

# **Mathematical Modeling for Cell Biology**

**CellBio 24 workshop**

**Sunday, December 15<sup>th</sup>**

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

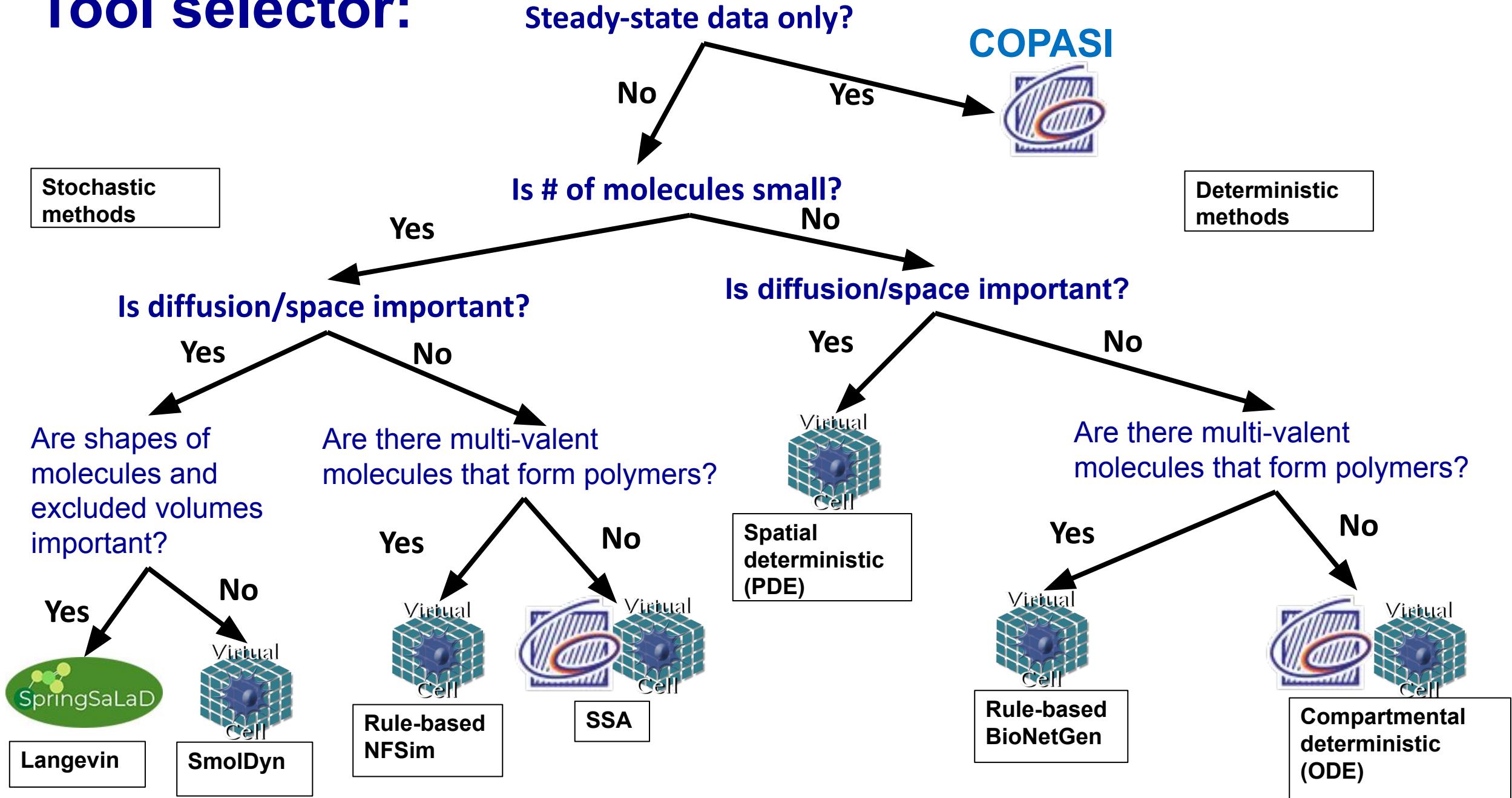
Introduce kinetic simulations, steady state analysis, parameter estimation, spatial modeling, rule-based models, demonstrating them using two modeling and simulation tools:

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.

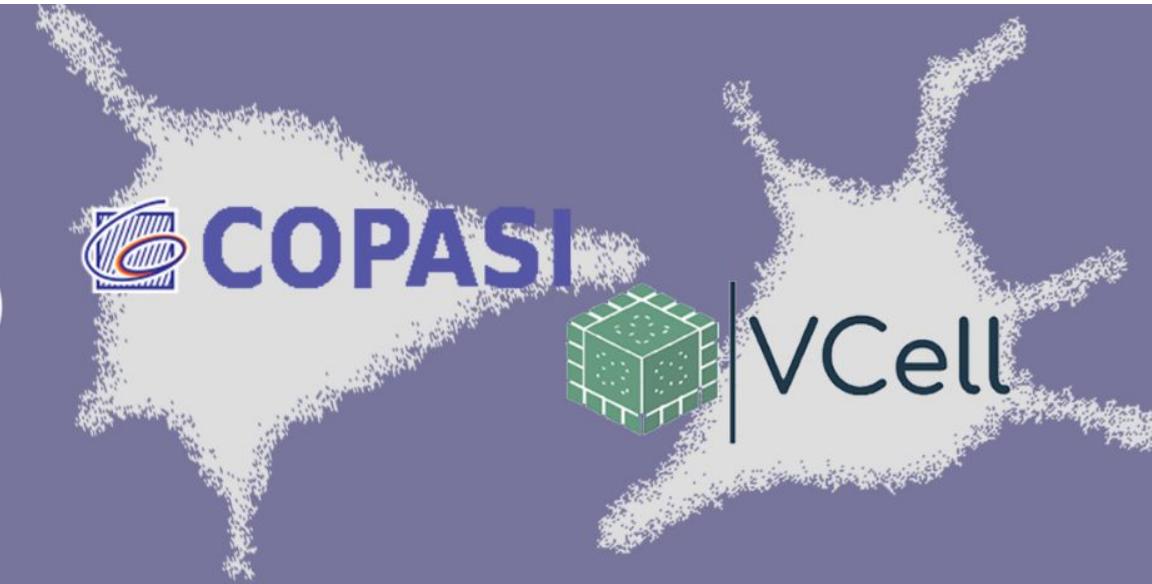
# CompCellBio workshops

<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**

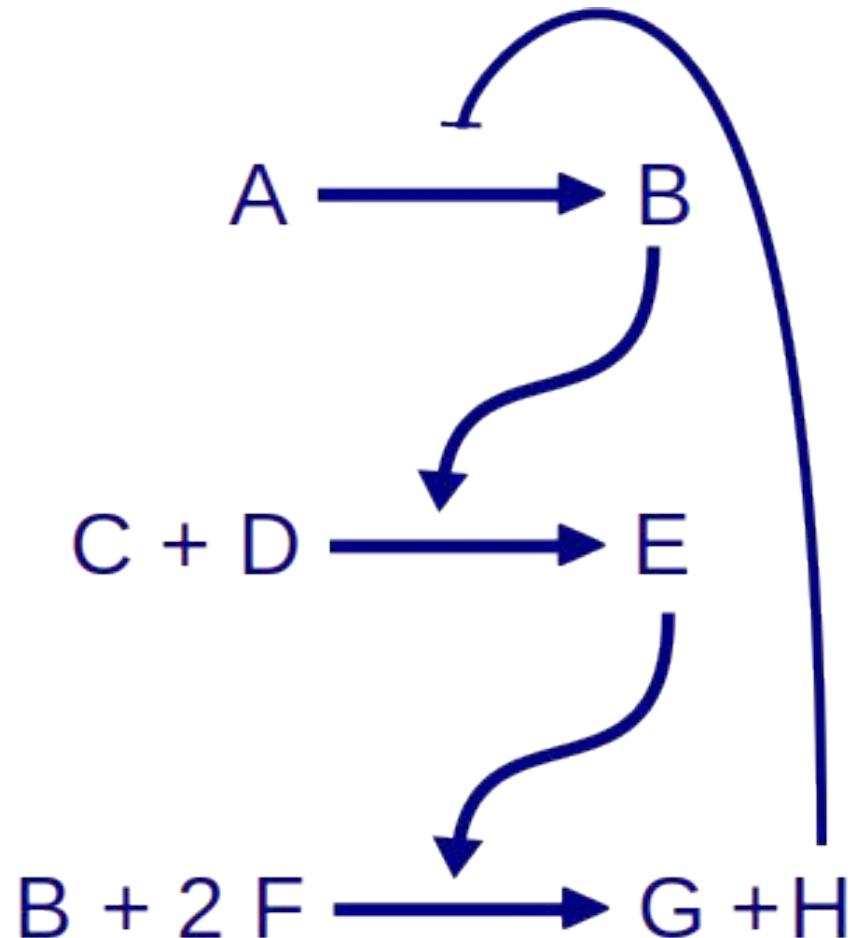
Farmington, CT, USA



# 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.

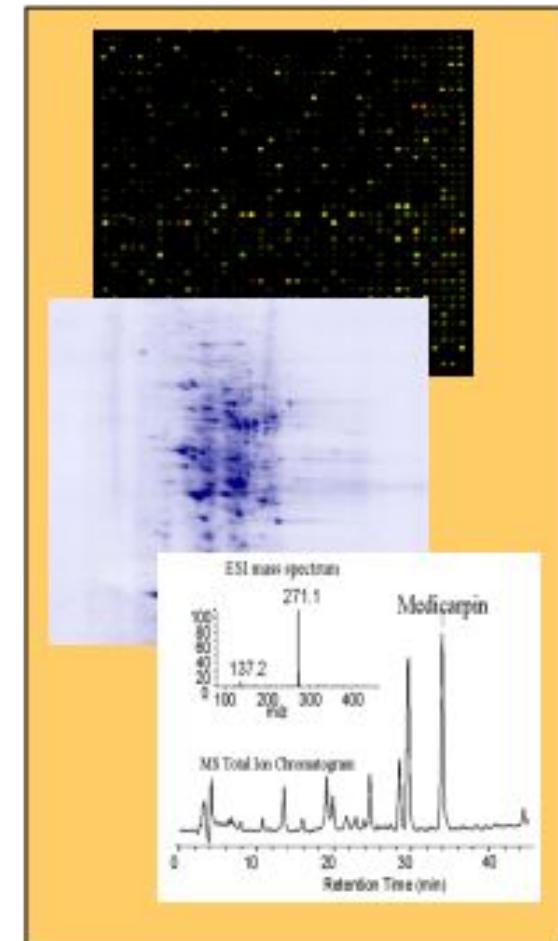
# Biochemical Process



Genome

Proteome

Metabolome



# Mathematical Model

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

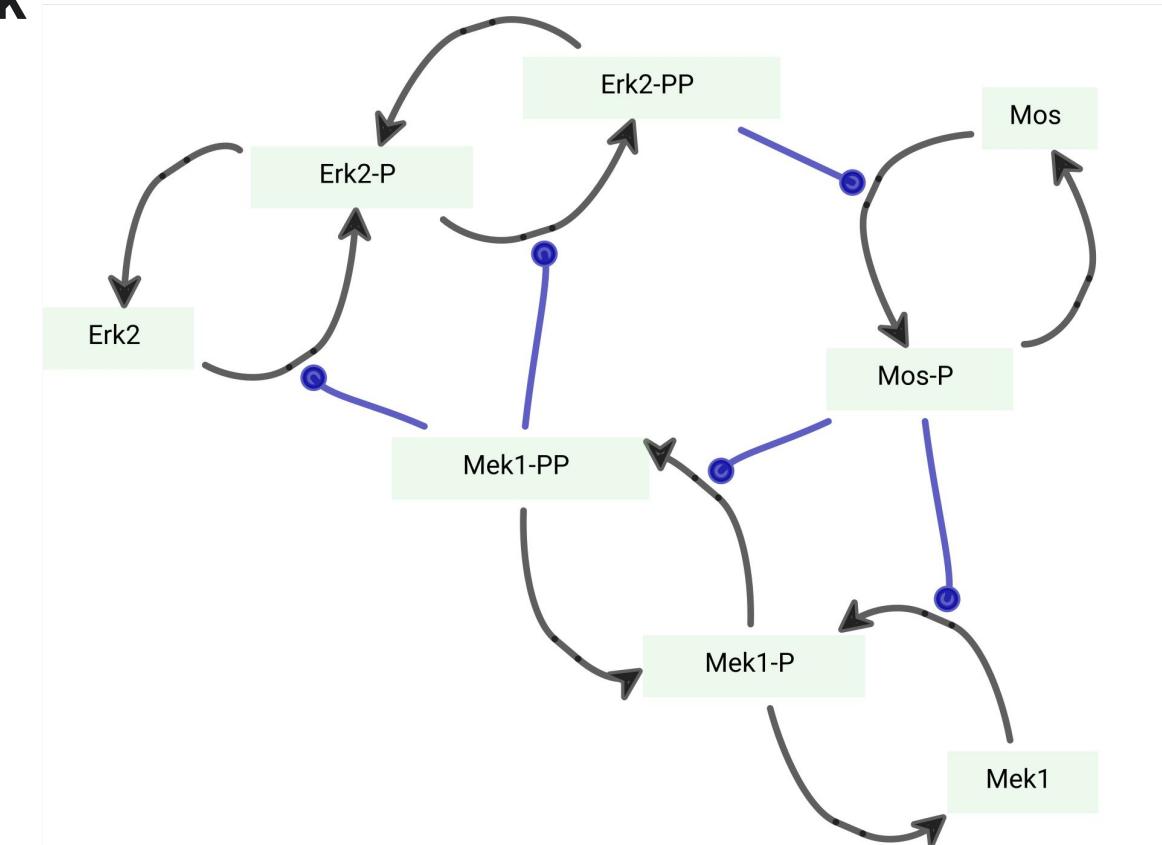
$$\dot{x} = N v \quad \text{with:}$$

$$x = \begin{pmatrix} x_1 \\ x_2 \\ \dots \\ x_n \end{pmatrix} \quad v = \begin{pmatrix} v_1 \\ v_2 \\ \dots \\ v_m \end{pmatrix}$$

# 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

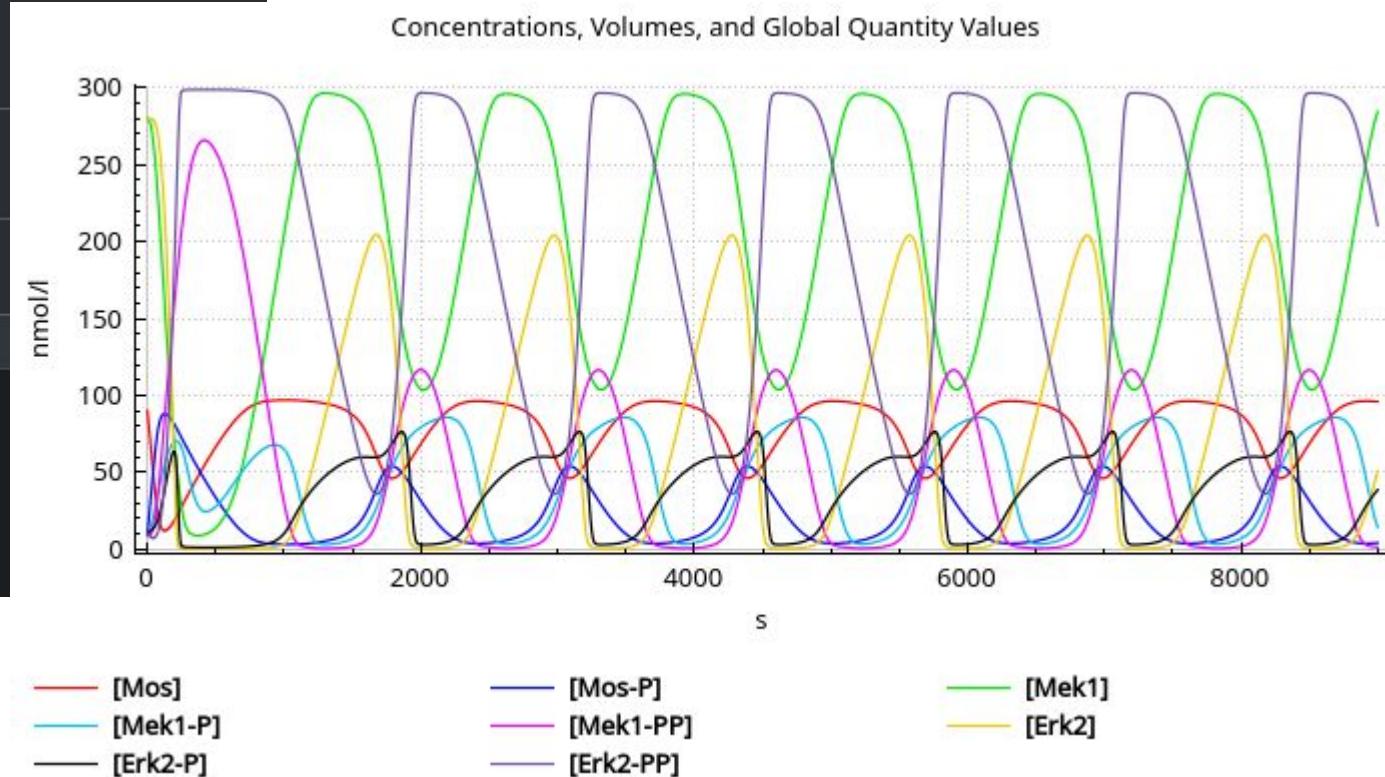
Output Events     Save Result in Memory

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

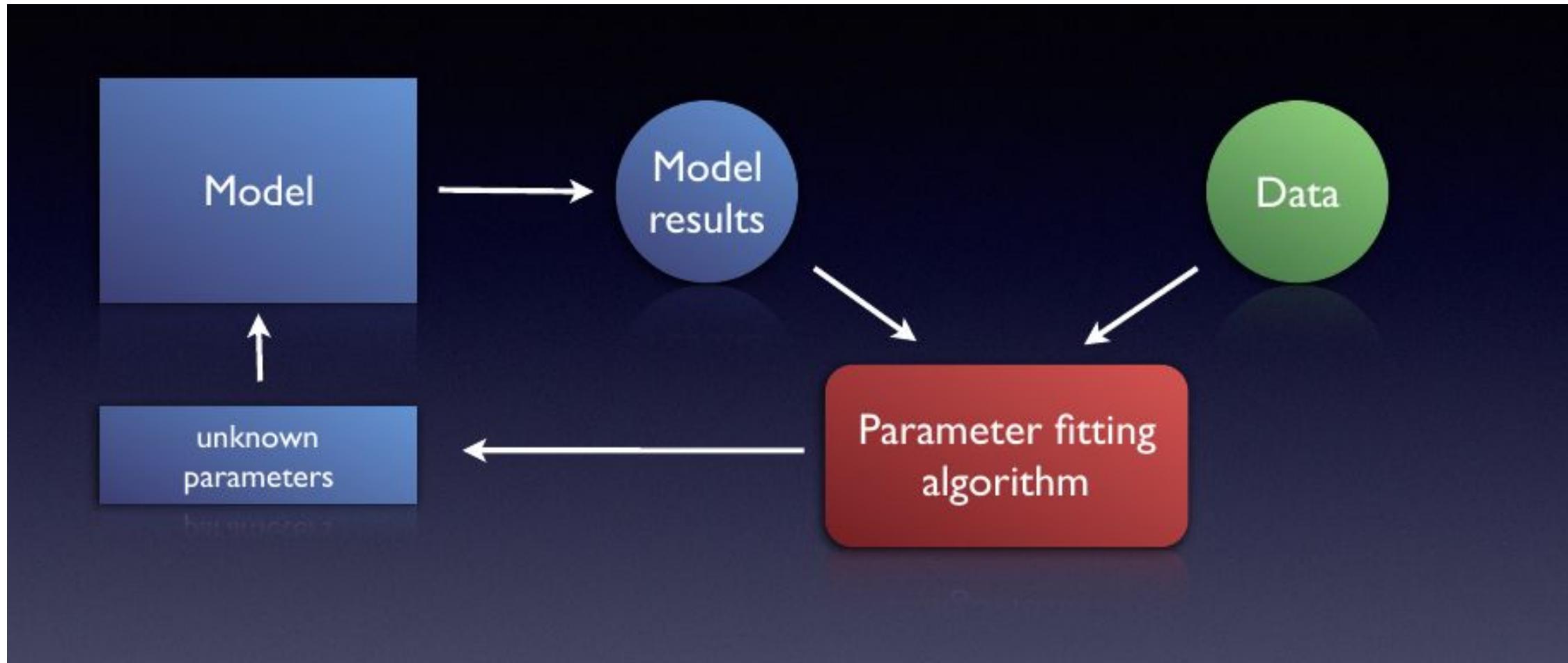


# Steady State

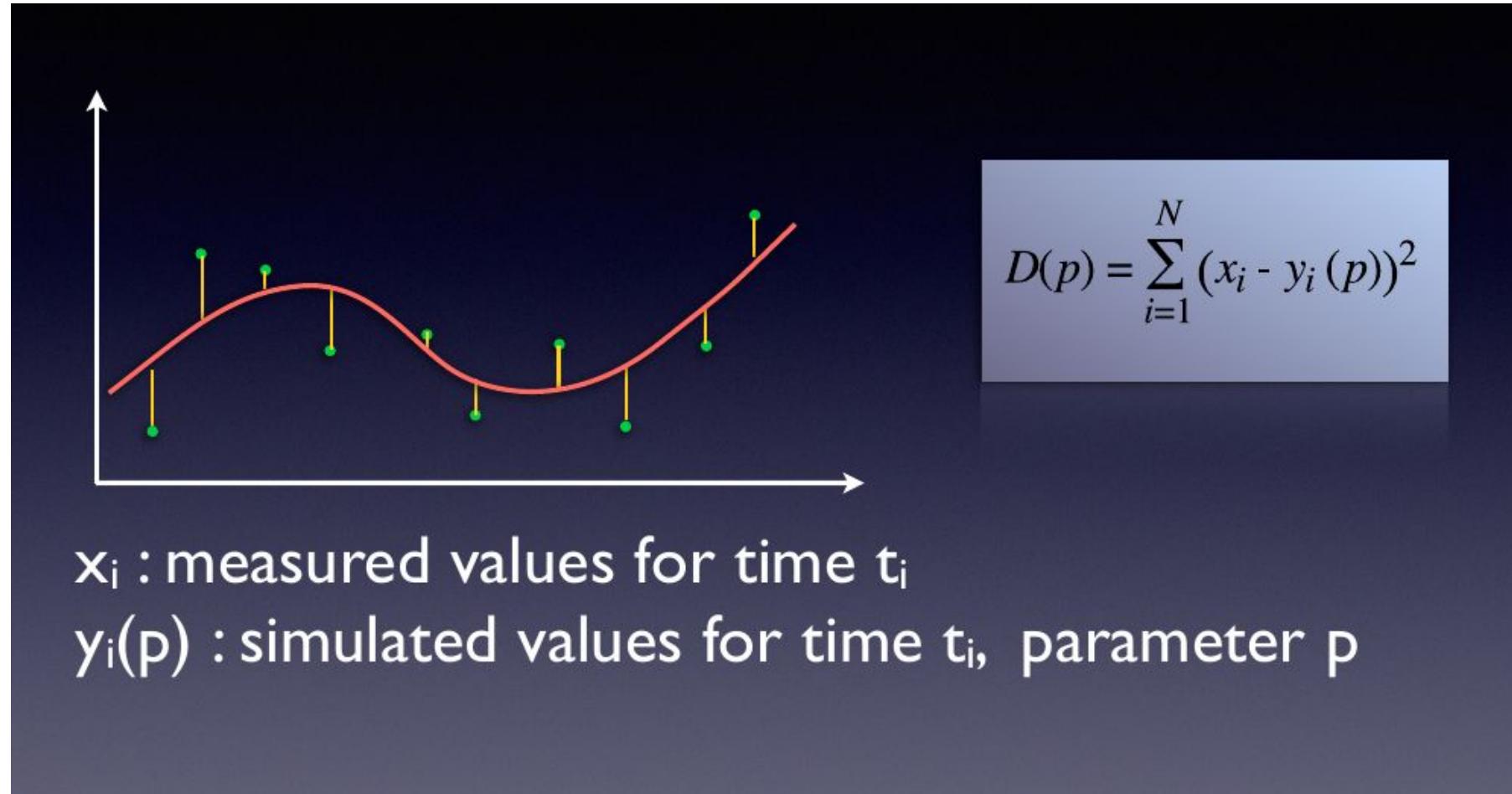
Steady State	
Name	Value
Resolution	1e-09
Derivation Factor	0.001
Use Newton	<input checked="" type="checkbox"/>
Use Integration	<input checked="" type="checkbox"/>
Use Back Integration	<input type="checkbox"/>
Accept Negative Concentrations	<input type="checkbox"/>
Iteration Limit	50
Maximum duration 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



# Parameter Estimation

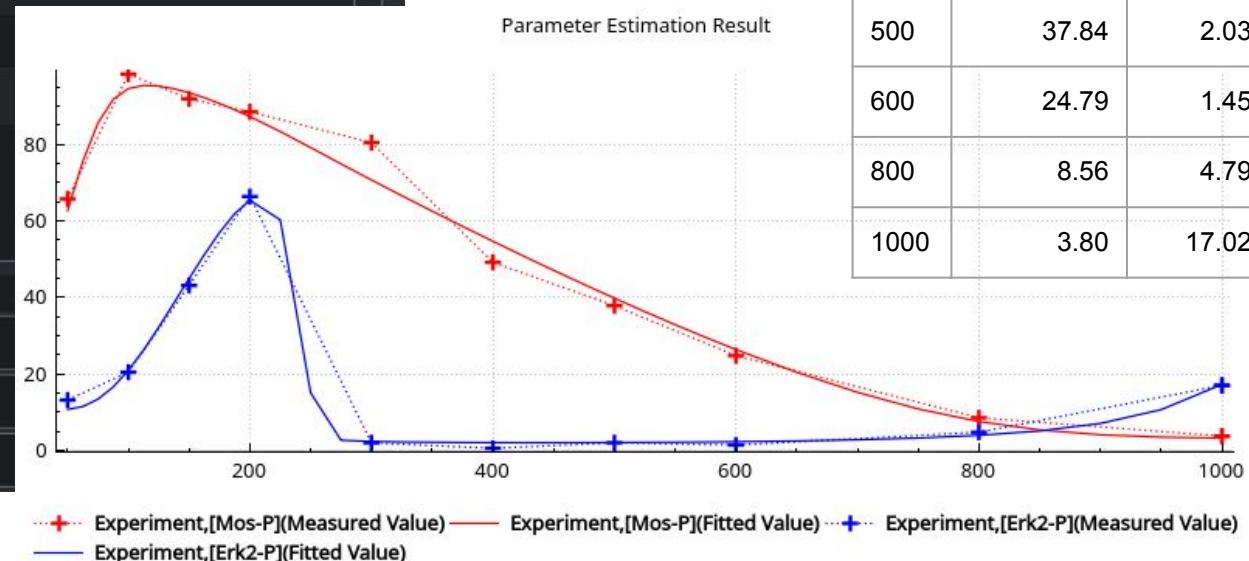
**Parameter Estimation**

update model    executable  
 Experimental Data    Validation Data  
 Randomize Start Values    Create Parameter Sets    Calculate Statistics    Use Time Sens

Parameters (6) Constraints (0)

1	$0.25 \leq (\text{MAPKK activation}).V1 \leq 4.75$ ; Start Value = 0.252586
2	$0.025 \leq (\text{MAPKK inactivation}).V2 \leq 0.475$ ; 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: (MAPKK activation).V1  
 Lower Bound: -Infinity   0.25  
 Upper Bound: +Infinity   4.75  
 Start Value: 0.252586



time	MAPKK-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](https://doi.org/10.1016/j.bpj.2023.06.013)

VCell BioModels referenced in publication

user: les

biomodel name: [FRAP\\_Membrane\\_Rel](#)

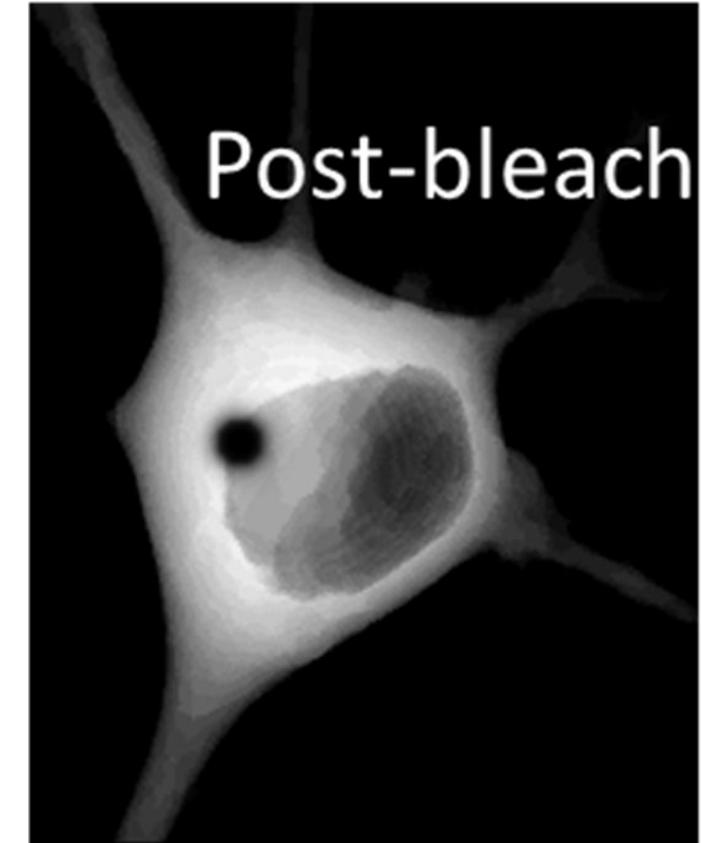
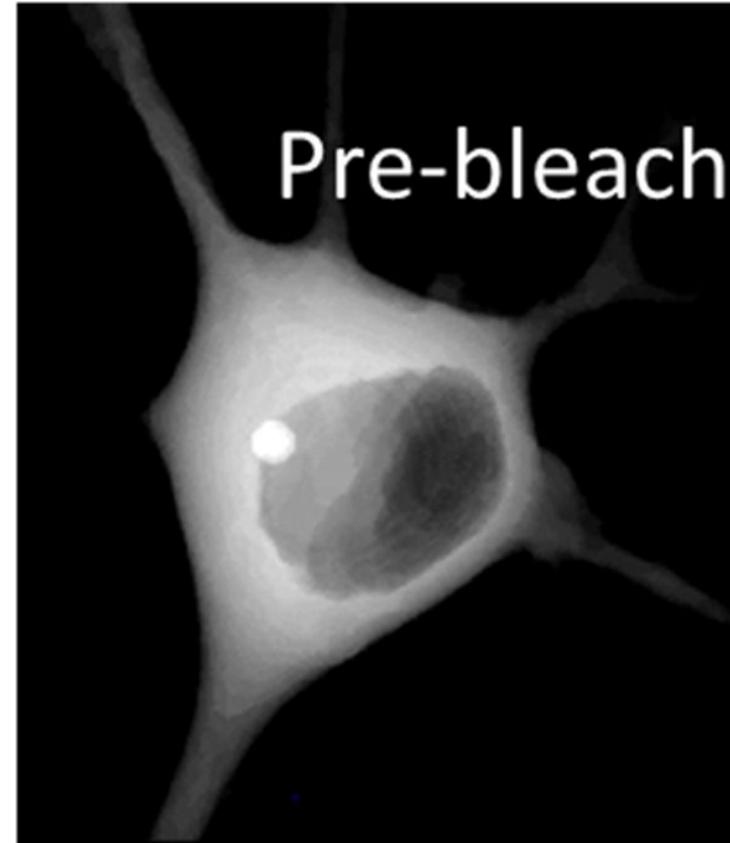
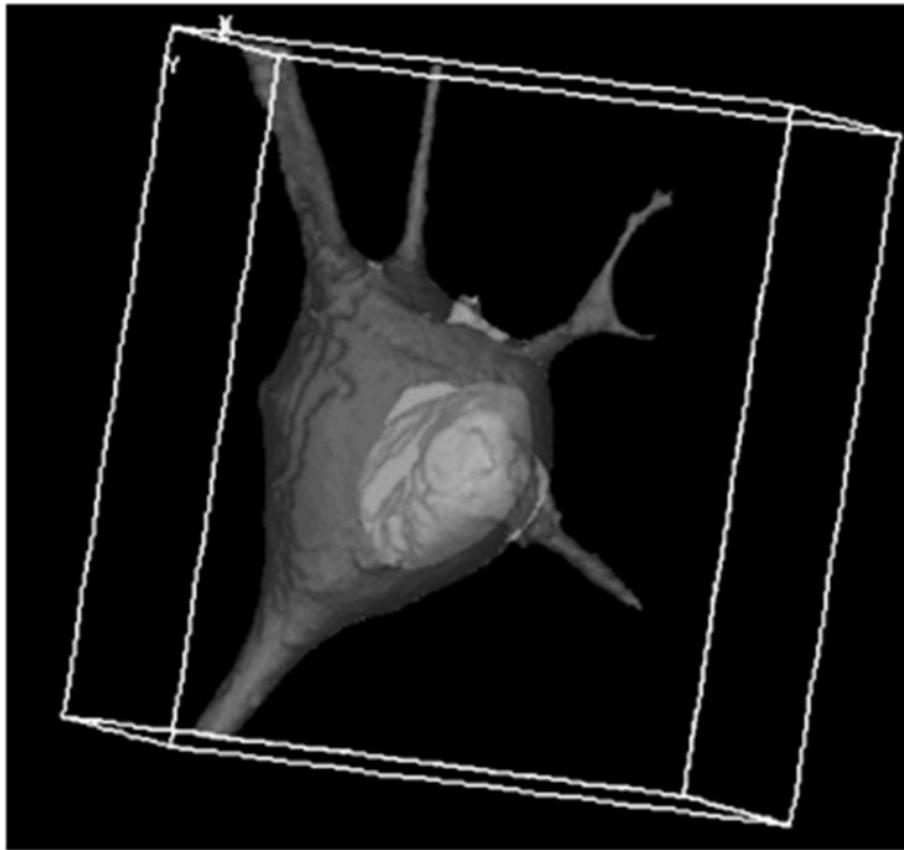
biomodel name: [FRAP\\_Cyt](#)

biomodel name: [FRAP\\_Cyt\\_Membrane\\_Binding](#)

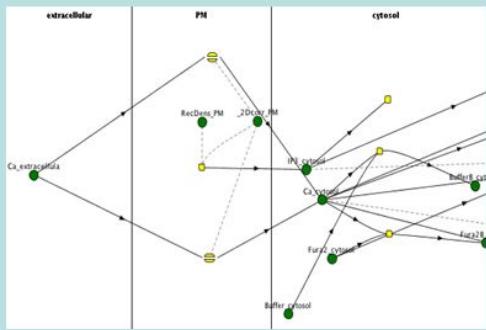
biomodel name: [FRAP Condensate Droplet](#)



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

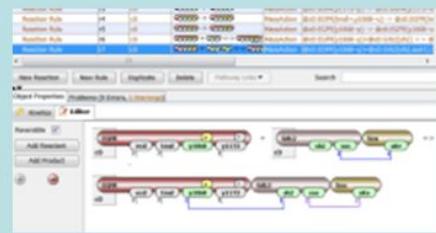


# Physiology (Biological Mechanisms)



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)

All structures and subdomains must be mapped to run a simulation. Use line tool or drop down menu in the 'subdomain' column.

Membrane boundary conditions are chosen alphabetically among the adjacent subdomains.

Structure	Subdomain	Size Ratio	X <sub>i</sub>	X <sub>j</sub>	Y <sub>i</sub>	Y <sub>j</sub>	Z <sub>i</sub>	Z <sub>j</sub>
Cyt	Cyto	1 : 1	F <sub>11</sub>	F <sub>12</sub>	F <sub>21</sub>	F <sub>22</sub>	F <sub>31</sub>	F <sub>32</sub>
EC	EC	1 : 1	F <sub>11</sub>	F <sub>12</sub>	F <sub>21</sub>	F <sub>22</sub>	F <sub>31</sub>	F <sub>32</sub>
M	Cyto(EC)	1 : 1						

### Choice of Simulation types:

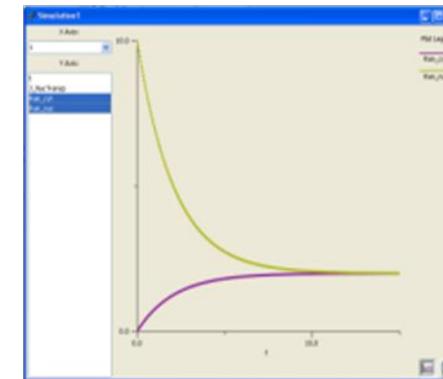
Ordinary Differential  
Equations

Partial Differential Equations

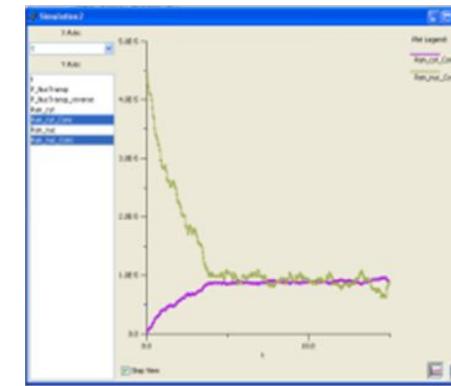
Non-Spatial Stochastic  
(Gillespie)

Spatial Stochastic  
(Smoldyn)

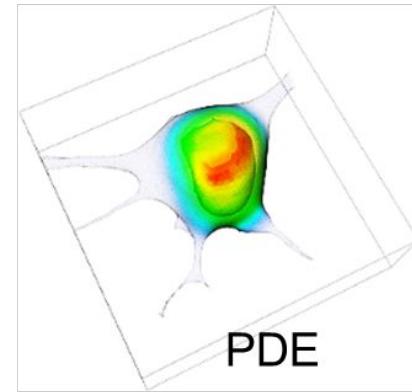
Hybrid Spatial  
Deterministic/stochastic  
Network Free Stochastic



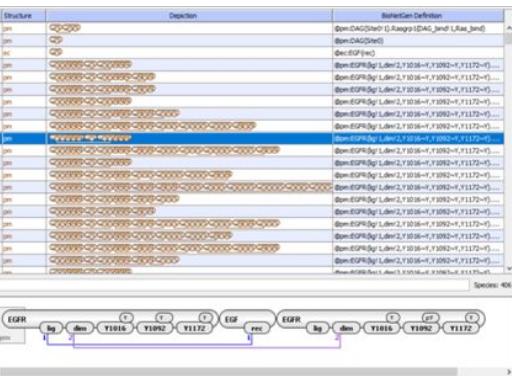
ODE



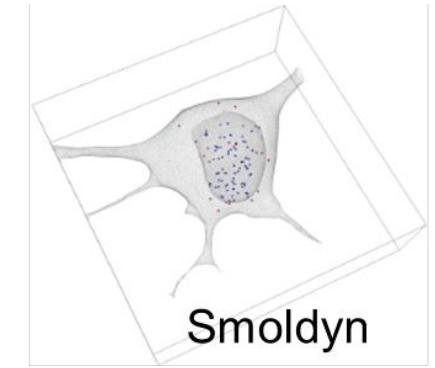
Nonspatial Stochastic  
(Gillespie, Hybrid)



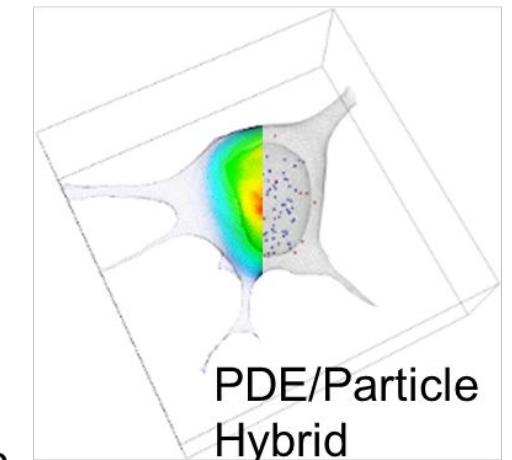
PDE



NFSim

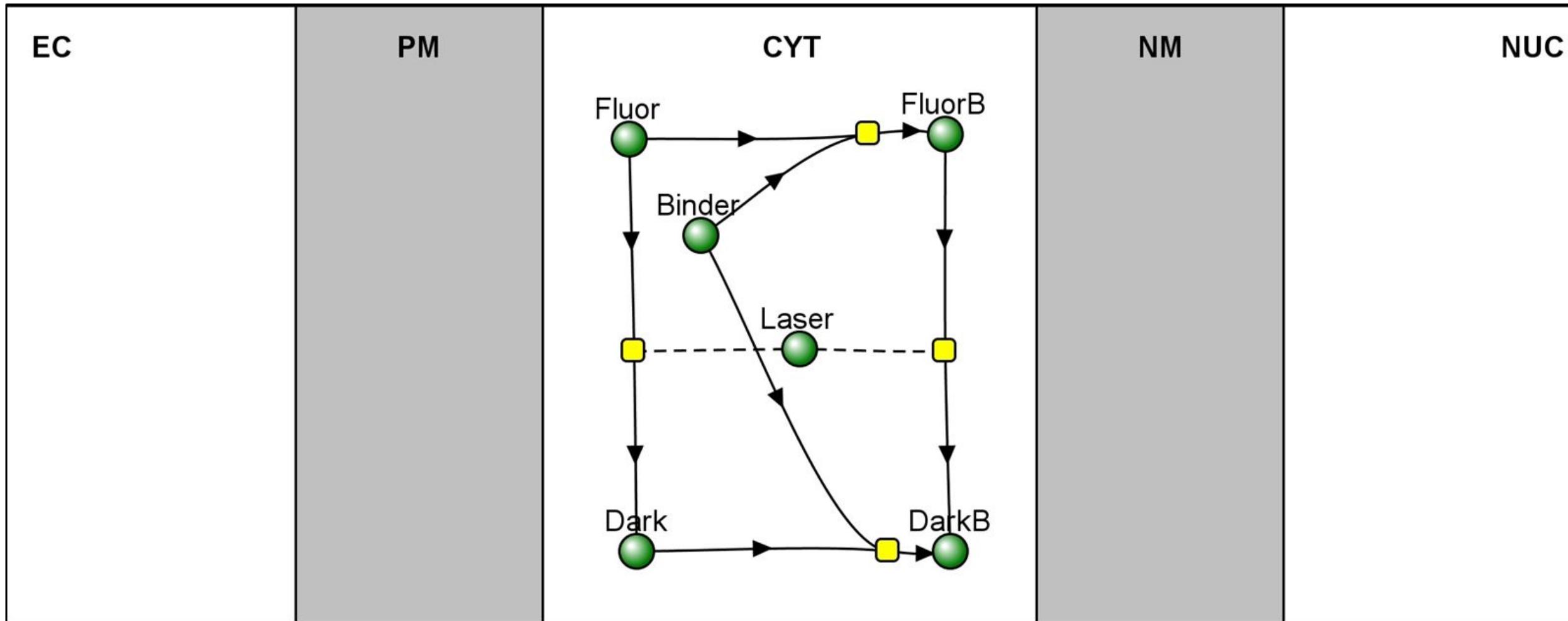


Smoldyn



PDE/Particle  
Hybrid

## 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)

 $d/dt$  Image-based bindin

VCell DB

BioModels

## Search

 frap[Advanced >>](#) Has[Search](#)[Show](#)

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

New Application ▾

Delete

More Copy Actions ▾

Compare...

Search



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)

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

**Geometry**  
**Specifications**  
**Protocols**  
**Simulations**

Parameters, Functions, Units, etc.

Pathway

VCell DB BMDB Pathway Comm

BioModels

Search  Advanced > Has Spatial

Search 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 ▾

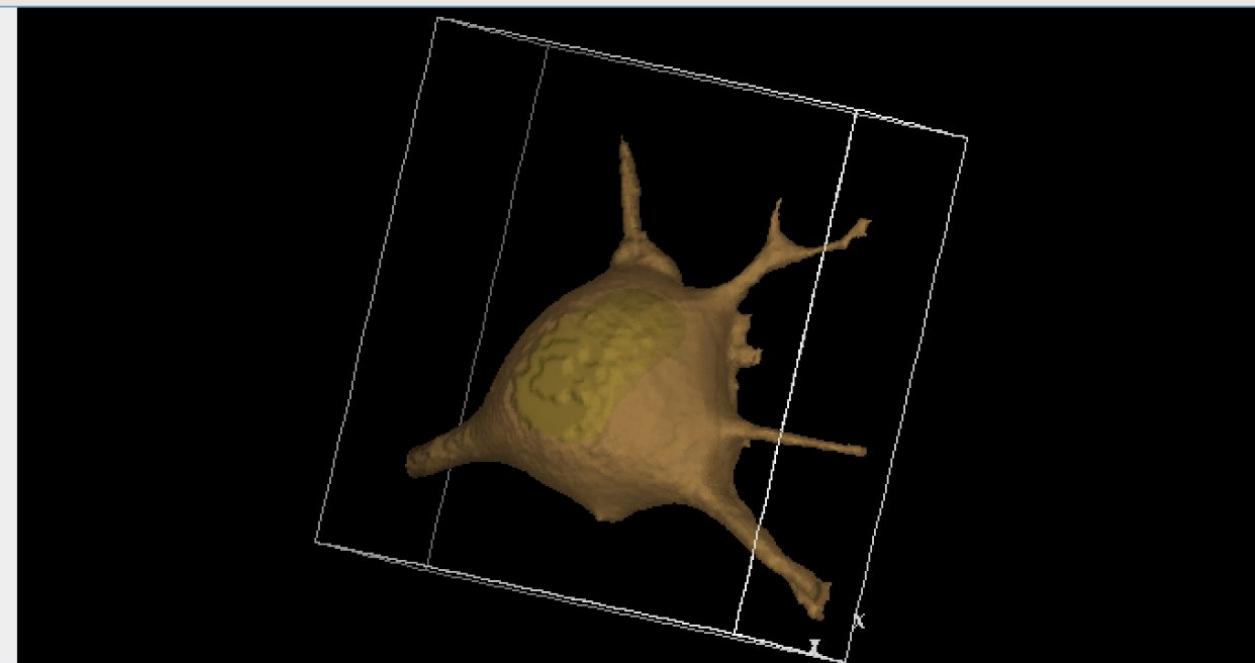
Name	Value
ec	
cytosol	
Nucleus	

Front Back Add Subdomain ▾ Delete

Slice View Surface View Geometric Region Details

Reset View

Opacity: -100, -75, -50, -25, -0



812MB / 1,241.5MB

$d/dt$  Image-based binding to li  
 $d/dt$  Large Liquid Droplet Edge  
 $d/dt$  Large Liquid Droplet Image  
 $d/dt$  Large Liquid Droplet Low K  
 $d/dt$  Liquid droplet Edge Dif Bar  
 $d/dt$  Liquid Droplet Low Kd, low  
 $d/dt$  Non spatial to determine S  
 $d/dt$  Small Liquid Droplet Edge I

## Geometry

## Specifications

## Protocols

VCell DB

BioModels

### Search

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[Advanced >>](#)

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Search

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Geometry

Specifications

Protocols

Simulations

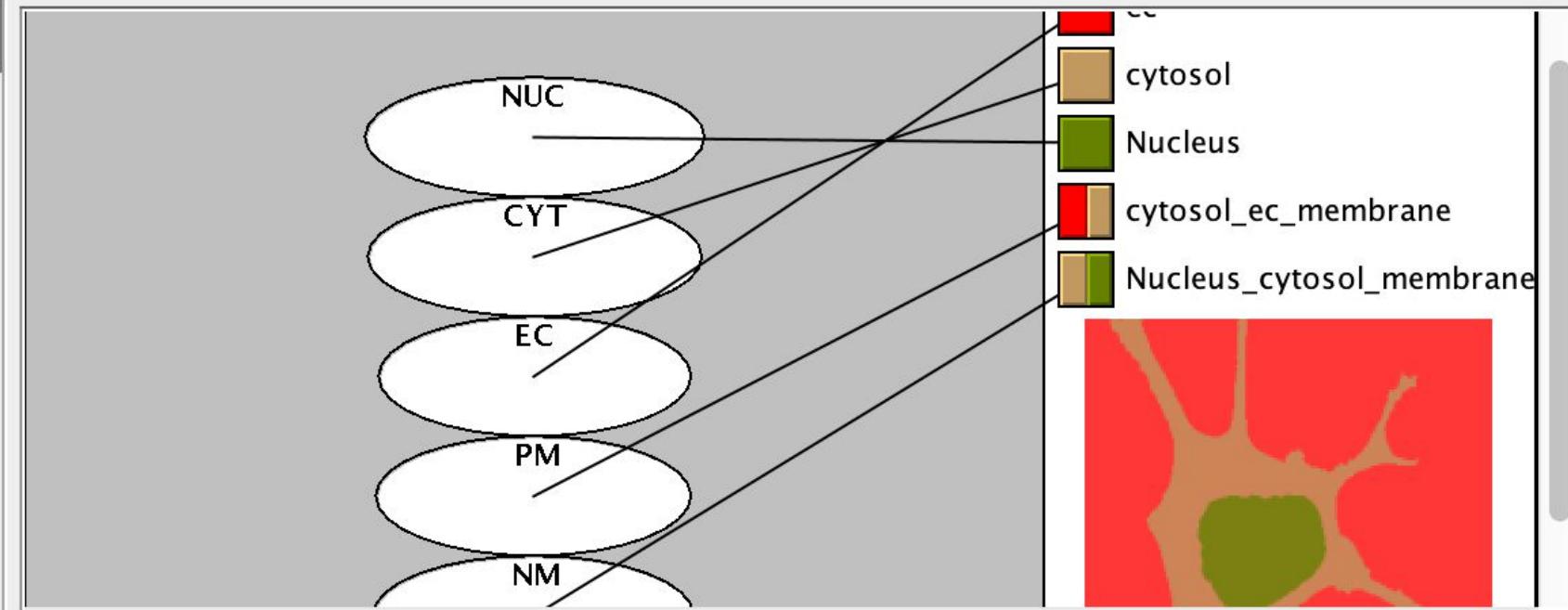
Structure Mapping

Geometry Definition

Kinematics



All structures and subdomains must be mapped to run a simulation. Use line tool or drop down menu in the 'subdomain' column.



Membrane boundary conditions are chosen alphabetically among the adjacent subdomains.

Structure	Subdomain	Size Ratio	X-	X+	Y-	Y+	Z-	Z+
NUC	Nucleus	1 [ 1 ]	Flux	Flux	Flux	Flux	Flux	Flux
CYT	cytosol	1 [ 1 ]	Flux	Flux	Flux	Flux	Flux	Flux
EC	ec	1 [ 1 ]	Flux	Flux	Flux	Flux	Flux	Flux
PM	cytosol_ec_m	1 [ 1 ]	Flux	Flux	Flux	Flux	Flux	Flux

## 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"/>	$((((x - 23.0) ^ 2.0) + ((y - 39.0) ^ 2.0) + ((z - 13.0) ^ 2.0)) < 4.0)$ · BinderD
Dark	CYT		<input type="checkbox"/>	<input type="checkbox"/>	0.0 [μM]	<input type="checkbox"/>	$((((x - 23.0) ^ 2.0) + ((y - 39.0) ^ 2.0) + ((z - 13.0) ^ 2.0)) < 4.0)$ · BinderD
Binder	CYT		<input type="checkbox"/>		$(591.4462440264 * (((x - 23.0) ^ 2.0) + ((y - 39.0) ^ 2.0) + ((z - 13.0) ^ 2.0)) < 4.0)$ · BinderD	<input type="checkbox"/>	$((((x - 23.0) ^ 2.0) + ((y - 39.0) ^ 2.0) + ((z - 13.0) ^ 2.0)) < 4.0)$ · BinderD
FluorB	CYT		<input checked="" type="checkbox"/>		$(8.553755973599845 * (((x - 23.0) ^ 2.0) + ((y - 39.0) ^ 2.0) + ((z - 13.0) ^ 2.0)) < 4.0)$ · BinderD	<input type="checkbox"/>	$((((x - 23.0) ^ 2.0) + ((y - 39.0) ^ 2.0) + ((z - 13.0) ^ 2.0)) < 4.0)$ · BinderD
Laser	CYT		<input type="checkbox"/>		$(\exp(-(((z - 10.0) ^ 2.0) / (2.0 * (\text{sigmaaxial})))) * BinderD)$	<input type="checkbox"/>	0.0 [μm².s⁻¹]
DarkB	CYT		<input type="checkbox"/>		0.0 [μM]	<input type="checkbox"/>	$((((x - 23.0) ^ 2.0) + ((y - 39.0) ^ 2.0) + ((z - 13.0) ^ 2.0)) < 4.0)$ · BinderD

Search 

Object Properties

Annotations

Problems (0 Errors, 1 Warnings)

Database File Info



Description	Parameter	Expression	Units
initial concentration for FluorB	initConc	$8.553755973599845 \cdot (((x - 23.0) ^ 2.0) + ((y - 39.0) ^ 2.0) + ((z - 13.0) ^ 2.0)) < 4.0)$ · BinderD	μM
diffusion constant for FluorB	diff	$((((x - 23.0) ^ 2.0) + ((y - 39.0) ^ 2.0) + ((z - 13.0) ^ 2.0)) < 4.0) \cdot BinderD$	μm².s⁻¹

 Geometry Specifications Protocols Simulations

Electrical

Events

 Rate Rules Assignment Rules

Microscope Measurements

**Fluorescence Function Name**

fluor

**Point Spread Function** Z Projection Gaussian

Sigma XY

Sigma Z

**Choose Fluorescent Species**

Dark

Binder

Laser

DarkB

FluorB

Fluor

&gt;&gt;

&lt;&lt;

## Simulations

## Output Functions

## Generated Math



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

## Object Properties

## Annotations

## Problems (0 Errors, 1 Warnings)

## Database File Info

## Annotation:

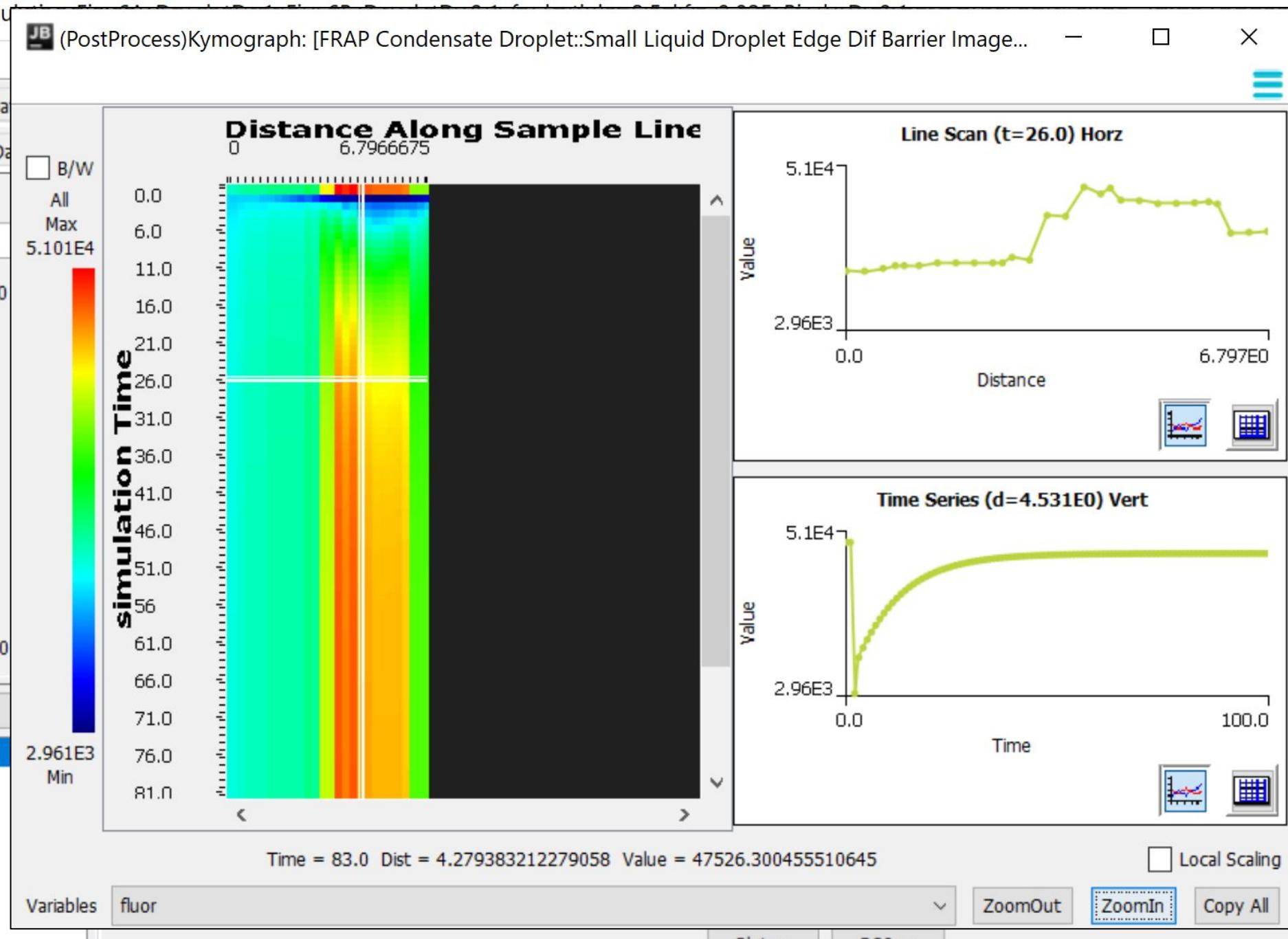
Fig. 6A. DropletD=1, Fig. 6B. DropletD=0.1; for both kr=2.5, kf = 0.025, BinderD=0.1

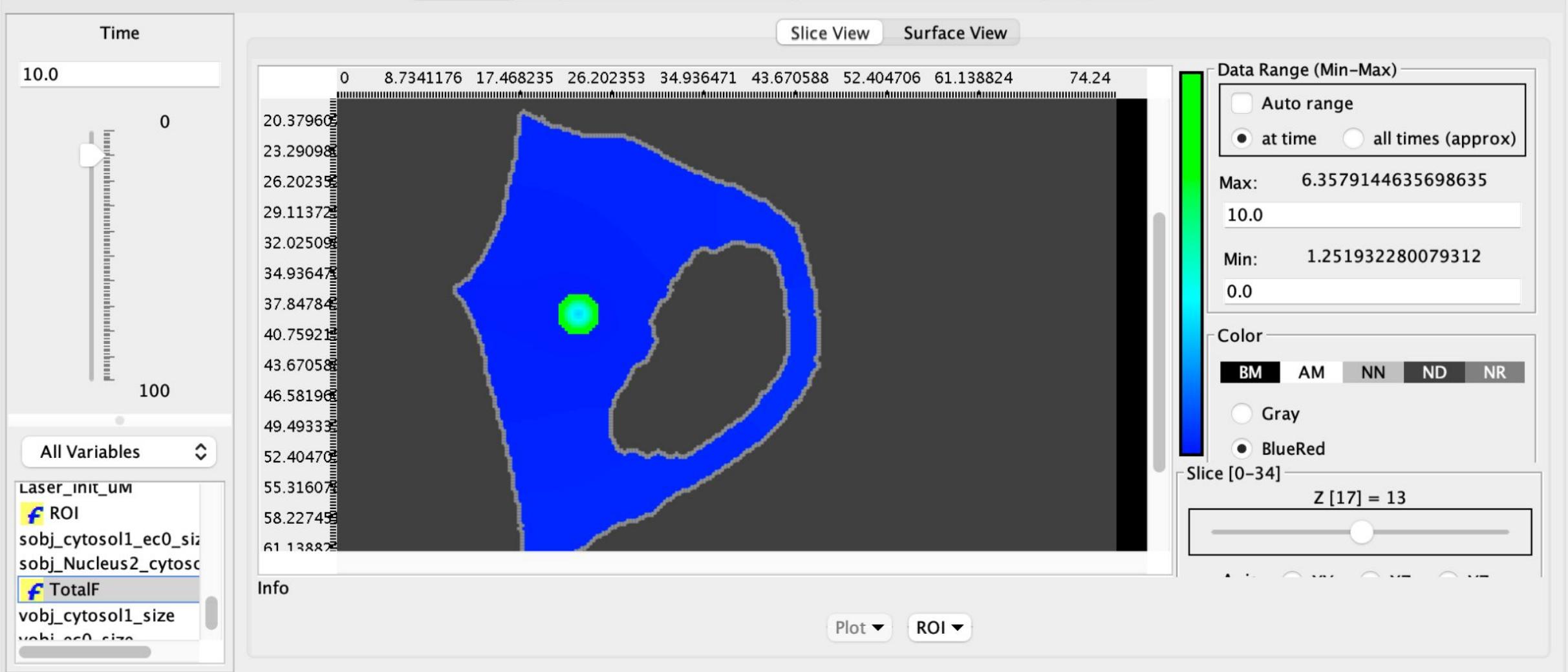
## Settings:

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





## Choose Parameter Values

DropletD

0.1

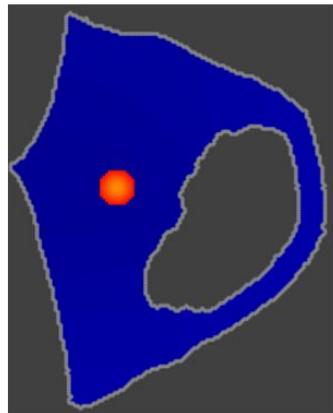
1.0

3.0

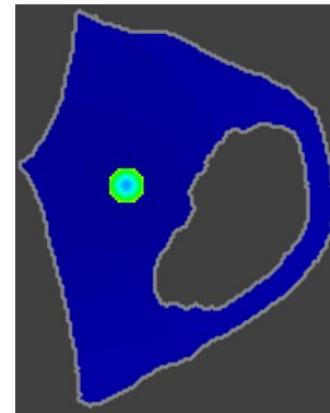
# Example 2: Using PDEs to simulate FRAP of a biomolecular condensate

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

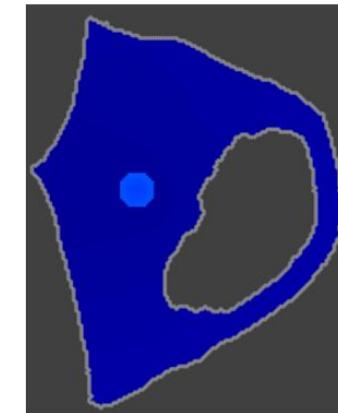
A.  $D=1 \mu\text{m}^2/\text{s}$   
 $k_r = 2.5 \text{ s}^{-1}$



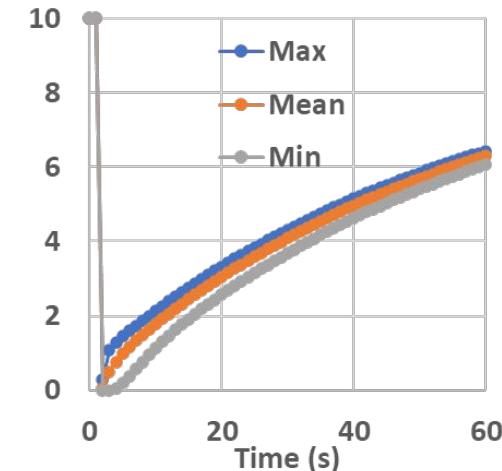
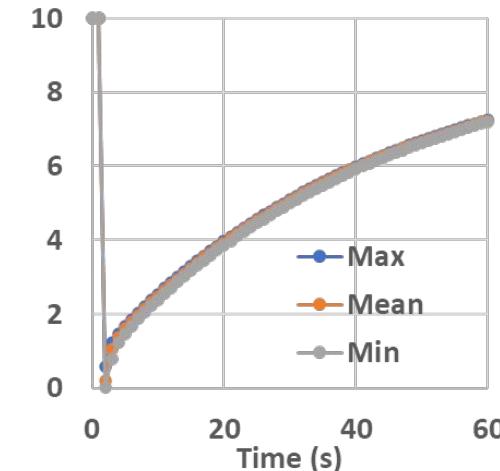
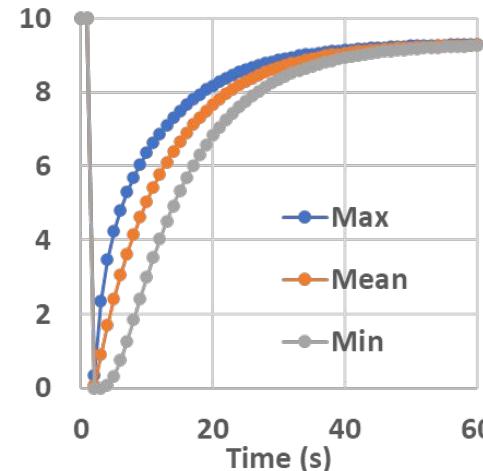
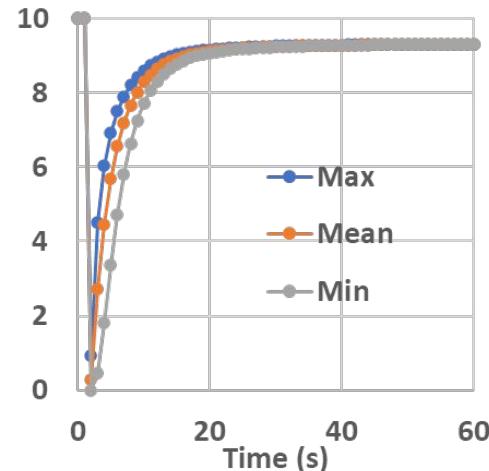
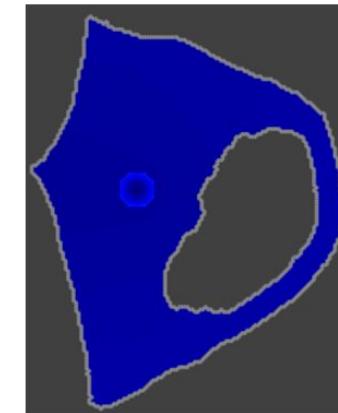
B.  $D=0.1 \mu\text{m}^2/\text{s}$   
 $k_r = 2.5 \text{ s}^{-1}$



C.  $D=1 \mu\text{m}^2/\text{s}$   
 $k_r = 0.025 \text{ s}^{-1}$

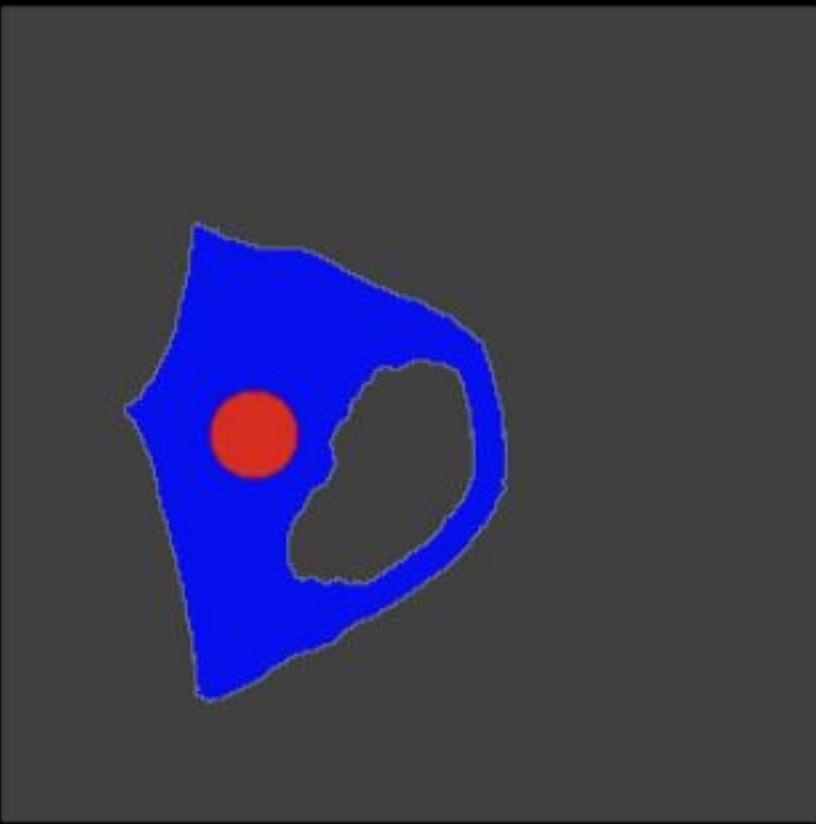


D.  $D=0.1 \mu\text{m}^2/\text{s}$   
 $k_r = 0.025 \text{ s}^{-1}$



# 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*

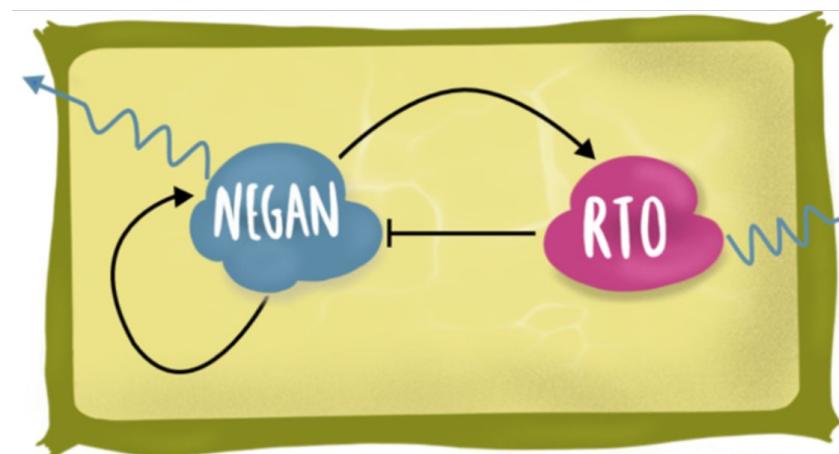
Archive

 Download Full Issue

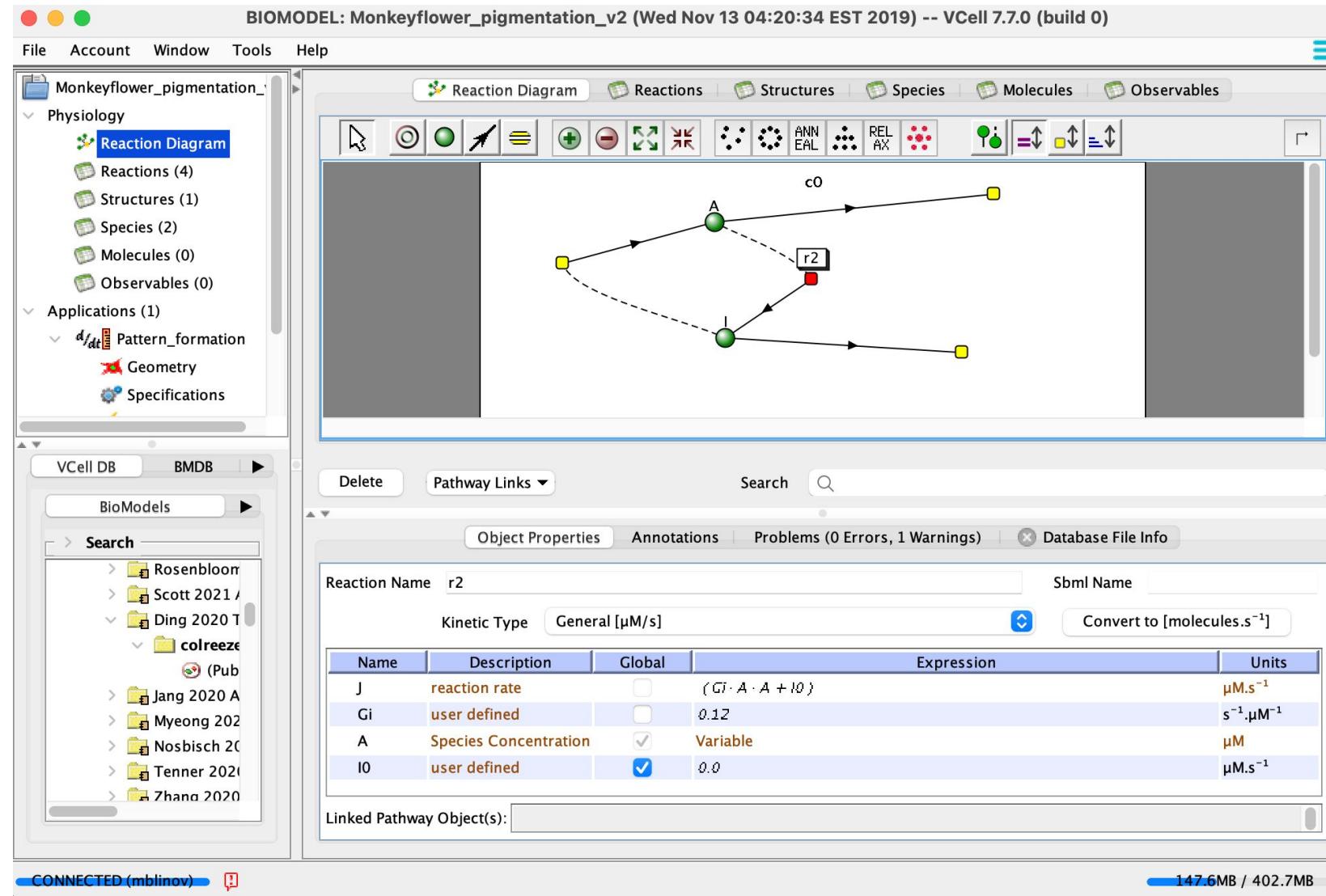
## Two MYB Proteins in a Self-Organizing Activator-Inhibitor System Produce Spotted Pigmentation Patterns

Baoqing Ding<sup>1,9</sup> · Erin L. Patterson<sup>2,3,8,9</sup> · Srinidhi V. Holalu<sup>2,3,9</sup> · ... · Michael L. Blinov<sup>6</sup> ·Benjamin K. Blackman  · Yao-Wu Yuan  ... 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



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

The screenshot shows the BIOMODEL software interface for a model named "Monkeyflower\_pigmentation\_v2".

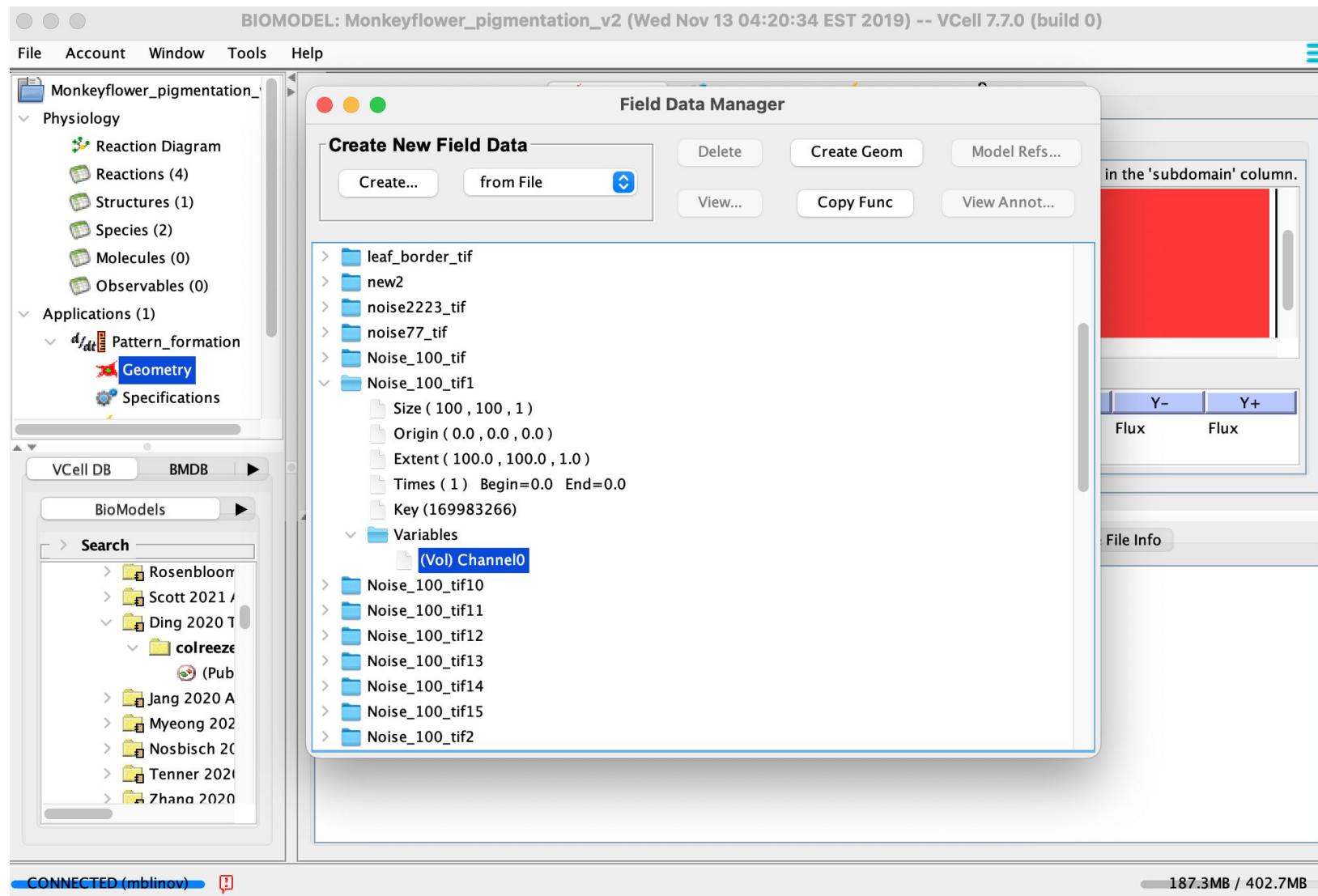
**Specifications Tab:**

Species	Structure	Depiction	Clamped	Rules	Initial Condition	Well Mixed	Diffusion Constant
A	c0	●	<input checked="" type="checkbox"/>		((vcField('Noise_100.tif1', 'Channel0', 0.0, 'Volume')) / 255.0) · 0.2	<input checked="" type="checkbox"/>	0.01 [ $\mu\text{m}^2 \cdot \text{s}^{-1}$ ]
I	c0	●	<input type="checkbox"/>		0.0 [ $\mu\text{M}$ ]	<input type="checkbox"/>	0.5 [ $\mu\text{m}^2 \cdot \text{s}^{-1}$ ]

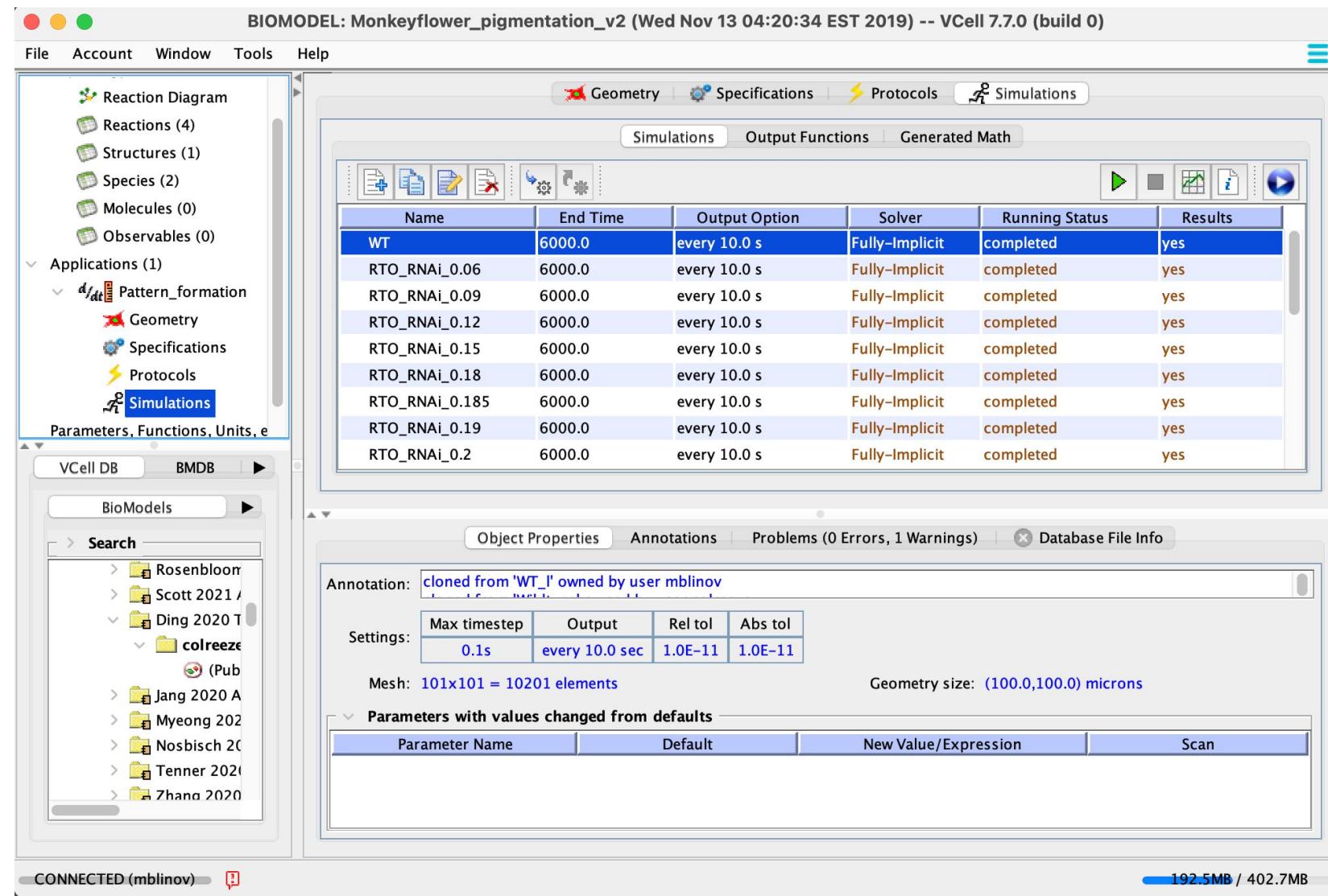
**Object Properties Panel:**

Description	Parameter	Expression	Units
initial concentration for A	initConc	<code>vcField ('Noise_100.tif1', 'Channel0', 0.0, 'Volume') / 255.0 · 0.2</code>	$\mu\text{M}$
diffusion constant for A	diff	0.01	$\mu\text{m}^2 \cdot \text{s}^{-1}$
Boundary Condition X- for A	BC_Xm	<zero flux>	$\mu\text{M} \cdot \mu\text{m} \cdot \text{s}^{-1}$
Boundary Condition X+ for A	BC_Xp	<zero flux>	$\mu\text{M} \cdot \mu\text{m} \cdot \text{s}^{-1}$
Boundary Condition Y- for A	BC_Ym	<zero flux>	$\mu\text{M} \cdot \mu\text{m} \cdot \text{s}^{-1}$
Boundary Condition Y+ for A	BC_Yp	<zero flux>	$\mu\text{M} \cdot \mu\text{m} \cdot \text{s}^{-1}$
Velocity X for A	Vel_X	<0.0>	$\mu\text{m} \cdot \text{s}^{-1}$
Velocity Y for A	Vel_Y	<0.0>	$\mu\text{m} \cdot \text{s}^{-1}$

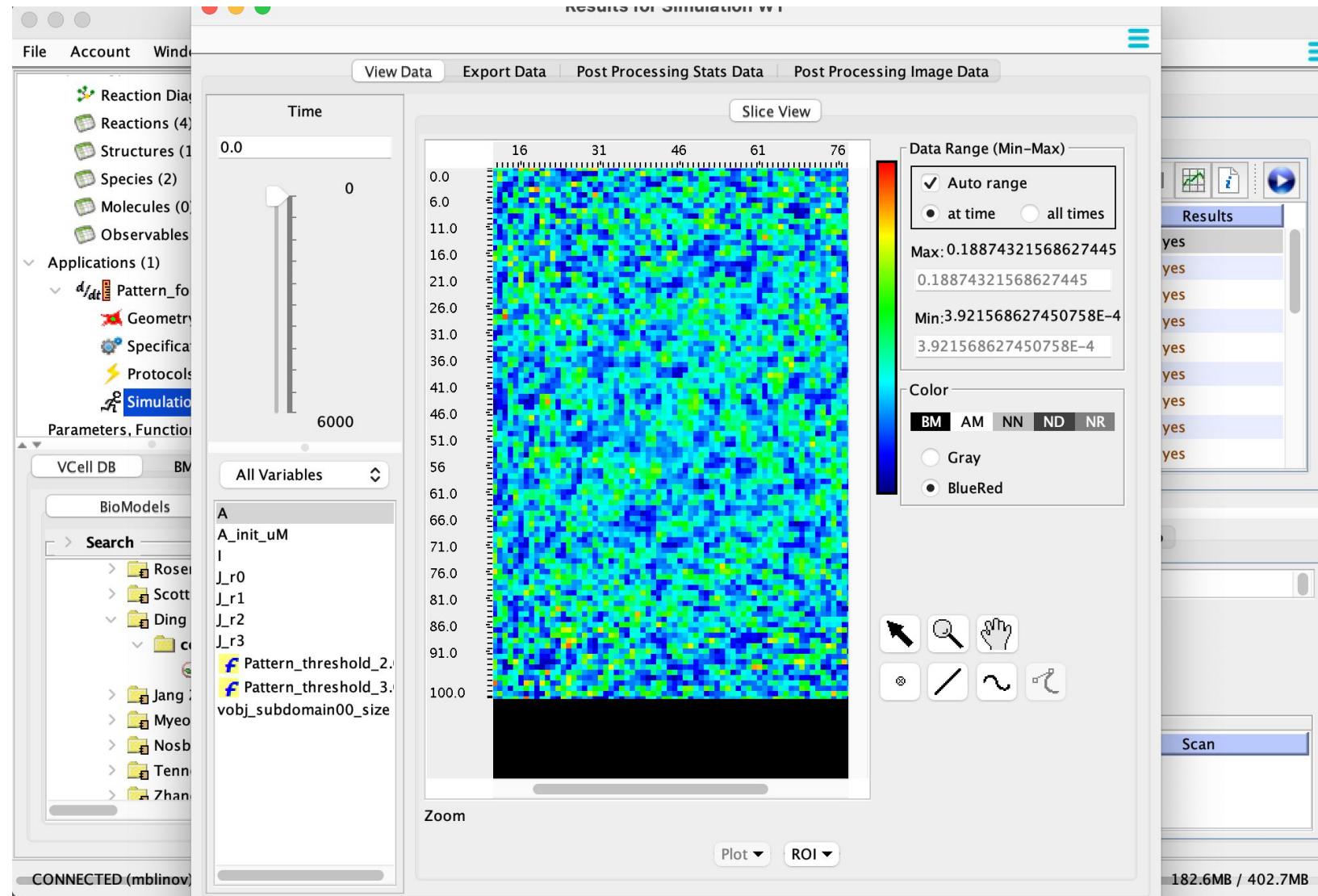
# In VCell non-uniform initial distribution are called field data



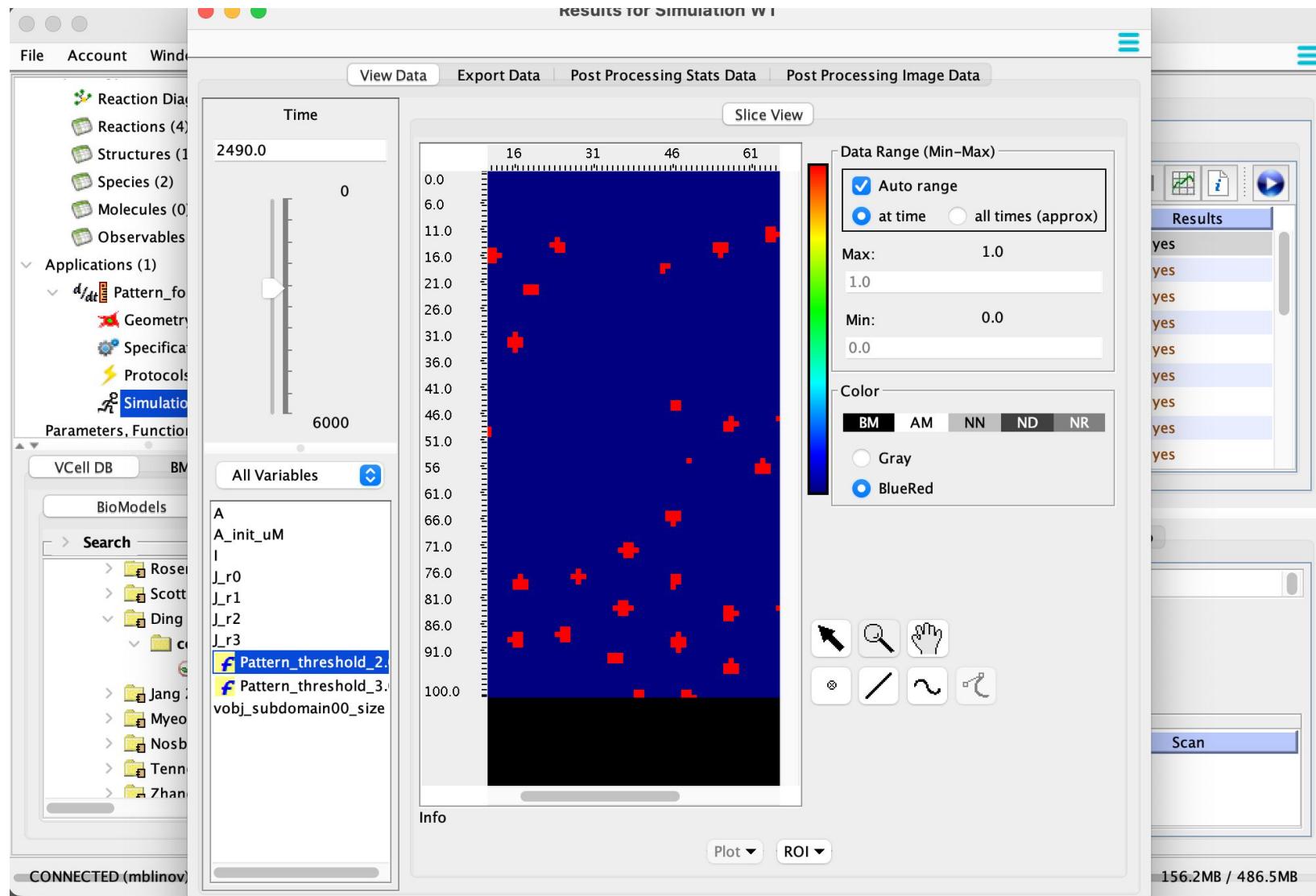
# Now we demonstrate how this data is used



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 Time

Export Table

BM Name	App Name	Sim Name	Time Slice	Format	Date Exported
Monkeyflower_pigmentation_v2	PatternFormation	WT	0.0/6000.0	N5	2024/11/22 15:00...
Tutorial_MultiApp	d/dt 3D pde	Simulation4	0.0/9.99999999999999...	N5	2024/11/19 15:13:...
Tutorial_MultiApp	d/dt 3D pde	Simulation4	0.0/9.99999999999999...	N5	2024/11/19 14:58:...
Rule-based_egfr_compart	d/dt 3D	Spatial_3D	0.0/12.0	N5	2024/11/19 14:09:...
Brown et al 2008 Purkinje 3D – 12 PF Sti...	d/dt 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...	d/dt 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	0.0/9.999999999990...	JPEG	2024/10/22 14:24:...
Brown et al 2008 Purkinje 3D – 12 PF Sti...	d/dt 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...	d/dt 3D PIP2_experimentally derived geom...	stimulated synthesis and lat d...	0.0/2.0	JPEG	2024/10/22 14:20:...
Tutorial_MultiApp	d/dt 3D pde	Simulation4	0.0/9.999999999999...	JPEG	2024/10/22 14:18:...

**Copy Link** **Delete Export** **Search**

Export Details

Properties

Variables List: [A]

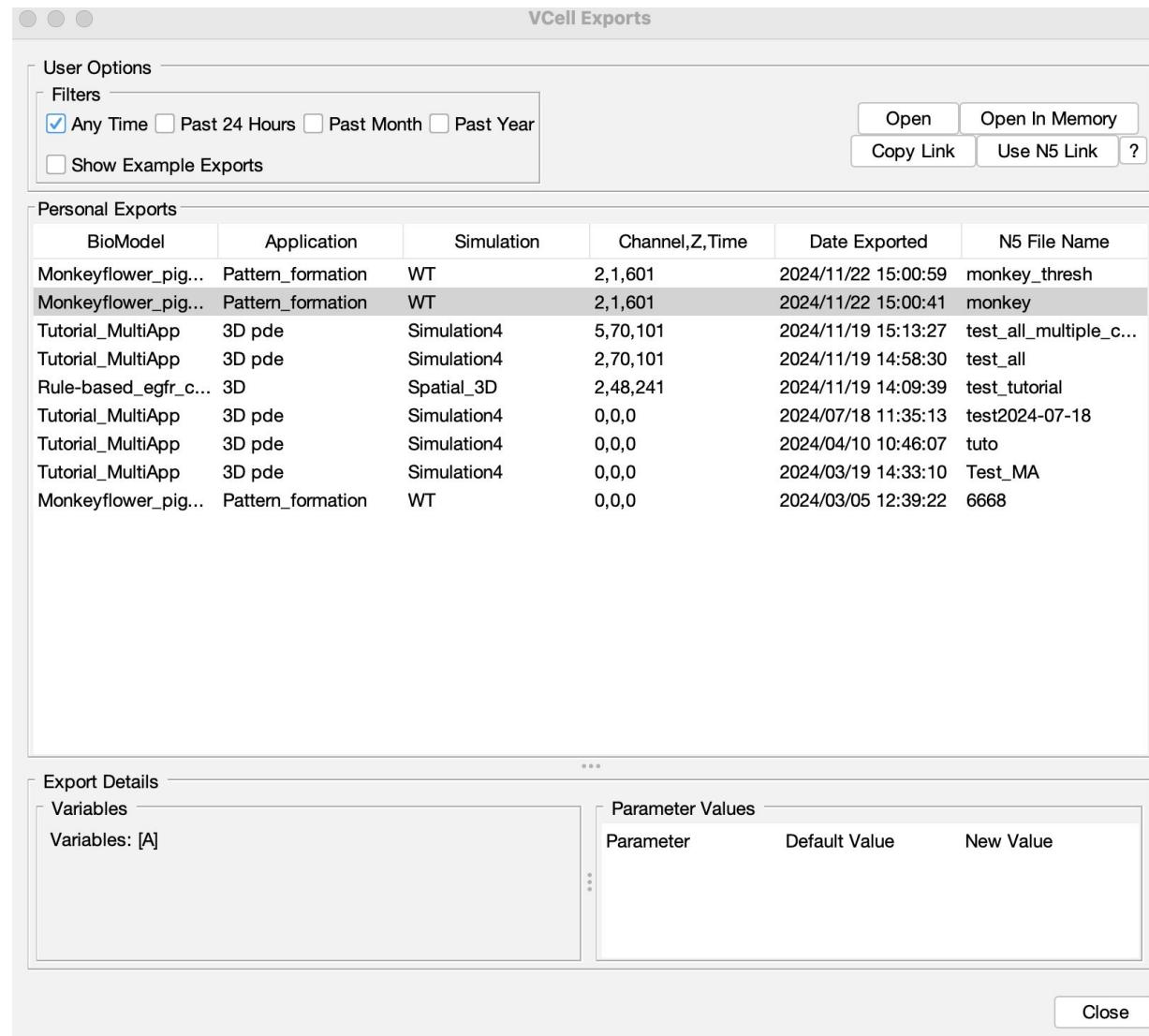
Simulation ID: SimID\_169880916\_0\_  
Name: monkey  
Link: <https://vcell.cam.uchc.edu/n5Data/mblinov/0d8874422cbdd77.n5?dataSetName=7115835095>

Parameters

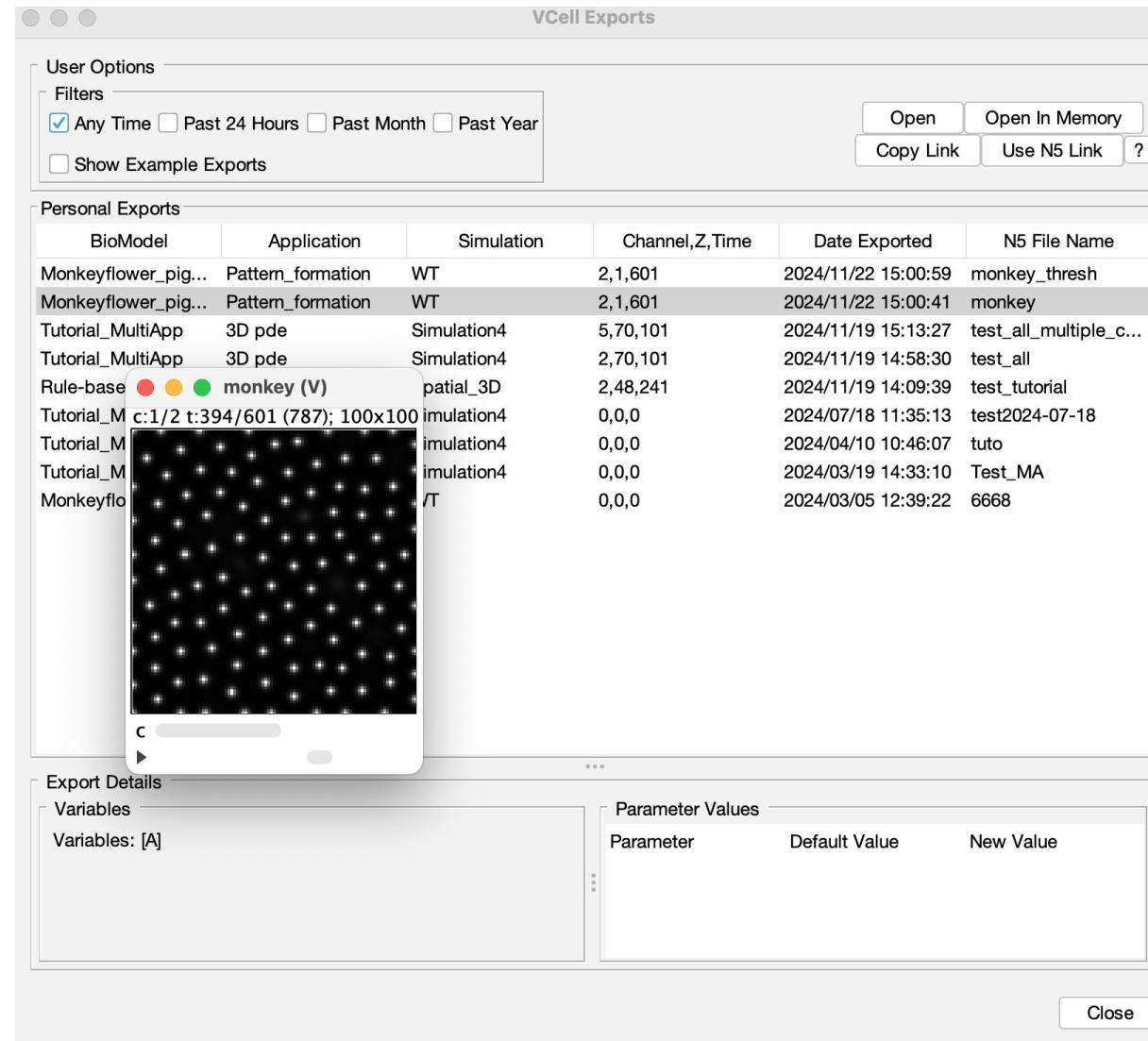
Parameter	Default Value	New Value
-----------	---------------	-----------

**Close**

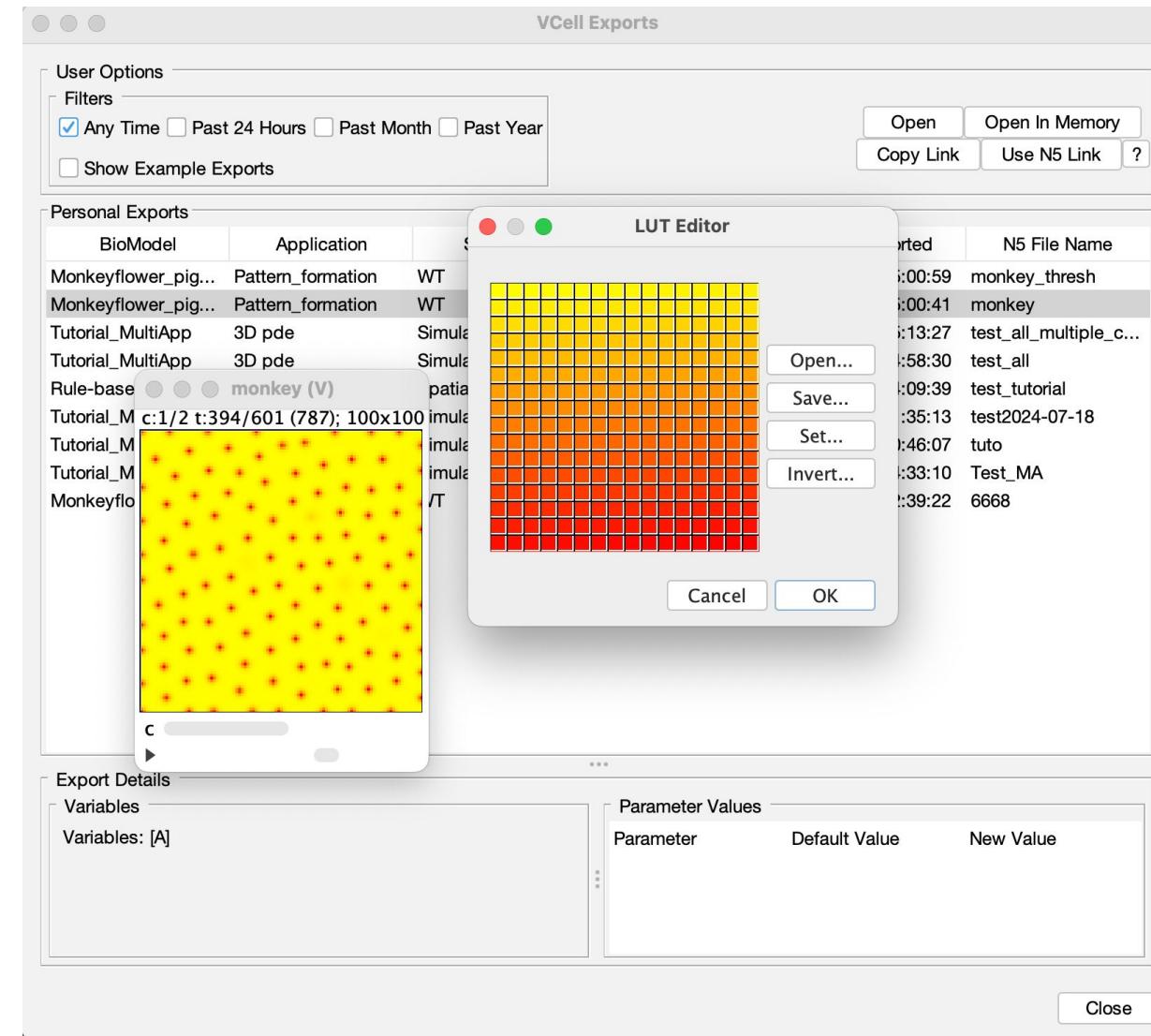
# These images are accessible from FIJI/ImageJ with VCell plugin as hyperstacks

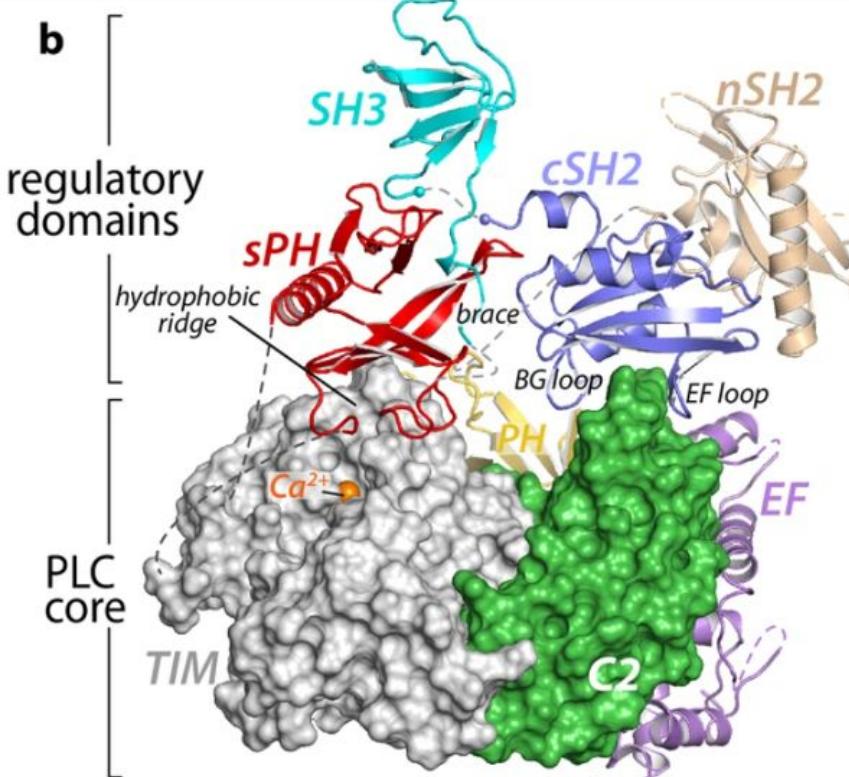


# These images are accessible from FIJI/ImageJ with VCell plugin as hyperstacks



# Using color LUT to compare VCell images with real data





# A kinetic model of phospholipase C- $\gamma$ 1 linking structure-based insights to dynamics of enzyme autoinhibition and activation

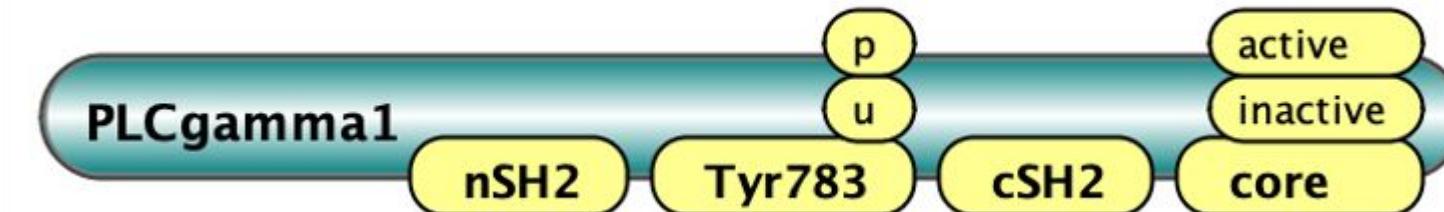
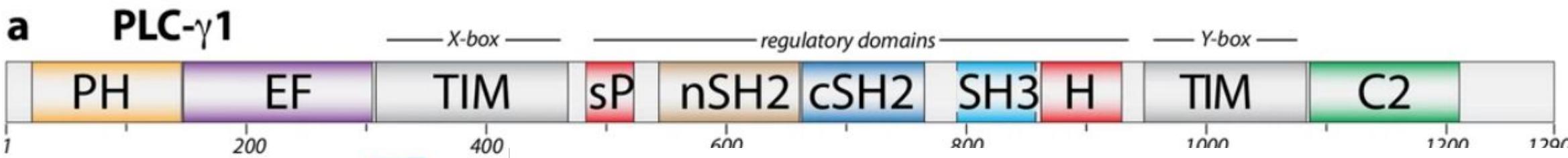
Received for publication, October 19, 2021, and in revised form, March 27, 2022. Published, Papers in Press, March 31, 2022,  
<https://doi.org/10.1016/j.jbc.2022.101886>

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Edited by Roger Colbran

**a** PLC- $\gamma$ 1



# Molecules

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)
- Structures (1)
- Species (2)
- Molecules (2)**
- Observables (9)

Applications (1)

- Application0

Parameters, Functions, Units, etc.

Pathway

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) 168.7MB / 486.5MB

# Reactions

BIMODEL: 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

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- Observables (9)

Applications (1)

- Application0

Parameters, Functions, Units, etc.

Pathway

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(pY!1).PLCgamma1(nSH2!1) ->
Reaction Rule r04	cell		MassAction			@cell:RTK(pY!1).PLCgamma1(nSH2!1,Ty783~p)
Reaction Rule r05	cell		MassAction			@cell:PLCgamma1(Tyr783~p) -> @cell:PLCgamma1(cSH21)
Reaction Rule r06	cell		MassAction			@cell:PLCgamma1(cSH21,core~inactive)
Reaction Rule r07	cell		MassAction			@cell:PLCgamma1(cSH21,core~inactive)
Reaction Rule r08	cell		MassAction			@cell:PLCgamma1(Tyr783~p,cSH2) -> @cell:PLCgamma1(cSH21,cSH2)
Reaction Rule r09	cell		MassAction			@cell:PLCgamma1(Tyr783~p!1,cSH2!1)
Reaction Rule r10	cell		MassAction			@cell:RTK(pY!1).PLCgamma1(nSH2!1,cSH2!1)
Reaction Rule r11	cell		MassAction			@cell:PLCgamma1(nSH2,core~inactive)
Reaction Rule r12	cell		MassAction			@cell:PLCgamma1(core~active) -> @cell:PLCgamma1(core~active)

New Reaction New Rule Duplicate Delete Pathway Links Search

Object Properties Annotations Problems (0 Errors, 1 Warnings)

Reversible

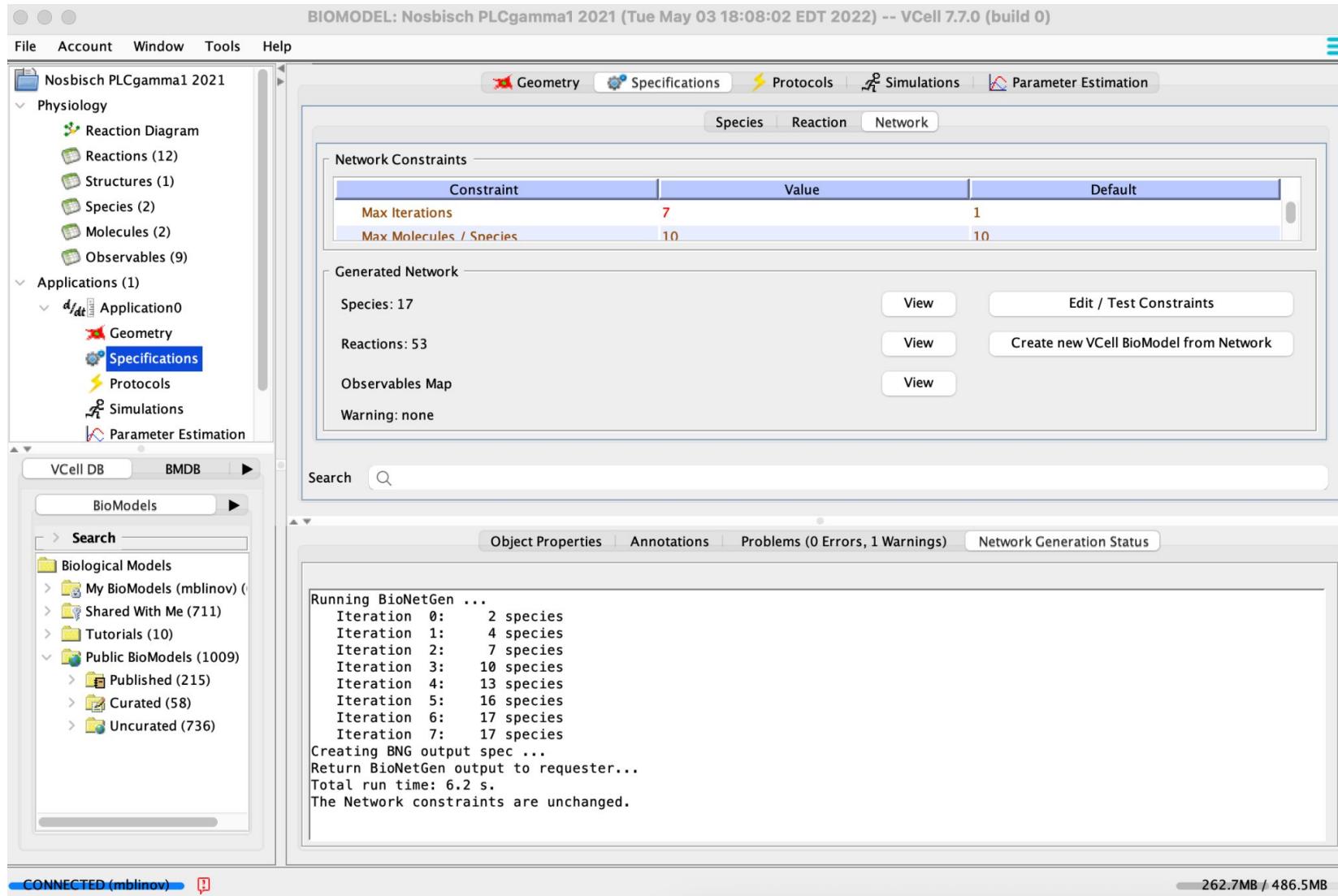
Add Reactant Add Product

Single Row Viewer  Show Molecule Color  Show Non-trivial  Show Differ...

Kinetics Editor

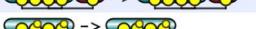
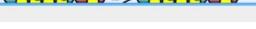
CONNECTED (mblinov) 189.9MB / 486.5MB

# Network generation

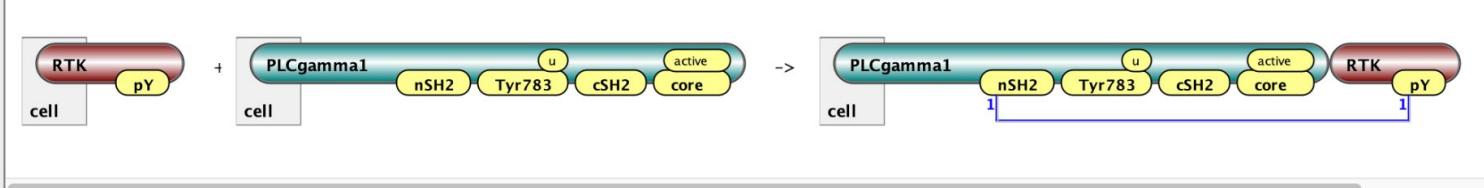


# Generated species and reactions

View Generated Reactions

Rule	Structure	Depiction	BioNetGen Definition
r02	cell		RTK(pY) + PLCgamma1(Tyr783~u,cSH2,core~active,nSH2) -> PLCgamma1(Tyr783~p,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~p1,cSH2!1,core~active,nSH2) -> PLCgamma1(Tyr783~p1,cSH2!1,core~active...)
r01	cell		RTK(pY) + PLCgamma1(Tyr783~u,cSH2!1,core~inactive!1,nSH2) -> PLCgamma1(Tyr783~u,cSH2!1,core~inactive...)
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~inactive...)
r01	cell		RTK(pY) + PLCgamma1(Tyr783~p,cSH2,core~inactive,nSH2) -> PLCgamma1(Tyr783~p,cSH2,core~inactive,n...)
r01	cell		RTK(pY) + PLCgamma1(Tyr783~p1,cSH2!1,core~inactive,nSH2) -> PLCgamma1(Tyr783~p1,cSH2!1,core~inactive...)
r03	cell		PLCgamma1(Tyr783~u,cSH2!1,core~inactive!1,nSH2!2).RTK(pY!2) -> RTK(pY) + PLCgamma1(Tyr783~u,cSH2!1,...)
r03	cell		PLCgamma1(Tyr783~u,cSH2,core~inactive,nSH2!1).RTK(pY!1) -> RTK(pY) + PLCgamma1(Tyr783~u,cSH2,core~inactive...)
r03	cell		PLCgamma1(Tyr783~p,cSH2!1,core~inactive!1,nSH2!2).RTK(pY!2) -> RTK(pY) + PLCgamma1(Tyr783~p,cSH2!1,core~inactive...)
r03	cell		PLCgamma1(Tyr783~p,cSH2,core~inactive,nSH2!1).RTK(pY!1) -> RTK(pY) + PLCgamma1(Tyr783~p,cSH2,core~inactive...)
r03	cell		PLCgamma1(Tyr783~p,cSH2,core~active,nSH2!1).RTK(pY!2) -> RTK(pY) + PLCgamma1(Tyr783~p,cSH2,core~active,nSH2!1)...
r03	cell		PLCgamma1(Tyr783~p1,cSH2!1,core~inactive,nSH2!2).RTK(pY!2) -> RTK(pY) + PLCgamma1(Tyr783~p1,cSH2!1,core~inactive...)
r03	cell		PLCgamma1(Tyr783~p1,cSH2!1,core~active,nSH2!2).RTK(pY!2) -> RTK(pY) + PLCgamma1(Tyr783~p1,cSH2!1,core~active,nSH2!2)...
r04	cell		PLCgamma1(Tyr783~u,cSH2!1,core~inactive!1,nSH2!2).RTK(pY!2) -> RTK(pY) + PLCgamma1(Tyr783~u,cSH2!1,core~inactive!1,nSH2!2)...
r04	cell		PLCgamma1(Tyr783~u,cSH2,core~inactive,nSH2!1).RTK(pY!1) -> RTK(pY) + PLCgamma1(Tyr783~u,cSH2,core~inactive,nSH2!1)...
r04	cell		PLCgamma1(Tyr783~p,cSH2!1,core~inactive!1,nSH2!2).RTK(pY!2) -> RTK(pY) + PLCgamma1(Tyr783~p,cSH2!1,core~inactive!1,nSH2!2)...
r04	cell		PLCgamma1(Tyr783~p,cSH2,core~inactive,nSH2!1).RTK(pY!1) -> RTK(pY) + PLCgamma1(Tyr783~p,cSH2,core~inactive,nSH2!1)...
r05	cell		PLCgamma1(Tyr783~u,cSH2!1,core~inactive!1,nSH2!2).RTK(pY!2) -> RTK(pY) + PLCgamma1(Tyr783~u,cSH2!1,core~inactive!1,nSH2!2)...
r05	cell		PLCgamma1(Tyr783~u,cSH2,core~inactive,nSH2!1).RTK(pY!2) -> RTK(pY) + PLCgamma1(Tyr783~u,cSH2,core~inactive,nSH2!1)...
r05	cell		PLCgamma1(Tyr783~p,cSH2!1,core~inactive!1,nSH2) -> RTK(pY) + PLCgamma1(Tyr783~p,cSH2!1,core~inactive!1,nSH2)...
r05	cell		PLCgamma1(Tyr783~p,cSH2,core~inactive,nSH2) -> RTK(pY) + PLCgamma1(Tyr783~p,cSH2,core~inactive,nSH2)...
r05	cell		PLCgamma1(Tyr783~p1,cSH2!1,core~inactive!1,nSH2) -> RTK(pY) + PLCgamma1(Tyr783~p1,cSH2!1,core~inactive!1,nSH2)...
r05	cell		PLCgamma1(Tyr783~p1,cSH2,core~inactive,nSH2) -> RTK(pY) + PLCgamma1(Tyr783~p1,cSH2,core~inactive,nSH2)...

Search  Reactions: 53



**Close**

# Observables

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)
- Structures (1)
- Species (2)
- Molecules (2)
- Observables (9)

Applications (1)

- d/  
Application0
- Geometry
- Specifications
- Protocols
- Simulations
- Parameter Estimation

VCell DB BMDB

BioModels

New Observable Duplicate Delete Pathway Links Search

Object Properties Annotations Problems (0 Errors, 1 Warnings)

Name	Structure	Depiction	Notes	BioNetGen Definition	Count
O0_RTKit	cell			RTK()	Molecules
O0_PLCl_tot	cell			PLCgamma1()	Molecules
O0_PLCl_active	cell			PLCgamma1(core~active!?)	Molecules
O0_PLCl_inactive	cell			PLCgamma1(core~inactive!?)	Molecules
O0_PLCl_pTyr783	cell			PLCgamma1(Tyr783~p!?)	Molecules
O0_PLCl_dpTyr783	cell			PLCgamma1(Tyr783~u!?)	Molecules
O0_PLCl_RTKit_bound_inactive	cell			RTK(pY1).PLCgamma1(nSH2!1,core~inactive!?)	Molecules
O0_PLCl_RTKit_bound	cell			RTK(pY1).PLCgamma1(nSH2!1)	Molecules
O0_PLCl_cytosol	cell			PLCgamma1(nSH2,core~inactive!?)	Molecules

Add Pattern

Multimolecular

Polymer of

- length = 2
- length > 1

Object Properties Annotations Problems (0 Errors, 1 Warnings)

PLCgamma1

cell

nSH2

Tyr783

p

cSH2

core

CONNECTED (mblinov)

236.8MB / 486.5MB