

Mathematical Modeling for Cell Biology

CellBio 24 workshop

Sunday, December 15th

In order of appearance: Stefan Hoops, Leslie Loew, Michael Blinov, Ann Cowan

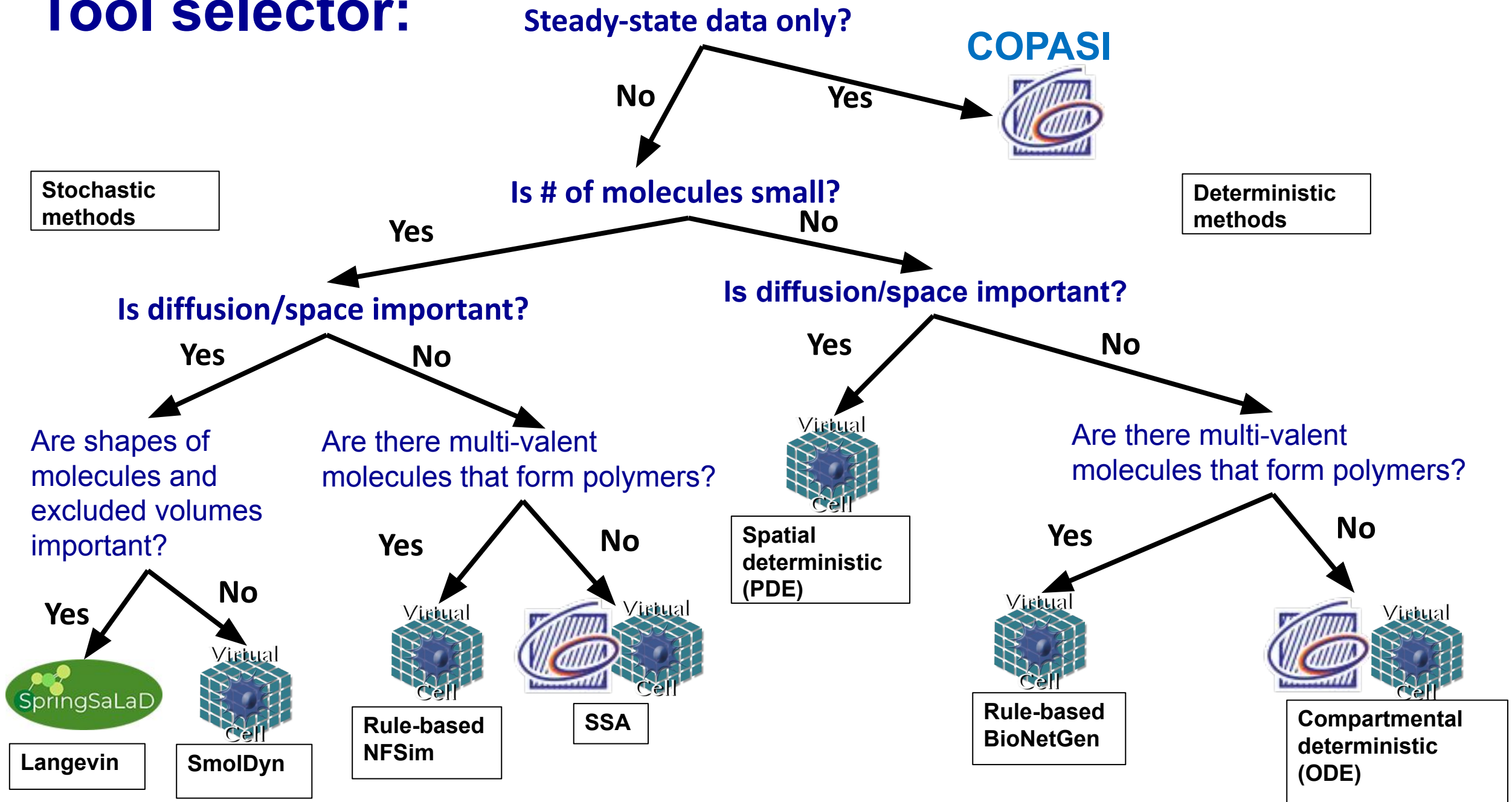
Introduce kinetic simulations, steady state analysis, parameter estimation, spatial modeling, rule-based models, demonstrating them using two modeling and simulation tools:

COPASI (<http://copasi.org>) and Virtual Cell (<http://vcell.org>).

This handout is available at: <https://compcellbio.org/assets/ASCB2024.pdf>

See also: <https://compcellbio.org/>

Tool selector:



Capabilities of our modeling tools:

METHODS	COPASI	VCell
Compartmental deterministic modeling (ODE)	✓	✓
Stochastic compartmental modeling (SSA)	✓	✓
Spatial deterministic modeling (PDE)		✓
Steady-state modeling	✓	
Stochastic differential equations (SDE)	✓	
Parameter fitting	✓	✓ (COPASI)
Compartmental rule-based modeling of multi-component molecules		✓ (BioNetGen)
Compartmental agent-based modeling of multi-component molecules		✓ (NFsim)
Spatial stochastic modeling		✓ (Smoldyn)
Spatial stochastic modeling accounting for volumes		✓ (SpringSalad)

Example models for today's workshop

1. **Steady-State, Time Course, and Parameter Fitting with COPASI** ([Negative feedback and ultrasensitivity can bring about oscillations in the mitogen-activated protein kinase cascades](#)) - presented by Stefan Hoops ([Biomodels Database: BIOMD0000000010](#))
2. **Using PDEs to simulate FRAP of a biomolecular condensate** (Cowan and Loew, Biophys. J. 2023, [PUBMED: 37353932](#)) - presented by Leslie Loew (<http://vcell.org/biomodel-255507058>)
3. **Using ImageJ to define initial concentration distribution in reaction-diffusion simulations** (Ding et al., 2020; Current Biology; [PUBMED:32155414](#)) - presented by Michael Blinov (<https://vcell.org/biomodel-169993006>)
4. **Rule-based modeling defining molecules and multi-molecular species** (Nosbisch et al., 2022, JBC; [PUBMED:35367415](#)) - presented by Michael Blinov (<https://vcell.org/biomodel-232498815>)

Learning resources

This presentation: <https://compcellbio.org/assets/ASCB2024.pdf>

COPASI:

<https://vcell.org/support>:

- Multiple Tutorials(including FRAP and Rule-based)

- Links to YouTube channel, CompCellBio lecture videos

Computational Cell Biology Courses

- Online Feb 24-28, 2025 <https://compcellbio.org/ccbworkshop>

- In person CCB Workshop, Summer 2025.

CompCellBio workshops

<https://compcellbio.org/ccbworkshop>

26th Annual CCB Workshop

February 24 - 28, 2025

Please note this is the online format.



**25th On-site Workshop
Computational Cell Biology
July 22-24, 2024**

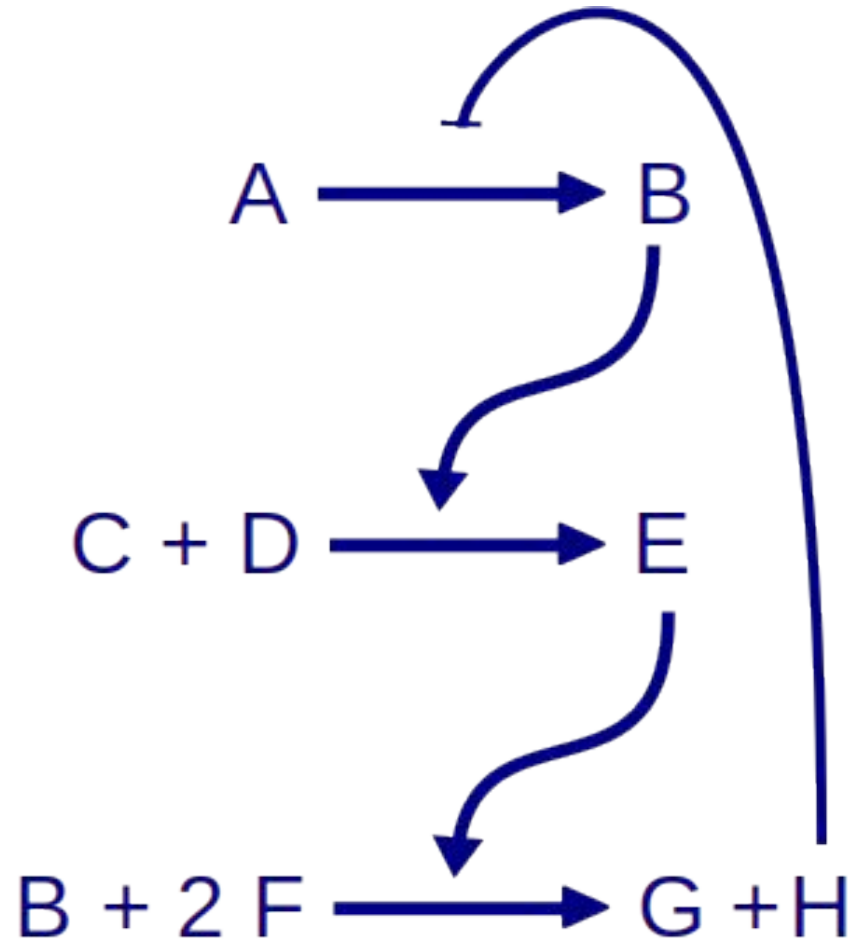
Farmington, CT, USA



COPASI Capabilities

- Time course (deterministic, stochastic, and hybrid algorithm)
- Steady state
- Stoichiometric analysis of the reaction network, including mass conservation analysis and elementary flux modes.
- Optimization of arbitrary components of the model using a range of diverse algorithms.
- Parameter estimation using a range of diverse optimization algorithms. This can be done over several different experiments simultaneously, including mixtures of steady-state and time course experiments.
- Local sensitivity analysis.
- Metabolic control analysis (a special form of sensitivity analysis).
- Time scale separation analysis; this allows definition of fast and slow components of the model, in a time-dependent way.
- Analysis of stochasticity using the linear noise approximation (allows estimating variances and co-variances even in the presence of large numbers of particles).
- Cross sections, which allow to characterize non-linear dynamics properties, such as oscillations and chaos.
- Lyapunov exponents, which allows to establish if the system dynamics are chaotic.

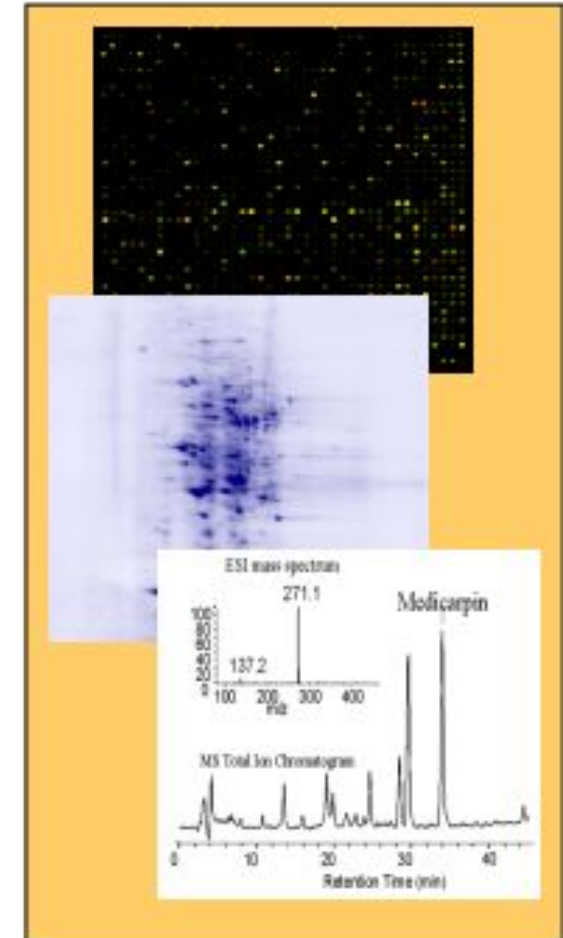
Biochemical Process



Genome

Proteome

Metabolome



Mathematical Model

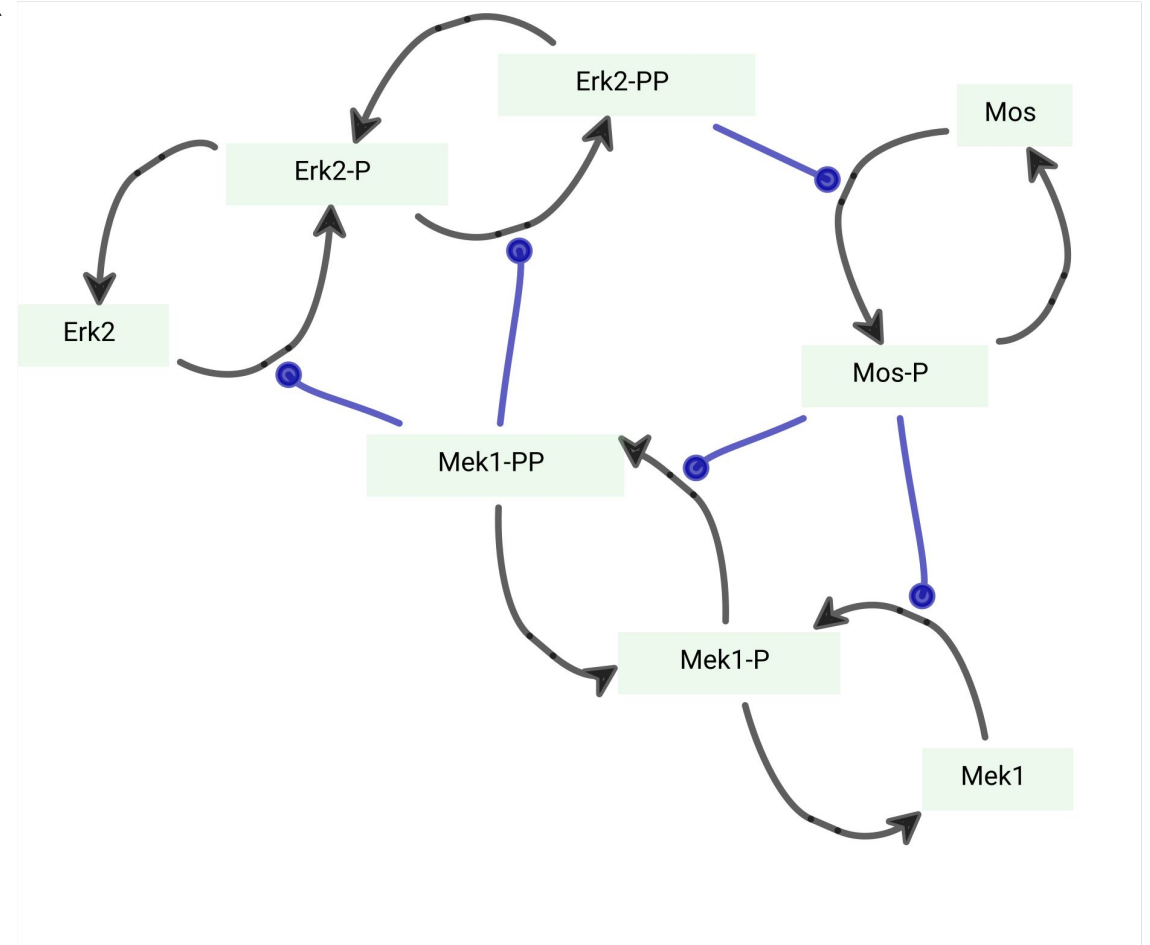
$$\begin{pmatrix} \dot{A} \\ \dot{B} \\ \dot{C} \\ \dot{D} \\ \dot{E} \\ \dot{F} \\ \dot{G} \\ \dot{H} \end{pmatrix} = \begin{pmatrix} -1 & 0 & 0 \\ 1 & 0 & -1 \\ 0 & -1 & 0 \\ 0 & -1 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & -2 \\ 0 & 0 & 1 \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} v_1(A, B, H) \\ v_2(B, C, D, E) \\ v_3(B, E, F, G, H) \end{pmatrix}$$

$$\dot{\mathbf{X}} = \mathbf{N} \mathbf{v} \quad \text{with:} \quad \mathbf{X} = \begin{pmatrix} X_1 \\ X_2 \\ \dots \\ X_n \end{pmatrix} \quad \mathbf{v} = \begin{pmatrix} v_1 \\ v_2 \\ \dots \\ v_m \end{pmatrix}$$

Example 1: COPASI

Kholodenko B. 2000: Negative feedback and ultrasensitivity can bring about oscillations in the mitogen-activated protein kinase cascades

- **Activated Mos activates Mek1**
- **Activated Mek1 activates Erk2**
- **Activated Erk2 activates Mos**



Time Course

Time Course

☐ update model ☒ executable

Duration, Intervals

Output Time Points

Duration [s] 9000

Intervals 1000

Interval Size [s] 9

☐ Automatic

☐ Start in Steady State

☐ Suppress Output Before [s] 0

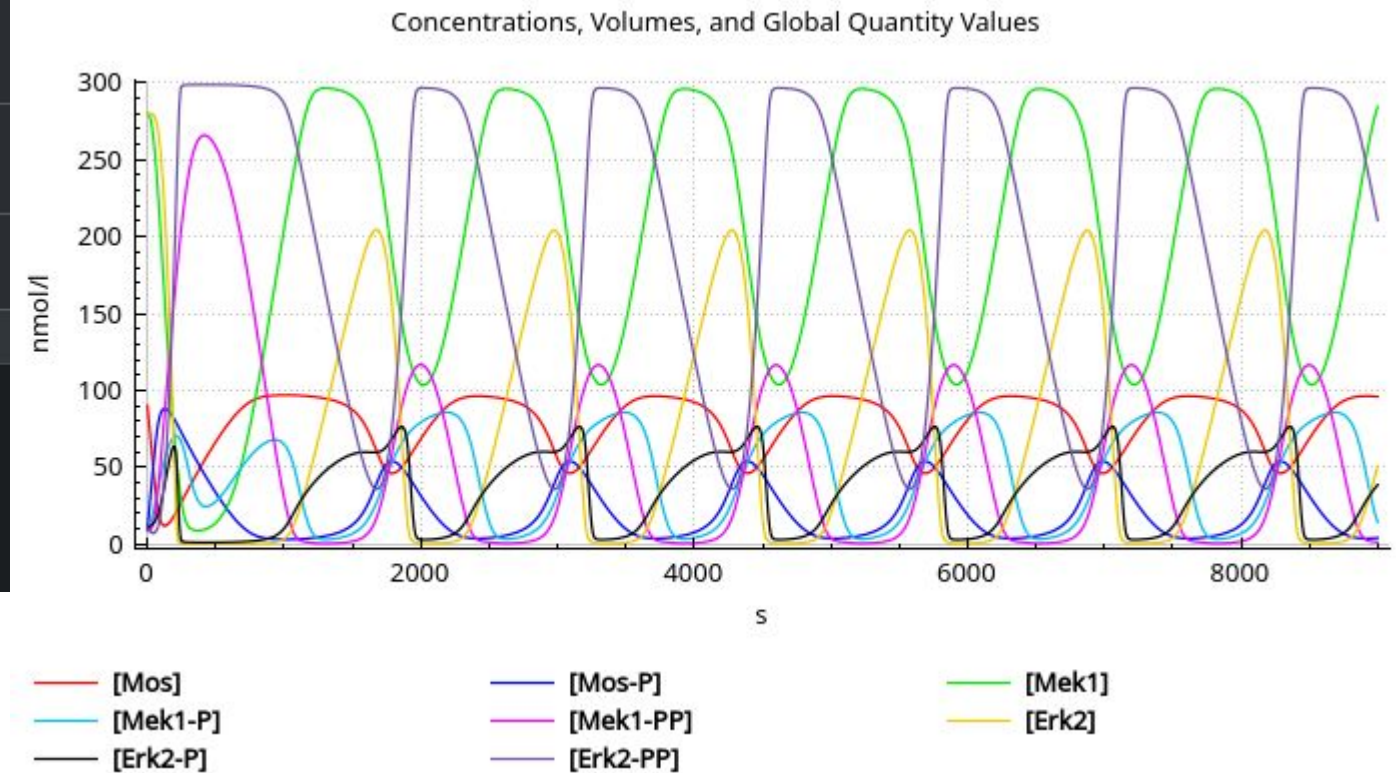
☐ Output Events ☒ Save Result in Memory

Integration Interval [s] 0 to 9000

Output Interval [s] 0 to 9000

Method Deterministic (LSODA)

Name	Value
Integrate Reduced Model	<input type="checkbox"/>
Relative Tolerance	1e-06
Absolute Tolerance	1e-12
Max Internal Steps	100000
Max Internal Step Size	0



Steady State

Steady State

Name	Value
Resolution	1e-09
Derivation Factor	0.001
Use Newton	<input checked="" type="checkbox"/>
Use Integration	<input checked="" type="checkbox"/>
Use Back Integration	<input type="checkbox"/>
Accept Negative Concentrations	<input type="checkbox"/>
Iteration Limit	50
Maximum duration for forward integration	1000000000
Maximum duration for backward integration	1000000
Target Criterion	Distance and Rate

Steady State Result

A steady state with given resolution was found.

Species Compartments Model Quantities Reactions **Stability** Jacobian (Com

KINETIC STABILITY ANALYSIS

The linear stability analysis based on the eigenvalues of the Jacobian matrix is only valid for steady states.

Summary:

This state is unstable,
transient states in its vicinity have oscillatory components.

Eigenvalue statistics:

Largest real part: 0.00158073

Largest absolute imaginary part: 0.00701841

The complex eigenvalues with the largest real part are: $0.00158073 + |-0.00701841i$

3 are purely real

0 are purely imaginary

2 are complex

0 are equal to zero

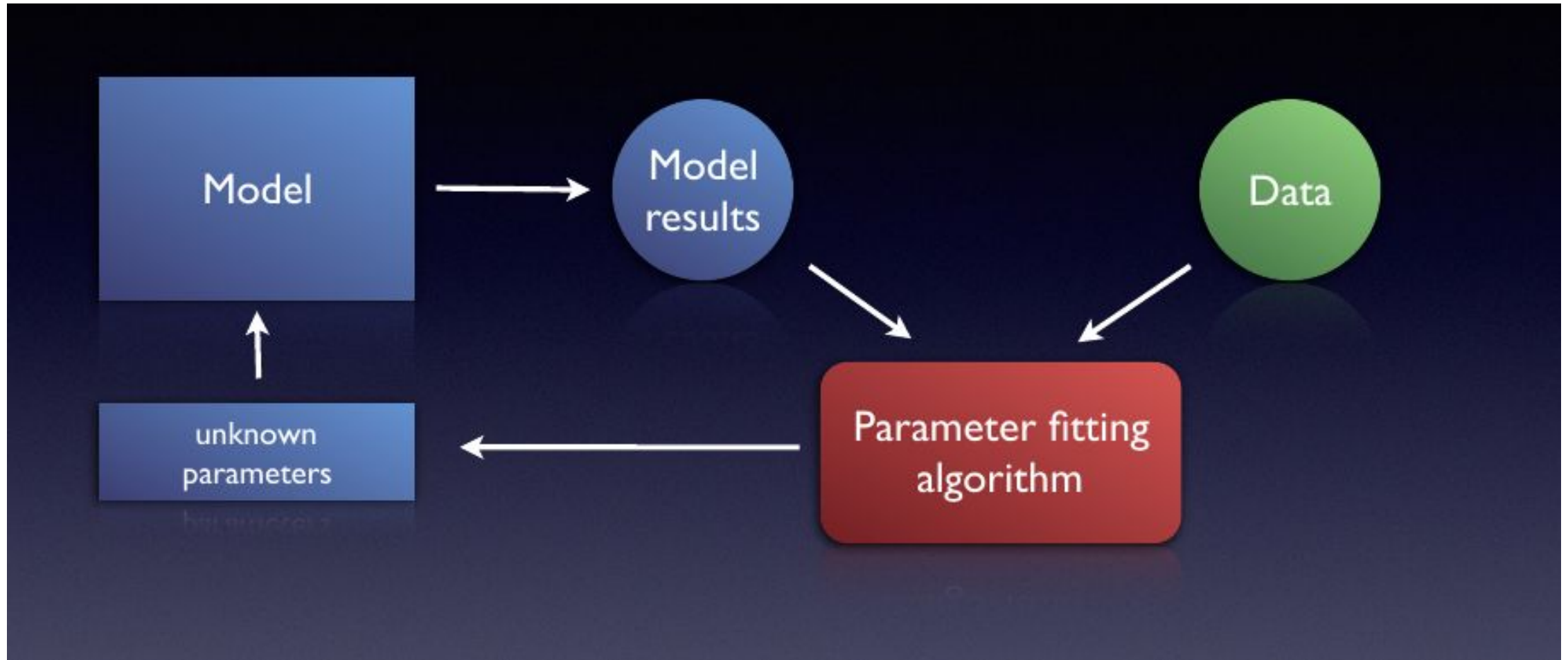
2 have positive real part

3 have negative real part

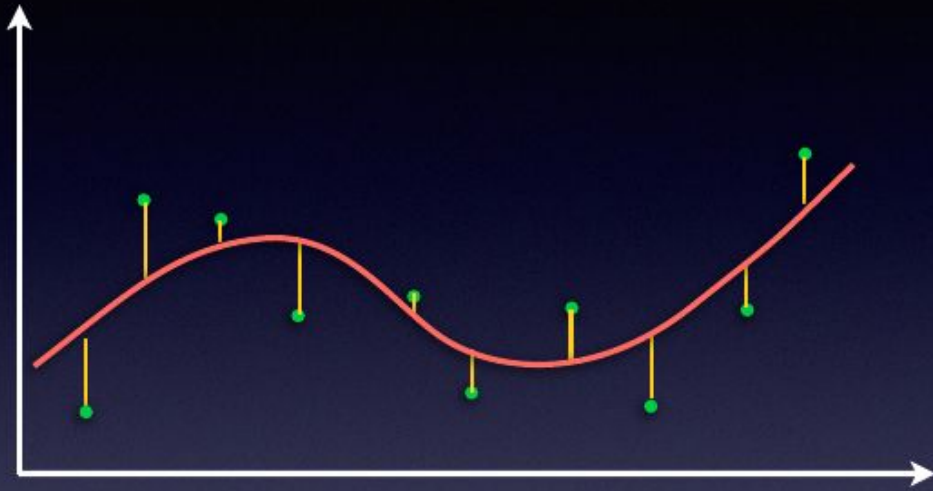
stiffness = 9.70885

time hierarchy = 0.186566

Parameter Estimation



Parameter Estimation



$$D(p) = \sum_{i=1}^N (x_i - y_i(p))^2$$

x_i : measured values for time t_i

$y_i(p)$: simulated values for time t_i , parameter p

Parameter Estimation

Parameter Estimation

☐ update model ☐ executable

☐ Randomize Start Values ☐ Create Parameter Sets ☒ Calculate Statistics ☐ Use Time Sens

Parameters (6) Constraints (0)

1	$0.25 \leq (\text{MAPKKK activation}).V1 \leq 4.75$; Start Value = 0.252586
2	$0.025 \leq (\text{MAPKKK inactivation}).V2 \leq 0.475$; Start Value = 0.410616
3	$0.075 \leq (\text{dephosphorylation of MAPKK-PP}).V5 \leq 1.425$; Start Value = 0.50374
4	$0.075 \leq (\text{dephosphorylation of MAPKK-P}).V6 \leq 1.425$; Start Value = 0.987345
5	$0.05 \leq (\text{dephosphorylation of MAPK-PP}).V9 \leq 0.95$; Start Value = 0.695592
6	$0.05 \leq (\text{dephosphorylation of MAPK-P}).V10 \leq 0.95$; Start Value = 0.745066

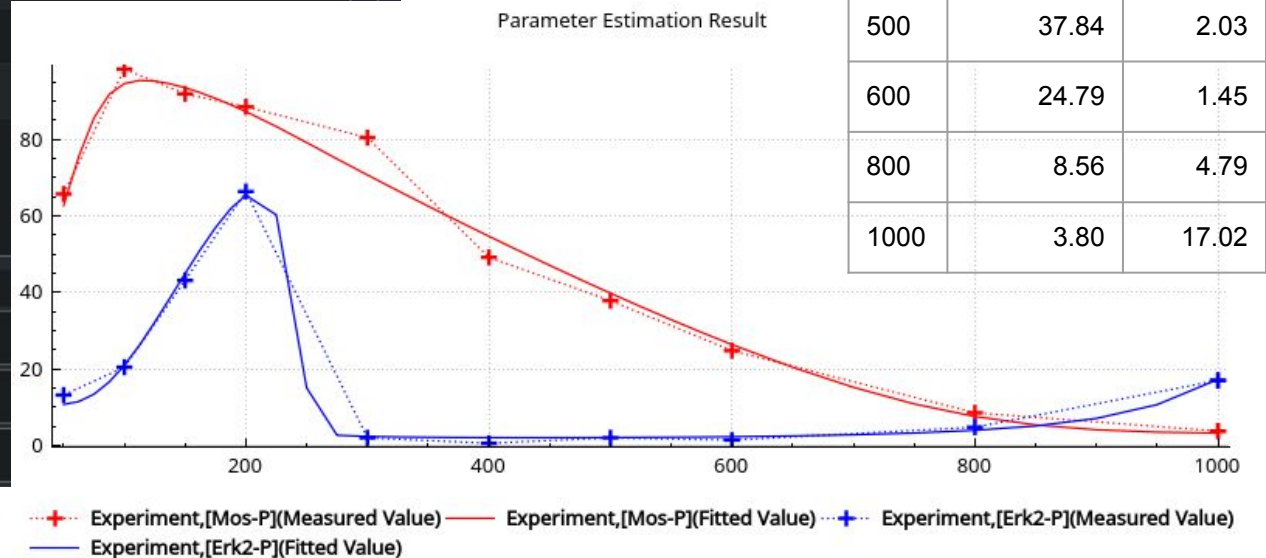
Object (MAPKKK activation).V1

Lower Bound ☐ - Infinity 0.25

Upper Bound ☐ + Infinity 4.75

Start Value 0.252586

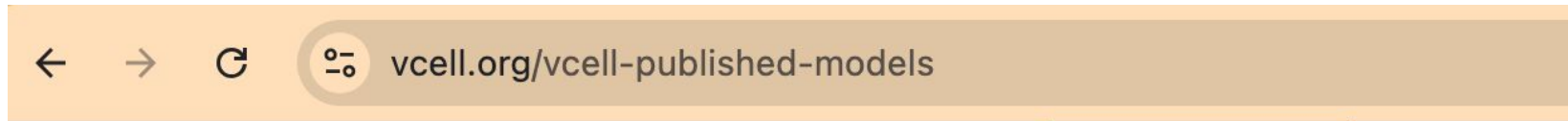
time	MAPKKK-P	MAPK-P
50	65.71	13.20
100	98.34	20.48
150	91.86	43.14
200	88.49	66.36
300	80.44	2.03
400	49.17	0.60
500	37.84	2.03
600	24.79	1.45
800	8.56	4.79
1000	3.80	17.02



VCell Capabilities

- Reaction - Diffusion - Advection - Electrophysiology
- 0, 1, 2 or 3D geometries, optionally from microscope images
- Deterministic and/or stochastic simulations
- Reaction networks or reaction rules
- Parameter scans and COPASI parameter estimation
- Database of models and model components
- Links to external model and pathway resources
- Biological Problems
 - Signaling and metabolic pathways
 - Intracellular trafficking
 - Ion channels
 - Virtual microscopy
 - Fluorescent indicators and probe redistribution

Example 2: Using PDEs to simulate FRAP of a biomolecular condensate



Beyond analytic solution: Analysis of FRAP experiments by spatial simulation of the forward problem.

Cowan, A.E. & Loew, L.M.

Biophys J. 2023 Jun 23;S0006-3495(23)00401-0

[PUBMED:37353932/](#)

[doi: 10.1016/j.bpj.2023.06.013](#)

VCell BioModels referenced in publication

user: les

biomodel name: [FRAP_Membrane_Rel](#)

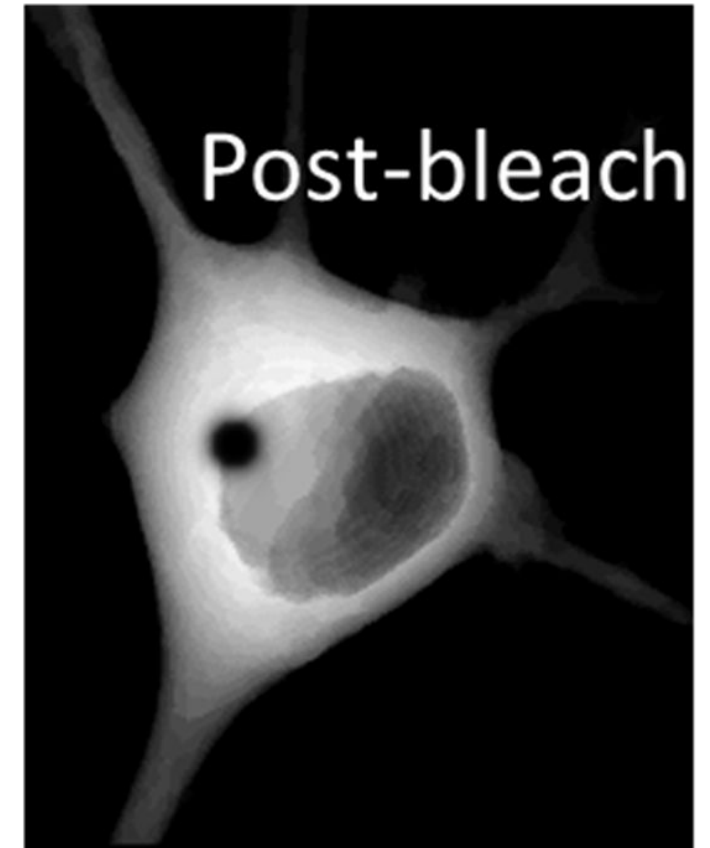
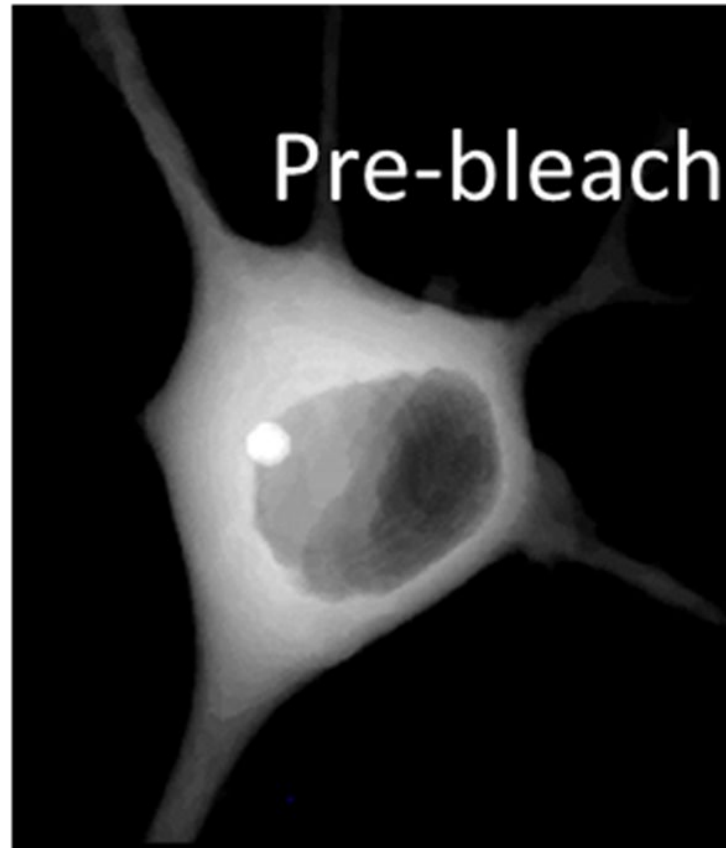
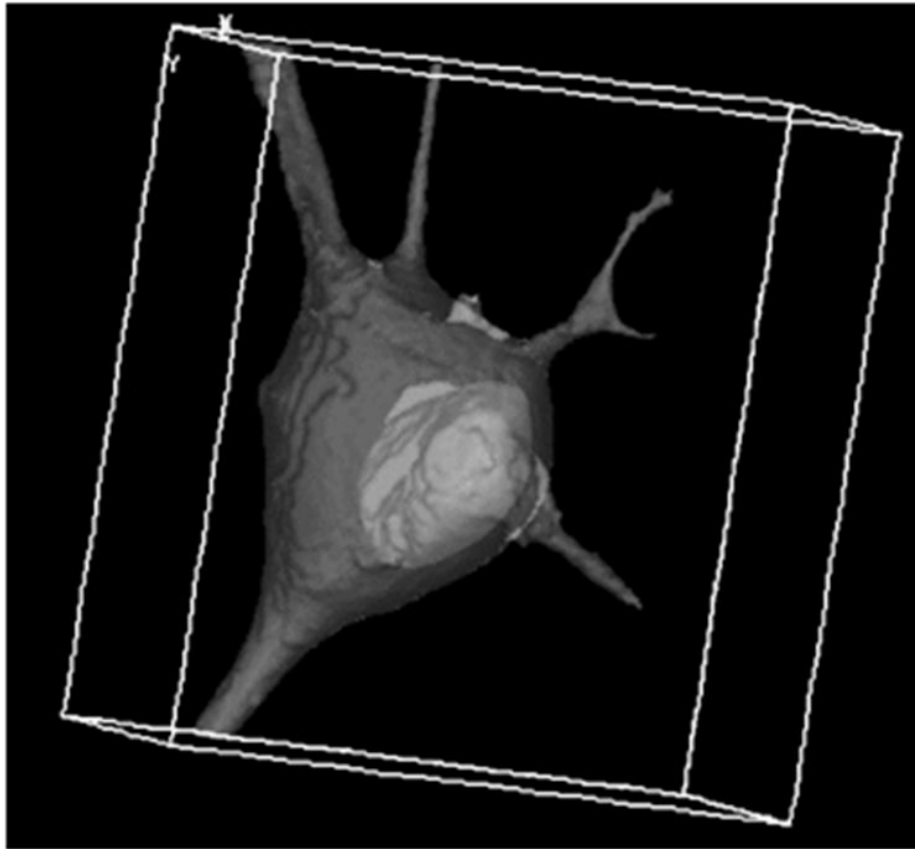
biomodel name: [FRAP_Cyt](#)

biomodel name: [FRAP_Cyt_Membrane_Binding](#)

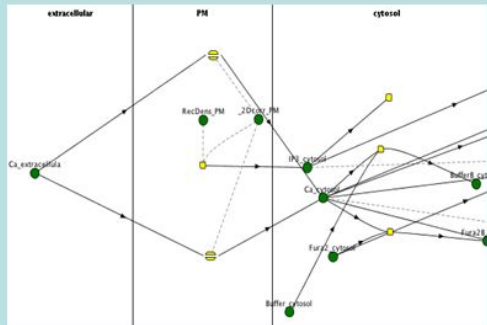
biomodel name: [FRAP Condensate Droplet](#)



Example 2: Using PDEs to simulate FRAP of a biomolecular condensate




Physiology (Biological Mechanisms)



Reaction/Transport Network

Or

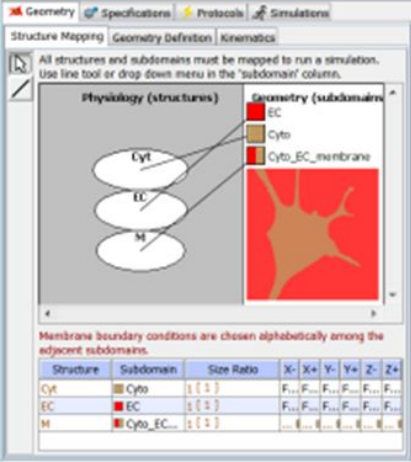


Rule-based modeling
(network free/agents
BioNetGen)

$$k_{on} * (IP3_cyt) * (IP3R_mem) - k_{off} * (IP3Rbound_mem)$$

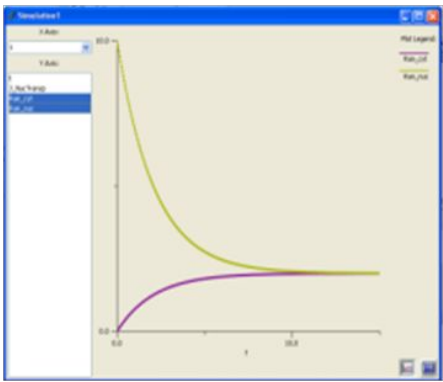
Reaction Rate Expressions

Applications (Physical Model)

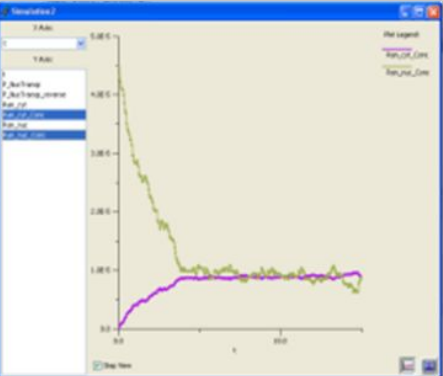


Choice of Simulation types:

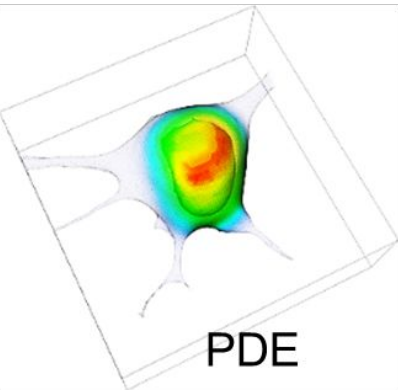
- Ordinary Differential Equations
- Partial Differential Equations
- Non-Spatial Stochastic (Gillespie)
- Spatial Stochastic (Smoldyn)
- Hybrid Spatial Deterministic/stochastic
- Network Free Stochastic



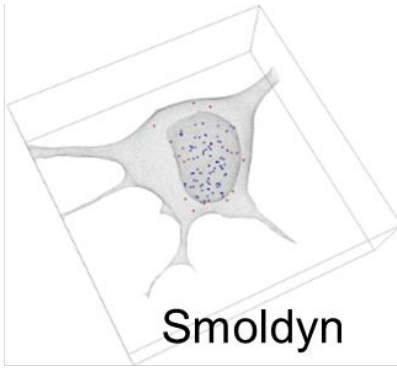
ODE



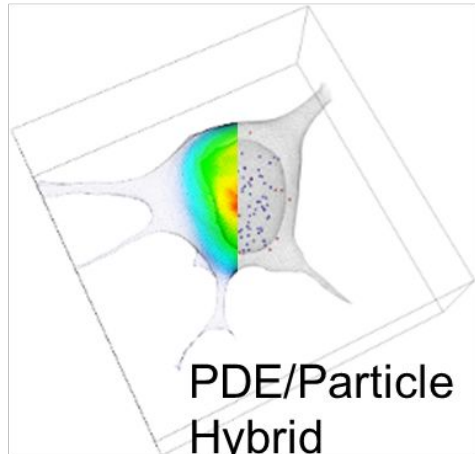
Nonspatial Stochastic
(Gillespie, Hybrid)



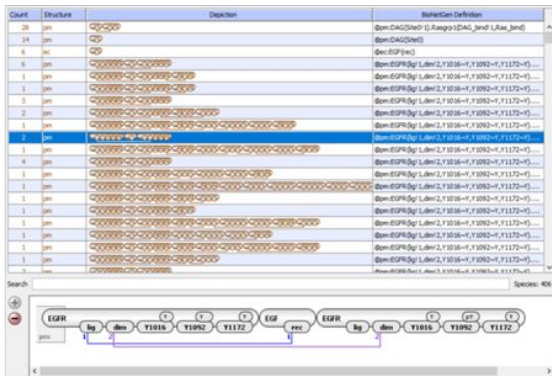
PDE



Smoldyn

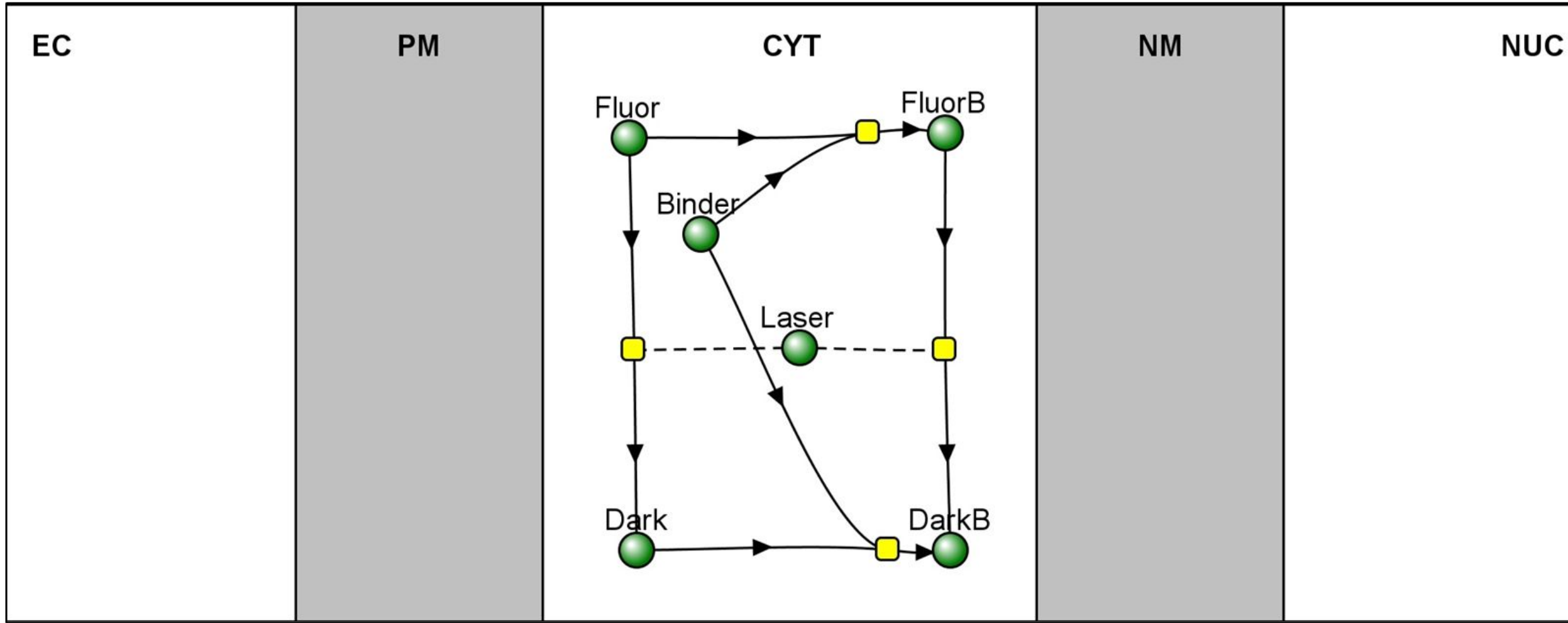


PDE/Particle
Hybrid



NFSim

Example 2: Using PDEs to simulate FRAP of a biomolecular condensate











FRAP Condensate Droplet

▼ Physiology

 Reaction Diagram Reactions (4) Structures (5) Species (6) Molecules (0) Observables (0)

▼ Applications (8)

>  Image-based binding

Name	Math Type	..
 Non spatial to determine SS	explicit network model, co...	(c...
 Image-based binding to liquid droplet, FRAP adjacent to droplet	explicit network model, 3D (...	(c...
 Large Liquid Droplet Edge Dif Barrier Image-based	explicit network model, 3D (...	(c...
 Liquid droplet Edge Dif Barrier Image-based adjacent bleach & FLIP	explicit network model, 3D (...	(c...
 Small Liquid Droplet Edge Dif Barrier Image-based	explicit network model, 3D (...	Sp...
 Large Liquid Droplet Low Kd, low [binder] Edge Dif Barrier Image-b...	explicit network model, 3D (...	(c...
 Liquid Droplet Low Kd, low [binder] Edge Dif Barrier Image-based	explicit network model, 3D (...	(c...
 Large Liquid Droplet Image-based half bleach	explicit network model, 3D (...	(c...

New Application ▼

Delete

More Copy Actions ▼

Compare...

Search



VCell DB ▶

BioModels ▶

▼ Search

 frap[Advanced >>](#)☐ Ha

Search

Sho

Object Properties

Annotations

Problems (0 Errors, 1 Warnings)

✕ Database File Info

Application Name Small Liquid Droplet Edge Dif Barrier Image-based

Description Spherical 2um condensate near nucleus. |

Summary

 math generated Widefield Bleach w fast binding_smaller droplet, BinderD=0 2Photon Bleach w default binding_smaller droplet, BinderD=0

Observables (0)

Applications (8)

- $\frac{d}{dt}$ Image-based binding to liquid drop
- $\frac{d}{dt}$ Large Liquid Droplet Edge Dif Barrie
- $\frac{d}{dt}$ Large Liquid Droplet Image-based I
- $\frac{d}{dt}$ Large Liquid Droplet Low Kd, low [b
- $\frac{d}{dt}$ Liquid droplet Edge Dif Barrier Imag
- $\frac{d}{dt}$ Liquid Droplet Low Kd, low [binder]
- $\frac{d}{dt}$ Non spatial to determine SS
- $\frac{d}{dt}$ Small Liquid Droplet Edge Dif Barrie

Geometry

Specifications

Protocols

Simulations

Parameters, Functions, Units, etc.

highway

VCell DB

BMDB

Pathway Comm

BioModels

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[Advanced >>](#)☐ Has Spatial

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Show All

Biological Models

> My BioModels (les) (27)

> Shared With Me (55)

> Tutorials (4)

Public BioModels (55)

> Published (13)

> Curated (0)

Geometry

Specifications

Protocols

Simulations

Structure Mapping

Geometry Definition

Kinematics

Domain: 3D, size=(74.24,74.24,26.0), origin=(0.0,0.0,0.0)

Edit Domain...

Export...

Edit Image

Replace Geometry ▾

Name

Value

- ec
- cytosol
- Nucleus

Front

Back

Add Subdomain ▾

Delete

Slice View

Surface View

Geometric Region Details

Reset View

Opacity

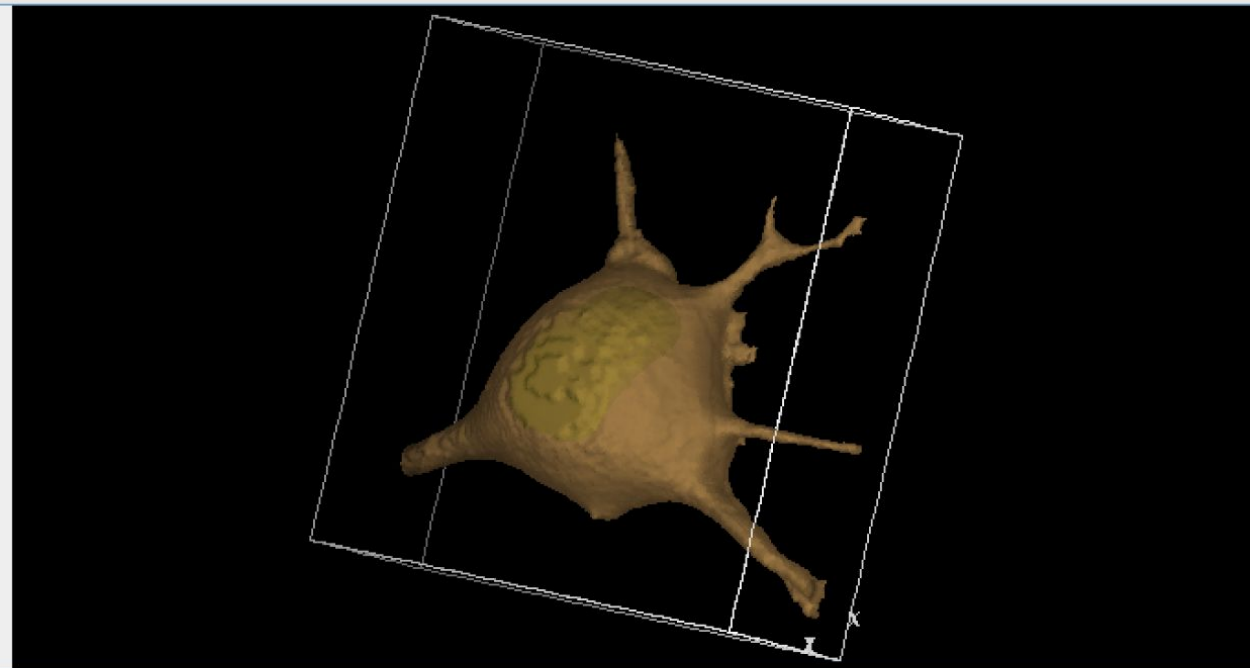
100

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50

25

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Geometry



Specifications



Protocols



Simulations

Species

Reaction

Network

Species	Structure	Depiction	Clamped	Rules	Initial Condition	Well Mixed	Diffusion Constant
Fluor	CYT		<input type="checkbox"/>		1.4462440264001468 μM	<input type="checkbox"/>	$(((((x - 23.0) \wedge 2.0) + ((y - 39.0) \wedge 2.0) + ((z - 13.0) \wedge 2.0) < 4.0) \cdot \text{FluorD}$
Dark	CYT		<input type="checkbox"/>		0.0 μM	<input type="checkbox"/>	$(((((x - 23.0) \wedge 2.0) + ((y - 39.0) \wedge 2.0) + ((z - 13.0) \wedge 2.0) < 4.0) \cdot \text{DarkD}$
Binder	CYT		<input type="checkbox"/>		$(591.4462440264 * (((x - 23.0) \wedge 2.0) + ((y - 39.0) \wedge 2.0) + ((z - 13.0) \wedge 2.0) < 4.0) \cdot \text{BinderD}$	<input type="checkbox"/>	$(((((x - 23.0) \wedge 2.0) + ((y - 39.0) \wedge 2.0) + ((z - 13.0) \wedge 2.0) < 4.0) \cdot \text{BinderD}$
FluorB	CYT		<input checked="" type="checkbox"/>		$(8.553755973599845 * (((x - 23.0) \wedge 2.0) + ((y - 39.0) \wedge 2.0) + ((z - 13.0) \wedge 2.0) < 4.0) \cdot \text{FluorBD}$	<input checked="" type="checkbox"/>	$(((((x - 23.0) \wedge 2.0) + ((y - 39.0) \wedge 2.0) + ((z - 13.0) \wedge 2.0) < 4.0) \cdot \text{FluorBD}$
Laser	CYT		<input type="checkbox"/>		$(\exp(-((z - 10.0) \wedge 2.0) / (2.0 * (\text{sigmaaxial}))) \cdot \text{LaserD}$	<input type="checkbox"/>	0.0 $\mu\text{m}^2 \cdot \text{s}^{-1}$
DarkB	CYT		<input type="checkbox"/>		0.0 μM	<input type="checkbox"/>	$(((((x - 23.0) \wedge 2.0) + ((y - 39.0) \wedge 2.0) + ((z - 13.0) \wedge 2.0) < 4.0) \cdot \text{DarkBD}$

Search



Object Properties

Annotations

Problems (0 Errors, 1 Warnings)



Database File Info

Description	Parameter	Expression	Units
initial concentration for FluorB	initConc	$8.553755973599845 \cdot (((x - 23.0) \wedge 2.0) + ((y - 39.0) \wedge 2.0) + ((z - 13.0) \wedge 2.0) < 4.0)$	μM
diffusion constant for FluorB	diff	$(((((x - 23.0) \wedge 2.0) + ((y - 39.0) \wedge 2.0) + ((z - 13.0) \wedge 2.0) < 4.0) \cdot \text{BinderD}$	$\mu\text{m}^2 \cdot \text{s}^{-1}$

Fluorescence Function Name

fluor

Point Spread Function

☒ Z Projection

☐ Gaussian

Sigma XY

Sigma Z

Choose Fluorescent Species

Dark
Binder
Laser
DarkB



>>

<<

FluorB
Fluor





Name	End Time	Output Option	Solver	Running Status	Results
No edge BarrierWidefield Bleach w fast binding_smaller droplet, BinderD=0	100.0	every 1.0 s	Fully-Impl...	completed	yes
No Edge BarrierWidefield Bleach w defalt binding_smaller droplet, BinderD=0	100.0	every 1.0 s	Fully-Impl...	completed	yes
No Edge BarrierWidefield Bleach w very slow binding_smaller droplet, Binde...	100.0	every 1.0 s	Fully-Impl...	completed	yes
Widefield Bleach w very slow binding_smaller droplet, BinderD=0	100.0	every 1.0 s	Fully-Impl...	completed	yes
Widefield Bleach w fast binding_smaller droplet, BinderD=0.1	100.0	every 1.0 s	Fully-Impl...	completed	yes
2Photon Bleach w default binding_smaller droplet, BinderD=0.1	100.0	every 1.0 s	Fully-Impl...	completed	yes
Fig. 7.B. With DropletD=1, EdgeD=0.1, kf=0.025, kr=2.5	100.0	every 1.0 s	Fully-Impl...	completed	yes
No edge BarrierWidefield Bleach w fast binding_smaller droplet, BinderD=0...	100.0	every 1.0 s	Fully-Impl...	completed	yes
Fig. 6A. DropletD=1, Fig. 6B. DropletD=0.1; for both kr=2.5, kf = 0.025, Bi...	100.0	every 1.0 s	Fully-Impl...	completed	yes
Fig. 6C. DropletD=1, Fig. 6D. DropletD=0.1; for both kr=0.025, kf = 0.000...	100.0	every 1.0 s	Fully-Impl...	completed	yes
Widefield Bleach w very slow binding_smaller droplet, BinderD=0.1	100.0	every 1.0 s	Fully-Impl...	completed	yes

Annotation: [Fig. 6A. DropletD=1, Fig. 6B. DropletD=0.1; for both kr=2.5, kf = 0.025, BinderD=0.1](#)

Settings:

Max timestep	Output	Rel tol	Abs tol
0.1s	every 1.0 sec	1.0E-7	1.0E-9

Mesh: 256x256x35 = 2293760 elements

Geometry size: (74.24,74.24,26.0) microns

View Data

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View Data

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2.0

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All Variables

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ZoomIn

Copy All

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Variables

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ZoomOut

ZoomIn

Copy All

Plot

ROI

Local Scaling

Time

2.0

0

100

All Variables

fluor

Variables

fluor

ZoomOut

ZoomIn

Copy All

Plot

ROI



View Data

Export Data

Post Processing Stats Data

Post Processing Image Data

Time

10.0

0



100

All Variables

Laser_init_um

f ROI

sobj_cytosol1_ec0_size

sobj_Nucleus2_cytosc

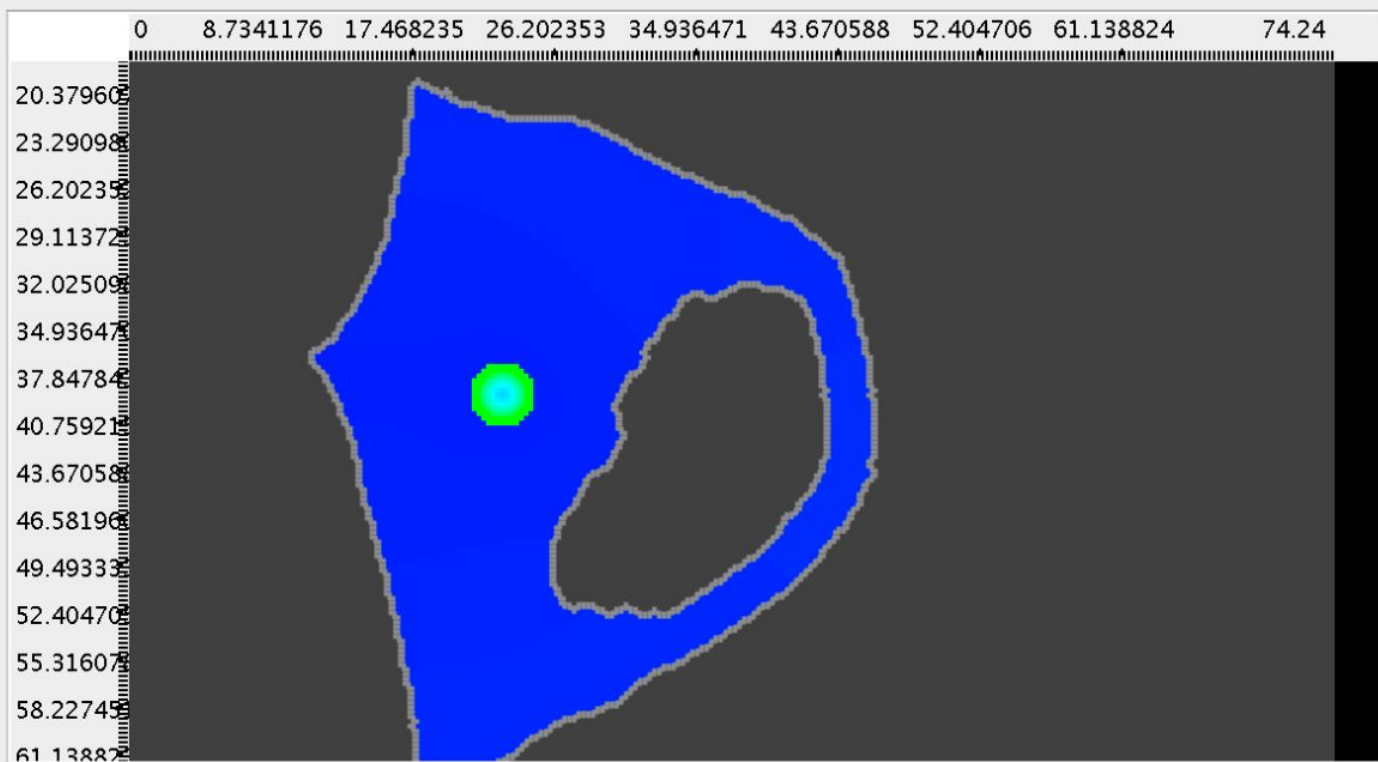
f TotalF

vobj_cytosol1_size

vobj_ec0_size

Slice View

Surface View



Info

Data Range (Min-Max)

☐ Auto range☒ at time☐ all times (approx)

Max: 6.3579144635698635

10.0

Min: 1.251932280079312

0.0

Color

BM

AM

NN

ND

NR

☐ Gray☒ BlueRed

Slice [0-34]

Z [17] = 13

Plot ▼

ROI ▼

Choose Parameter Values

DropletD

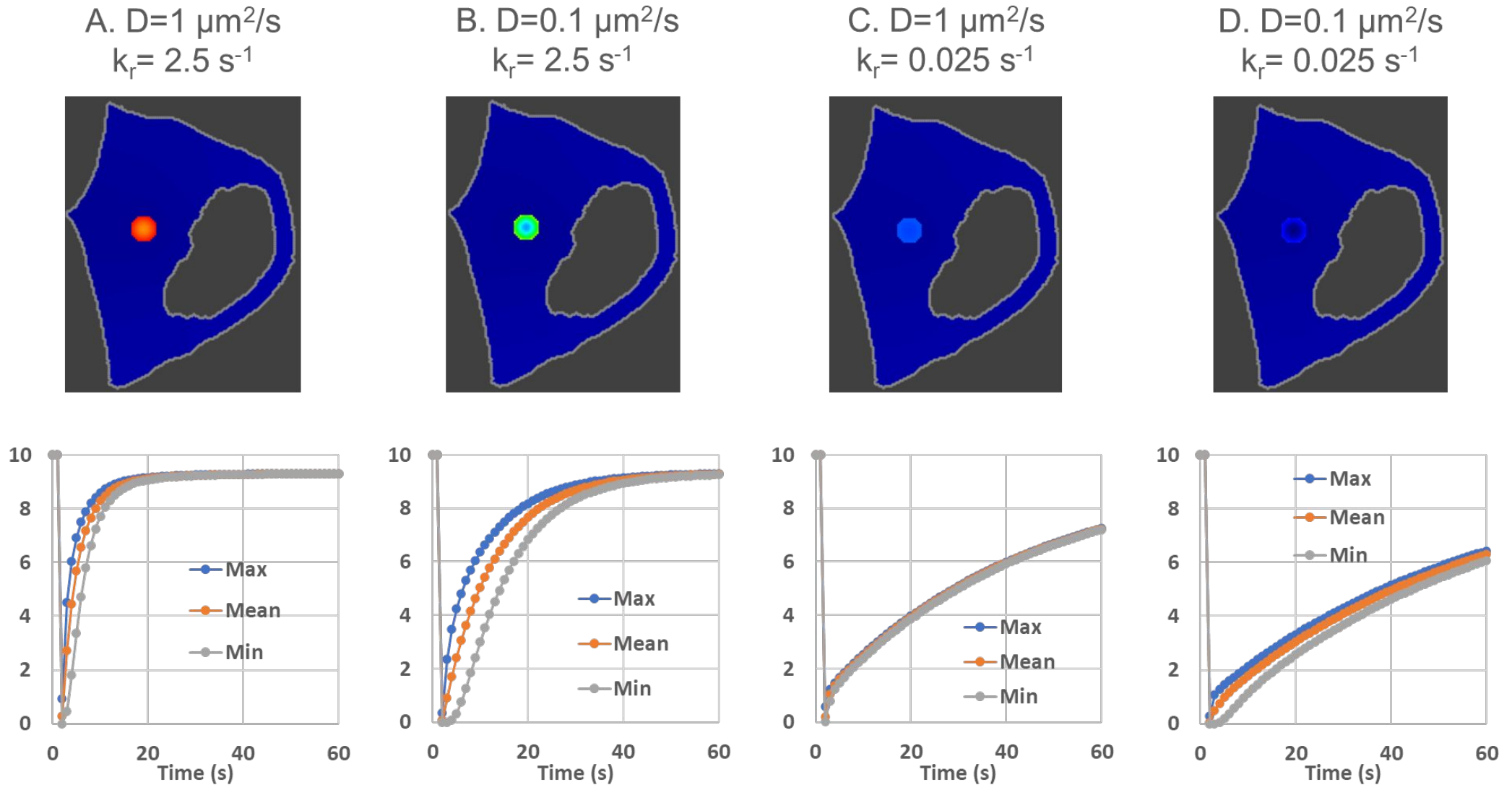
0.1

1.0

3.0

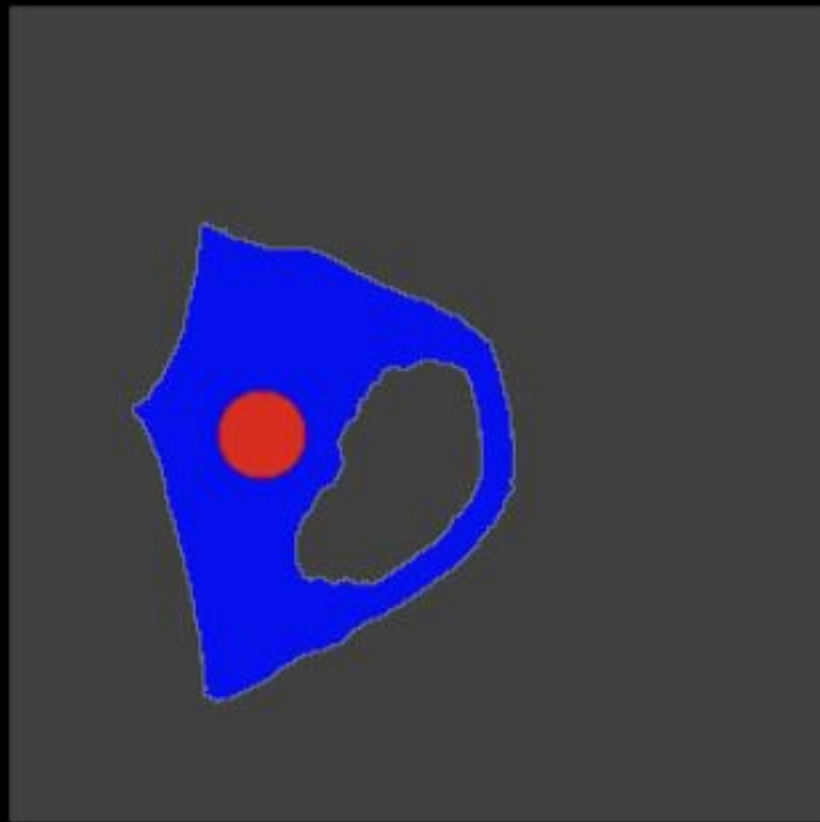
Example 2: Using PDEs to simulate FRAP of a biomolecular condensate

Figure 6 from Cowan and Loew, *Biophys. J.* 2023



Half bleach of a large droplet (Fig. 8b)

(movie exported directly from VCell)



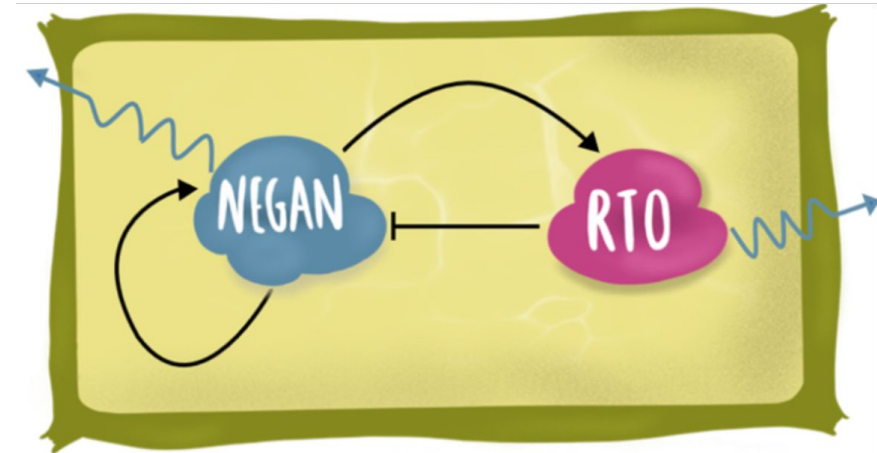
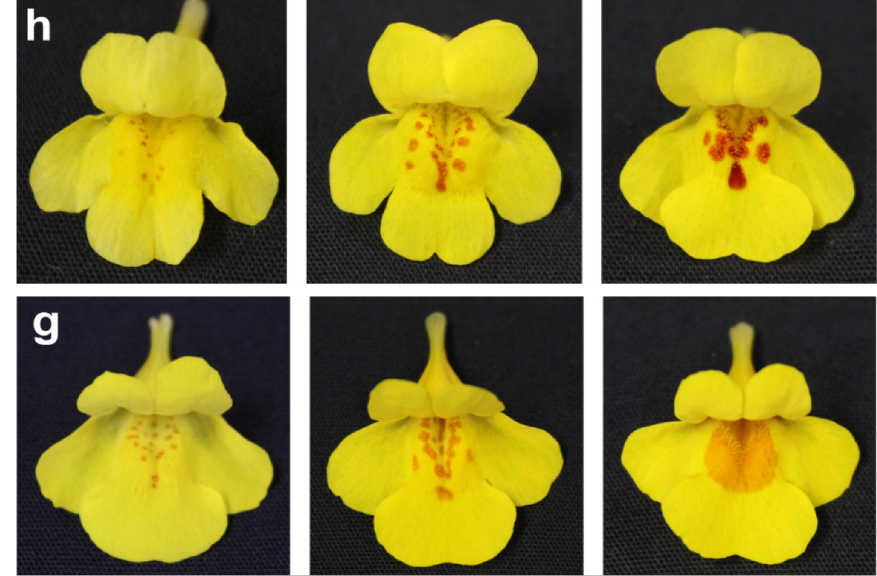
*Simulation experiments can be directly compared to microscopy experiments to answer questions like:
is it dissociation kinetics or intradroplet viscosity that controls the dynamics of biomolecular condensates?*

ARTICLE · Volume 30, Issue 5, P802-814.E8, March 09, 2020 · [Open](#)[Archive](#)[Download Full Issue](#)

Two MYB Proteins in a Self-Organizing Activator-Inhibitor System Produce Spotted Pigmentation Patterns

[Baoqing Ding](#)^{1,9} · [Erin L. Patterson](#)^{2,3,8,9} · [Srinidhi V. Holalu](#)^{2,3,9} · ... · [Michael L. Blinov](#)⁶ · [Benjamin K. Blackman](#)^{2,3,10} ✉ · [Yao-Wu Yuan](#)^{1,7} ✉ ... [Show more](#)

Monkeyflowers are a diverse genus of angiosperms that produce many beautiful and unique pigmentation patterns. Reaction-diffusion model with slow activator and fast repressor (Turing system) is known to generate patterns.



Using a simple Turing model to simulate pattern development

BIOMODEL: Monkeyflower_pigmentation_v2 (Wed Nov 13 04:20:34 EST 2019) -- VCell 7.7.0 (build 0)

File Account Window Tools Help

Monkeyflower_pigmentation_v2

- Physiology
 - Reaction Diagram
 - Reactions (4)
 - Structures (1)
 - Species (2)
 - Molecules (0)
 - Observables (0)
- Applications (1)
 - d/dt Pattern_formation
 - Geometry
 - Specifications

VCell DB BMDB

BioModels

Search

- Rosenbloom
- Scott 2021
- Ding 2020 T
- colreeze (Pub)
- Jang 2020 A
- Myeong 202
- Nosbisch 20
- Tenner 202
- Zhana 2020

Reaction Diagram

Reactions

Structures

Species

Molecules

Observables

Reaction Diagram

Reaction Name: r2

Kinetic Type: General [$\mu\text{M}/\text{s}$]

Convert to [molecules.s^{-1}]

Name	Description	Global	Expression	Units
J	reaction rate	<input type="checkbox"/>	$\{ G \cdot A \cdot A + I0 \}$	$\mu\text{M.s}^{-1}$
Gi	user defined	<input type="checkbox"/>	0.12	$\text{s}^{-1}.\mu\text{M}^{-1}$
A	Species Concentration	<input checked="" type="checkbox"/>	Variable	μM
I0	user defined	<input checked="" type="checkbox"/>	0.0	$\mu\text{M.s}^{-1}$

Linked Pathway Object(s):

CONNECTED (mblinov)

147.6MB / 402.7MB

The initial species distributions can be defined from images (e.g. fluorescent image)

BIOMODEL: Monkeyflower_pigmentation_v2 (Wed Nov 13 04:20:34 EST 2019) -- VCell 7.7.0 (build 0)

File Account Window Tools Help

Monkeyflower_pigmentation_v2

- Physiology
 - Reaction Diagram
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- Applications (1)
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VCell DB BMDB

BioModels

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- Rosenbloom
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 - colreeze (Pub)
- Jang 2020 A
- Myeong 202
- Nosbisch 20
- Tenner 2021
- Zhana 2020

Geometry Specifications Protocols Simulations

Species Reaction Network

Species	Structure	Depiction	Clamped	Rules	Initial Condition	Well Mixed	Diffusion Constant
A	c0		<input type="checkbox"/>		((vcField('Noise_100.tif1',	<input type="checkbox"/>	0.01 [$\mu\text{m}^2.\text{s}^{-1}$]
I	c0		<input type="checkbox"/>		0.0 [μM]	<input type="checkbox"/>	0.5 [$\mu\text{m}^2.\text{s}^{-1}$]

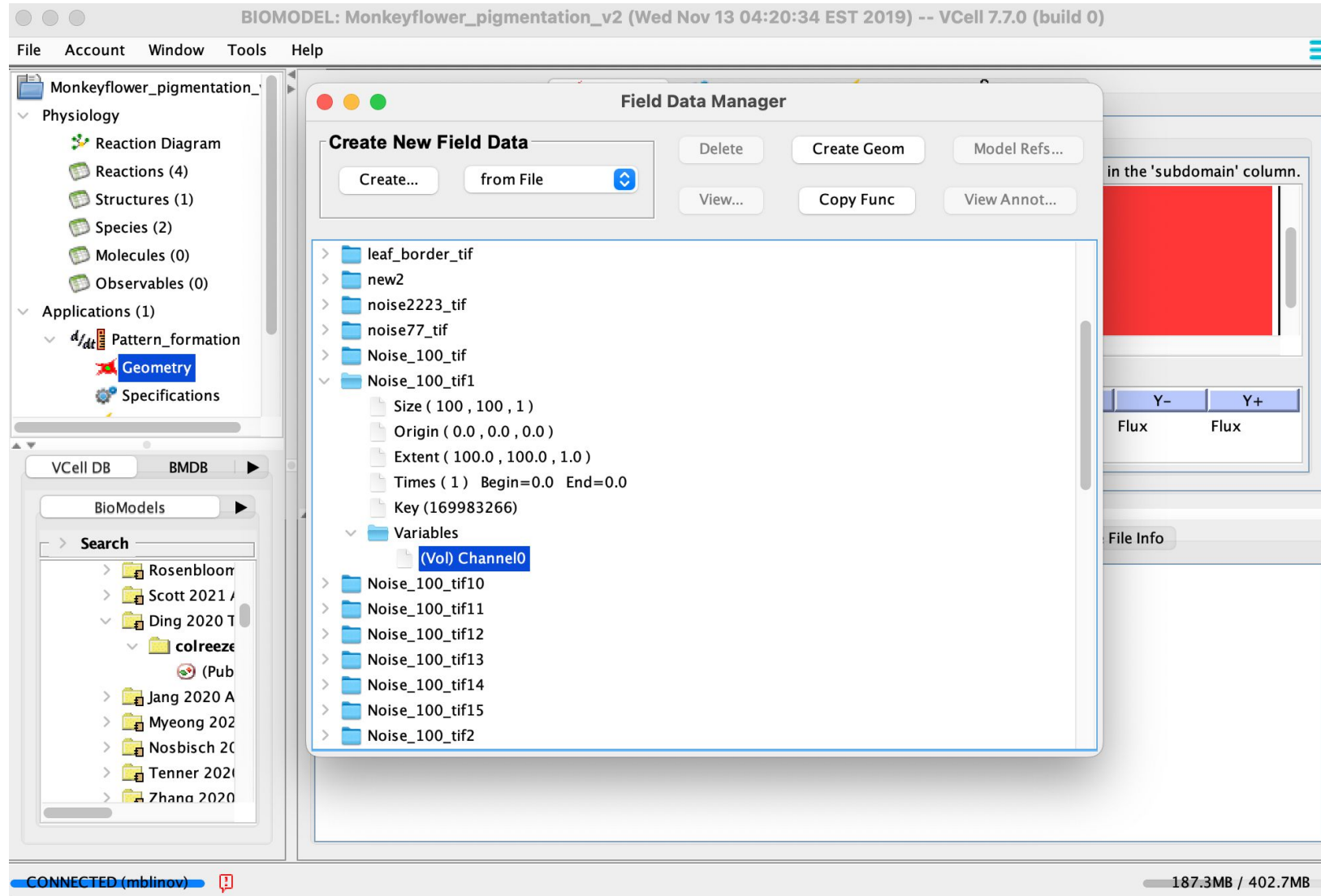
Search

Object Properties Annotations Problems (0 Errors, 1 Warnings) Database File Info

Description	Parameter	Expression	Units
initial concentration for A	initConc	$\frac{\text{vcField}('Noise_100_tif1', 'Channel0', 0.0, 'Volume')}{255.0} \cdot 0.2$	μM
diffusion constant for A	diff	0.01	$\mu\text{m}^2.\text{s}^{-1}$
Boundary Condition X- for A	BC_Xm	<zero flux>	$\mu\text{M}.\mu\text{m}.\text{s}^{-1}$
Boundary Condition X+ for A	BC_Xp	<zero flux>	$\mu\text{M}.\mu\text{m}.\text{s}^{-1}$
Boundary Condition Y- for A	BC_Ym	<zero flux>	$\mu\text{M}.\mu\text{m}.\text{s}^{-1}$
Boundary Condition Y+ for A	BC_Yp	<zero flux>	$\mu\text{M}.\mu\text{m}.\text{s}^{-1}$
Velocity X for A	Vel_X	<0.0>	$\mu\text{m}.\text{s}^{-1}$
Velocity Y for A	Vel_Y	<0.0>	$\mu\text{m}.\text{s}^{-1}$

CONNECTED (mblinov) 152.9MB / 402.7MB

In VCell non-uniform initial distribution are called field data



Now we demonstrate how this data is used

BIOMODEL: Monkeyflower_pigmentation_v2 (Wed Nov 13 04:20:34 EST 2019) -- VCell 7.7.0 (build 0)

File Account Window Tools Help

Reaction Diagram
Reactions (4)
Structures (1)
Species (2)
Molecules (0)
Observables (0)
Applications (1)
 Pattern_formation
 Geometry
 Specifications
 Protocols
 Simulations
Parameters, Functions, Units, e

VCeDB BMDB

BioModels

Search

- Rosenbloom
- Scott 2021
- Ding 2020 T
 - colreeze (Pub
- Jang 2020 A
- Myeong 202
- Nosbisch 20
- Tenner 202
- Zhana 2020

Geometry Specifications Protocols Simulations

Simulations Output Functions Generated Math

Name	End Time	Output Option	Solver	Running Status	Results
WT	6000.0	every 10.0 s	Fully-Implicit	completed	yes
RTO_RNAi_0.06	6000.0	every 10.0 s	Fully-Implicit	completed	yes
RTO_RNAi_0.09	6000.0	every 10.0 s	Fully-Implicit	completed	yes
RTO_RNAi_0.12	6000.0	every 10.0 s	Fully-Implicit	completed	yes
RTO_RNAi_0.15	6000.0	every 10.0 s	Fully-Implicit	completed	yes
RTO_RNAi_0.18	6000.0	every 10.0 s	Fully-Implicit	completed	yes
RTO_RNAi_0.185	6000.0	every 10.0 s	Fully-Implicit	completed	yes
RTO_RNAi_0.19	6000.0	every 10.0 s	Fully-Implicit	completed	yes
RTO_RNAi_0.2	6000.0	every 10.0 s	Fully-Implicit	completed	yes

Object Properties Annotations Problems (0 Errors, 1 Warnings) Database File Info

Annotation: cloned from 'WT_1' owned by user mblinov

Settings:

Max timestep	Output	Rel tol	Abs tol
0.1s	every 10.0 sec	1.0E-11	1.0E-11

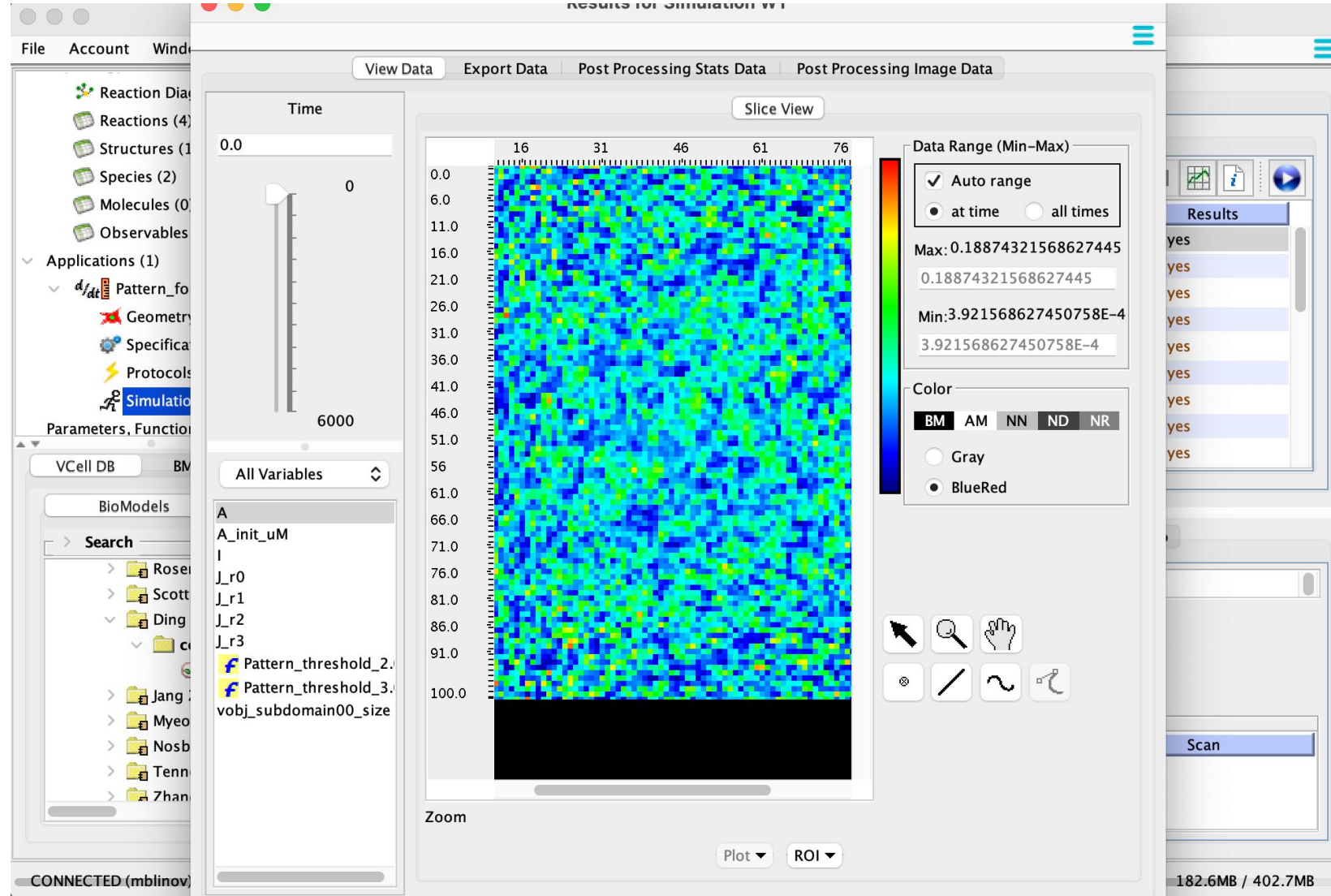
Mesh: 101x101 = 10201 elements Geometry size: (100.0,100.0) microns

Parameters with values changed from defaults

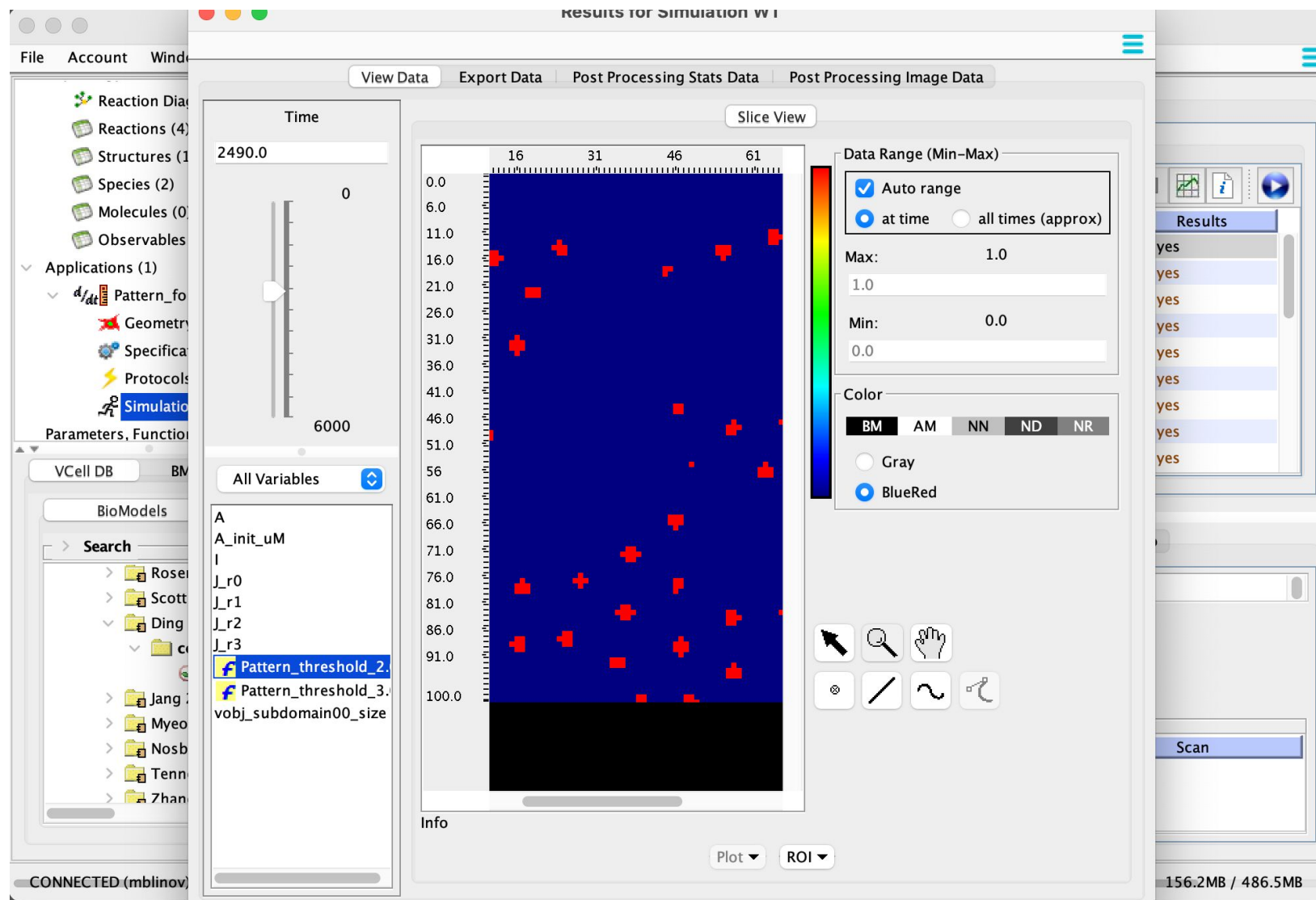
Parameter Name	Default	New Value/Expression	Scan
----------------	---------	----------------------	------

CONNECTED (mblinov) 192.5MB / 402.7MB

Initial condition imported from image (e.g. noise generated in ImageJ)



End result of the simulation



To compare with experimental data, we can export in multiple formats, including N5

View Exported Data

User Options

Export Type

☒ C...☒ HDF5☒ QUICKTIME☒ GIF☒ JPEG☒ NRRD☒ UCD☒ UNSTRUCT☒ IMAGE☒ PLY☒ N5

Time Interval

☐ Past 24 hours☐ Past Month☐ Past Year☒ Any Tim

Export Table

BM Name	App Name	Sim Name	Time Slice	Format	Date Exported
Monkeyflower_pigmentation_v2	Pattern_formation	WT	0.0/6000.0	N5	2024/11/22 15:00:...
Tutorial_MultiApp	3D pde	Simulation4	0.0/9.999999999999...	N5	2024/11/19 15:13:...
Tutorial_MultiApp	3D pde	Simulation4	0.0/9.999999999999...	N5	2024/11/19 14:58:...
Rule-based_egfr_compart	3D	Spatial_3D	0.0/12.0	N5	2024/11/19 14:09:...
Brown et al 2008 Purkinje 3D – 12 PF Sti...	3D PIP2_experimentally derived geom...	stimulated synthesis and lat d...	0.0/2.0	JPEG	2024/10/22 14:34:...
Brown et al 2008 Purkinje 3D – 12 PF Sti...	3D PIP2_experimentally derived geom...	stimulated synthesis and lat d...	0.0/2.0	JPEG	2024/10/22 14:26:...
Tutorial_MultiApp	Stoch Spatial	1000 particles	0.0/9.999999999999...	JPEG	2024/10/22 14:24:...
Brown et al 2008 Purkinje 3D – 12 PF Sti...	3D PIP2_experimentally derived geom...	stimulated synthesis and lat d...	0.0/2.0	GIF	2024/10/22 14:21:...
Brown et al 2008 Purkinje 3D – 12 PF Sti...	3D PIP2_experimentally derived geom...	stimulated synthesis and lat d...	0.0/2.0	JPEG	2024/10/22 14:20:...
Tutorial_MultiApp	3D pde	Simulation4	0.0/9.999999999999...	JPEG	2024/10/22 14:18:...

Copy Link

Delete Export

Search

Export Details

Properties

Variables List: [A]

Simulation ID: SimID_169880916_0_

Name: monkey

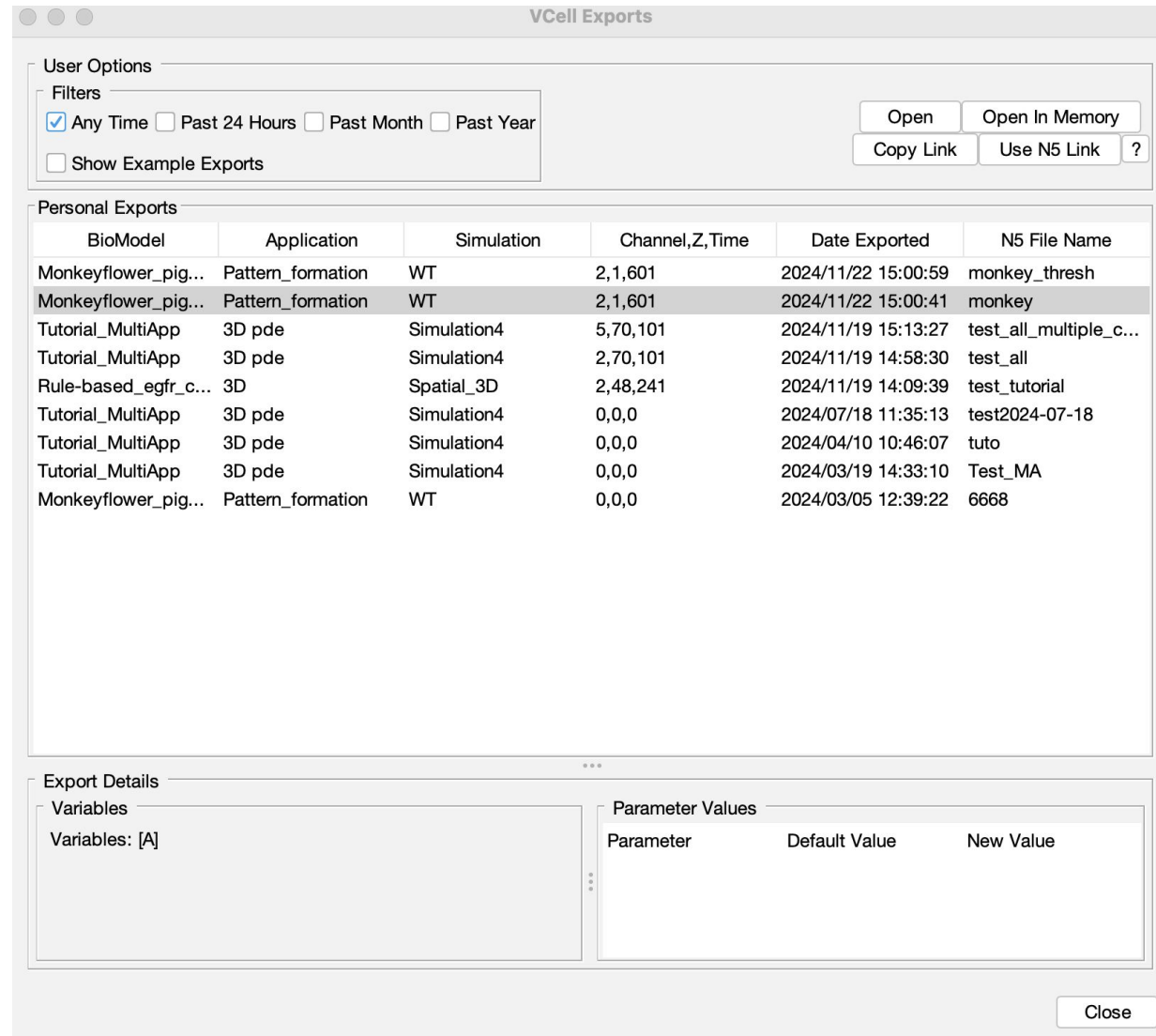
Link: <https://vcell.cam.uchc.edu/n5Data/mblinov/0d8874422cbdd77.n5?dataSetName=7115835095>

Parameters

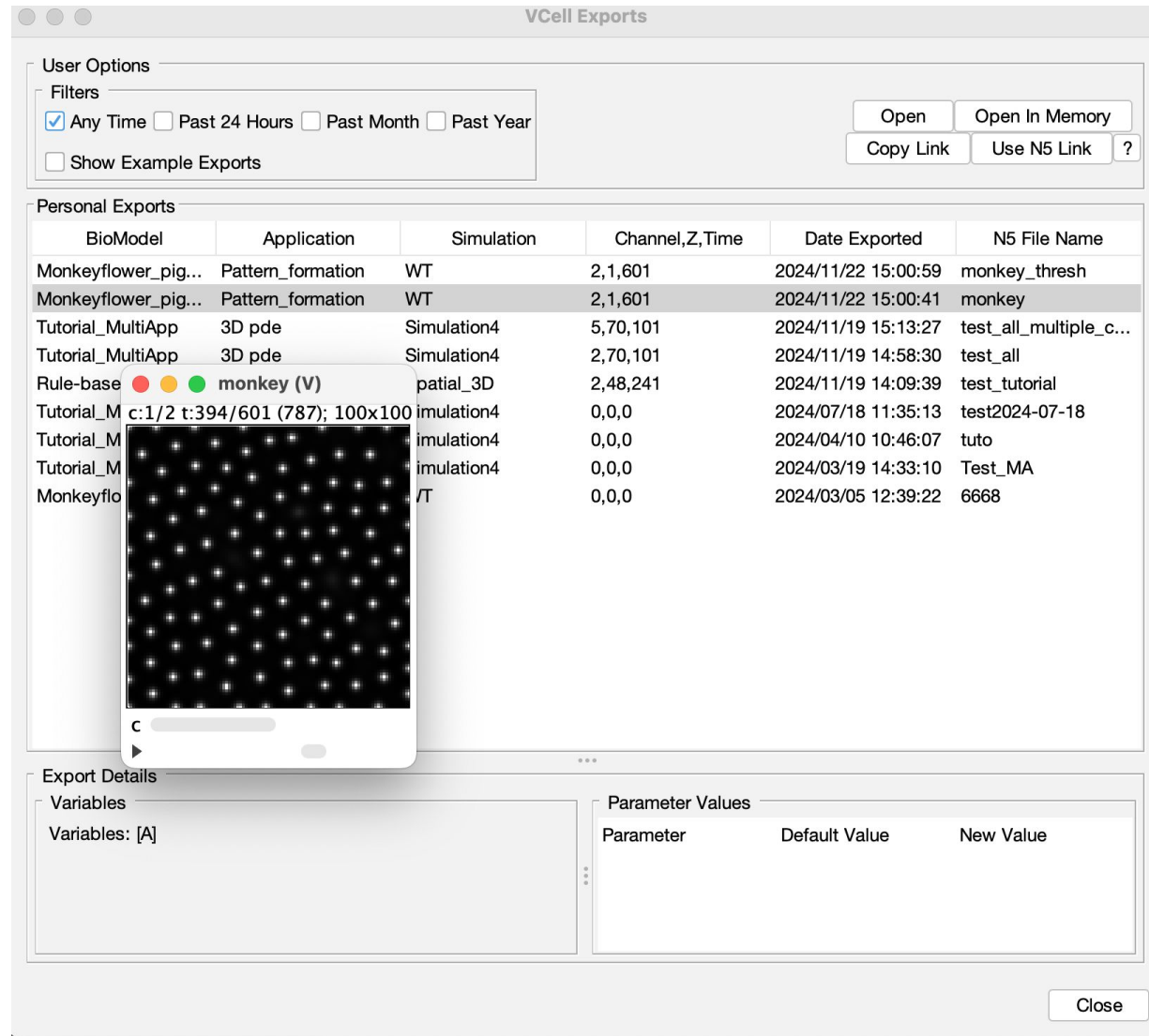
Parameter	Default Value	New Value
-----------	---------------	-----------

Close

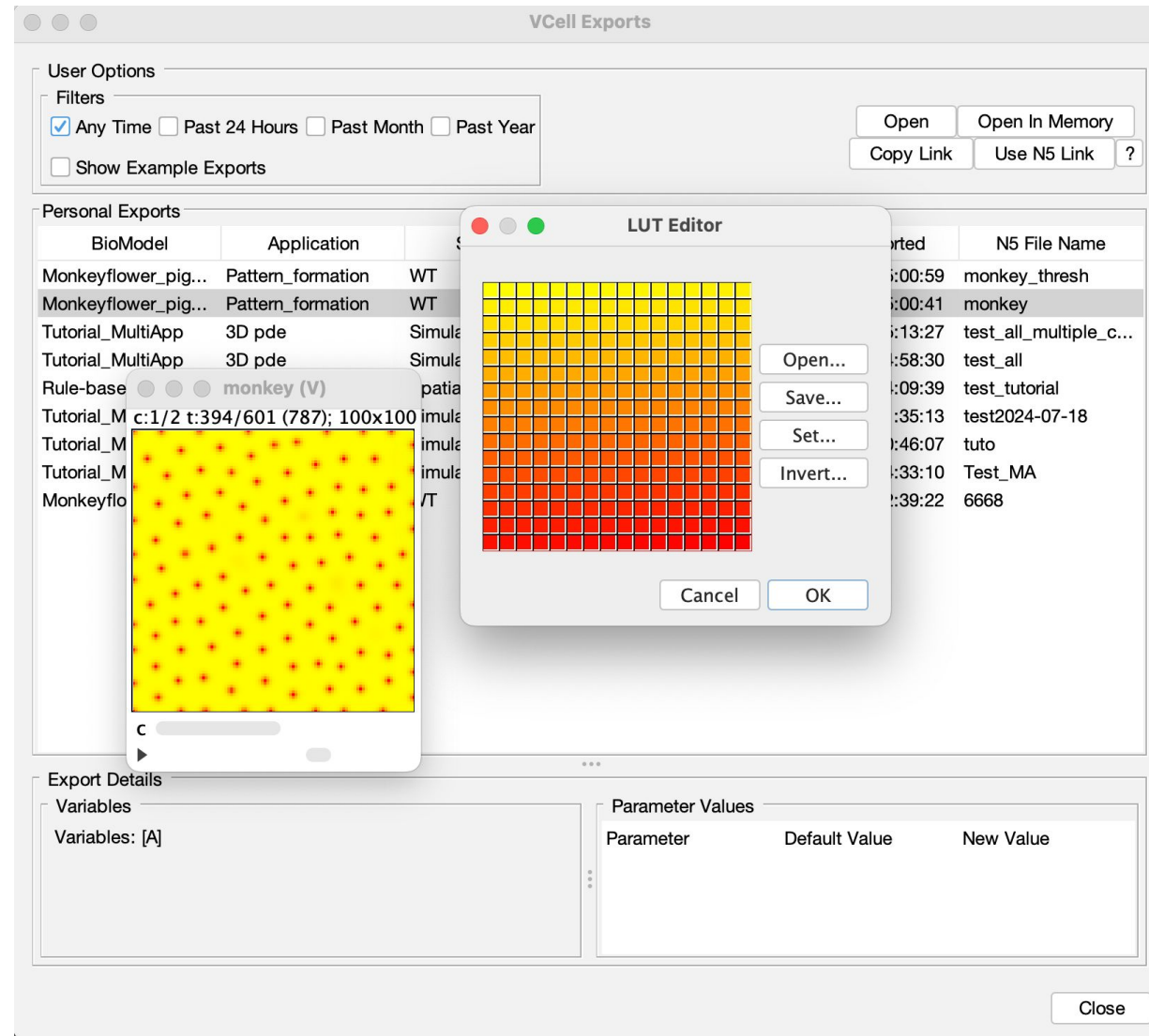
These images are accessible from FIJI/ImageJ with VCell plugin as hyperstacks

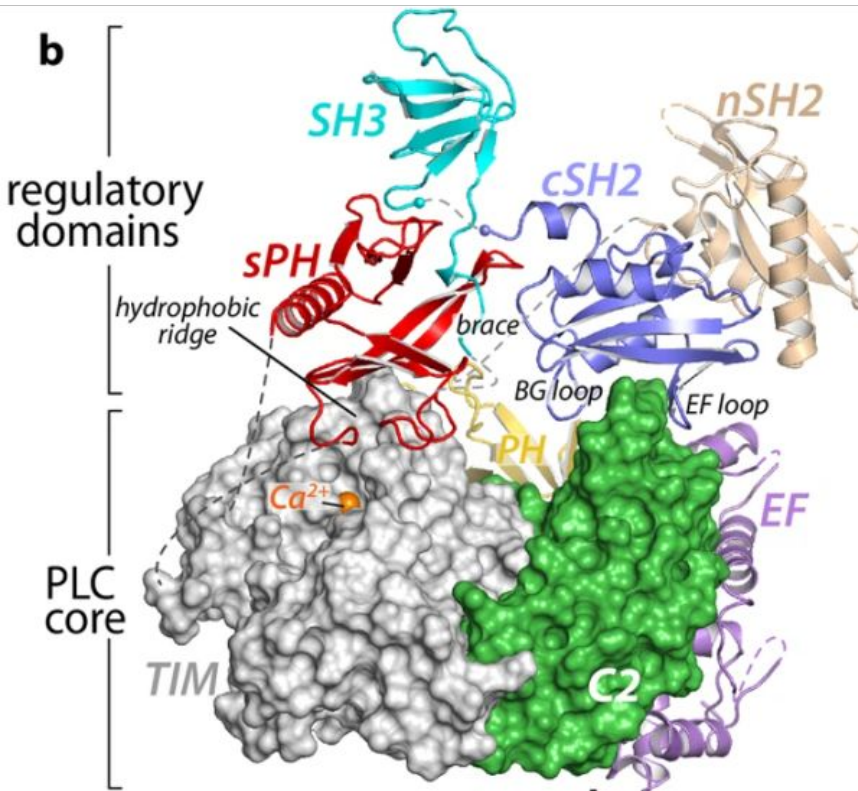


These images are accessible from FIJI/ImageJ with VCell plugin as hyperstacks



Using color LUT to compare VCell images with real data





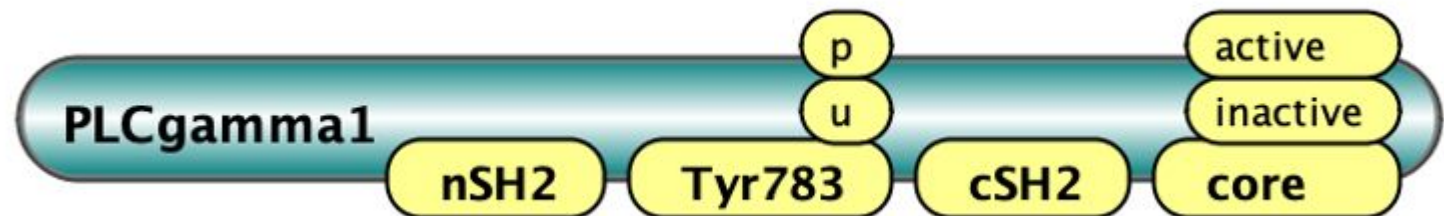
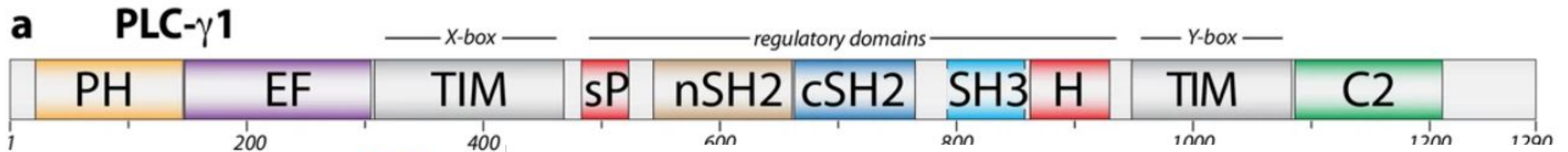
A kinetic model of phospholipase C- γ 1 linking structure-based insights to dynamics of enzyme autoinhibition and activation

Received for publication, October 19, 2021, and in revised form, March 27, 2022 Published, Papers in Press, March 31, 2022,
<https://doi.org/10.1016/j.jbc.2022.101886>

Jamie L. Nosbisch¹, James E. Bear², and Jason M. Haugh^{3,*}

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Edited by Roger Colbran



Molecules

BIOMODEL: Nobsisch PLCgamma1 2021 (Tue May 03 18:08:02 EDT 2022) -- VCell 7.7.0 (build 0)

File Account Window Tools Help

Nobsisch PLCgamma1 2021

- Physiology
 - Reaction Diagram
 - Reactions (12)
 - Structures (1)
 - Species (2)
 - Molecules (2)**
 - Observables (9)
- Applications (1)
 - > $\frac{d}{dt}$ Application0
 - Parameters, Functions, Units, etc.
 - Pathway




VCell DB BMDB

BioModels

Search

- Biological Models
 - > My BioModels (mblinov)
 - > Shared With Me (711)
 - > Tutorials (10)
 - > Public BioModels (1009)
 - > Published (215)
 - > Curated (58)
 - > Uncurated (736)

Reaction Diagram Reactions Structures Species **Molecules** Observables

Name	Depiction	Notes	Link	BioNetGen Definition
RTK				RTK(pY)
PLCgamma1				PLCgamma1(nSH2,Tyr783~u~p,cSH2,core~inactive~active)

New Molecule Delete Pathway Links Search


Object Properties Annotations Problems (0 Errors, 1 Warnings)

Anchor Molecule

☒ No restrictions

☐ Only these:

☐ cell



Pathway Links

Linked Pathway Object(s):

CONNECTED (mblinov) 168.7 MB / 486.5 MB

Reactions

BIOMODEL: Nosbisch PLCgamma1 2021 (Tue May 03 18:08:02 EDT 2022) -- VCell 7.0 (build 0)

File Account Window Tools Help

Nosbisch PLCgamma1 2021

- Physiology
 - Reaction Diagram
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VCeI DB BMDB

BioModels

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 - Published (215)
 - Curated (58)
 - Uncurated (736)

Reaction Diagram Reactions Structures Species Molecules Observables

Reaction	Name	Structure	Depiction	Kinetics	Notes	Link
Reaction Rule r01	cell		MassAction			@cell:RTK(pY)+@cell:PLCgamma1(nSH2)
Reaction Rule r02	cell		MassAction			@cell:RTK(pY)+@cell:PLCgamma1(nSH2)
Reaction Rule r03	cell		MassAction			@cell:RTK(pY11).PLCgamma1(nSH2!1) ->
Reaction Rule r04	cell		MassAction			@cell:RTK(pY11).PLCgamma1(nSH2!1, Tyr
Reaction Rule r05	cell		MassAction			@cell:PLCgamma1(Tyr783~p) -> @cell:
Reaction Rule r06	cell		MassAction			@cell:PLCgamma1(cSH2, core~inactive)
Reaction Rule r07	cell		MassAction			@cell:PLCgamma1(Tyr783~p, cSH2) ->
Reaction Rule r08	cell		MassAction			@cell:PLCgamma1(Tyr783~p!1, cSH2!1)
Reaction Rule r09	cell		MassAction			@cell:RTK(pY11).PLCgamma1(nSH2!1, co
Reaction Rule r10	cell		MassAction			@cell:PLCgamma1(nSH2, core~inactive)
Reaction Rule r11	cell		MassAction			@cell:PLCgamma1(nSH2, core~inactive)
Reaction Rule r12	cell		MassAction			@cell:PLCgamma1(core~active) -> @ce

New Reaction New Rule Duplicate Delete Pathway Links Search

Object Properties Annotations Problems (0 Errors, 1 Warnings)

Kinetics Editor

Reversible ☐ + -

Add Reactant

Add Product

☐ Single Row Viewer

☒ Show Molecule Color

☒ Show Non-trivial

☐ Show Differen...

CONNECTED (mblinov)

189.9MB / 486.5MB

Network generation

BIOMODEL: Nosbisch PLCgamma1 2021 (Tue May 03 18:08:02 EDT 2022) -- VCell 7.7.0 (build 0)

File Account Window Tools Help

Nosbisch PLCgamma1 2021

- Physiology
 - Reaction Diagram
 - Reactions (12)
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- Applications (1)
 - Application0
 - Geometry
 - Specifications**
 - Protocols
 - Simulations
 - Parameter Estimation

VCell DB BMDB

BioModels

Search

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 - Uncurated (736)

Geometry Specifications Protocols Simulations Parameter Estimation

Species Reaction Network

Network Constraints

Constraint	Value	Default
Max Iterations	7	1
Max Molecules / Species	10	10

Generated Network

Species: 17 [View](#) [Edit / Test Constraints](#)

Reactions: 53 [View](#) [Create new VCell BioModel from Network](#)

Observables Map [View](#)

Warning: none

Search

Object Properties Annotations Problems (0 Errors, 1 Warnings) Network Generation Status

```
Running BioNetGen ...
Iteration 0: 2 species
Iteration 1: 4 species
Iteration 2: 7 species
Iteration 3: 10 species
Iteration 4: 13 species
Iteration 5: 16 species
Iteration 6: 17 species
Iteration 7: 17 species
Creating BNG output spec ...
Return BioNetGen output to requester...
Total run time: 6.2 s.
The Network constraints are unchanged.
```

CONNECTED (mblinov) 262.7MB / 486.5MB

Generated species and reactions

View Generated Reactions

Rule	Structure	Depiction	BioNetGen Definition
r02	cell		RTK(pY) + PLCgamma1(Tyr783~u,cSH2,core~active,nSH2) -> PLCgamma1(Tyr783~u,cSH2,core~active,nSH2!...
r02	cell		RTK(pY) + PLCgamma1(Tyr783~p,cSH2,core~active,nSH2) -> PLCgamma1(Tyr783~p,cSH2,core~active,nSH2!...
r02	cell		RTK(pY) + PLCgamma1(Tyr783~p!1,cSH2!1,core~active,nSH2) -> PLCgamma1(Tyr783~p!1,cSH2!1,core~activ...
r01	cell		RTK(pY) + PLCgamma1(Tyr783~u,cSH2!1,core~inactive!1,nSH2) -> PLCgamma1(Tyr783~u,cSH2!1,core~inact...
r01	cell		RTK(pY) + PLCgamma1(Tyr783~u,cSH2,core~inactive,nSH2) -> PLCgamma1(Tyr783~u,cSH2,core~inactive,n...
r01	cell		RTK(pY) + PLCgamma1(Tyr783~p,cSH2!1,core~inactive!1,nSH2) -> PLCgamma1(Tyr783~p,cSH2!1,core~inact...
r01	cell		RTK(pY) + PLCgamma1(Tyr783~p,cSH2,core~inactive,nSH2) -> PLCgamma1(Tyr783~p,cSH2,core~inactive,n...
r01	cell		RTK(pY) + PLCgamma1(Tyr783~p!1,cSH2!1,core~inactive,nSH2) -> PLCgamma1(Tyr783~p!1,cSH2!1,core~ina...
r03	cell		PLCgamma1(Tyr783~u,cSH2!1,core~inactive!1,nSH2!2).RTK(pY!2) -> RTK(pY) + PLCgamma1(Tyr783~u,cSH2!...
r03	cell		PLCgamma1(Tyr783~u,cSH2,core~inactive,nSH2!1).RTK(pY!1) -> RTK(pY) + PLCgamma1(Tyr783~u,cSH2,cor...
r03	cell		PLCgamma1(Tyr783~p,cSH2!1,core~inactive!1,nSH2!2).RTK(pY!2) -> RTK(pY) + PLCgamma1(Tyr783~p,cSH2!...
r03	cell		PLCgamma1(Tyr783~u,cSH2,core~active,nSH2!1).RTK(pY!1) -> RTK(pY) + PLCgamma1(Tyr783~u,cSH2,core~...
r03	cell		PLCgamma1(Tyr783~p,cSH2,core~inactive,nSH2!1).RTK(pY!1) -> RTK(pY) + PLCgamma1(Tyr783~p,cSH2,cor...
r03	cell		PLCgamma1(Tyr783~p,cSH2,core~active,nSH2!1).RTK(pY!1) -> RTK(pY) + PLCgamma1(Tyr783~p,cSH2,core~...
r03	cell		PLCgamma1(Tyr783~p!1,cSH2!1,core~inactive,nSH2!2).RTK(pY!2) -> RTK(pY) + PLCgamma1(Tyr783~p!1,cSH...
r03	cell		PLCgamma1(Tyr783~p!1,cSH2!1,core~active,nSH2!2).RTK(pY!2) -> RTK(pY) + PLCgamma1(Tyr783~p!1,cSH2!...
r04	cell		PLCgamma1(Tyr783~u,cSH2!1,core~inactive!1,nSH2!2).RTK(pY!2) -> PLCgamma1(Tyr783~p,cSH2!1,core~ina...
r04	cell		PLCgamma1(Tyr783~u,cSH2,core~inactive,nSH2!1).RTK(pY!1) -> PLCgamma1(Tyr783~p,cSH2,core~inactive,...
r04	cell		PLCgamma1(Tyr783~u,cSH2,core~active,nSH2!1).RTK(pY!1) -> PLCgamma1(Tyr783~p,cSH2,core~active,nSH...
r05	cell		PLCgamma1(Tyr783~p,cSH2!1,core~inactive!1,nSH2!2).RTK(pY!2) -> PLCgamma1(Tyr783~u,cSH2!1,core~ina...
r05	cell		PLCgamma1(Tyr783~p,cSH2!1,core~inactive!1,nSH2) -> PLCgamma1(Tyr783~u,cSH2!1,core~inactive!1,nSH2)
r05	cell		PLCgamma1(Tyr783~p,cSH2,core~inactive,nSH2!1).RTK(pY!1) -> PLCgamma1(Tyr783~u,cSH2,core~inactive...

Search

Reactions: 53

+

->

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Observables

BIOMODEL: Nosbisch PLCgamma1 2021 (Tue May 03 18:08:02 EDT 2022) -- VCell 7.7.0 (build 0)

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Nosbisch PLCgamma1 2021

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Reaction Diagram Reactions Structures Species Molecules Observables

Name	Structure	Depiction	Notes	BioNetGen Definition	Count
O0_RTK_tot	cell			RTK()	Molecules
O0_PLCgamma1_tot	cell			PLCgamma1()	Molecules
O0_PLCgamma1_active	cell			PLCgamma1(core~active!?)	Molecules
O0_PLCgamma1_inactive	cell			PLCgamma1(core~inactive!?)	Molecules
O0_PLCgamma1_pTyr783	cell			PLCgamma1(Tyr783~p!?)	Molecules
O0_PLCgamma1_dpTyr783	cell			PLCgamma1(Tyr783~u!?)	Molecules
O0_PLCgamma1_RTK_bound_inactive	cell			RTK(pY11).PLCgamma1(nSH2!1,core~inactive!?)	Molecules
O0_PLCgamma1_RTK_bound	cell			RTK(pY11).PLCgamma1(nSH2!1)	Molecules
O0_PLCgamma1_cytosol	cell			PLCgamma1(nSH2,core~inactive!?)	Molecules

New Observable Duplicate Delete Pathway Links Search

Object Properties Annotations Problems (0 Errors, 1 Warnings)

Add Pattern

Multimolecular

Polymer of

length = 2

length > 1

+

-

cell

PLCgamma1

nSH2 Tyr783 cSH2 core

236.8MB / 486.5MB