
 - Job 2685

Starting Job 2757
Starting Job 2758
Starting Job 2759
Starting Job 2760

Attributes:

solver	runge-kutta
time-step	4e-2
<input type="checkbox"/> name	...
<input checked="" type="checkbox"/> time-scaling	20

Symbols

Symbol	Description
APC	Anaphase-pr...
c	division timeout
cc	cellcount
CDK1	Cyclin-depen...
cell	divisions
celltype	
d	Michaelis co...
K	Hill coefficient
n	portion
p	Polo-like kin...
Plk1	

Plugins

Plugin	Category
Constant	Container
ConstantVector	Container
DiffEqn	Math
Function	Math
Rule	Math
VectorFunction	Math
VectorRule	Math

Continuous Process Plugins
Instantaneous Process Plugins
ModelStructure
Symbols
MathExpressions
Plugins
Concepts
ContactLogger

Environment for tightly coupled **Rule** and **DiffEqn**. Expressions with a **System** are synchronously updated and may contain recurrence relations.

- **solver**: numerical solver for DiffEqn: Euler (1st order), Heun (aka explicit trapezoid rule, 2nd order) or Runge-Kutta (4th order)
- **time-step**: integration step size.
- **time-scaling** (optional): scales the dynamics of **System** to the simulation time. Equivalent to multiplying all **DiffEqn** in the **System** with a scalar.

Note: Systems define their own **Scope**. This implies that values of symbols defined within a **System** are not accessible outside of the **System**.

Model loaded successfully

Models

Editor

Attributes

Symbols

System

Documentation

Morpheus - CellCycle.xml

Open Save local Start Stop

Documents

- CellCycle.xml
 - Description
 - Global
 - Space
 - Time
 - CellTypes**
 - CPM
 - CellPopulations
 - Analysis
 - ParamSweep
- ActivatorInhibitor_2D.xml
 - Description
 - Global
 - Space
 - Time
 - Analysis
 - ParamSweep
- CellSorting_2D.xml
 - Description
 - Global
 - Space
 - Time

JobQueue FixBoard

Process Progress

- BIOMD00000000...
- Example-Activat...
- Example-Activat...
- Example-Activat...
- Example-Autocri...
- Example-CellCycle
 - Job 2761**
 - Job 2760
 - Job 2759
 - Job 2758
 - Job 2757
 - Job 2756
 - Job 2755
 - Job 2686
 - Job 2685

Starting Job 2757
Starting Job 2758
Starting Job 2759
Starting Job 2760

Continuous Process Plugins
Instantaneous Process Plugins
ModelStructure
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Environment for tightly coupled **Rule** and **DiffEqn**. Expressions with a **System** are synchronously updated and may contain recurrence relations.

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Model loaded successfully

Symbol	Description
APC	Anaphase-pr...
c	division timeout
cc	cellcount
CDK1	Cyclin-depen...
cell	divisions
celltype	Michaelis co...
d	Hill coefficient
K	Polo-like kin...
n	portion
p	
Plk1	

Plugin	Category
Constant	Container
ConstantVector	Container
DiffEqn	Math
Function	Math
Rule	Math
VectorFunction	Math
VectorRule	Math

Models

Editor

Attributes

Symbols

Plugins

System

Documentation

Morpheus - CellCycle.xml

Open Save local Start Stop

CellType

- Property
- Property
- Property
- System

 - DiffEqn
 - Expression
 - DiffEqn
 - DiffEqn
 - Constant
 - Property
 - Property
 - Property
 - Property
 - VolumeConstraint
 - SurfaceConstraint
 - Event
 - Condition
 - Rule
 - CellDivision
 - Condition
 - Triggers

cells

CDK1 =
Plk1 =
APC =

dCDK1 / dt =
dPlk1 / dt =
dAPC / dt =
n =
K =
a1 =
a2 =
a3 =
β1 =
β2 =
β3 =
p =
d =
c =
cc =
Vt =
c =

Attributes:

solver	runge-kutta
time-step	4e-2
<input type="checkbox"/> name	...
<input checked="" type="checkbox"/> time-scaling	20

Symbol

Symbol	Description
APC	Anaphase-pr...
c	division timeout
cc	cellcount
CDK1	Cyclin-depen...
cell	divisions
celltype	Michaelis co...
d	Hill coefficient
K	portion
n	Polo-like kin...
p	
Plk1	

Plugin

Plugin	Category
Constant	Container
ConstantVector	Container
DiffEqn	Math
Function	Math
Rule	Math
VectorFunction	Math
VectorRule	Math

Continuous Process Plugins
Instantaneous Process Plugins
ModelStructure
Symbols
MathExpressions
Plugins
Concepts
ContactLogger

Environment for tightly coupled Rule and DiffEqn. Expressions with a System are synchronously updated and may contain recurrence relations.

- solver:** numerical solver for DiffEqn: Euler (1st order), Heun (aka explicit trapezoid rule, 2nd order) or Runge-Kutta (4th order)
- time-step:** integration step size.
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Model loaded successfully

Models

Editor

Attributes

Symbols

Plugins

System

Docs

Morpheus - CellCycle.xml

Continuous Process Plugins
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ModelStructure
Symbols
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Plugins
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ContactLogger

Environment for tightly coupled **Rule** and **DiffEqn**. Expressions with a **System** are synchronously updated and may contain recurrence relations.

- **solver**: numerical solver for DiffEqn: Euler (1st order), Heun (aka explicit trapezoid rule, 2nd order) or Runge-Kutta (4th order)
- **time-step**: integration step size.
- **time-scaling** (optional): scales the dynamics of **System** to the simulation time. Equivalent to multiplying all **DiffEqn** in the **System** with a scalar.

Note: Systems define their own **Scope**. This implies that values of symbols defined within a **System** are not accessible outside

Model loaded successfully

Models

Editor

Attributes

Symbols

Plugins

Job archive

Documentation

System

Docs

The screenshot shows the Morpheus software interface with several panels:

- Editor Panel:** Displays an XML model structure for "CellCycle.xml". It includes sections for CellType, System, and various properties and equations.
- Attributes Panel:** Shows simulation parameters: solver (runge-kutta), time-step (4e-2), and time-scaling (20).
- Symbols Panel:** Lists symbols with their descriptions: APC, c, cc, CDK1, cell, celltype, d, K, n, p, Plk1, and Vt.
- Plugins Panel:** Lists available plugins categorized by type: Constant, ConstantVector, DiffEqn, Function, Rule, VectorFunction, and VectorRule.
- Documentation Panel:** Provides detailed information about the System component, including its environment, rules, and expressions.
- Job archive:** A list of completed jobs with progress bars.
- Bottom Status:** Text indicating the model was loaded successfully.

Starting Job 2757
Starting Job 2758
Starting Job 2759
Starting Job 2760

Model loaded successfully

Models

Editor

Attributes

Symbols

Plugins

Job archive

Messages

System

Docs

Continuous Process Plugins

Instantaneous Process Plugins

ModelStructure

Symbols

MathExpressions

Plugins

Concepts

ContactLogger

Documentation

CellCycle.xml

Description

Global

Space

Time

CellTypes

CPM

CellPopulations

Analysis

ParamSweep

ActivatorInhibitor_2D.xml

Description

Global

Space

Time

Analysis

ParamSweep

CellSorting_2D.xml

Description

Global

Space

Time

Analysis

ParamSweep

JobQueue

FixBoard

Process

BIOMD00000000...

Example-Activat...

Example-Activat...

Example-Activat...

Example-Autocri...

Example-CellCycle

Job 2761

Job 2760

Job 2759

Job 2758

Job 2757

Job 2756

Job 2755

Job 2686

Job 2685

Starting Job 2761

Starting Job 2758

Starting Job 2759

Starting Job 2760

Plugin

Constant

ConstantVector

DiffEqn

Function

Rule

VectorFunction

VectorRule

Attributes:

solver	runge-kutta
time-step	4e-2
<input type="checkbox"/> name	...
<input checked="" type="checkbox"/> time-scaling	20

Symbol

Symbol	Description
APC	Anaphase-pr...
c	division timeout
cc	cellcount
CDK1	Cyclin-depen...
cell	divisions
celltype	Michaelis co...
d	Hill coefficient
K	portion
n	Polo-like kin...
p	
Plk1	

Model loaded successfully

Models

Job archive

Editor

Attributes

Symbols

Plugins

Docs

Start / Stop

Continuous Process Plugins

Instantaneous Process Plugins

ModelStructure

Symbols

MathExpressions

Plugins

Concepts

ContactLogger

System

MathExpressions

Environment for tightly coupled **Rule** and **DiffEqn**. Expressions with a **System** are synchronously updated and may contain recurrence relations.

- **solver**: numerical solver for DiffEqn: Euler (1st order), Heun (aka explicit trapezoid rule, 2nd order) or Runge-Kutta (4th order)
- **time-step**: integration step size.
- **time-scaling** (optional): scales the dynamics of **System** to the simulation time. Equivalent to multiplying all **DiffEqn** in the **System** with a scalar.

Note: Systems define their own **Scope**. This implies that values of symbols defined within a **System** are not accessible outside

Model loaded successfully

The screenshot shows the Morpheus software interface with several open windows:

- Models**: A sidebar listing XML files: CellCycle.xml, ActivationIntracellular_2D.xml, and CellSorting_2D.xml.
- Job archive**: A list of jobs with progress bars, including Job 2761 (selected), Job 2760, Job 2759, Job 2758, Job 2757, Job 2756, Job 2755, Job 2686, and Job 2685.
- Editor**: The main workspace showing the XML structure of a model. It includes sections for CellType, System, and other components like DiffEqn and Property.
- Attributes**: A table showing attributes for a system, including solver (runge-kutta), time-step (4e-2), and time-scaling (20).
- Symbols**: A table listing symbols with their descriptions: APC, c, cc, CDK1, cell, celltype, d, K, n, p, Plk1, etc.
- Plugins**: A table listing available plugins categorized by type: Constant, ConstantVector, DiffEqn, Function, Rule, VectorFunction, and VectorRule.
- Docs**: A documentation panel listing various components: Continuous Process Plugins, Instantaneous Process Plugins, ModelStructure, Symbols, MathExpressions, Plugins, Concepts, and ContactLogger.

Models

Job archive

Messages

Morpheus - CellCycle.xml

local

Start Stop

Documents

CellCycle.xml
Description
Global
Space
Time
CellTypes
CPM
CellPopulations
Analysis
ParamSweep
ActivatorInhibitor_2D.xml
Description
Global
Space
Time
Analysis
ParamSweep
CellSorting_2D.xml
Documentation JobQueue FixBoard

Output

Job 2761: Example-CellCycle

Stop Output Folder Terminal Create movie

Name Size Kind

plot_1.000.png 5 KB png File

plot_0.950.png 5 KB png File

plot_0.900.png 5 KB png File

plot_0.850.png 5 KB png File

plot_0.800.png 5 KB png File

plot_0.750.png 5 KB png File

plot_0.700.png 5 KB png File

plot_0.650.png 5 KB png File

Preview

Time Schedule Performance Table

```
+ 82.42% = 21230.92[ms] | CPM [Vt] -> [cell.center]
+ 6.32% = 1627.84[ms] | CellDivision [CDK1,c] ->
[Vt,c,cell.center,d]
+ 6.01% = 1546.87[ms] | Gnuplotter [CDK1] -> []
+ 4.70% = 1211.54[ms] | DependencyGraph [] -> []
+ 0.37% = 95.89[ms] | Logger [APC,CDK1,Plk1] ->
[]
+ 0.10% = 24.82[ms] | System
[K,n,α1,α2,α3,β1,β2,β3] -> [APC,CDK1,Plk1]
+ 0.01% = 1.80[ms] | Event [CDK1] -> [c]
```

==== Simulation finished ====
Init Time = 0s 102ms
Wall Time = 25s 758ms
CPU Time = 22s 210ms (4 threads)

Memory peak = 29.5703 Mb
Deleting scope root
Deleting scope CellType[cells]

Model loaded successfully

Models

Job archive

Messages

Morpheus - CellCycle.xml

local

Start Stop

Documents

CellCycle.xml
Description
Global
Space
Time
CellTypes
CPM
CellPopulations
Analysis
ParamSweep
ActivatorInhibitor_2D.xml
Description
Global
Space
Time
Analysis
ParamSweep
CellSorting_2D.xml
Documentation JobQueue FixBoard

Output

Job 2761: Example-CellCycle

Stop Output Folder Terminal Create movie

Name Size Kind

plot_1.000.png 5 KB png File

plot_0.950.png 5 KB png File

plot_0.900.png 5 KB png File

plot_0.850.png 5 KB png File

plot_0.800.png 5 KB png File

plot_0.750.png 5 KB png File

plot_0.700.png 5 KB png File

plot_0.650.png 5 KB png File

Time Schedule Performance Table

+ 82.42% = 21230.92[ms] | CPM [Vt] -> [cell.center]

+ 6.32% = 1627.84[ms] | CellDivision [CDK1,c] -> [Vt,c,cell.center,d]

+ 6.01% = 1546.87[ms] | Gnuplotter [CDK1] -> []

+ 4.70% = 1211.54[ms] | DependencyGraph [] -> []

+ 0.37% = 95.89[ms] | Logger [APC,CDK1,Plk1] -> []

+ 0.10% = 24.82[ms] | System

[K,n, $\alpha_1,\alpha_2,\alpha_3,\beta_1,\beta_2,\beta_3$] -> [APC,CDK1,Plk1]

+ 0.01% = 1.80[ms] | Event [CDK1] -> [c]

--- Simulation finished ---

Init Time = 0s 102ms

Wall Time = 25s 758ms

CPU Time = 22s 210ms (4 threads)

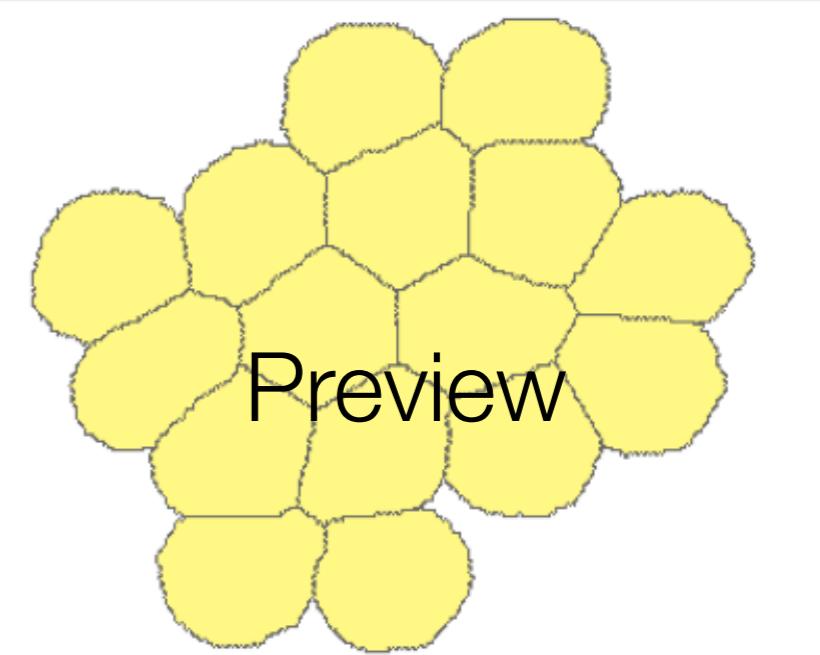
Memory peak = 29.5703 Mb

Deleting scope root

Deleting scope CellType[cells]

Preview

Model loaded successfully



Models

Job archive

Messages

Morpheus - CellCycle.xml

local

Start Stop

Documents

CellCycle.xml
Description
Global
Space
Time
CellTypes
CPM
CellPopulations
Analysis
ParamSweep
ActivatorInhibitor_2D.xml
Description
Global
Space
Time
Analysis
ParamSweep
CellSorting_2D.xml
Documentation JobQueue FixBoard

Output file browser

Job 2761: Example-CellCycle

Stop Output Folder Terminal Create movie

Name Size Kind

plot_1.000.png	5 KB	png File
plot_0.950.png	5 KB	png File
plot_0.900.png	5 KB	png File
plot_0.850.png	5 KB	png File
plot_0.800.png	5 KB	png File
plot_0.750.png	5 KB	png File
plot_0.700.png	5 KB	png File
plot_0.650.png	5 KB	png File

Time Schedule Performance Table

```
+ 82.42% = 21230.92[ms] | CPM [Vt] -> [cell.center]
+ 6.32% = 1627.84[ms] | CellDivision [CDK1,c] ->
[Vt,c,cell.center,d]
+ 6.01% = 1546.87[ms] | Gnuplotter [CDK1] -> []
+ 4.70% = 1211.54[ms] | DependencyGraph [] -> []
+ 0.37% = 95.89[ms] | Logger [APC,CDK1,Plk1] ->
[]
+ 0.10% = 24.82[ms] | System
[K,n,α1,α2,α3,β1,β2,β3] -> [APC,CDK1,Plk1]
+ 0.01% = 1.80[ms] | Event [CDK1] -> [c]
```

==== Simulation finished ====
Init Time = 0s 102ms
Wall Time = 25s 758ms
CPU Time = 22s 210ms (4 threads)

Memory peak = 29.5703 Mb
Deleting scope root
Deleting scope CellType[cells]

Preview

Model loaded successfully

Models

Job archive

Messages

Output file browser

Simulation output

Preview

Morpheus - CellCycle.xml

Job 2761: Example-CellCycle

Stop Output Folder Terminal Create movie

Name Size Kind

plot_1.000.png	5 KB	png File
plot_0.950.png	5 KB	png File
plot_0.900.png	5 KB	png File
plot_0.850.png	5 KB	png File
plot_0.800.png	5 KB	png File
plot_0.750.png	5 KB	png File
plot_0.700.png	5 KB	png File
plot_0.650.png	5 KB	png File

Time Schedule Performance Table

```
+ 82.42% = 21230.92[ms] | CPM [Vt] -> [cell.center]
+ 6.32% = 1627.84[ms] | CellDivision [CDK1,c] ->
[Vt,c,cell.center,d]
+ 6.01% = 1546.87[ms] | Gnuplotter [CDK1] -> []
+ 4.70% = 1211.54[ms] | DependencyGraph [] -> []
+ 0.37% = 95.89[ms] | Logger [APC,CDK1,Plk1] ->
[]
+ 0.10% = 24.82[ms] | System
[K,n,α1,α2,α3,β1,β2,β3] -> [APC,CDK1,Plk1]
+ 0.05% = 1.45[ms] | Event [CDK1,c]
```

==== Simulation finished ====
Init Time = 0s 102ms
Wall Time = 25s 758ms
CPU Time = 22s 210ms (4 threads)

Memory peak = 29.5703 Mb
Deleting scope root
Deleting scope CellType[cells]

Model loaded successfully

Models

Job archive

Messages

Output file browser

Simulation output

Tools

Preview

Morpheus - CellCycle.xml

Job 2761: Example-CellCycle

Time Schedule Performance Table

```
+ 82.42% = 21230.92[ms] | CPM [Vt] -> [cell.center]
+ 6.32% = 1627.84[ms] | CellDivision [CDK1,c] ->
[Vt,c,cell.center,d]
+ 6.01% = 1546.87[ms] | Gnuplotter [CDK1] -> []
+ 4.70% = 1211.54[ms] | DependencyGraph [] -> []
+ 0.37% = 95.89[ms] | Logger [APC,CDK1,Plk1] ->
[]
+ 0.10% = 24.82[ms] | System
[K,n,α1,α2,α3,β1,β2,β3] -> [APC,CDK1,Plk1]
+ 0.05% = 13.81[ms] | Event [CDK1,c]
```

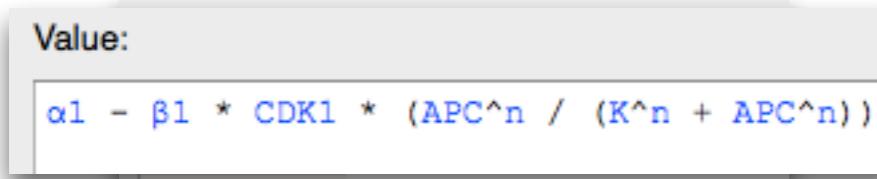
==== Simulation finished ====
Init Time = 0s 102ms
Wall Time = 25s 758ms
CPU Time = 22s 210ms (4 threads)

Memory peak = 29.5703 Mb
Deleting scope root
Deleting scope CellType[cells]

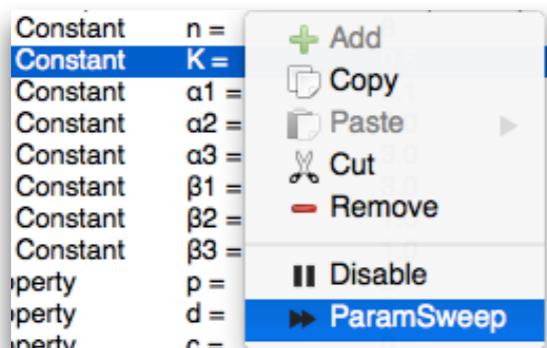
Model loaded successfully

Graphical user interface

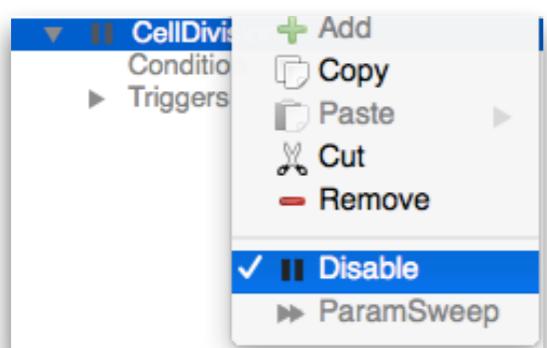
Features



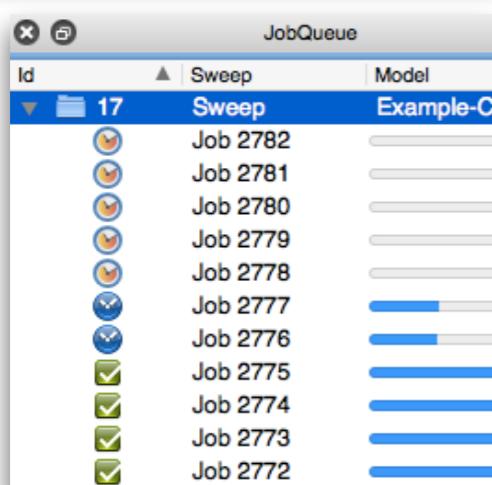
Mathematical expressions
In familiar in-fix notation



Re-use models
Stored in job archive



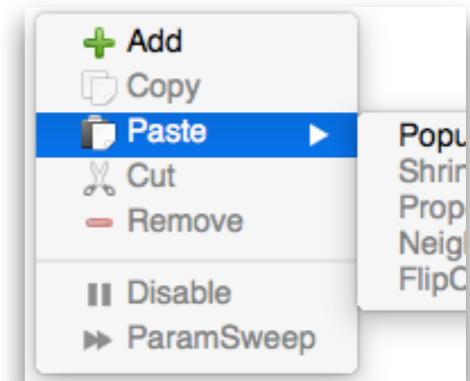
Parameter exploration
Batch simulation within GUI



Create movies
From image sequences



Temporarily disable elements
Testing and debugging



Copy-paste elements
Between different models

Job scheduling
Multithreading and parallel simulation

Graphical user interface

Data export and visualization

Gnuplotter

Visualize cell Properties and Field

Logger

Data export in csv or matrix format
and versatile tool for plotting

HistogramLogger

Compute frequency distributions
and visualization

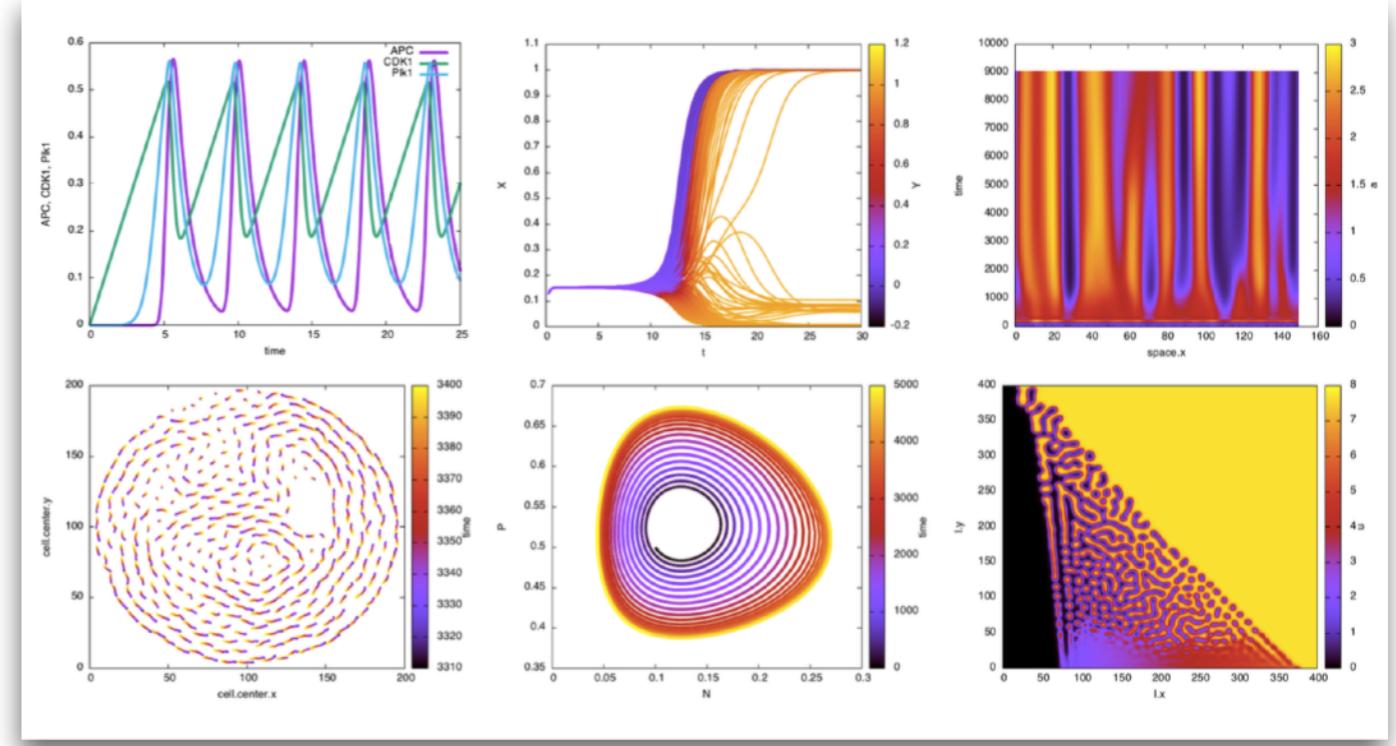
TIFFPlotter

Export multichannel TIFF stacks
with OME (open microscopy) header

Graphical user interface

Data export and visualization

Gnuplotter
Visualize cell Properties and Field



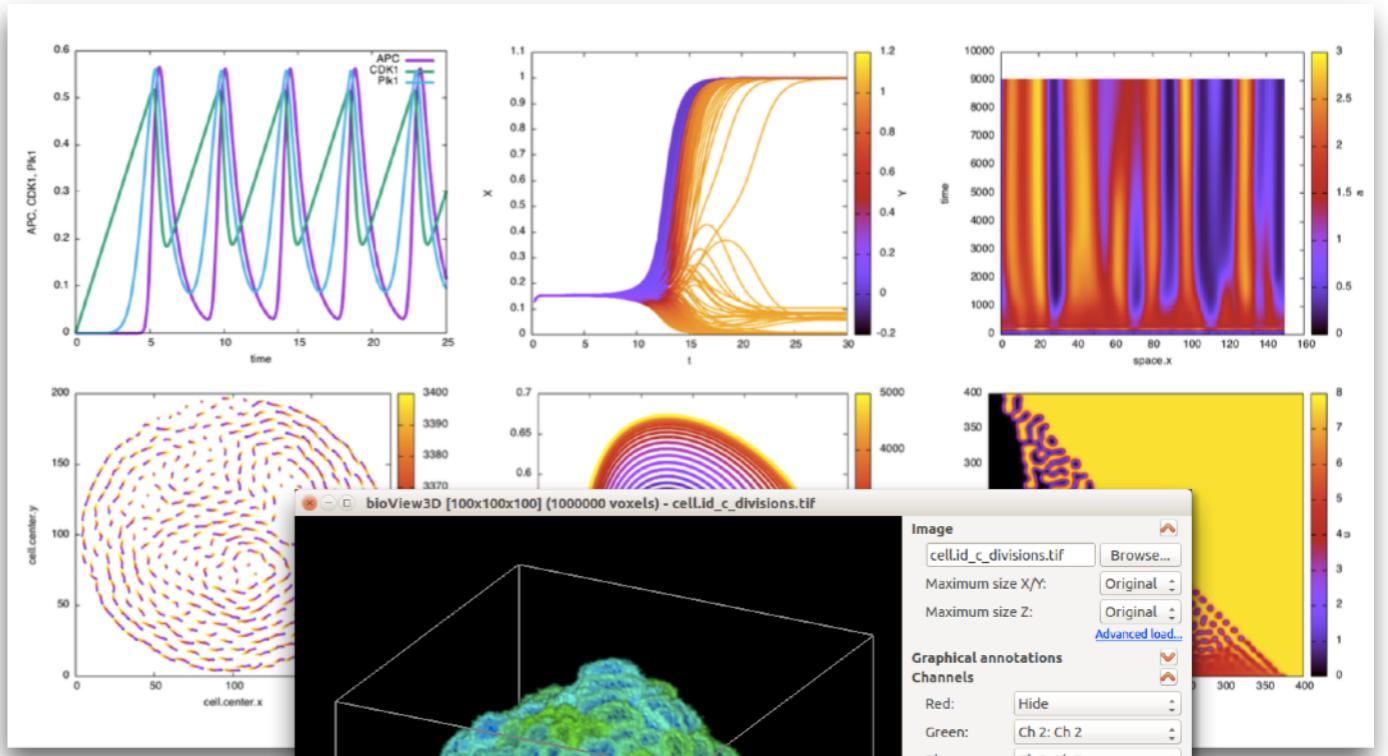
HistogramLogger
Compute frequency distributions
and visualization

TIFFPlotter
Export multichannel TIFF stacks
with OME (open microscopy) header

Graphical user interface

Data export and visualization

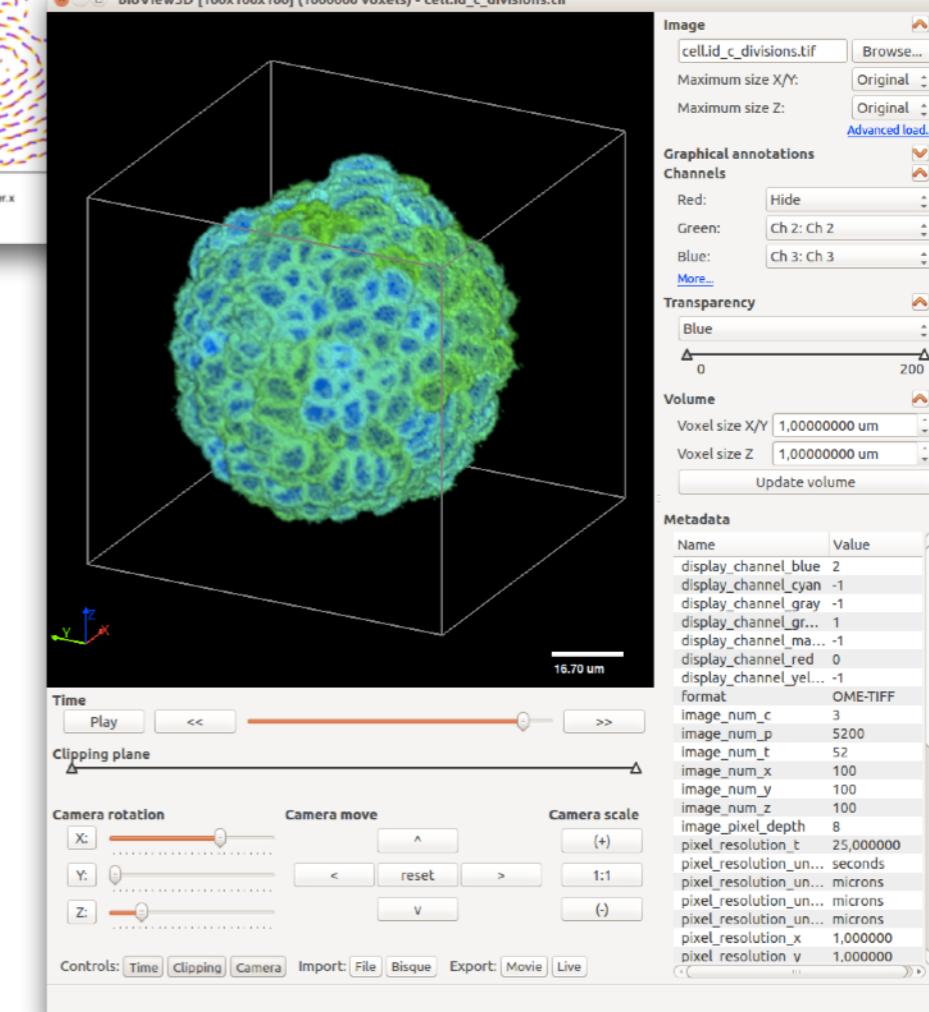
Gnuplotter
Visualize cell Properties and Field



Logger
Data export in csv or matrix format
and versatile tool for plotting

HistogramLogger
Compute frequency distributions
and visualization

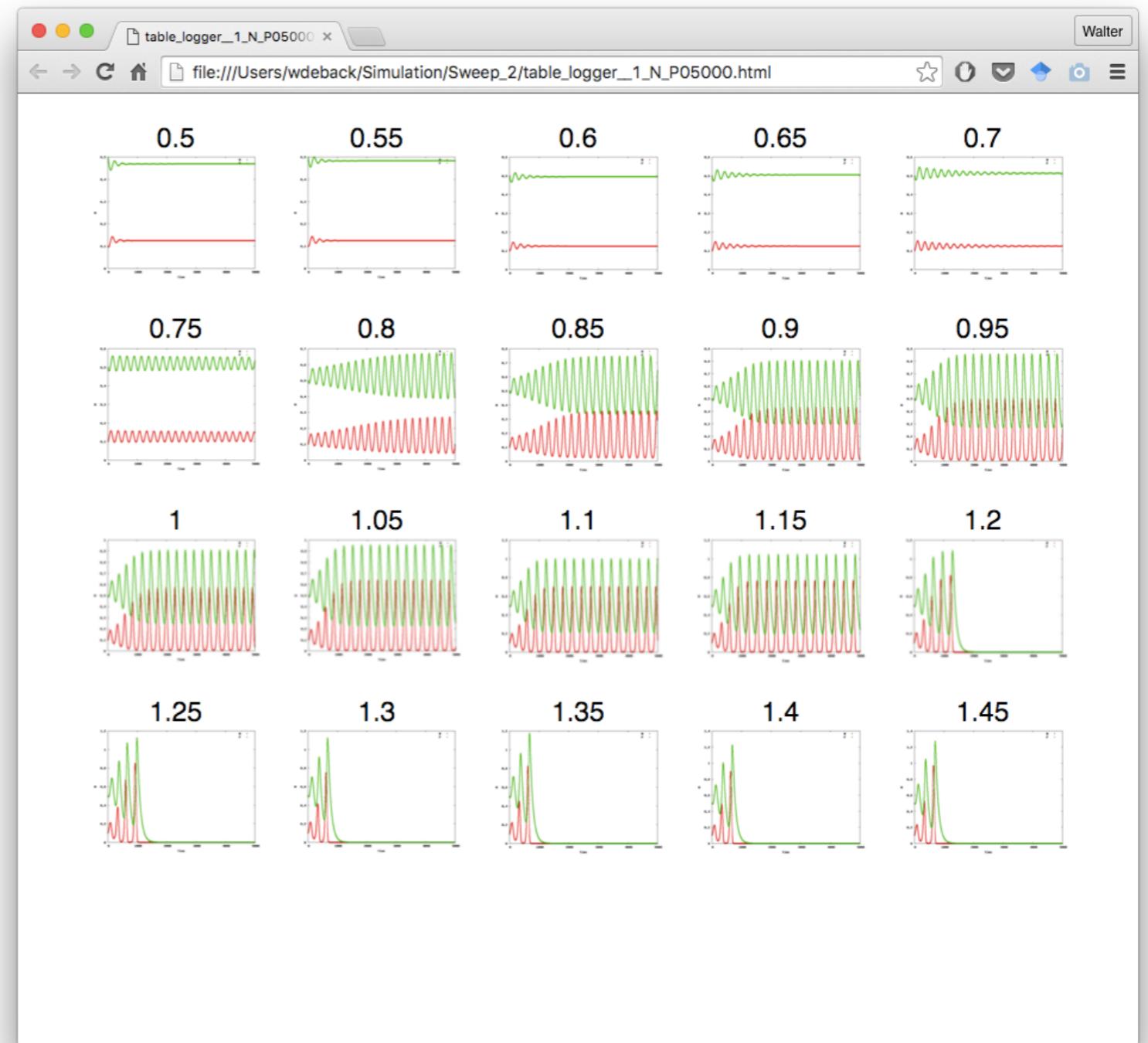
TIFFPlotter
Export multichannel TIFF stacks
with OME (open microscopy) header



Graphical user interface

Image table

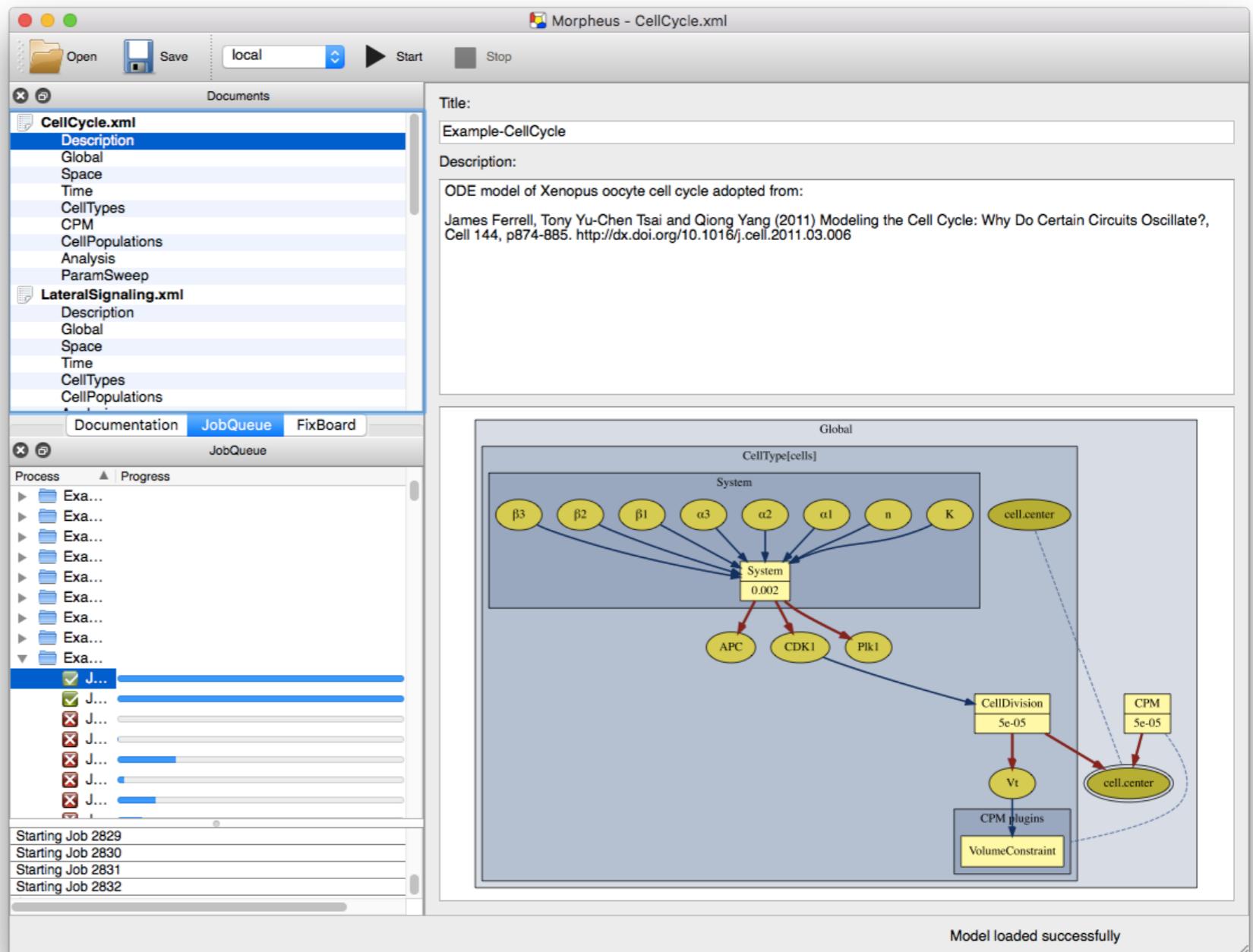
Table of images or movies
Visually inspect results of
parameter sweeps (HTML5)



Graphical user interface

Symbol dependency graph

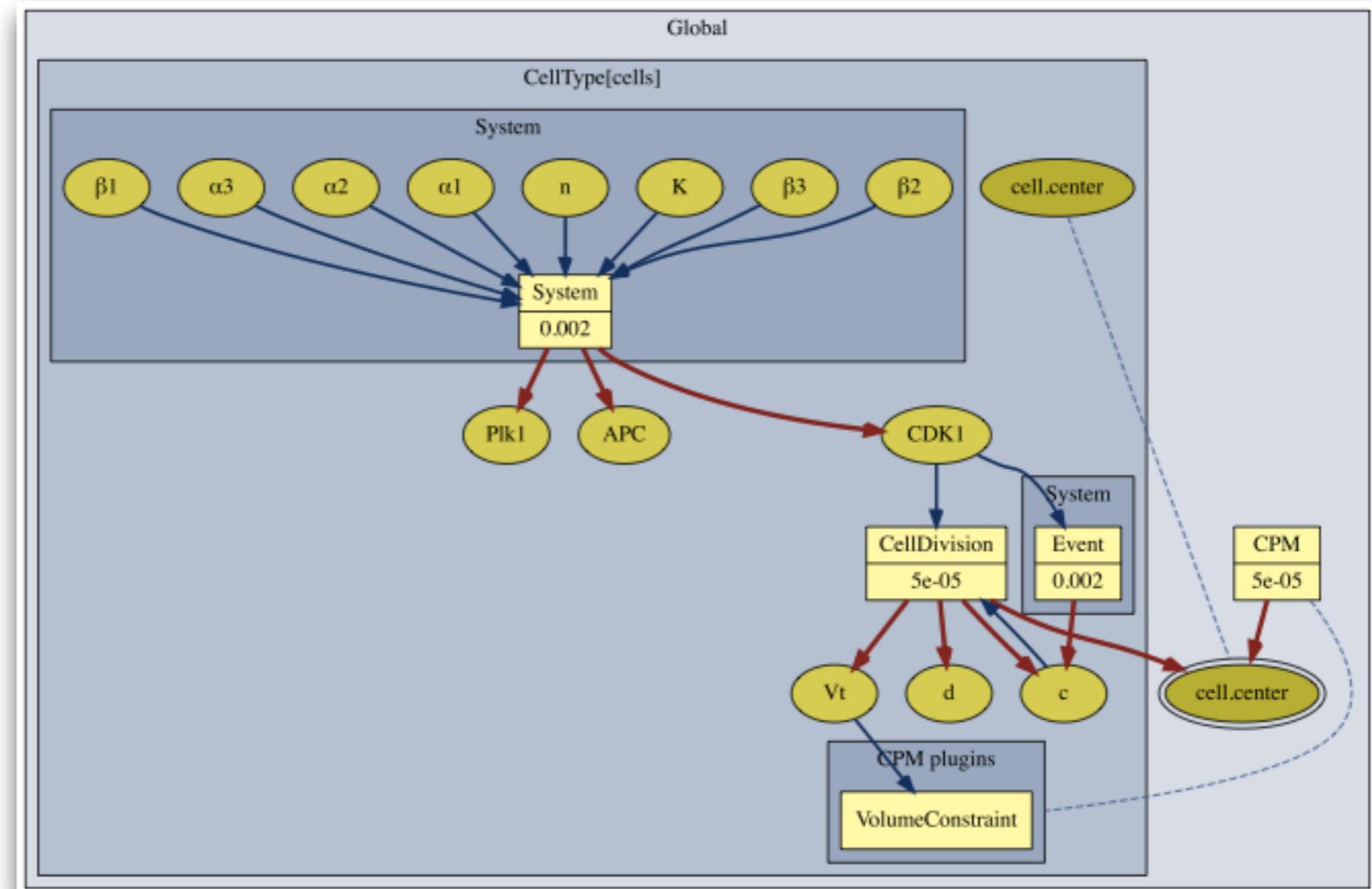
Graphical representation
of model dependencies
Logic and information flow
in multi-scale models



Graphical user interface

Symbol dependency graph

Graphical representation
of model dependencies
Logic and information flow
in multi-scale models



Morpheus in education

Morpheus in education

Teaching mathematical and computational modeling

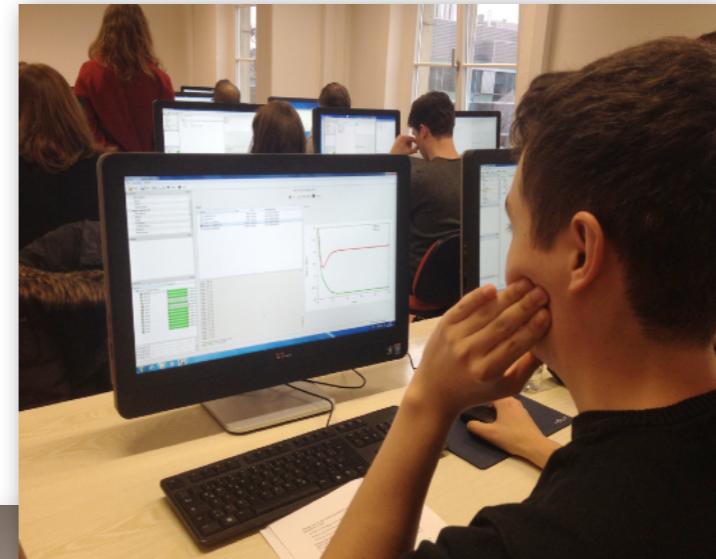
Lecture course
Introduction to mathematical biology
TU Dresden

Practical course
Modeling of pattern formation in tissues
DIGS-BB (biomedicine and bioengineering)

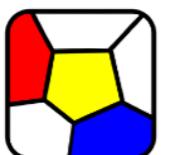
Summer school
Math. modeling of tissue mechanics
Euro. Mathematical Society (EMS) and ESMTB

Workshop
Computational stem cell biology
German Stem Cell Network (GSCN)

Workshop
Multi-scale modeling of biological systems
National University La Plata, Buenos Aires



Workshop on “Computational Stem Cell Biology”
organized by German Stem Cell Network (GSCN)

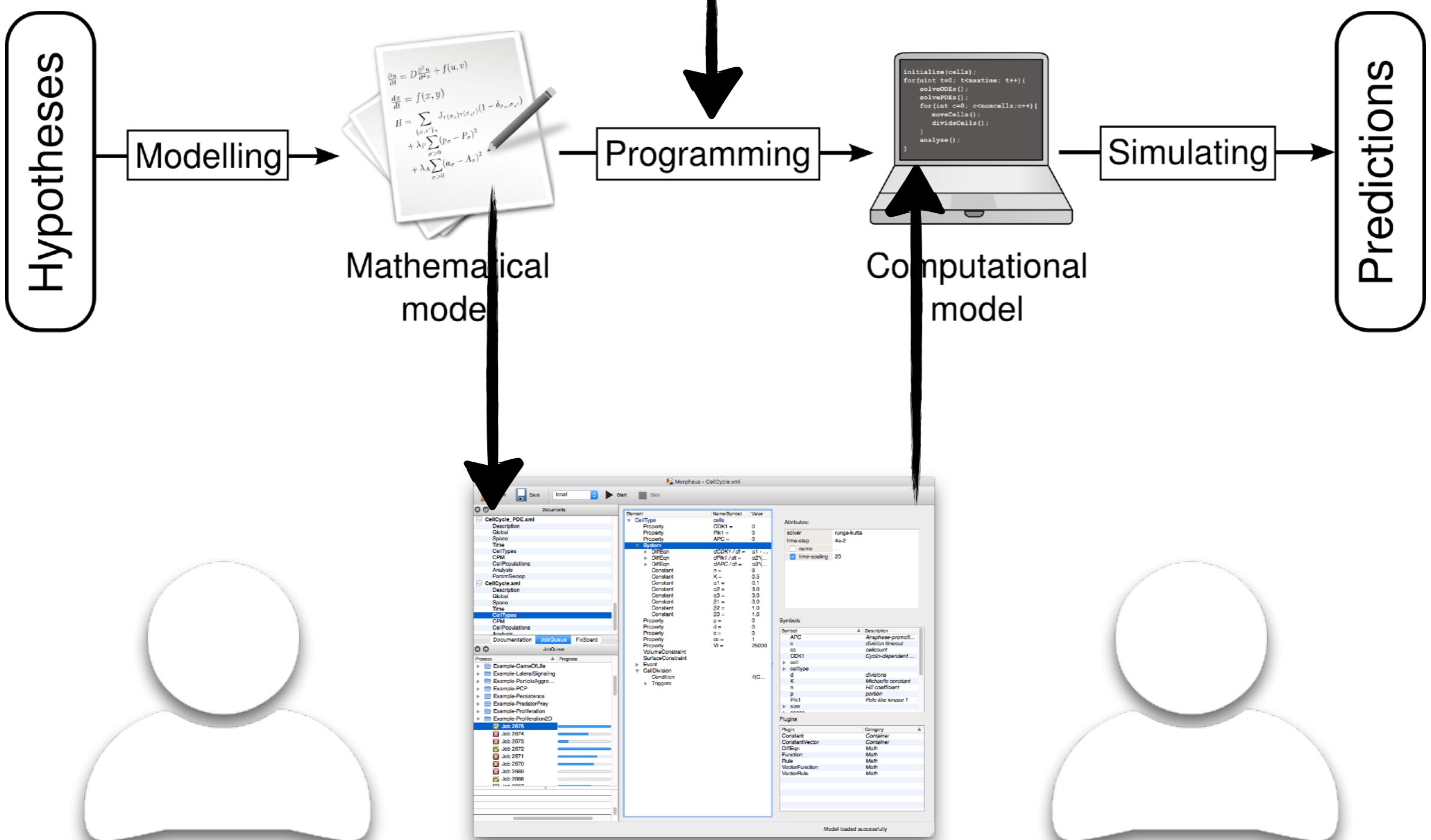


Morpheus

open-source framework for
multiscale & multicellular
systems simulation

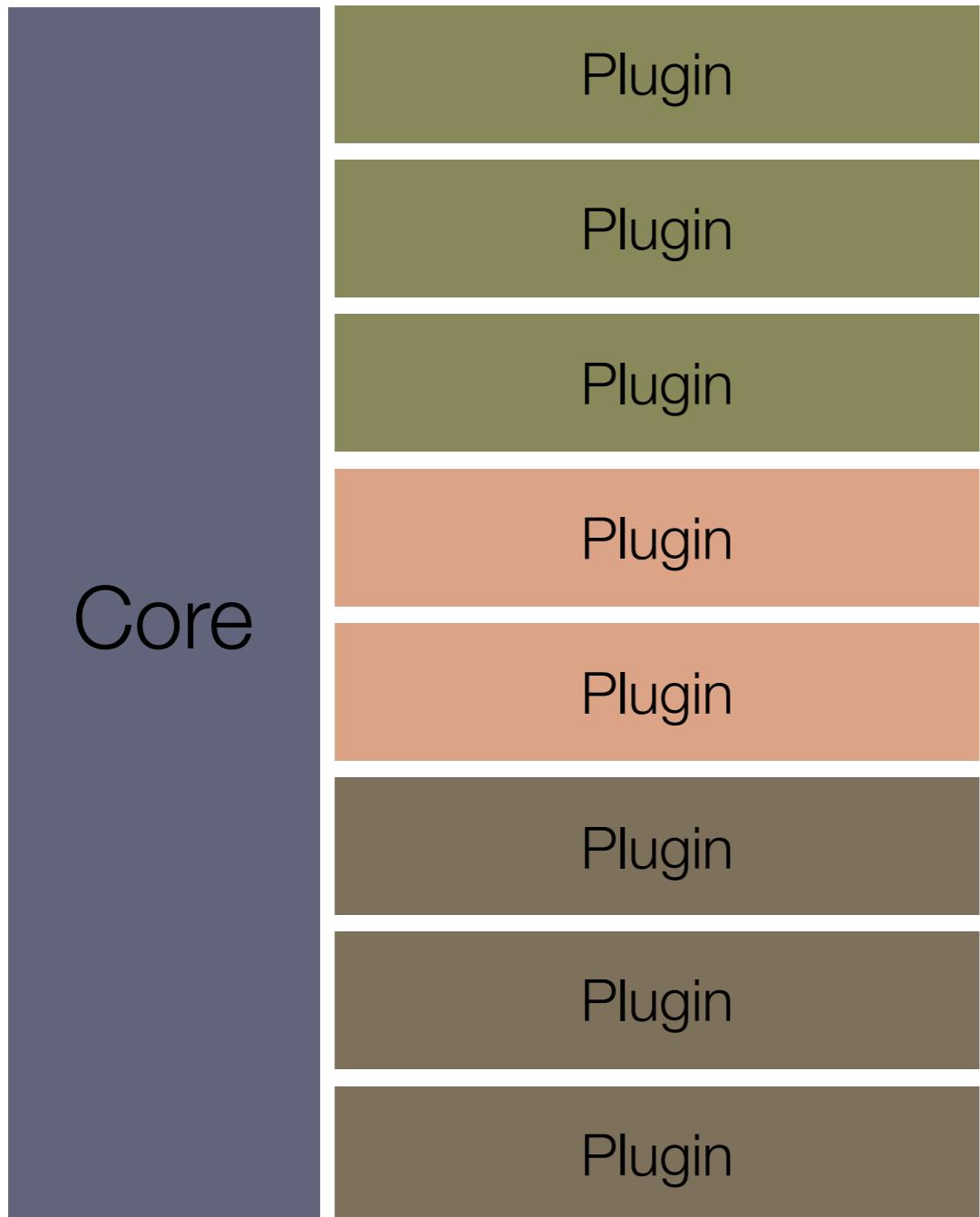
Plugin development

Open-source framework



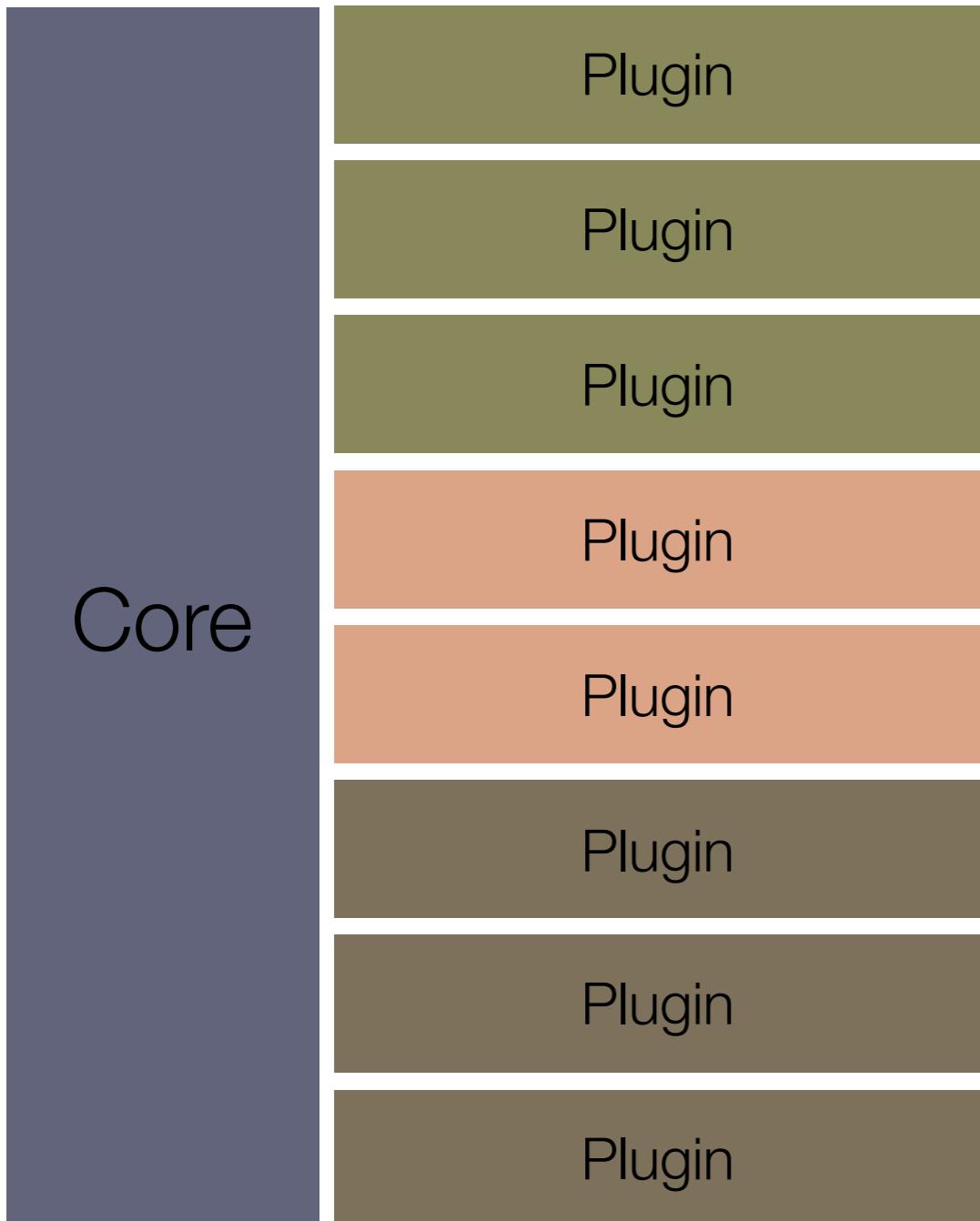
Plugin architecture

Categories of plugins



Plugin architecture

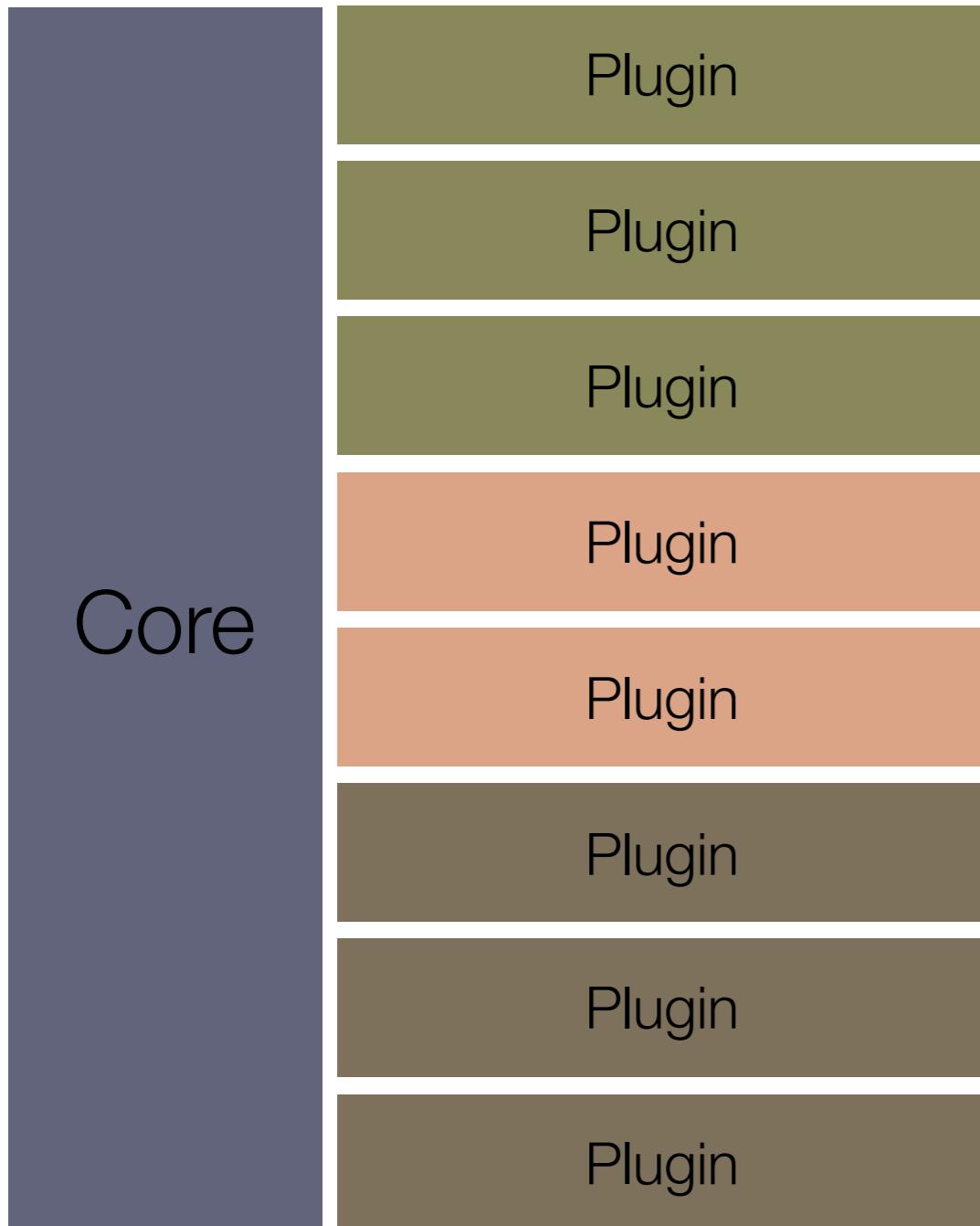
Categories of plugins



Initialization plugins
Cell configurations

Plugin architecture

Categories of plugins

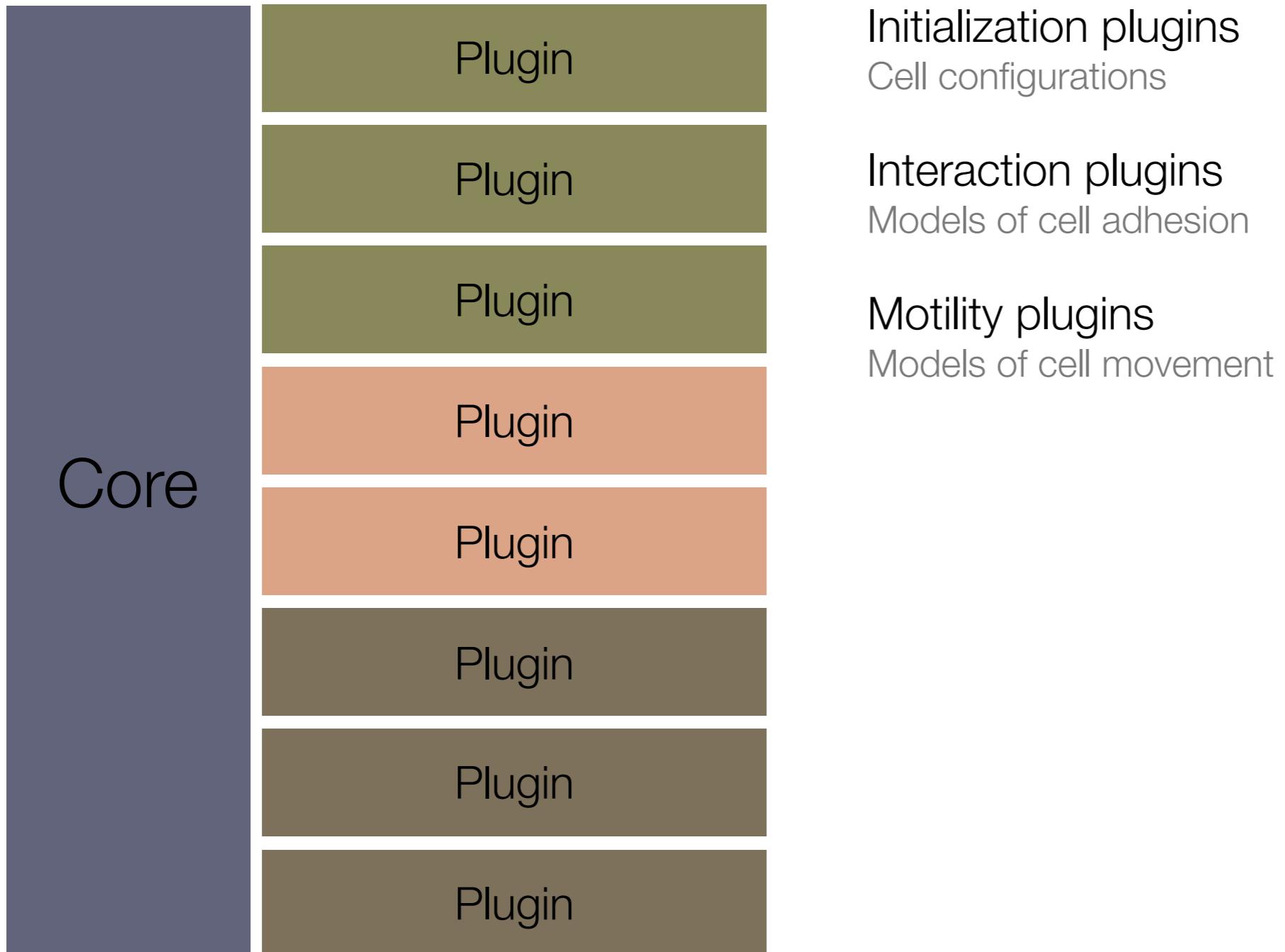


Initialization plugins
Cell configurations

Interaction plugins
Models of cell adhesion

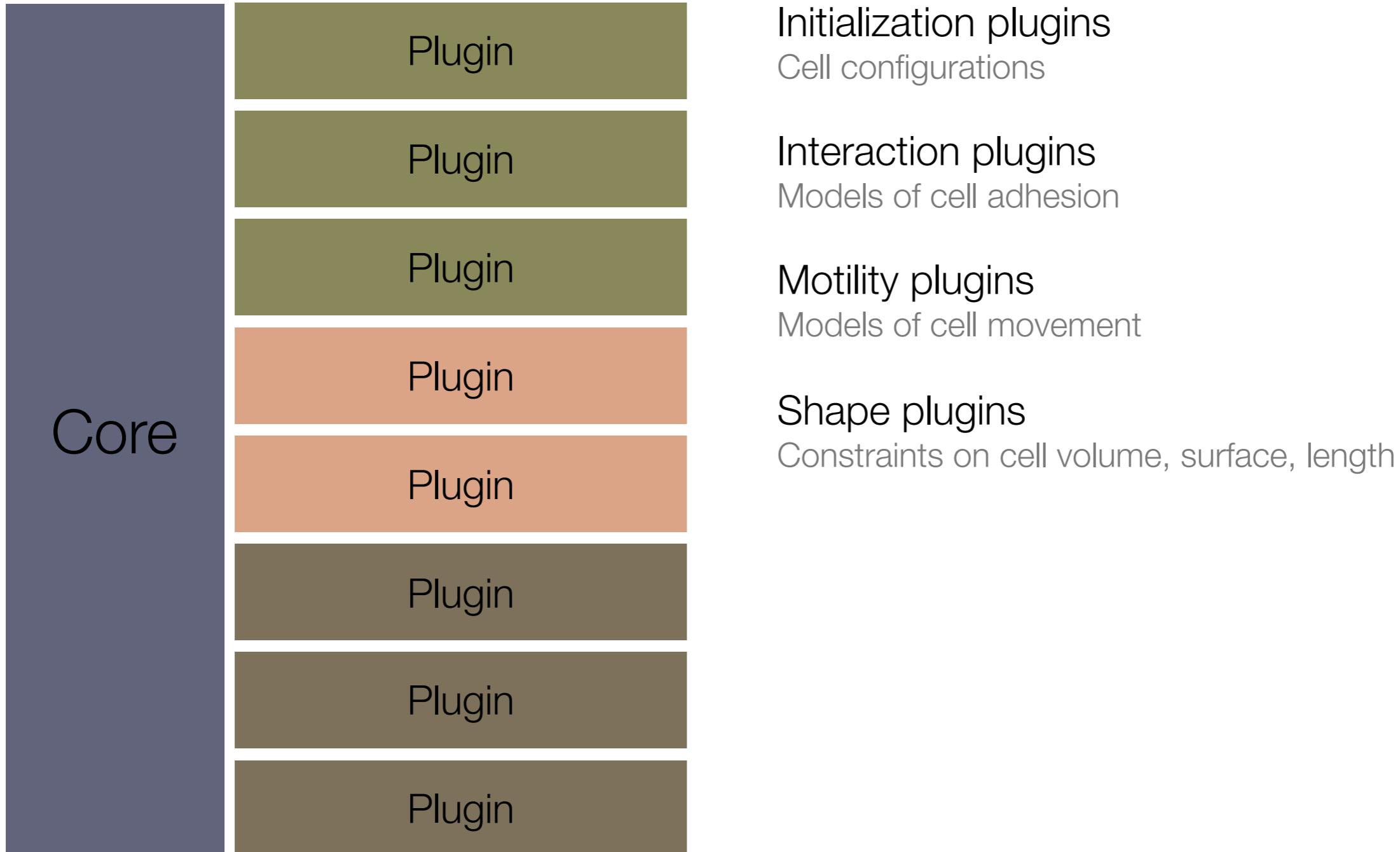
Plugin architecture

Categories of plugins



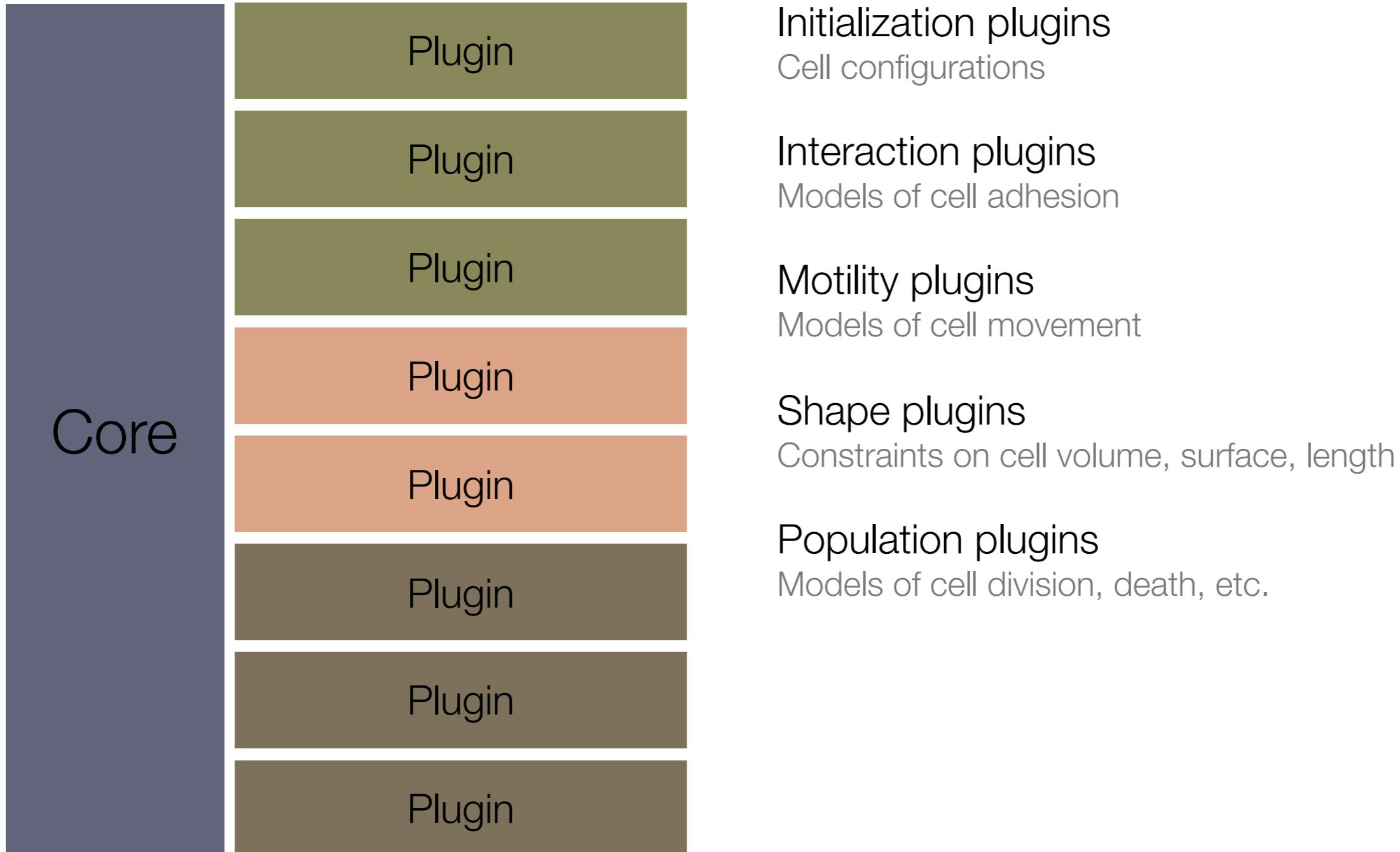
Plugin architecture

Categories of plugins



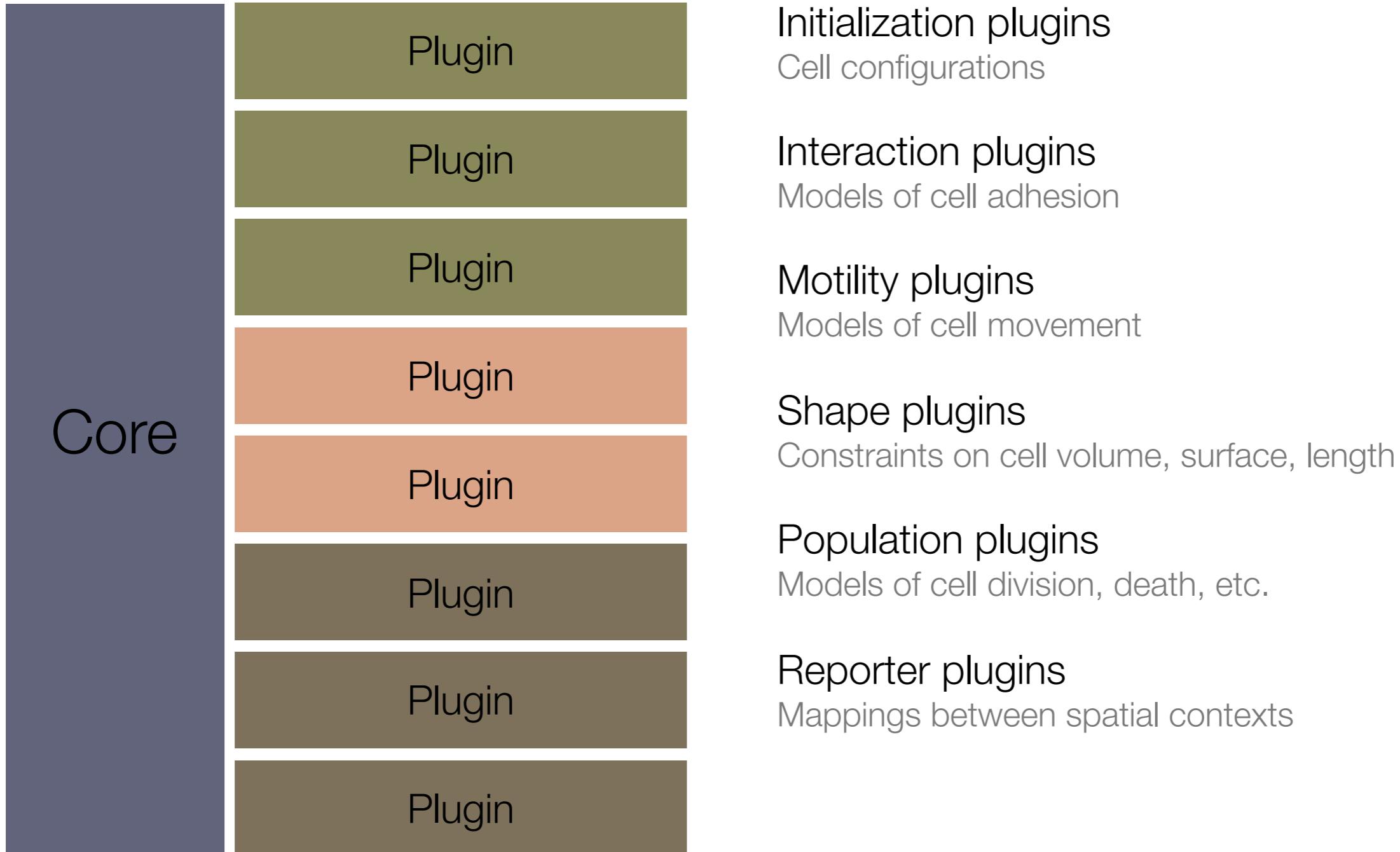
Plugin architecture

Categories of plugins



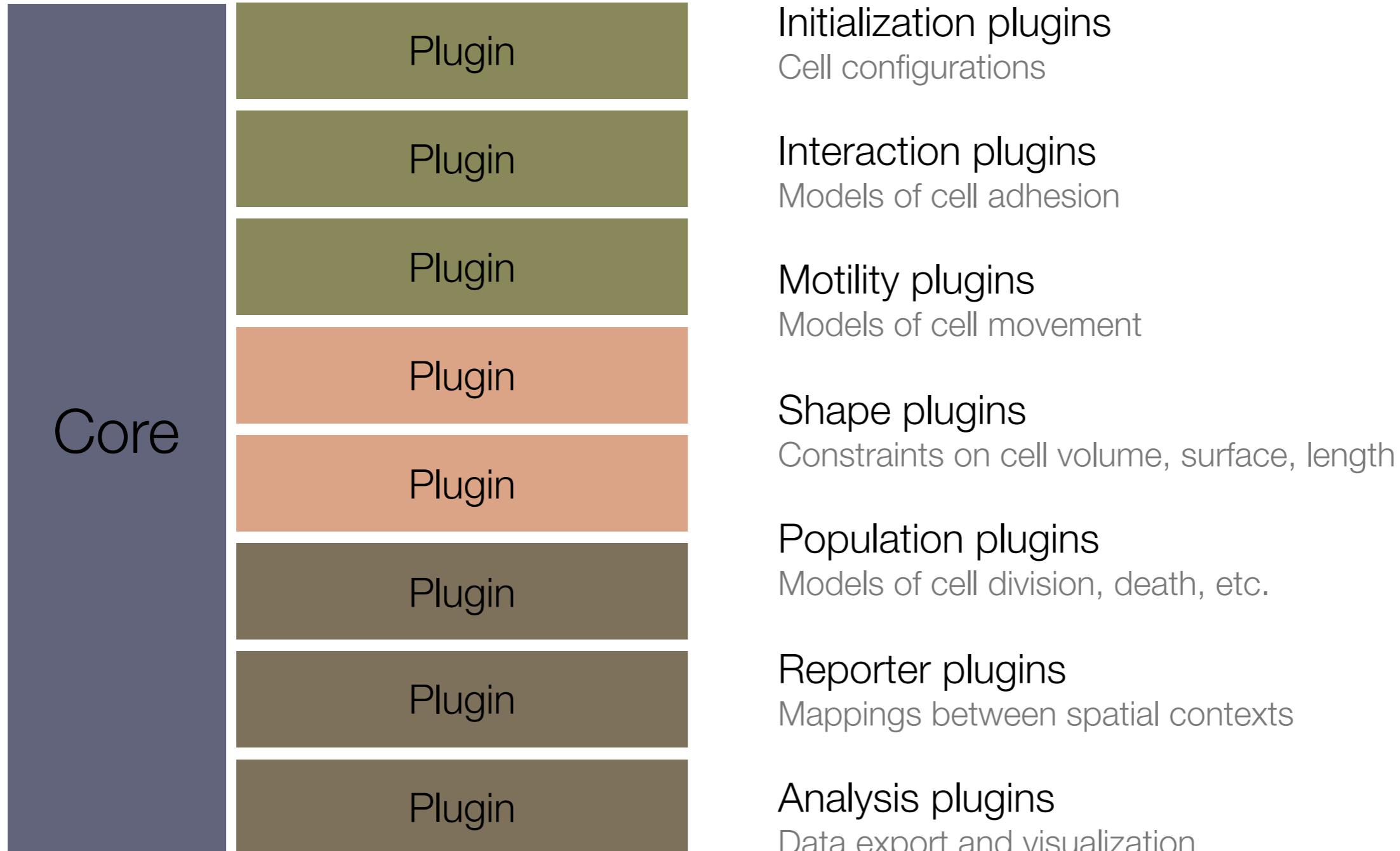
Plugin architecture

Categories of plugins



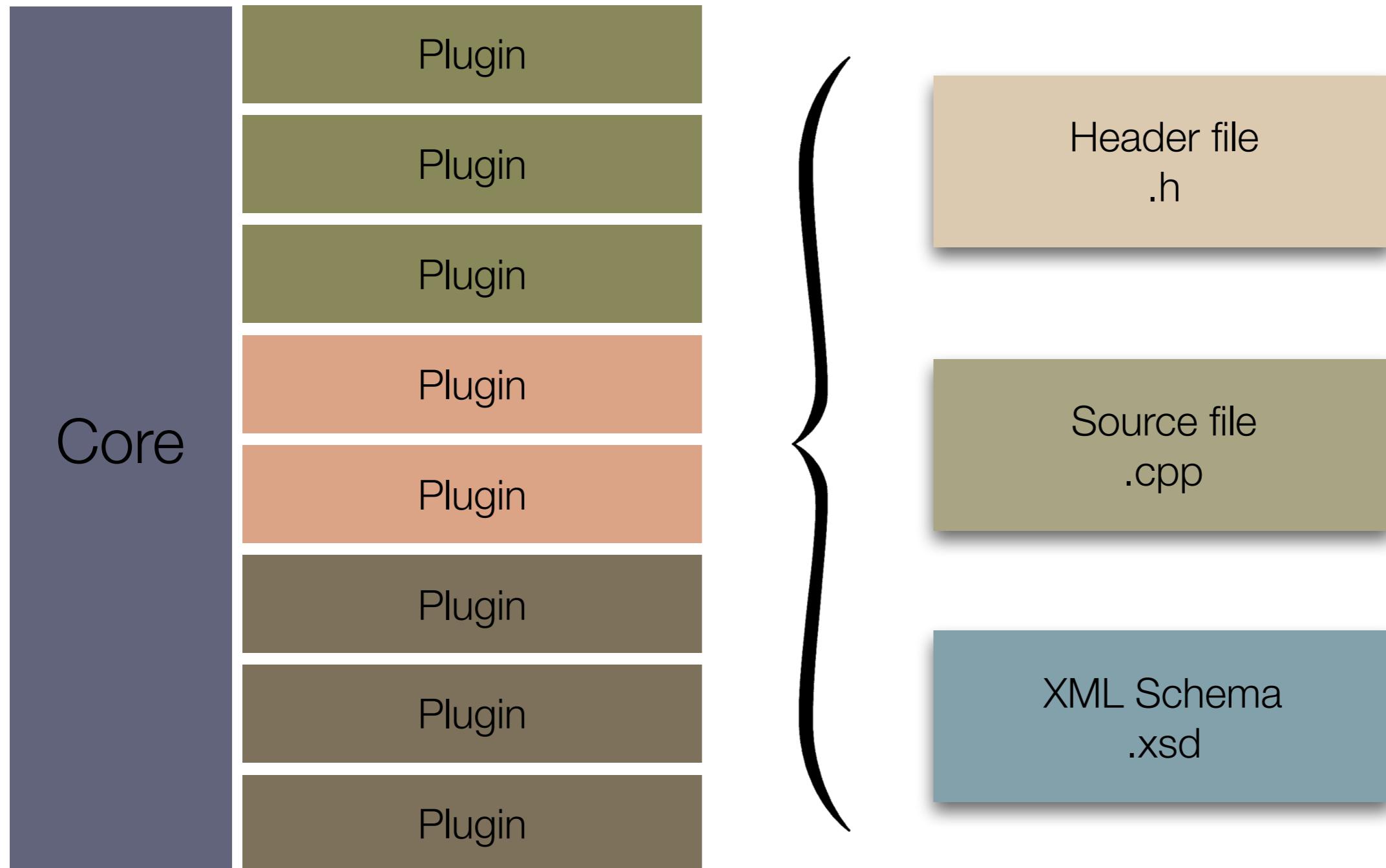
Plugin architecture

Categories of plugins



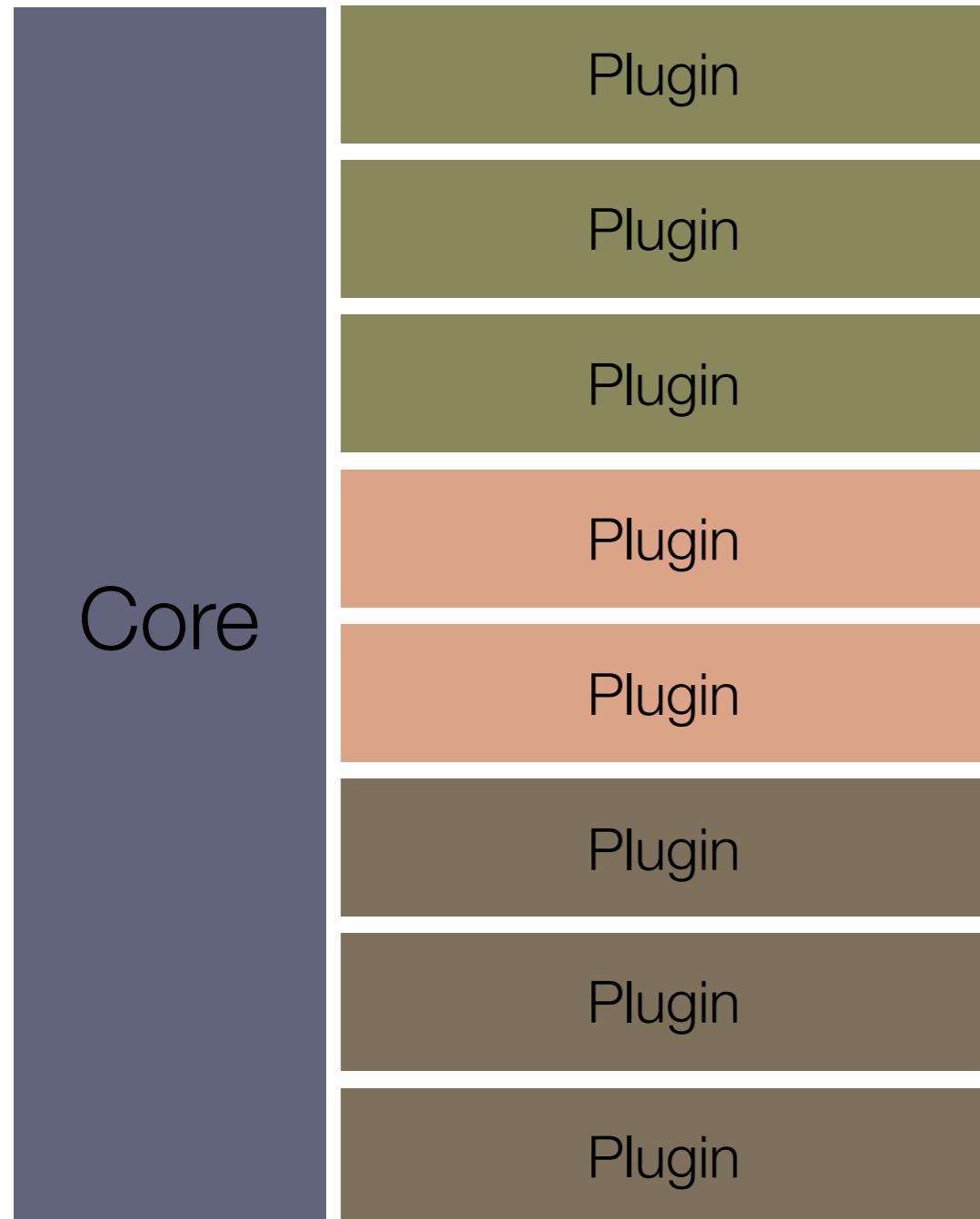
Plugin architecture

Structure of plugin



Plugin architecture

Structure of plugin



XSD

myPlugin.xsd

```
<xs:schema>
<xs:complexType name="MyPlugin">
  <xs:annotation>
    <xs:documentation>Documentation of MyPlugin

Documentation



Attributes



Header



myPlugin.h



```
#include "core/interfaces.h"
#include "core/simulation.h"
#include "core/celltype.h"

class MyPlugin : public Analysis_Listener
{
public:
 DECLARE_PLUGIN("MyPlugin");
 NetworkLogger() {};
 virtual void loadFromXML(const XMLNode);
 virtual void notify(double time);
 virtual void init(double time);

private:
 string symbolstr, celltypestr;
 SymbolAccessor<double> symbol;
 shared_ptr<const CellType> celltype;
};
```



Inherit interface



Override functions



Symbol references



Implementation



myPlugin.cpp



```
#include "myPlugin.h"
REGISTER_PLUGIN(MyPlugin);

void MyPlugin::loadFromXML(const XMLNode Node)
{
 Analysis_Listener::loadFromXML(Node);
 getXMLAttribute(Node, "celltype", celltypestr);
 getXMLAttribute(Node, "symbol", symbolstr);
}

void MyPlugin::init(double time)
{
 Analysis_Listener::init(time);
 celltype = CPM::findCellType(celltypestr);
 symbol = SIM::findSymbol<double>(symbolstr, celltype);
}

void MyPlugin::notify(double time)
{
 Analysis_Listener::notify(time);
 for(uint c=0; c < celltype->getCellIDs().size(); c++) {
 double value = CPM::getCell(cells[c]).get(symbol);
 // do something
 }
}
```



Read parameters



Initialize references



Use symbols


```

Plugin architecture

XML Schema

XSD

myPlugin.xsd

```
<xs:schema>
  <xs:complexType name="MyPlugin">
    <xs:annotation>
      <xs:documentation>Documentation of MyPlugin
    </xs:annotation>
    <xs:attribute name="interval" type="cpmDouble"      use="required"/>
    <xs:attribute name="celltype" type="cpmCellTypeRef" use="optional"/>
    <xs:attribute name="symbol"   type="cpmSymbolRef"   use="required"/>
  </xs:complexType>
</xs:schema>
```

Documentation

Attributes

Plugin architecture

Header file

Header

myPlugin.h

```
#include "core/interfaces.h"
#include "core/simulation.h"
#include "core/celltype.h"

class MyPlugin : public Analysis_Listener
{
public:
    DECLARE_PLUGIN("MyPlugin");
    NetworkLogger() {};
    virtual void loadFromXML(const XMLNode);
    virtual void notify(double time);
    virtual void init(double time);

private:
    string symbolstr, celltypestr;
    SymbolAccessor<double> symbol;
    shared_ptr<const CellType> celltype;
};
```

Inherit interface

Override functions

Symbol references

Plugin architecture

Source file

Implementation

myPlugin.cpp

```
#include "myPlugin.h"
REGISTER_PLUGIN(MyPlugin);

void MyPlugin::loadFromXML(const XMLNode Node)
{
    Analysis_Listener::loadFromXML( Node );
    getXMLAttribute(Node, "celltype", celltypestr);
    getXMLAttribute(Node, "symbol", symbolstr);
}

void MyPlugin::init(double time)
{
    Analysis_Listener::init(time);
    celltype = CPM::findCellType(celltypestr);
    symbol   = SIM::findSymbol<double>(symbolstr, celltype);
}

void MyPlugin::notify(double time)
{
    Analysis_Listener::notify(time);
    for(uint c=0; c < celltype->getCellIDs().size(); c++) {
        double value = CPM::getCell( cells[c] ).get( symbol );
        // do something
    }
}
```

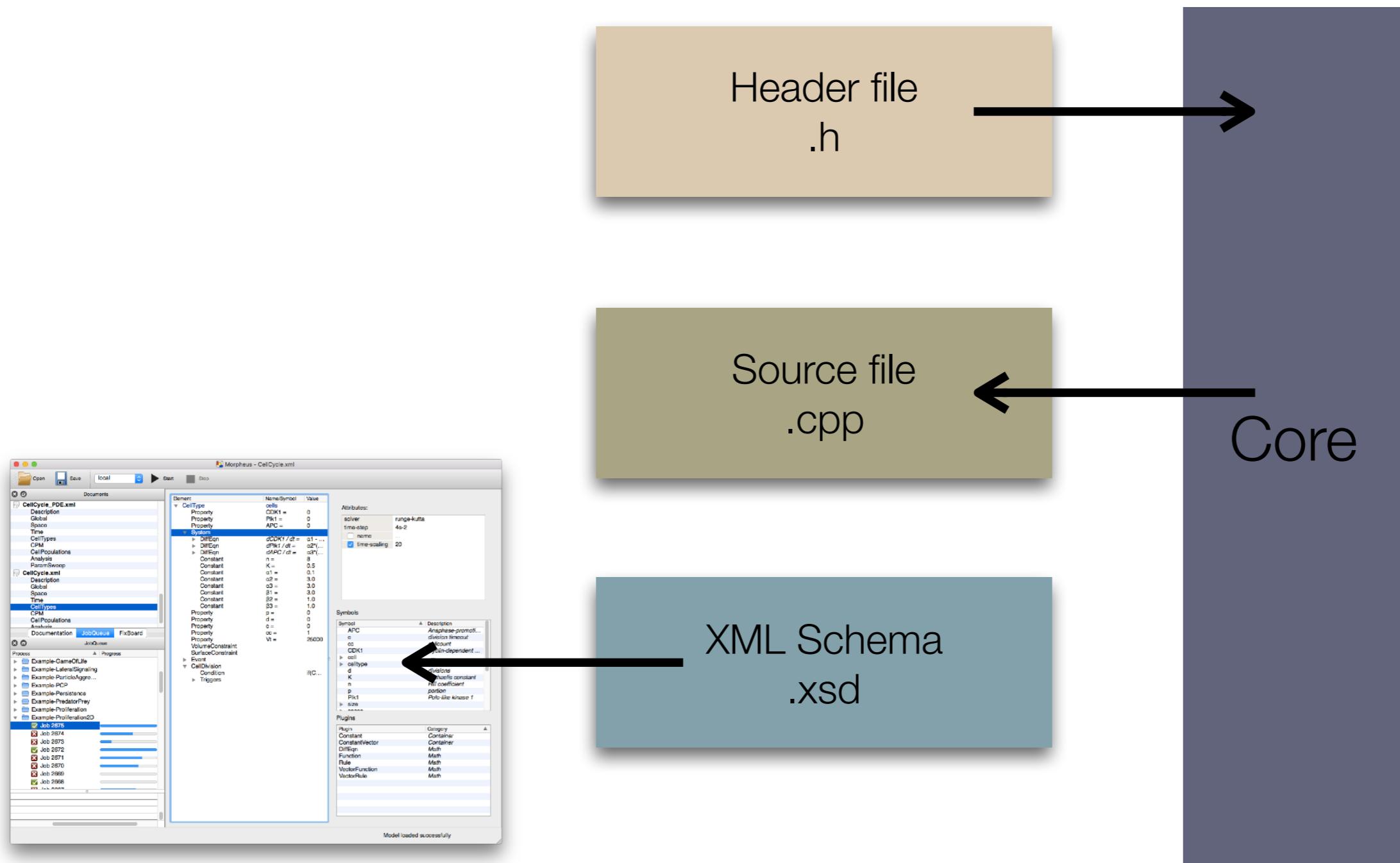
Read parameters

Initialize references

Use symbols

Plugin architecture

Integration into framework



Code Repository

gitlab.com/morpheus.lab

Git repository
distributed version control

BSD License
permissive open-source

Issue tracker
bugs and features

Documentation
plugin development

Community
distributed development

The screenshot shows the GitLab interface for the 'morpheus.lab / morpheus' project. The left sidebar contains navigation links: Go to group, Project (selected), Activity, Files, Commits, Builds (0), Graphs, Milestones, Issues (7), Merge Requests (2), Members, Labels, Wiki, Forks, and a user icon for 'wdeback'. The main content area displays the project details: 'morpheus' with a yellow and blue geometric logo. A brief description states: 'Morpheus is a modeling and simulation environment for multiscale and multicellular systems biology. It is developed by Jörn Starruß and Walter de Back at the TU Dresden, Germany.' Below this are statistics: 28 commits, 1 branch, 0 tags, 63.73 MB, and a 'License' button. Buttons for 'Unstar' (3), 'Fork' (3), and download options ('SSH', 'git@gitlab.com:morpheus.lab/morpheus.git') are also present. At the bottom, a commit history entry shows 'c4a762e1 Fixes #9 · a day ago by Jörn Starruß'. The footer contains a 'Morpheus' section with a detailed description and developer information.

morpheus.lab / morpheus

morpheus

Morpheus is a modeling and simulation environment for multiscale and multicellular systems biology. It is developed by Jörn Starruß and Walter de Back at the TU Dresden, Germany.

SSH git@gitlab.com:morpheus.lab/morpheus.git

28 commits 1 branch 0 tags 63.73 MB License Add Changelog Add Contribution guide

c4a762e1 Fixes #9 · a day ago by Jörn Starruß

Morpheus

Morpheus is a modeling and simulation environment for the study of multiscale and multicellular systems. For further information look at <https://imc.zih.tu-dresden.de/wiki/morpheus>.

Morpheus has been developed by Jörn Starruß and Walter de Back at the Center for High Performance Computing at the Technische Universität Dresden, Germany.

Code Repository

gitlab.com/morpheus.lab

Git repository
distributed version control

BSD License
permissive open-source

Issue tracker
bugs and features

Documentation
plugin development

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The screenshot shows a Mac OS X browser window displaying the GitLab project page for 'morpheus.lab / morpheus'. The page includes a sidebar with navigation links like Project, Activity, Files, Commits, Builds, Graphs, Milestones, Issues (7), Merge Requests (2), Members, Labels, Wiki, Forks, and a user icon for 'wdeback'. The main content area features a logo consisting of four overlapping colored squares (red, yellow, blue, white) and the project name 'morpheus'. A brief description states: 'Morpheus is a modeling and simulation environment for multiscale and multicellular systems biology. It is developed by Jörn Starruß and Walter de Back at the TU Dresden, Germany.' Below this is a code block showing the command to clone the repository: `git clone git@gitlab.com:morpheus.lab/morpheus.git morpheus`. The 'Morpheus' section contains a detailed description of the project's purpose and development team.

morpheus.lab / morpheus

Search

morpheus

Morpheus is a modeling and simulation environment for multiscale and multicellular systems biology. It is developed by Jörn Starruß and Walter de Back at the TU Dresden, Germany.

```
git clone git@gitlab.com:morpheus.lab/morpheus.git morpheus
cd morpheus
mkdir build
cd build
cmake ..
make && sudo make install
```

Morpheus

Morpheus is a modeling and simulation environment for the study of multiscale and multicellular systems. For further information look at <https://imc.zih.tu-dresden.de/wiki/morpheus>.

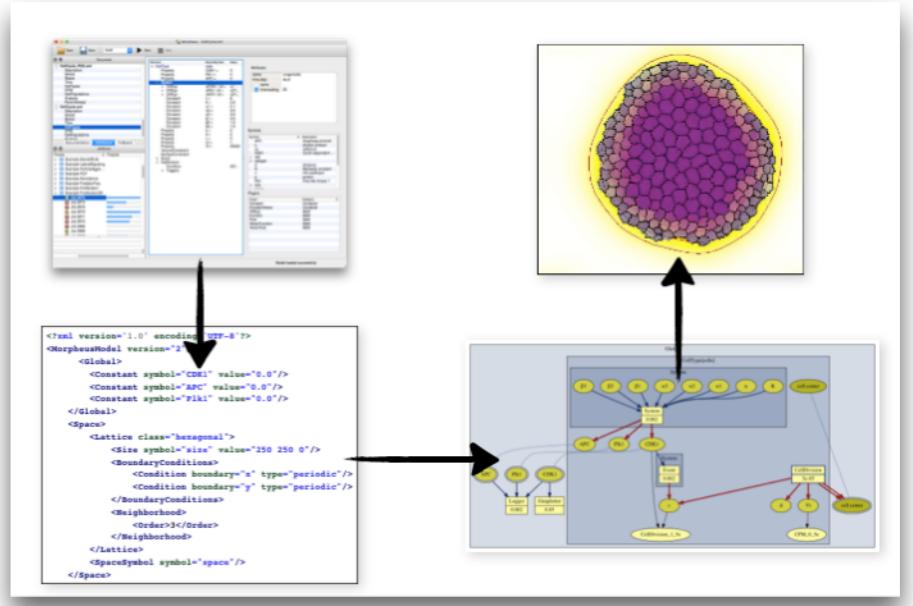
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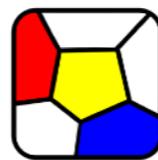
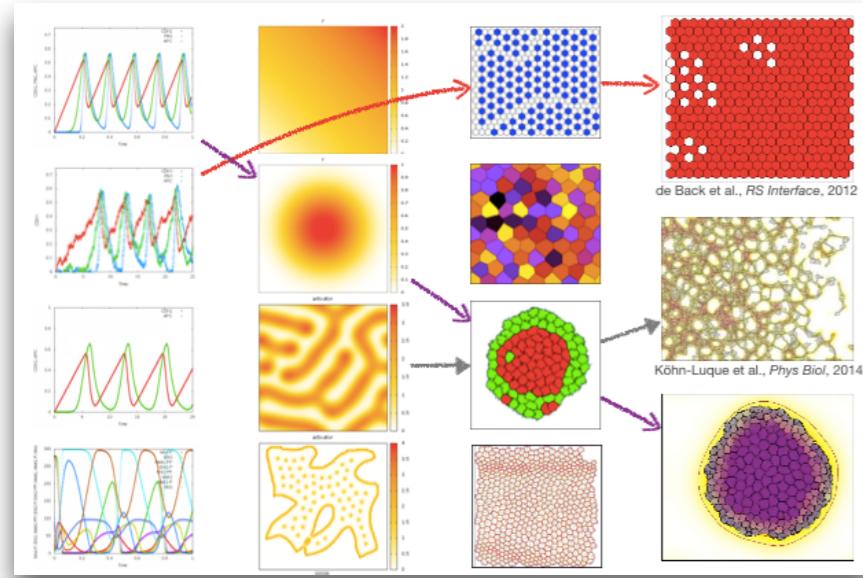
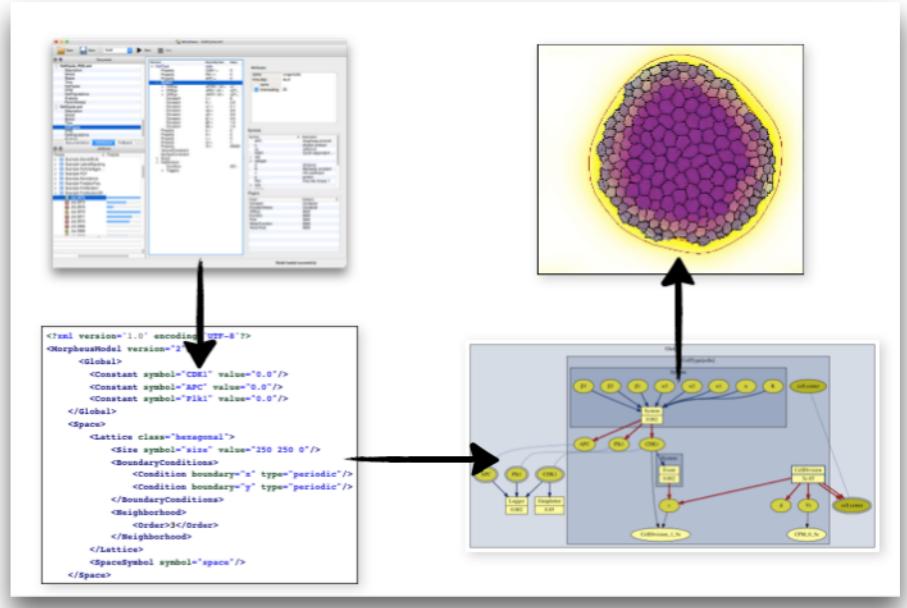
Morpheus



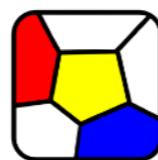
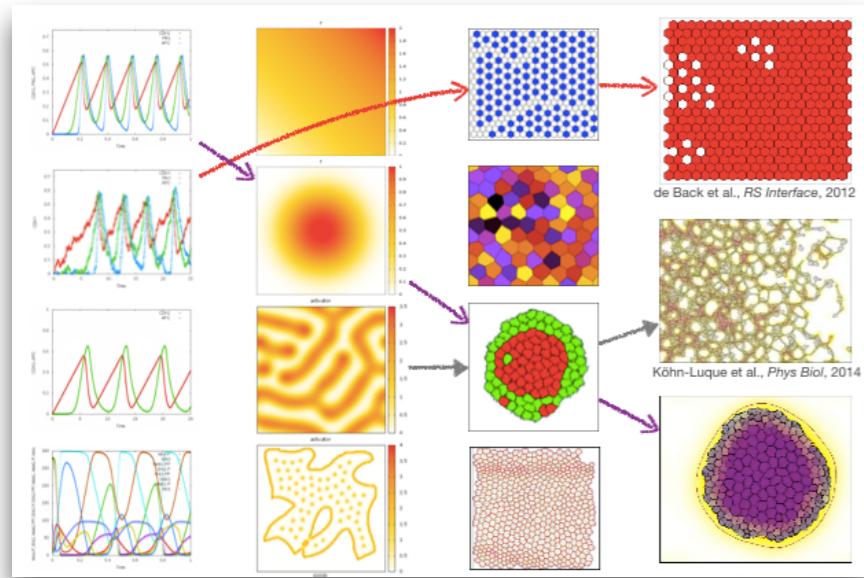
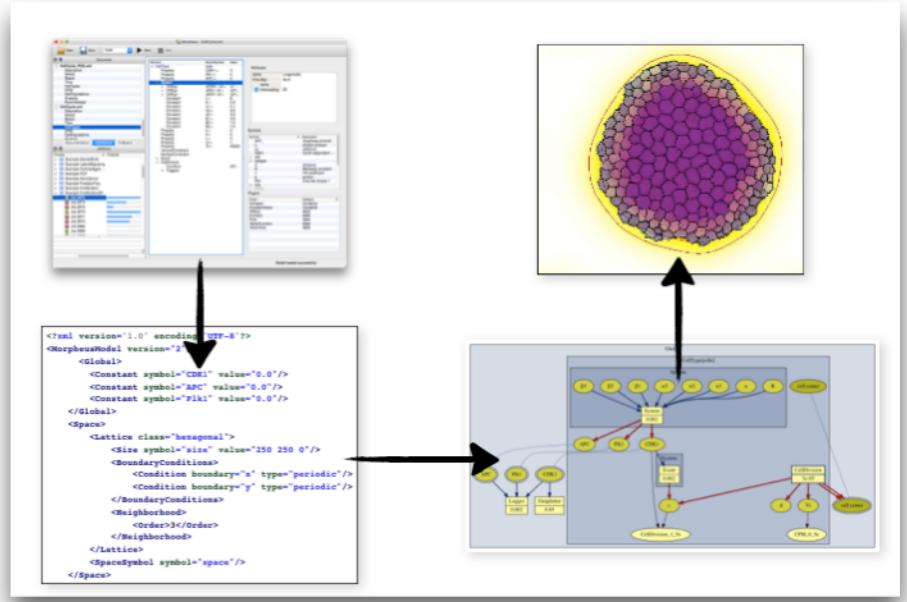
Morpheus



Morpheus



Morpheus



Morpheus

Documentation

- Continuous Process Plugins
- Hybridous Process Plugins
- ModelStructure
- MathExpressions
- Plugins
- Concurrent
- ContextLogger

System

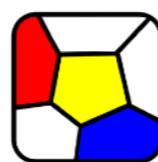
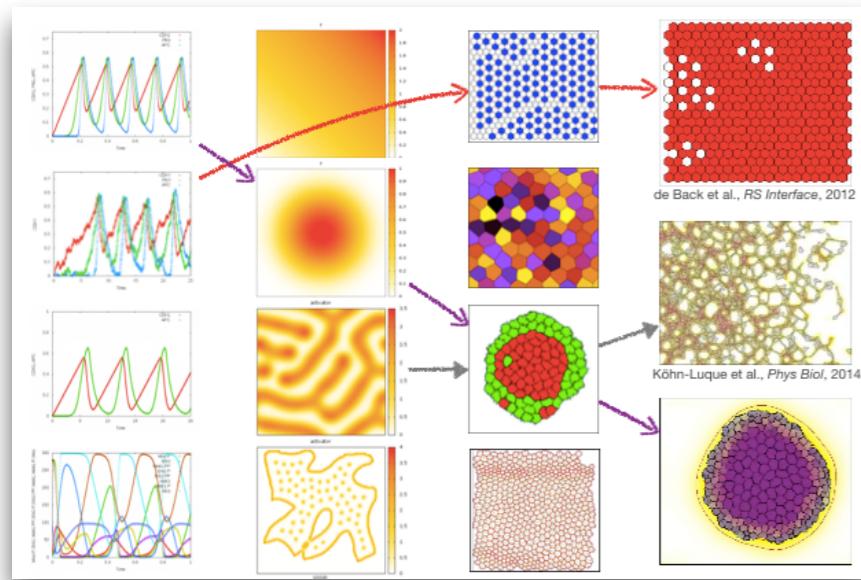
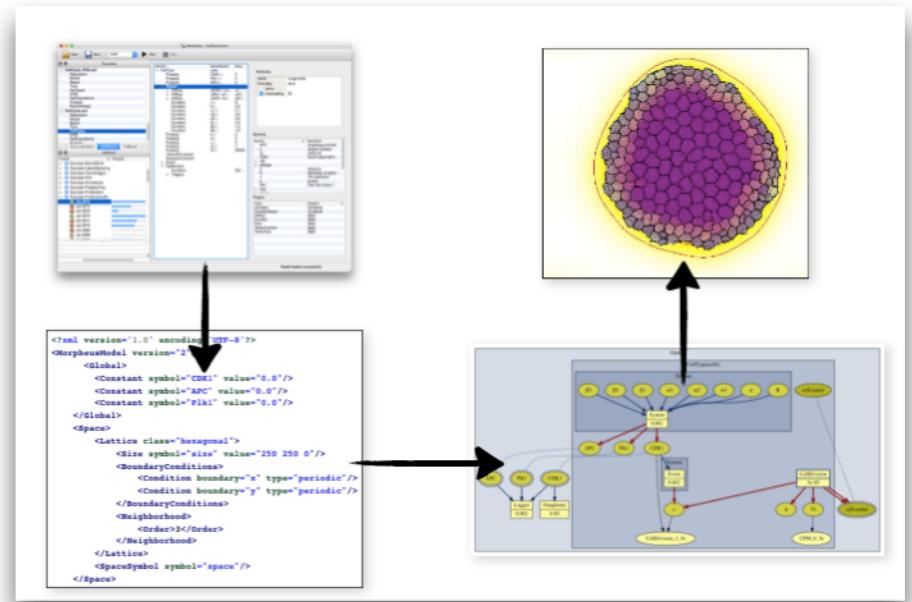
MathExpressions

Environment for tightly coupled Rule and DiffEqn. Expressions with a System are synchronously updated and may contain recurrence relations.

- solver: numerical solver for DiffEqn: Euler (1st order), Heun (aka explicit trapezoid rule, 2nd order) or Runge-Kutta (4th order)
- time-step: integration step size.
- time-scaling (optional): scales the dynamics of System to the simulation time. Equivalent to multiplying all DiffEqn in the System with a scalar.

Note: Systems define their own Scope. This implies that values of symbols defined within a System are not accessible outside of the System.

Model loaded successfully



Morpheus

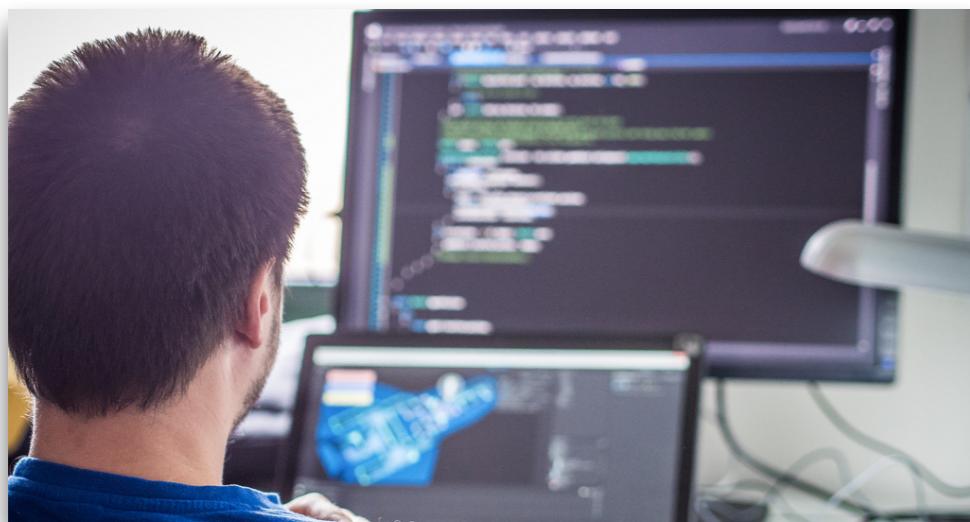
System

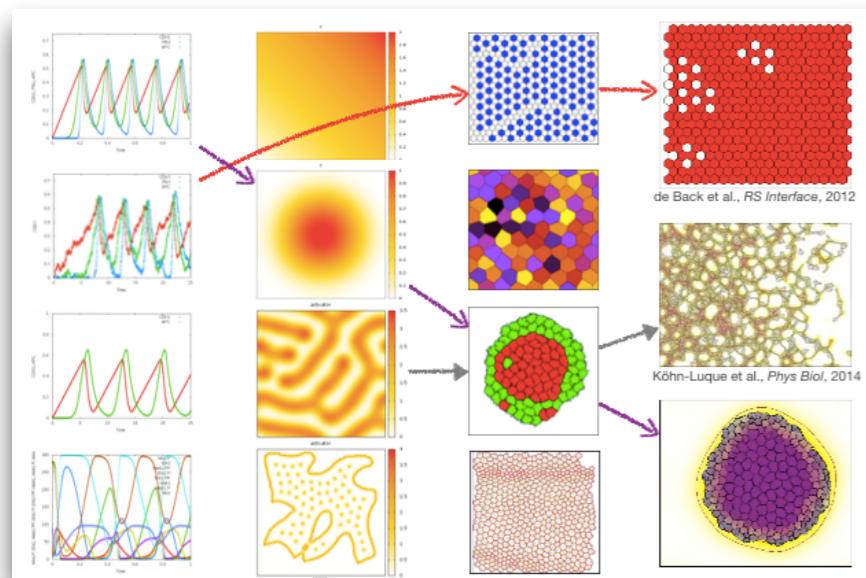
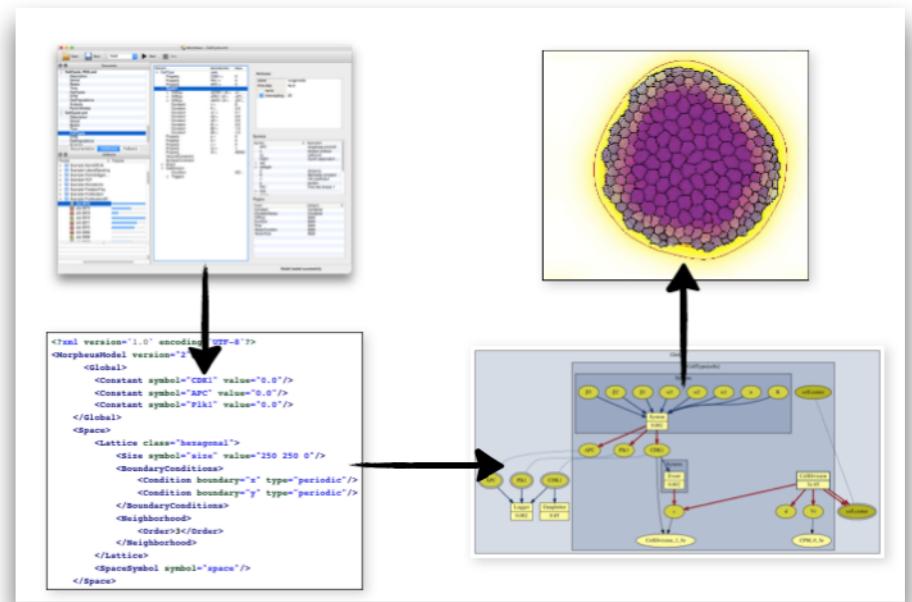
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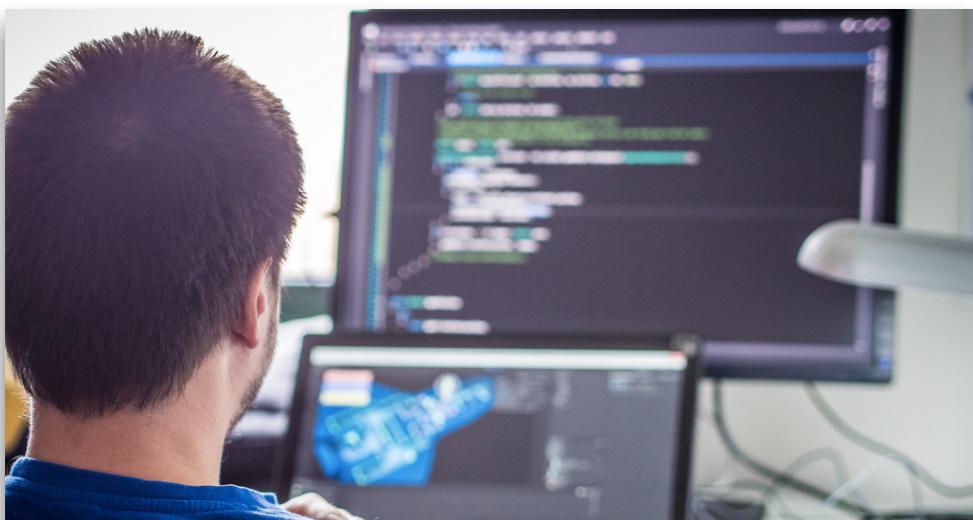
Model loaded successfully





Morpheus

A screenshot of the Morpheus software interface. It shows a hierarchical tree view of model files (CellType, System, Plugins, Symbols), a central workspace with a system diagram, and a status bar at the bottom. Icons for Windows, Mac, and Linux are shown.



A screenshot of a GitLab project page for 'morpheus.lab / morpheus'. It shows the repository details, a file viewer, and a large, colorful 3D visualization of a cell structure.

Future directions

Modeling

- Lattice-free modeling
 - Particle methods
PPM, Sbalzarini, MPI-CBG
 - Vertex models
Chaste as back-end?
- Image-based modeling
 - Integration with Fiji
Tomancak, MPI-CBG
- Adaptive time-stepping
 - Boost ODEInt

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The screenshot shows the homepage of BMC Biophysics, a journal published by BioMed Central. The header features the BioMed Central logo and the text "The Open Access Publisher". A search bar and a "MENU" button are also present. The main navigation menu includes "ABOUT", "ARTICLES" (which is underlined), and "SUBMISSION GUIDELINES". A large, dark rectangular box on the left contains the text "BMC Biophysics". Below the main content area, there is a "RESEARCH ARTICLE" section titled "OPEN ACCESS" followed by the article title: "The biophysical nature of cells: potential cell behaviours revealed by analytical and computational studies of cell surface mechanics". The authors listed are Ramiro Magno, Verônica A Grieneisen, and Athanasius FM Marée. At the bottom, there is copyright information: "BMC Biophysics 2015 8:8 | DOI: 10.1186/s13628-015-0022-x | © Magno et al.; licensee BioMed Central. 2015" and publication details: "Received: 21 November 2014 | Accepted: 24 April 2015 | Published: 12 May 2015".

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- Of modelers
 - User forum
 - Support
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- MSc projects
- Course material
- E-learning material

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Community

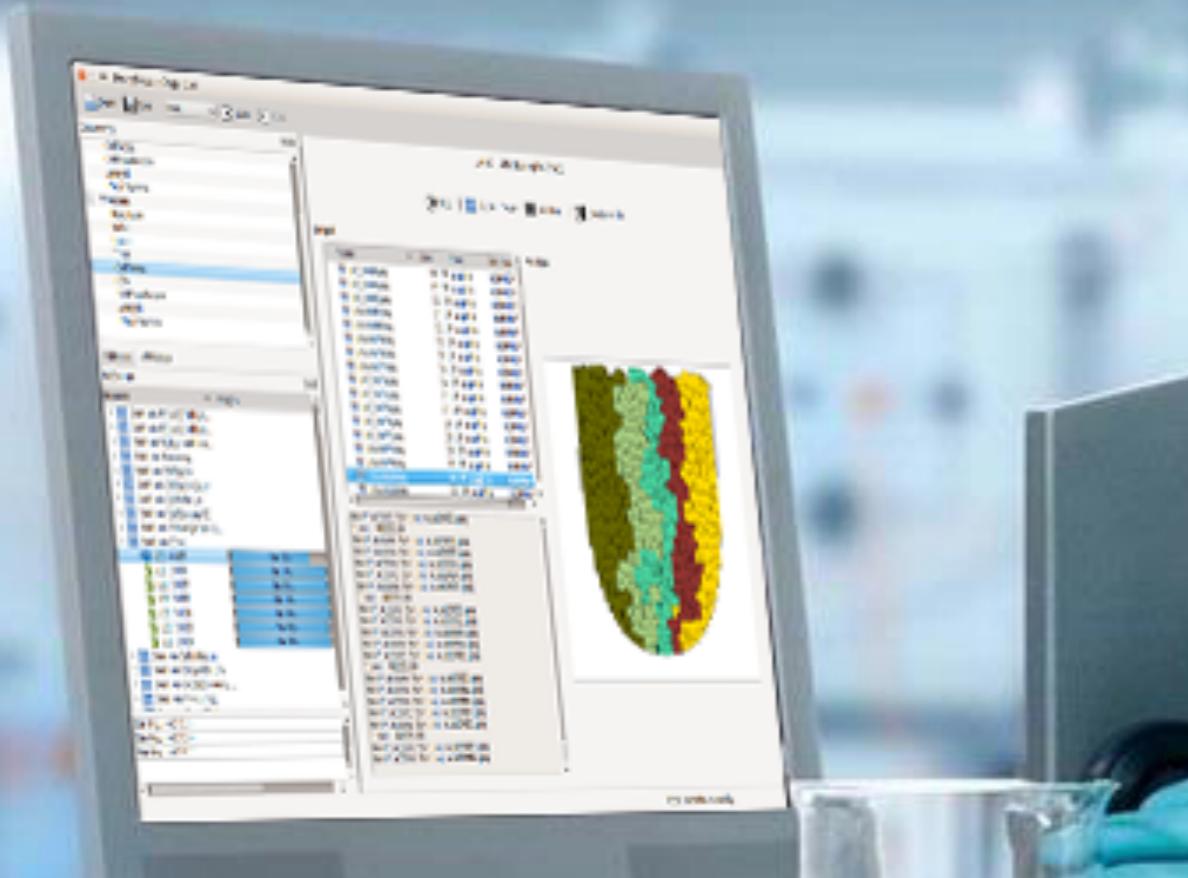
- Of modelers
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Education

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- Course material
- E-learning material

MorpheusML

- Model repository
- SED-ML
- COMBINE archive
- Standardization



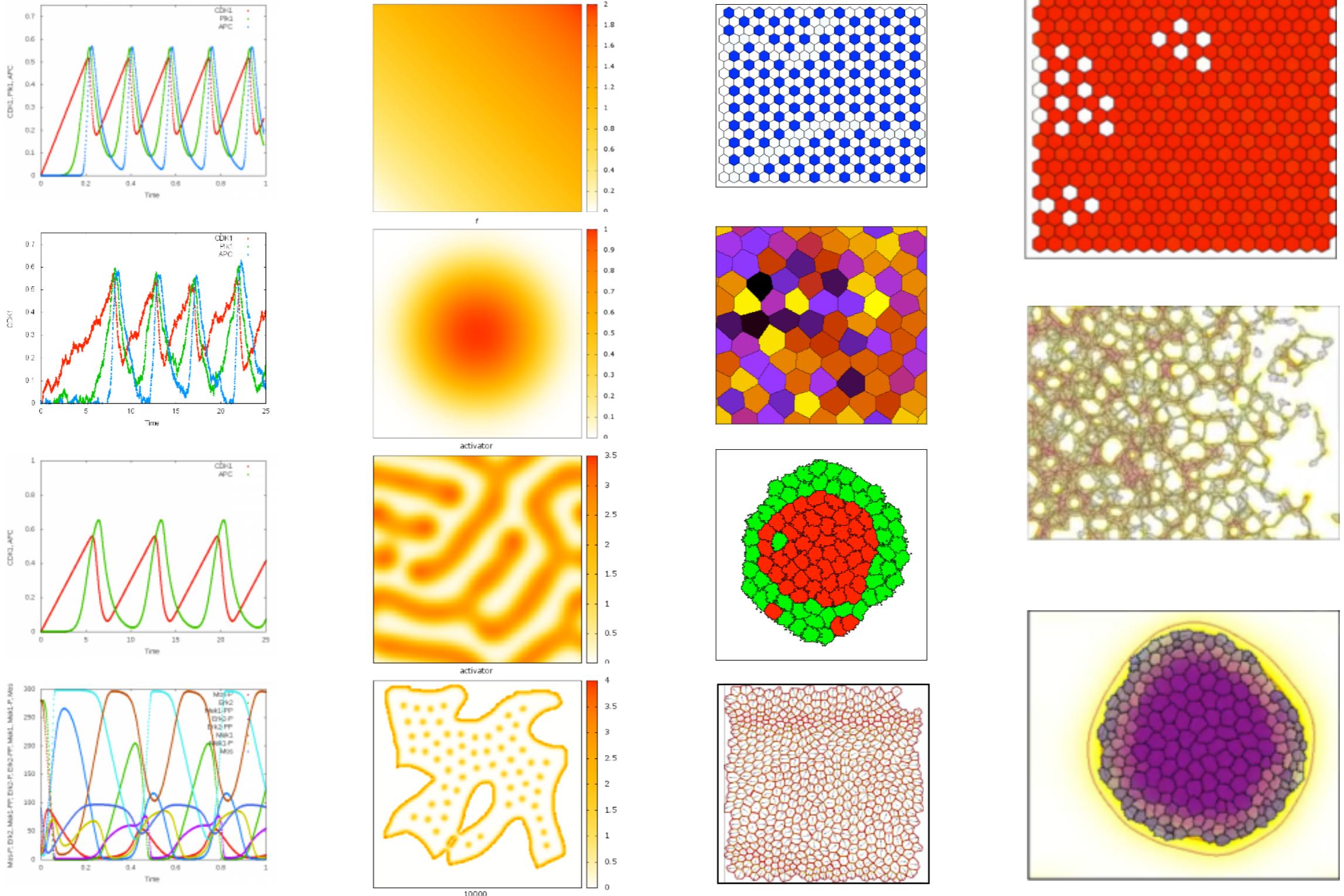
 Morpheus
modeling environment for
multicellular systems biology

Jörn Starruß &
Walter de Back
TU Dresden



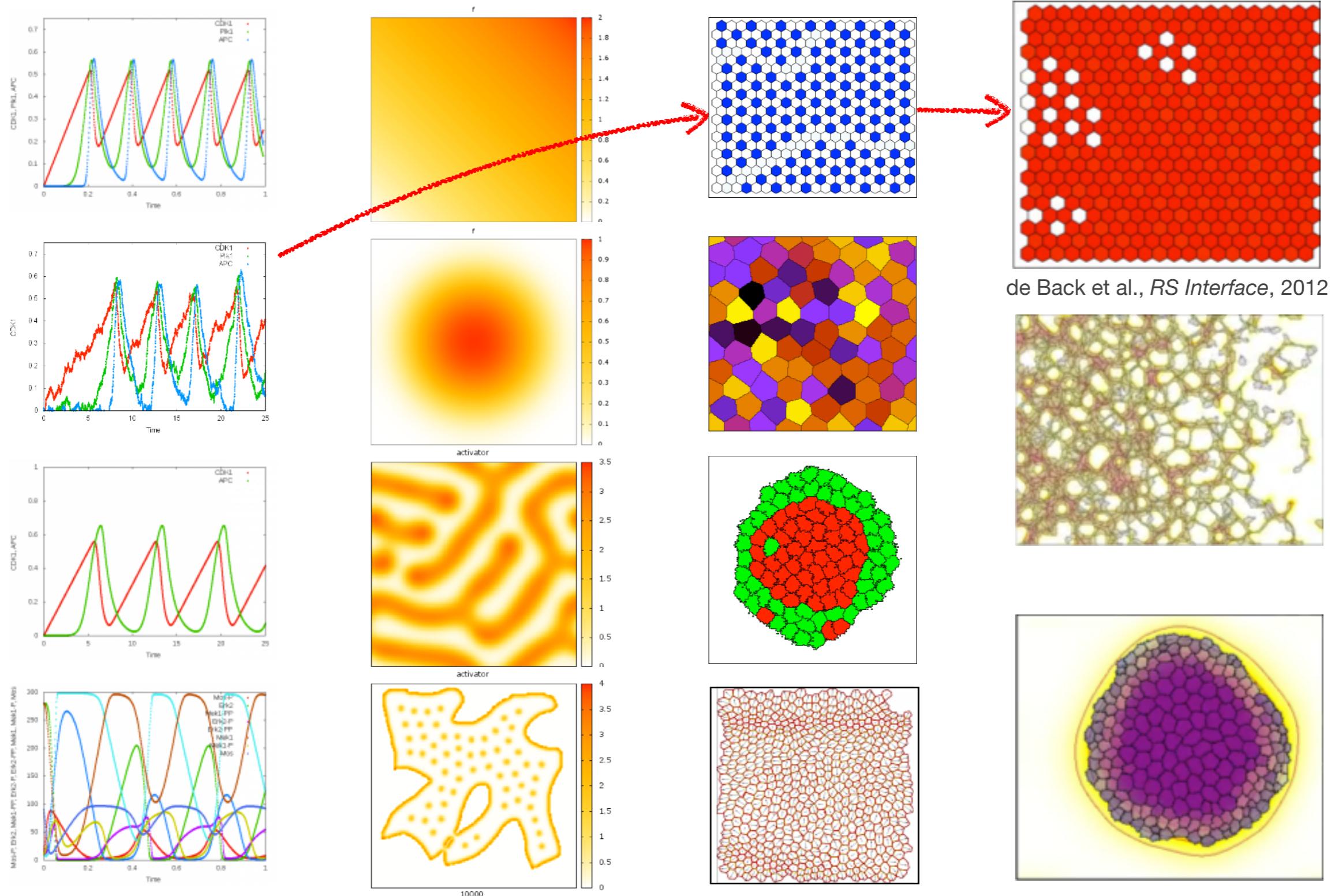
Multi-scale models

Coupling model formalisms



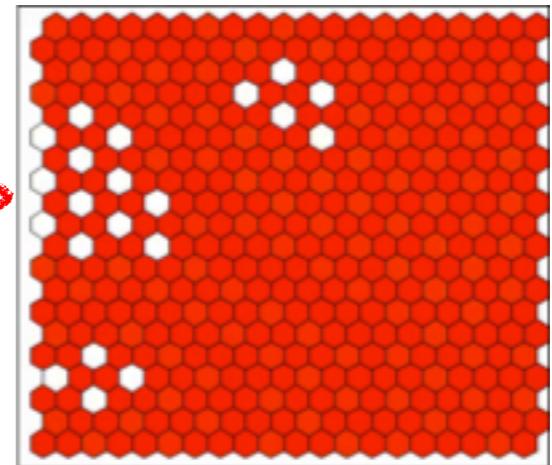
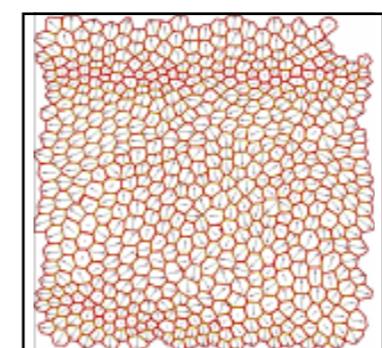
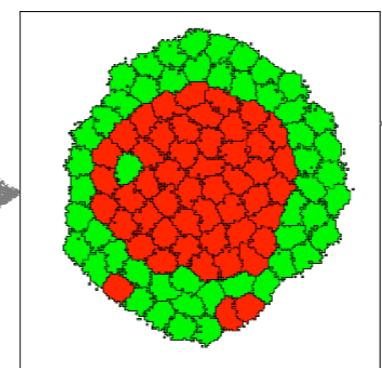
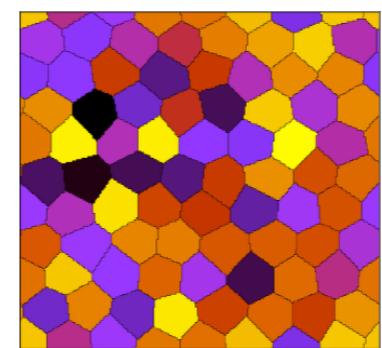
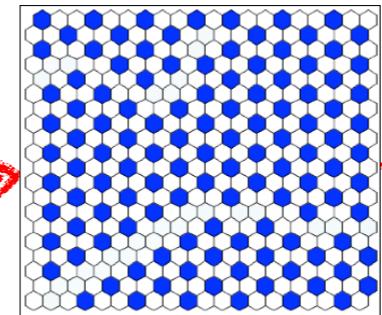
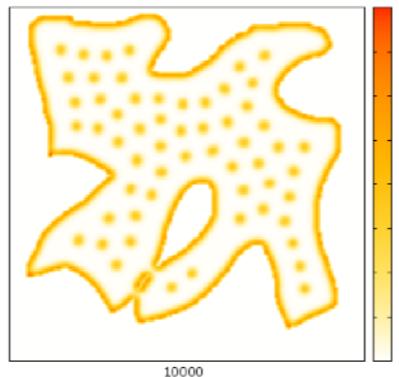
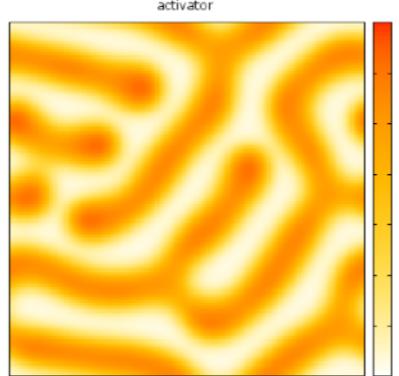
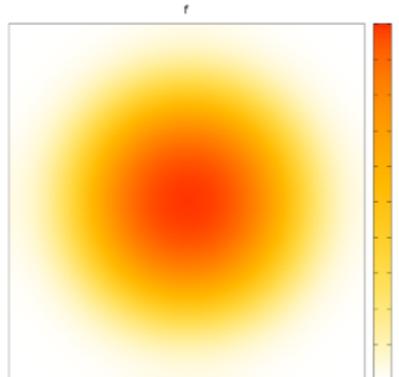
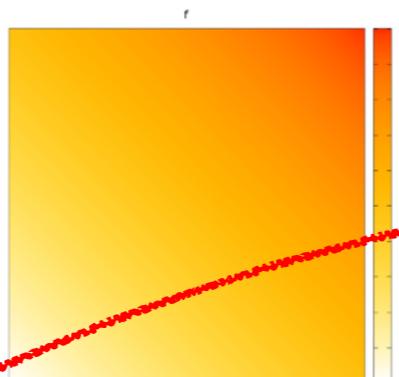
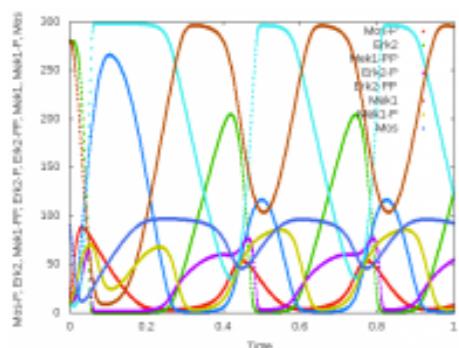
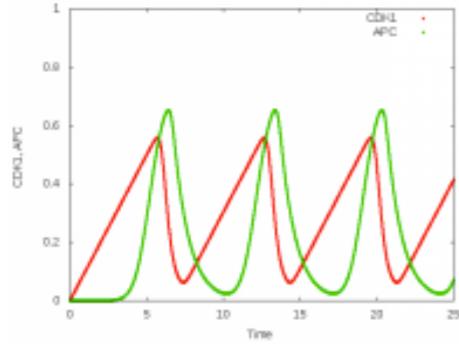
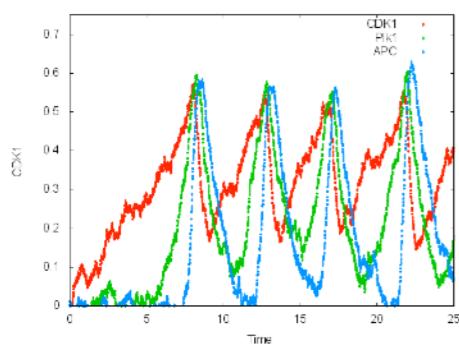
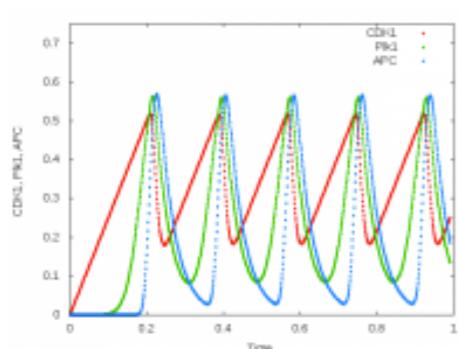
Multi-scale models

Coupling model formalisms

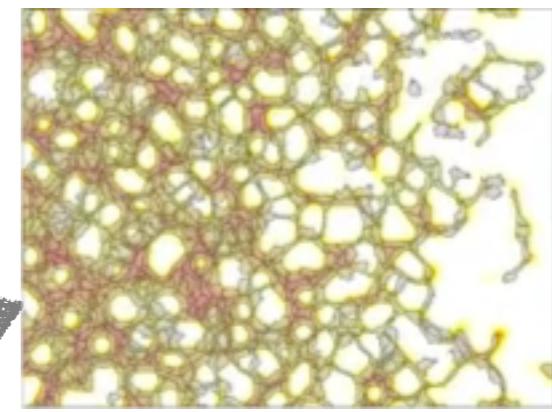


Multi-scale models

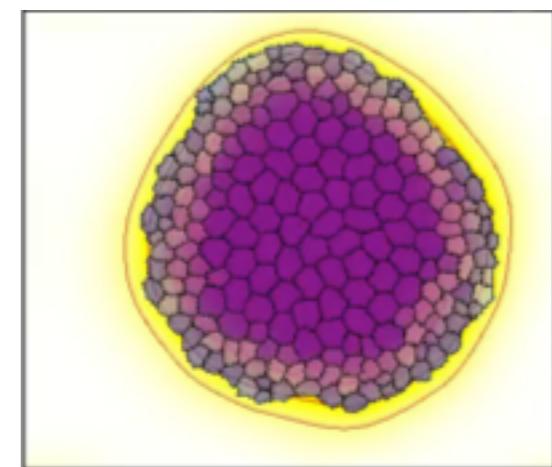
Coupling model formalisms



de Back et al., *RS Interface*, 2012

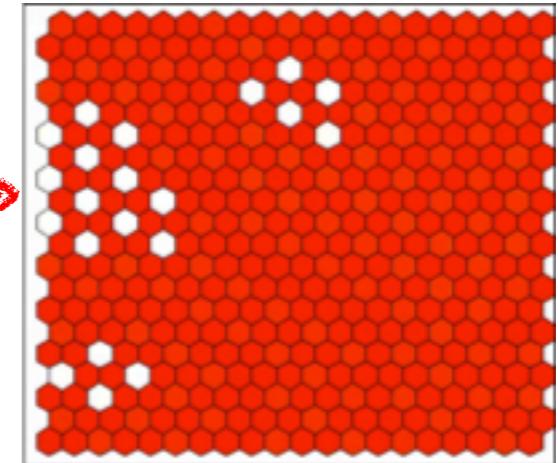
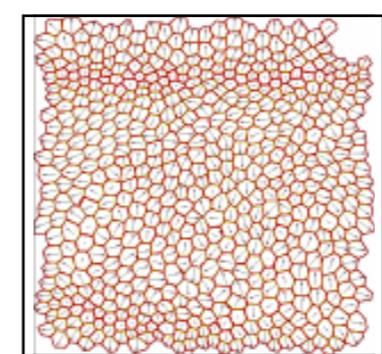
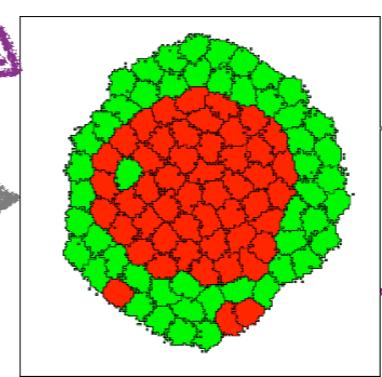
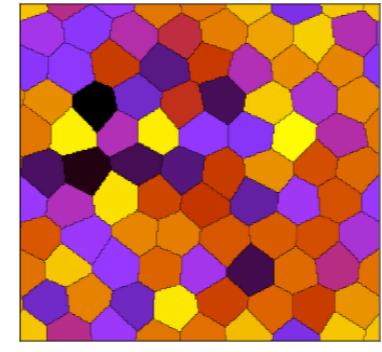
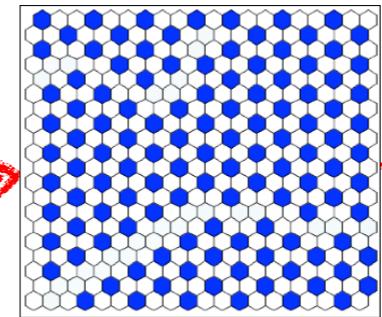
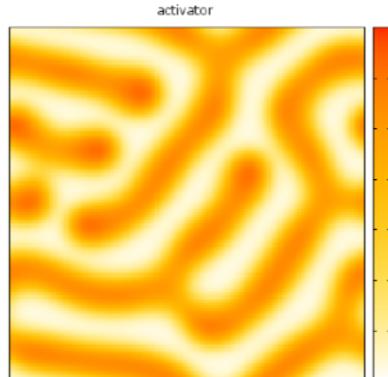
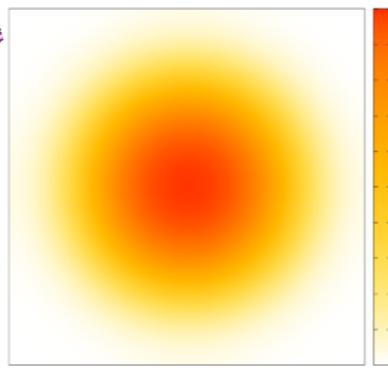
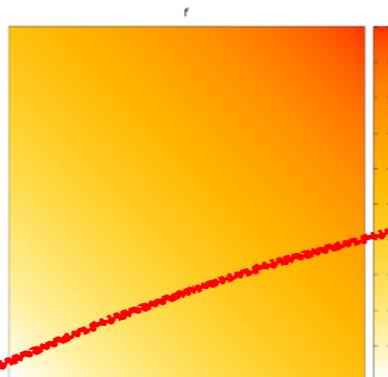
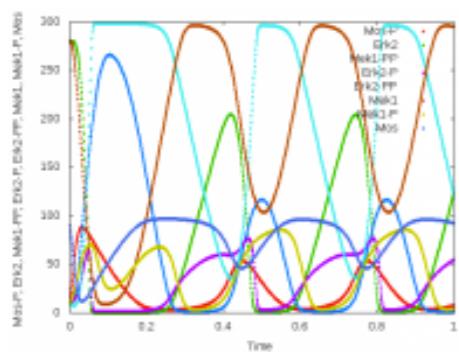
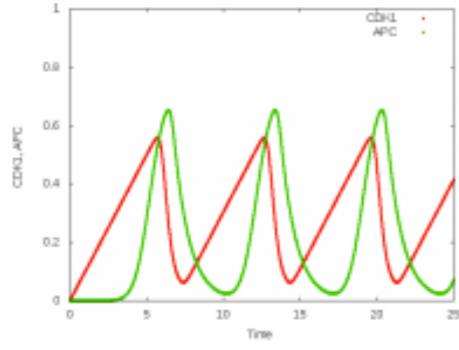
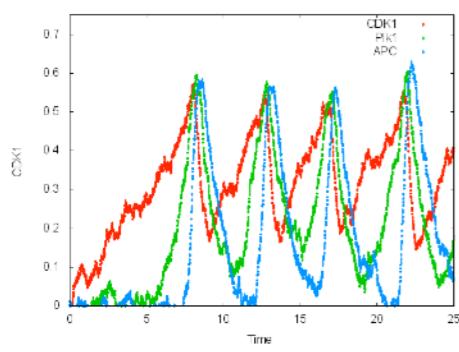
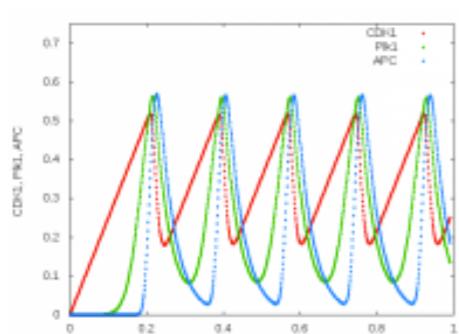


Köhn-Luque et al., *Phys Biol*, 2014

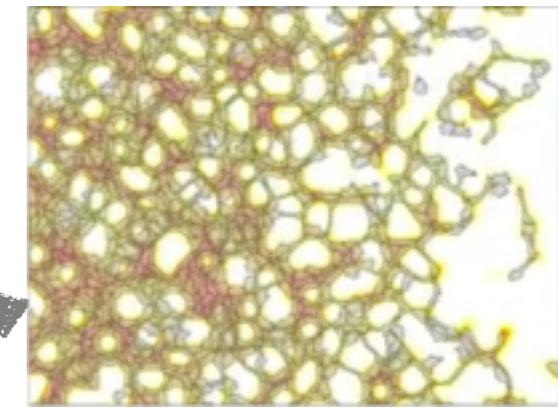


Multi-scale models

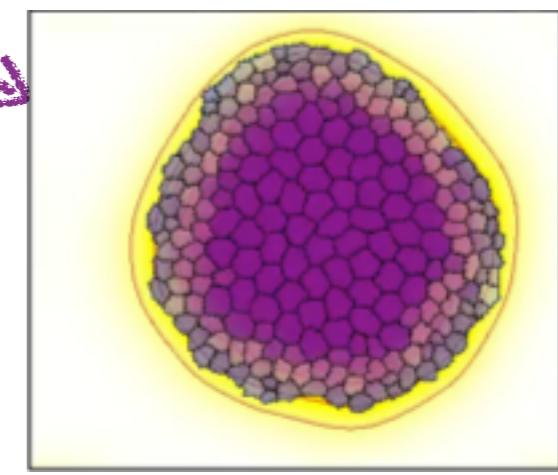
Coupling model formalisms



de Back et al., *RS Interface*, 2012



Köhn-Luque et al., *Phys Biol*, 2014



Morpheus - CellCycle.xml

Open Save local Start Stop

Documents

- CellCycle_PDE.xml
- Description Global Space Time CellTypes CPM CellPopulations Analysis ParamSweep
- Cellcycle.xml**
- Description Global Space Time **CellTypes**
- CPM CellPopulations Analysis
- ParamSweep

CellTypes

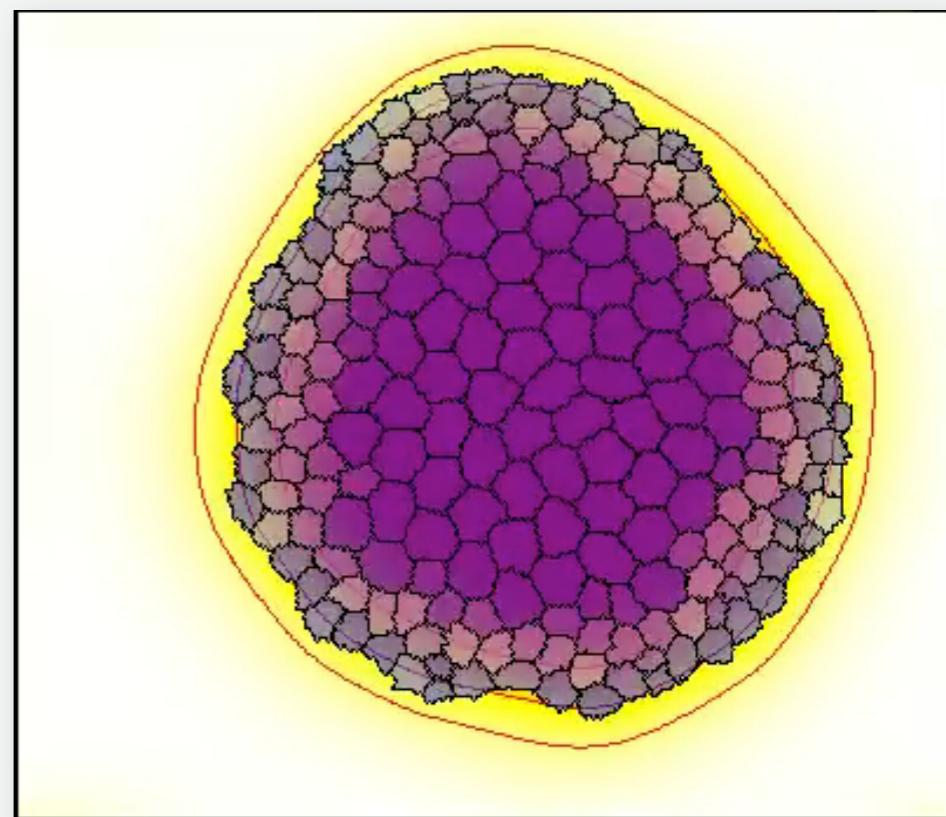
Documentation JobQueue FixBoard

Process

- Example-GameOfLife
- Example-LateralSignaling
- Example-ParticleAggregates
- Example-PCP
- Example-Persistence
- Example-PredatorPrey
- Example-Proliferation
- Example-Proliferation2D

Job Queue

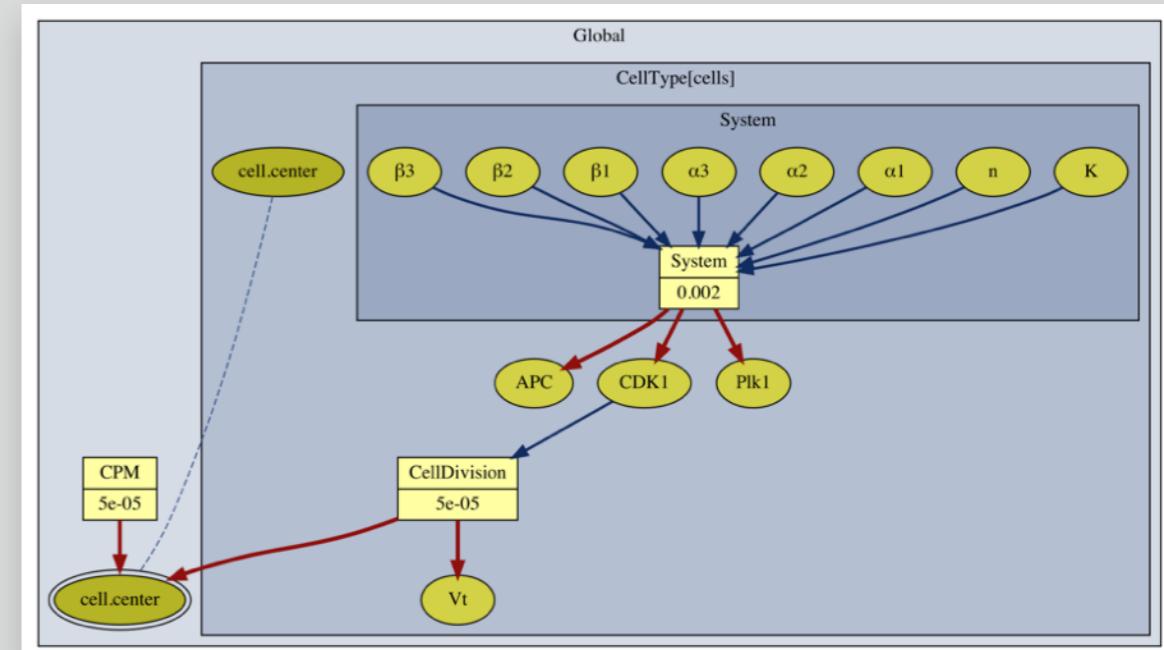
Model loaded successfully



```

<?xml version='1.0' encoding='UTF-8'?>
<MorpheusModel version="2">
  <Global>
    <Constant symbol="CDK1" value="0.0"/>
    <Constant symbol="APC" value="0.0"/>
    <Constant symbol="Plk1" value="0.0"/>
  </Global>
  <Space>
    <Lattice class="hexagonal">
      <Size symbol="size" value="250 250 0"/>
      <BoundaryConditions>
        <Condition boundary="x" type="periodic"/>
        <Condition boundary="y" type="periodic"/>
      </BoundaryConditions>
      <Neighborhood>
        <Order>3</Order>
      </Neighborhood>
    </Lattice>
    <SpaceSymbol symbol="space"/>
  </Space>

```



Morpheus - CellCycle.xml

Open Save local start Stop

Documents

CellCycle_PDE.xml

Description Global Space Time CellTypes CPM CellPopulations Analysis ParamSweep Cellcycle.xml Description Global Space Time CellTypes CPM CellPopulations Analysis ParamSweep Cellcycle

CellTypes CPM CellPopulations Analysis ParamSweep Cellcycle

Documentation JobQueue FixBoard

Process

- Example-GameOfLife
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- Example-Proliferation2D

Plugins

Model loaded successfully

Element

Element	Name/Symbol	Value	
CellType	Property	CDK1 = 0	
	Property	Plk1 = 0	
	Property	APC = 0	
	System	Diffeq	$dCDK1 / dt = \alpha_1 \cdot \beta_1 \cdot APC \cdot CDK1 - \alpha_2 \cdot Plk1 \cdot CDK1$
		Diffeq	$dPlk1 / dt = \alpha_2 \cdot APC \cdot CDK1 - \alpha_3 \cdot Plk1^2$
		Diffeq	$dAPC / dt = \alpha_3 \cdot Plk1^2 - \alpha_4 \cdot APC$
		Constant	n = 8
		Constant	K = 0.5
		Constant	$\alpha_1 = 0.1$
		Constant	$\alpha_2 = 3.0$
Constant		$\alpha_3 = 3.0$	
Constant		$\alpha_4 = 1.0$	
Property	p = 0		
Property	d = 0		
Property	c = 0		
Property	cc = 1		
VolumeConstraint	Vt = 25000		
SurfaceConstraint			
Event			
CellDivision			
Condition			
Triggers			

Attributes:

solver	runge-kutta
time-step	4e-2
<input type="checkbox"/> name	
<input checked="" type="checkbox"/> time-scaling	20

Symbols

Symbol	Description
APC	Anaphase-promoting complex
c	division timeout
cc	cellcount
CDK1	Cyclin-dependent kinase 1
cell	celltype
divisions	Michaelis constant
d	Hill coefficient
K	portion
n	Polo-like kinase 1
p	size

Plugins

Plugin	Category
Constant	Container
ConstantVector	Container
Diffeq	Math
Function	Math
Rule	Math
VectorFunction	Math
VectorRule	Math

