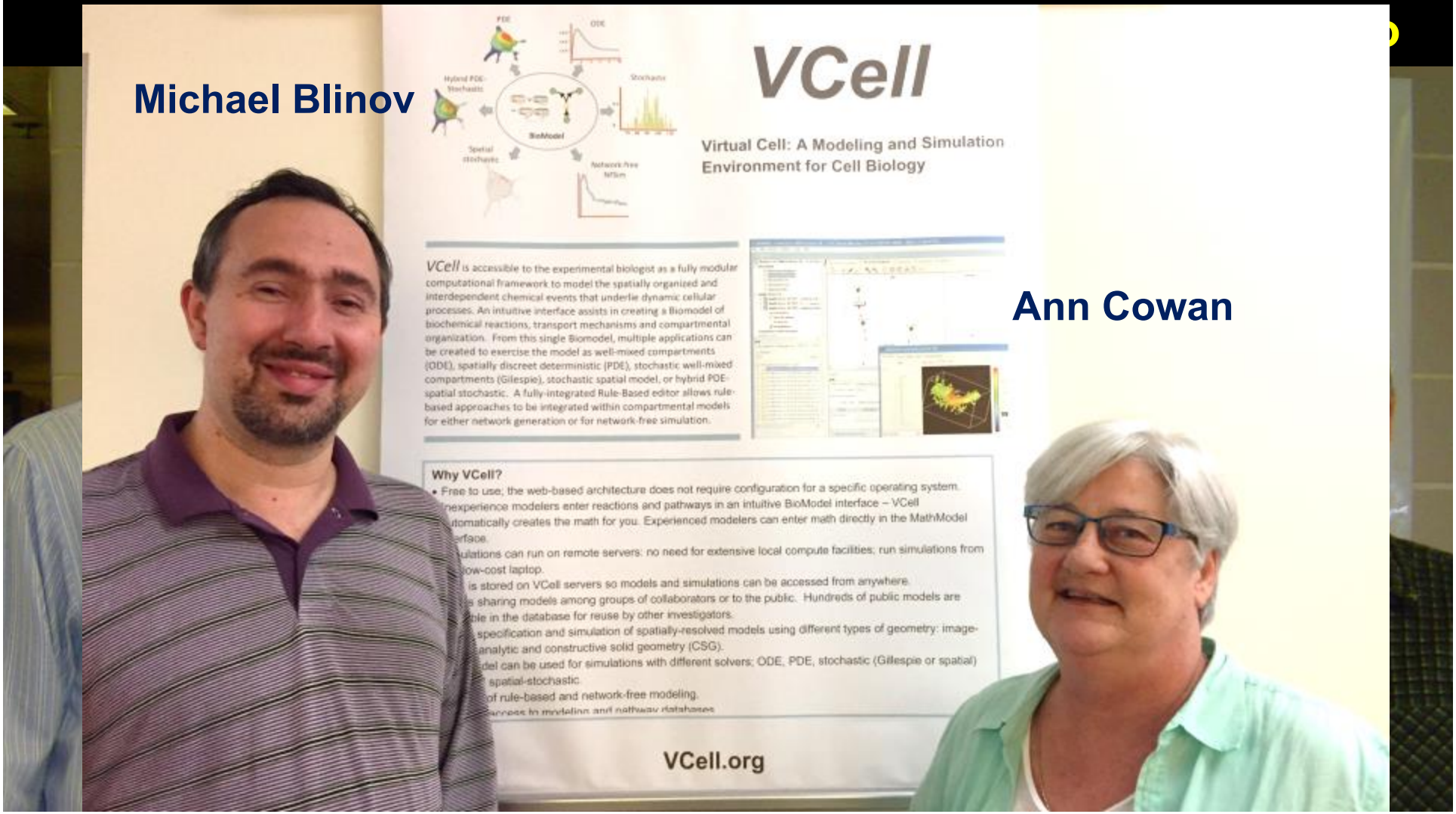
http://vcell.org

The Virtual Cell Project

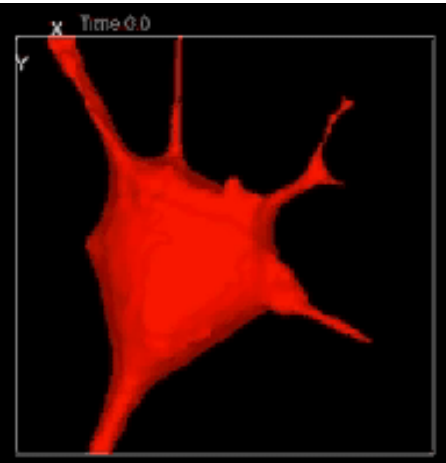
National Institute of General Medical Sciences

Biomedical Technology Research Centers

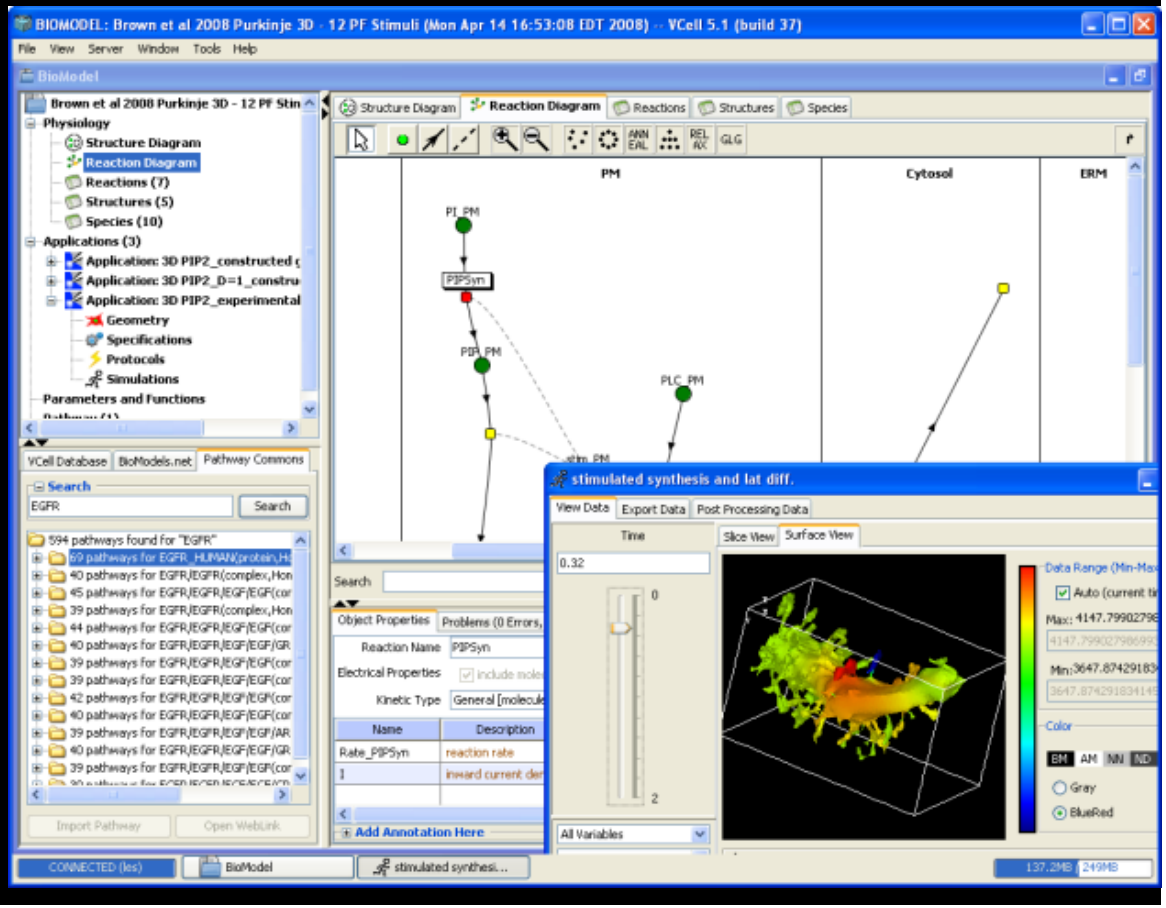


The Virtual Cell Project

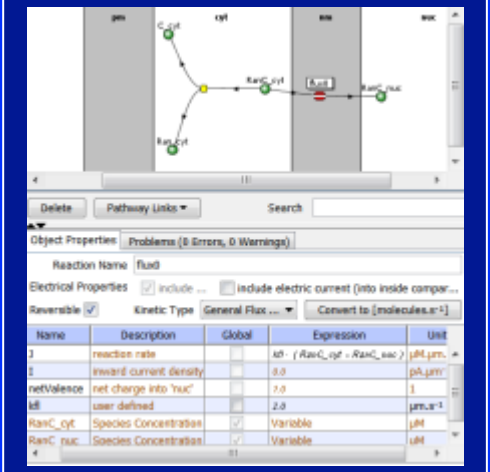
$$\frac{\partial C_i}{\partial t} = -\mathrm{div}\boldsymbol{F}_i + R_i$$



- ✓5,800 users who built models
- ✓Graphical interface for biologists & physical scientists
- ✓Reactions, diffusion, advection, membrane transport, electrophysiology
- ✓Compartmental (ODE), spatial (PDE), deterministic and stochastic simulations
- ✓Rule-based & network-free modeling options
- ✓Searchable model database
- ✓Pathway database support
- ✓Experimental data integration
- ✓Virtual Microscopy

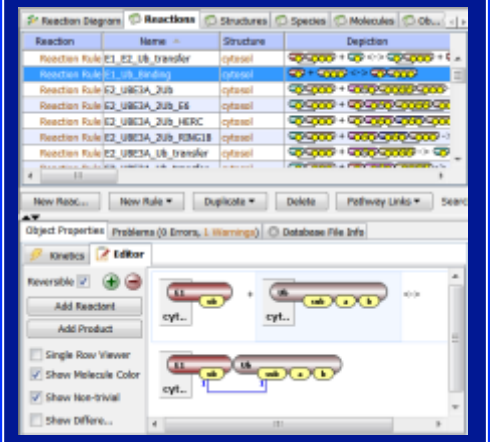


Physiology



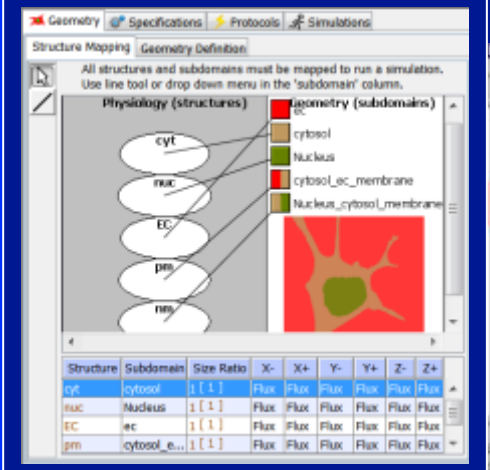
Reactions and Fluxes as explicit networks

and/or



Rules

Applications

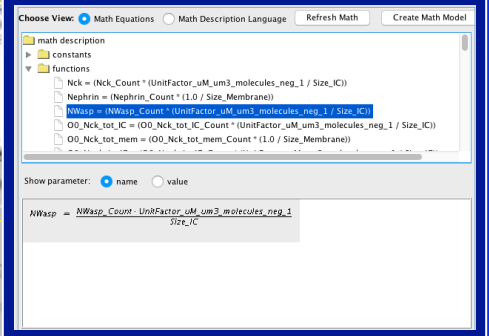


Topology ⟶ Geometry

ODE, Stochastic, PDE, Spatial Stochastic, Hybrid PDE/ Stochastic, Network-Free

Initial Conditions, Boundary Conditions, Diffusion, Advection, Disable Reactions, Clamp Species, Electrophysiology Protocols, Network Generation, Events

Math Description

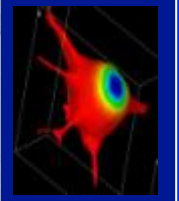


VCMDL

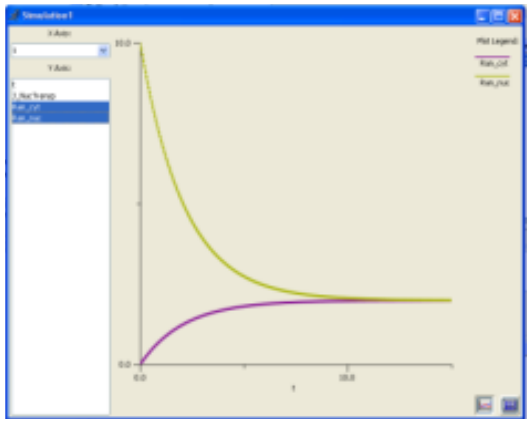
Simulations

Duration, Solver, Mesh Size, Parameter Scans, Parameter Estimation, Sensitivity

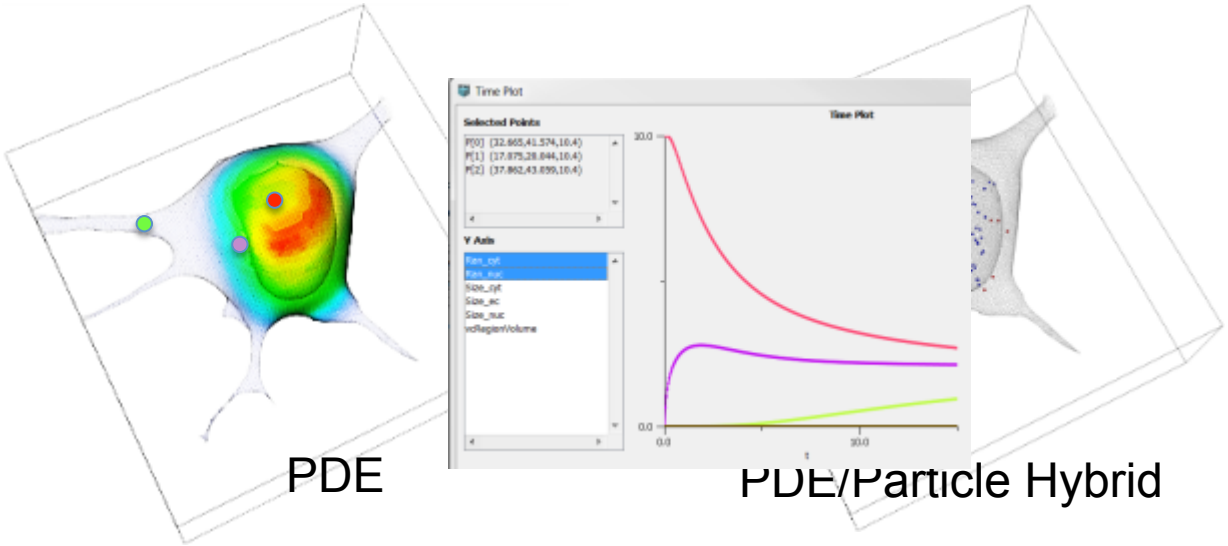
Results



Simulations with Multiple Physical Approximations

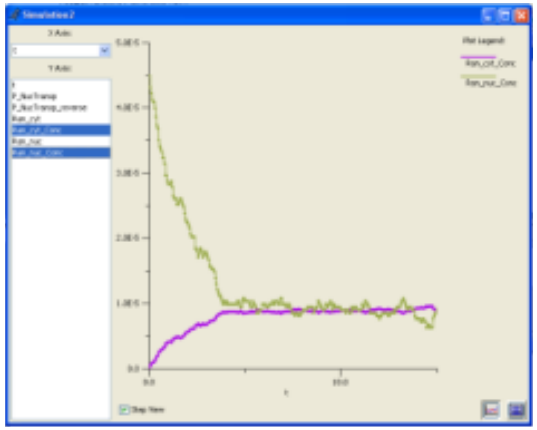


ODE

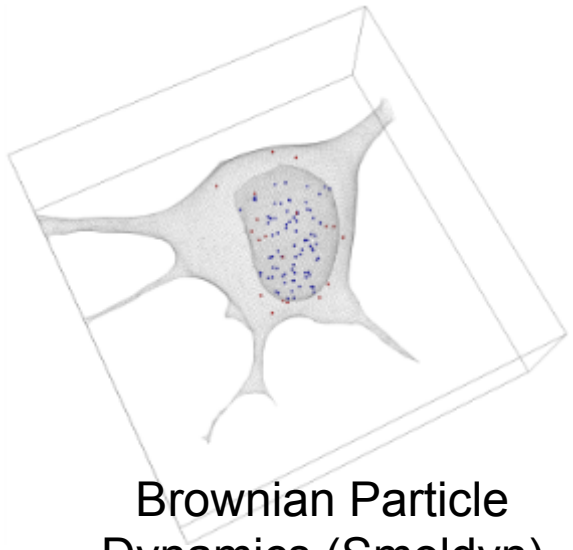


PDE

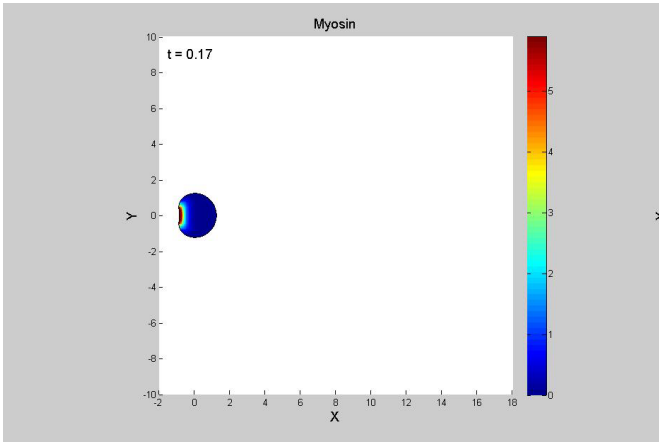
PDE/Particle Hybrid



Nonspatial Stochastic
(Gillespie, Hybrid, NFSim)

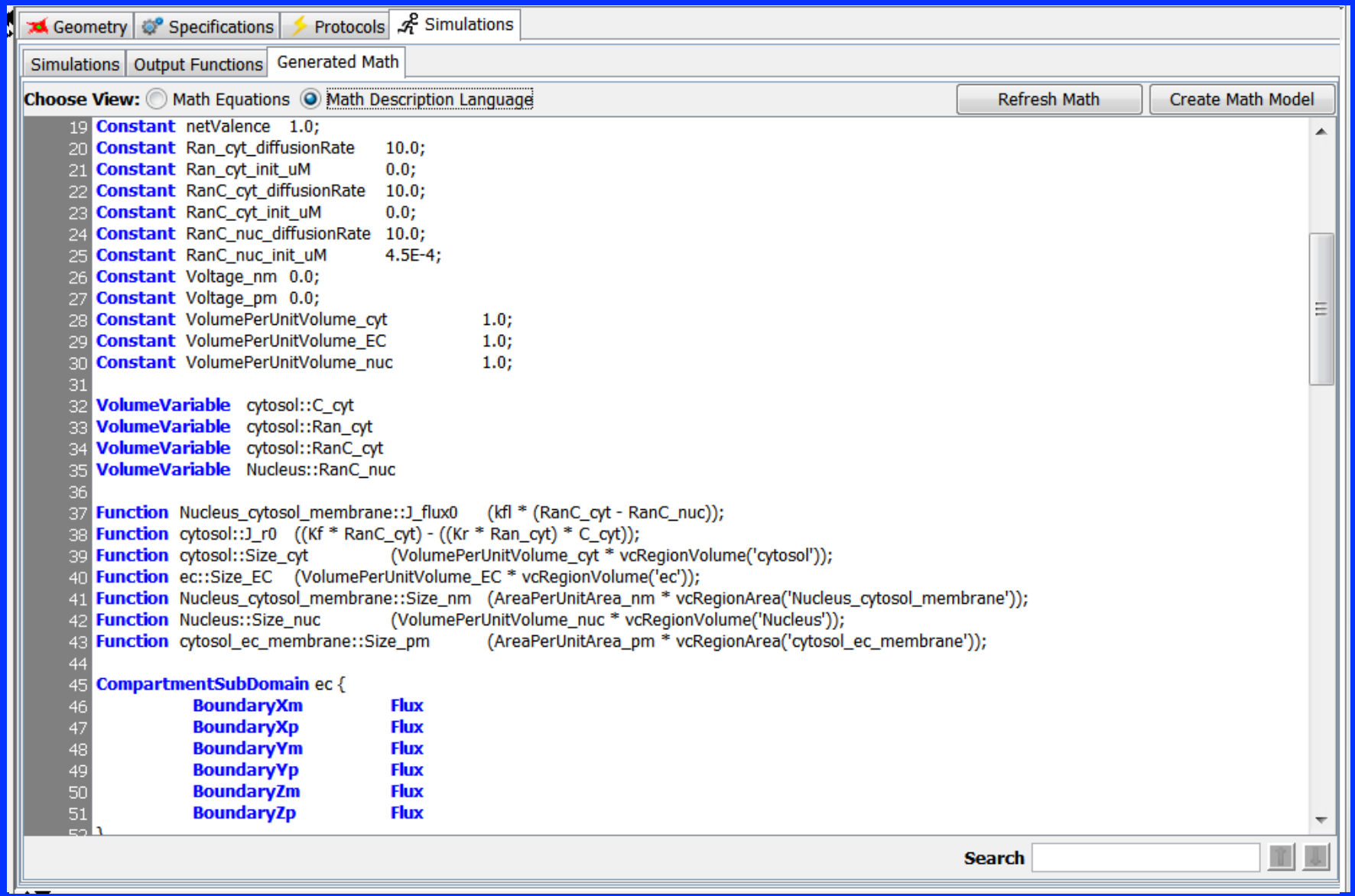


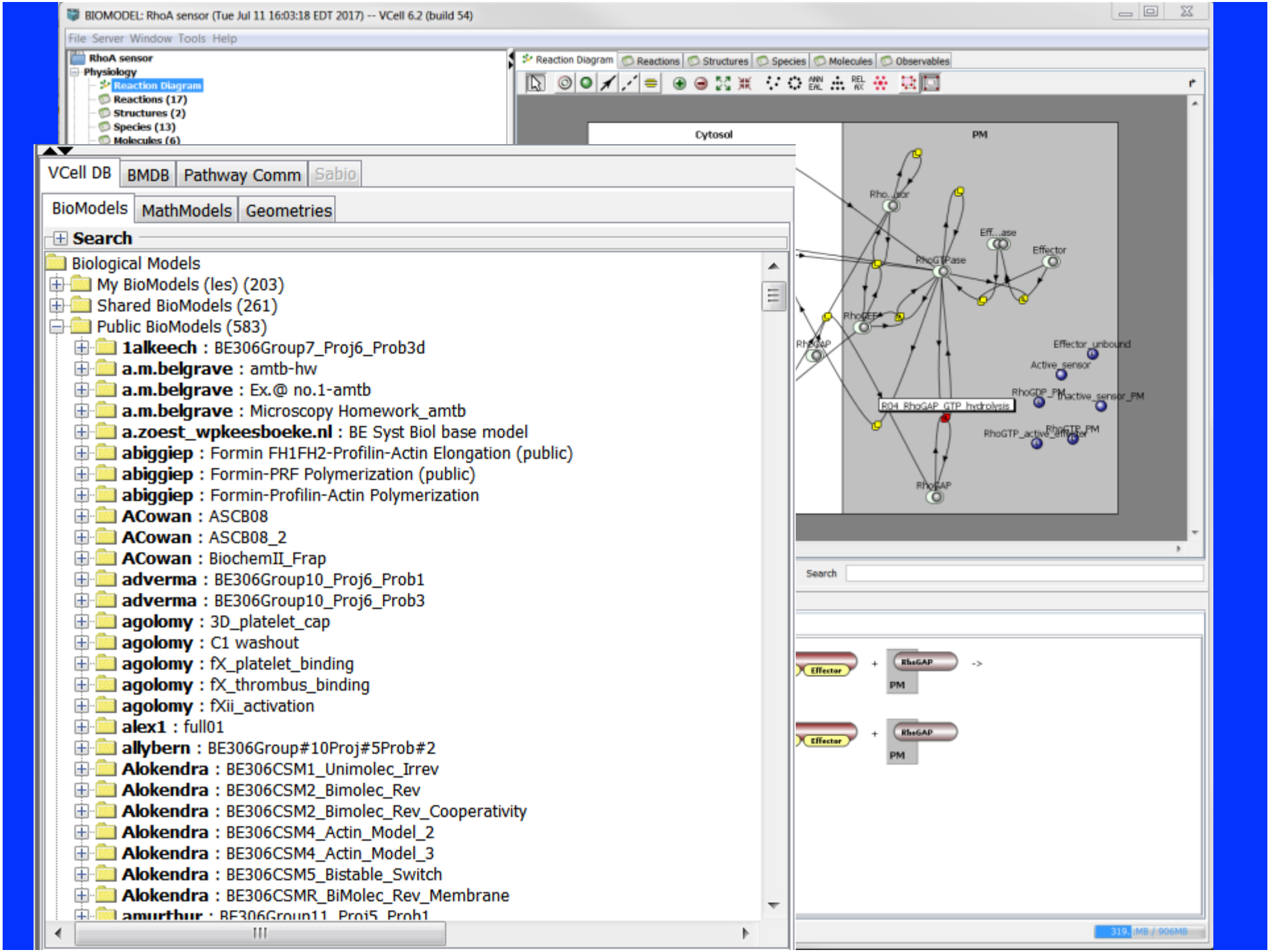
Brownian Particle
Dynamics (Smoldyn)

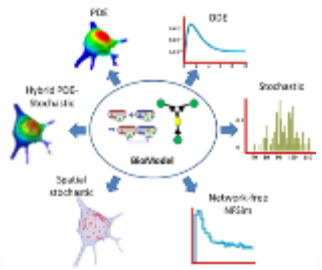


Moving Boundary Problems
COMING SOON IN 2D

BioModel → MathModel




BIOMODEL: RhoA sensor (Tue Jul 11 16:03:18 EDT 2017) -- VCell 6.2 (build 54)
File Server Window Tools Help
RhoA sensor
Physiology
Reaction Diagram
Reactions (17)
Structures (2)
Species (13)
Molecules (6)
Reaction Diagram
Reactions
Structures
Species
Molecules
Observables
Cytosol
PM
RhoGTPase
Effector
RhoGEF
RhoGAP
Effector_unbound
Active_sensor
R04_RhoGAP_GTP_hydrolysis
Inactive_sensor_PM
VCell DB
BMDB
Pathway Comm
Sabio
BioModels
MathModels
Geometries
Search
Biological Models
My BioModels (les) (203)
Shared BioModels (261)
Public BioModels (583)
1alkeech : BE306Group7_Proj6_Prob3d
a.m.belgrave : amtb-hw
a.m.belgrave : Ex.@ no.1-amtb
a.m.belgrave : Microscopy Homework_amtb
a.zoest_wpkeesboeke.nl : BE Syst Biol base model
abiggiep : Formin FH1FH2-Profilin-Actin Elongation (public)
abiggiep : Formin-PRF Polymerization (public)
abiggiep : Formin-Profilin-Actin Polymerization
ACowan : ASCB08
ACowan : ASCB08_2
ACowan : BiochemII_Frap
adverma : BE306Group10_Proj6_Prob1
adverma : BE306Group10_Proj6_Prob3
agolomy : 3D_platelet_cap
agolomy : C1 washout
agolomy : fX_platelet_binding
agolomy : fX_thrombus_binding
agolomy : fXii_activation
alex1 : full01
allybern : BE306Group#10Proj#5Prob#2
Alokendra : BE306CSM1_Unimolec_Irrev
Alokendra : BE306CSM2_Bimolec_Rev
Alokendra : BE306CSM2_Bimolec_Rev_Cooperativity
Alokendra : BE306CSM4_Actin_Model_2
Alokendra : BE306CSM4_Actin_Model_3
Alokendra : BE306CSM5_Bistable_Switch
Alokendra : BE306CSMR_BiMolec_Rev_Membrane
Search
Effector
RhoGAP
PM
319 MB / 906MB



VCELL

National Resource for Cell Analysis and Modeling

ModelBricks

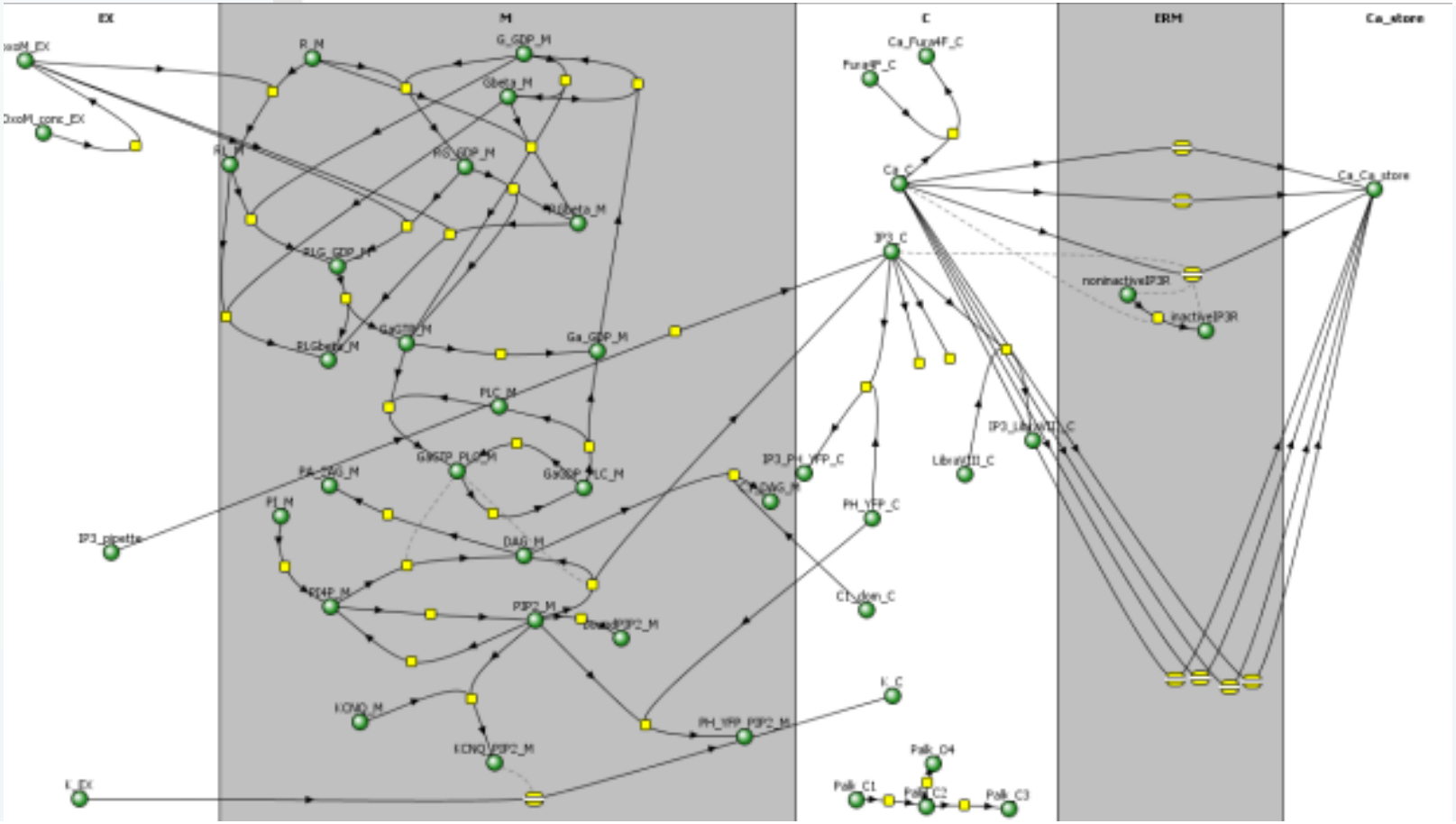
Public model from Bertil Hille lab

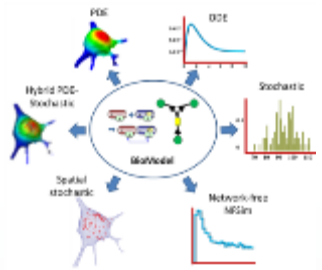
JGP Home » 2013 Archive » 1 May » 141 (5): 537

Research Article

Quantitative properties and receptor reserve of the DAG and PKC branch of G_q-coupled receptor signaling

Björn H. Falkenburger, Eamonn J. Dickson, Bertil Hille





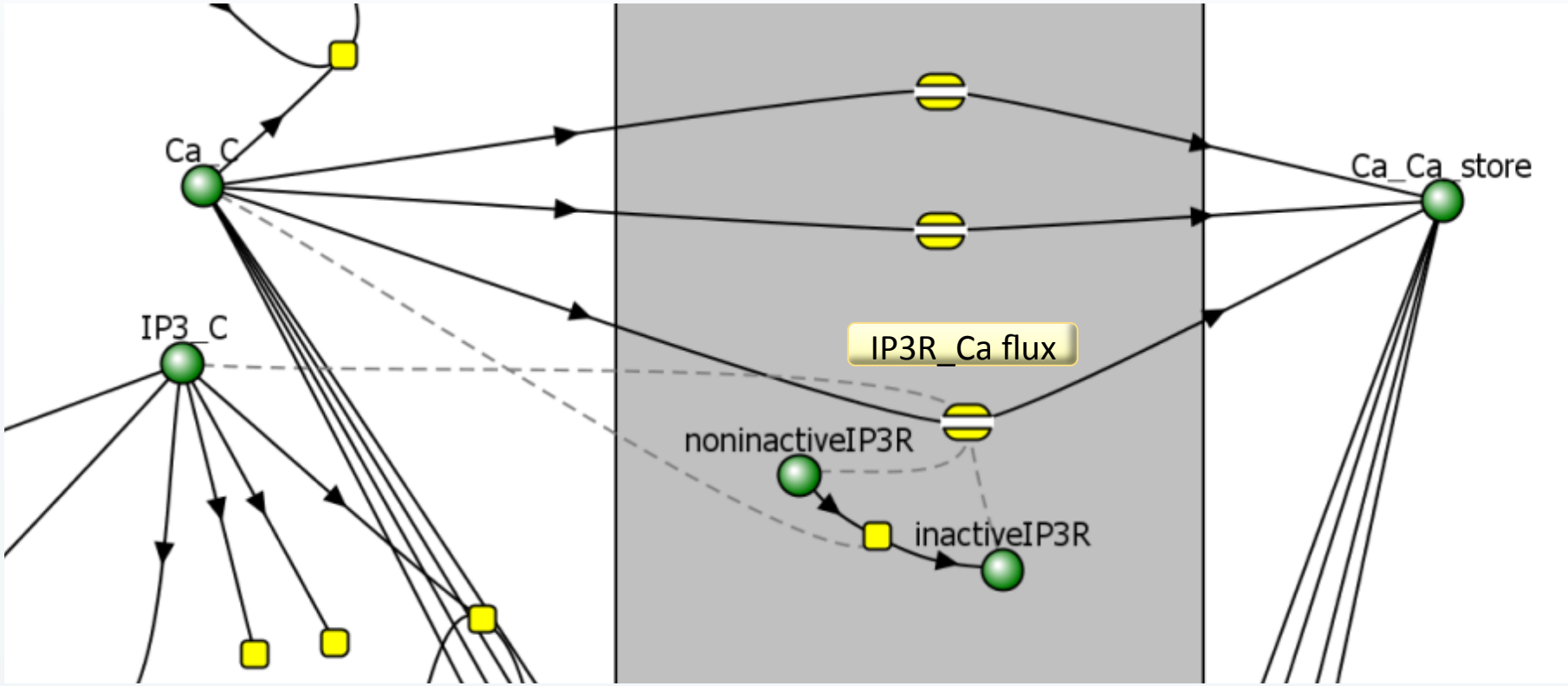
VCELL

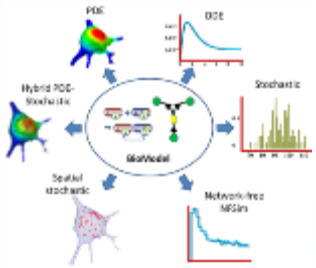
National Resource for Cell Analysis and Modeling

ModelBricks concept

- Containers for small, reusable VCell models that can be used in larger models
- Fully annotated
- Can be created by users and submitted for curation
- Carry parameter information and citation information
- Provides an incentive for users to create ModelBricks
- Molecular details included, no ambiguity to the intended composition of the species
- Are VCell models, therefore can be stored in VCell database, searched and exported to other formats
- VCell API integration with website provides infrastructure to disseminate the ModelBricks

Vcell submodel





VCELL

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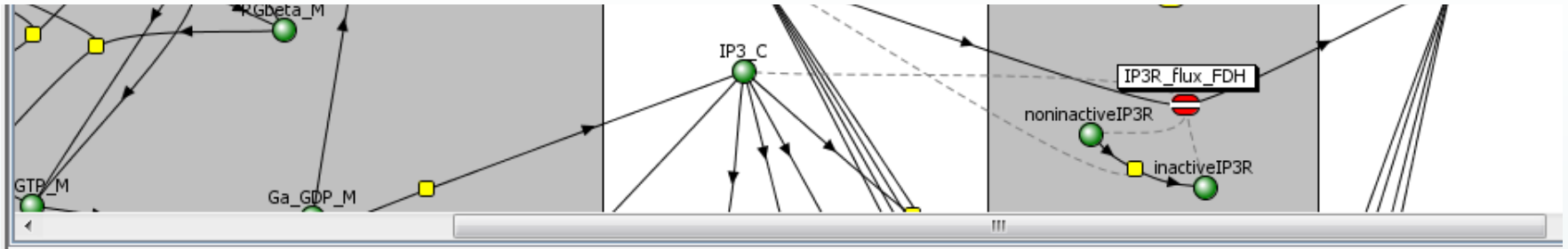
Defined kinetics



Delete | Pathway Links | Search

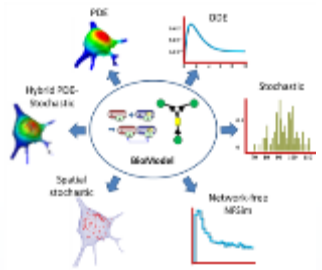
Object Properties | Problems (0 Errors, 10 Warnings) | Database File Info

Reaction Name: IP3R_flux_FDH

Electrical Properties: include molecular flux; include electric current (into inside compartment "Ca_store")

Reversible | Kinetic Type: General Flux Density (μM-μm/s) | Convert to [molecules

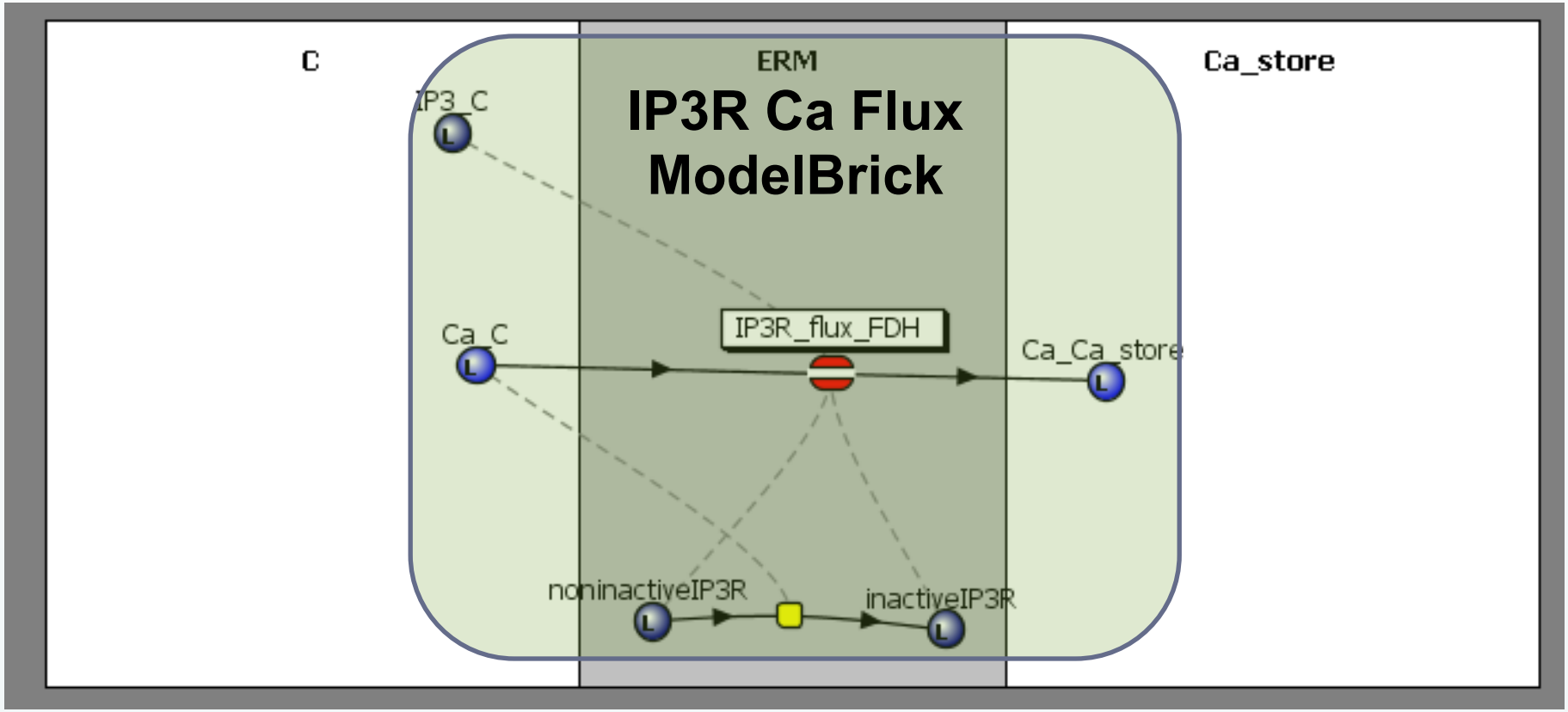
Name	Description	Global	Expression	Units
J	reaction rate		$-r\_FDH \cdot Jmax2 \cdot \left(1.0 - \frac{Ca\_C}{Ca\_Ca\_store}\right) \cdot \left(\frac{h \cdot IP3\_C \cdot Ca\_C}{(IP3\_C + KD\_IP3\_IP3R) \cdot (Ca\_C + KD\_act\_Ca\_IP3R)}\right)^{3.0}$	μM.μm.s^{-1}
I	inward current density		0.0	pA.μm^{-2}
netValence	net charge into 'Ca_store'		0.0	1
Jmax2	user defined		200.0	μM.μm.s^{-1}
r_FDH	Global Parameter	☑	1.0	1
Ca_C	Species Concentration	☑	Variable	μM
Ca_Ca_store	Species Concentration	☑	Variable	μM
h	Global Parameter	☑	$\frac{noninactiveIP3R}{(noninactiveIP3R + inactiveIP3R)}$	1
IP3_C	Species Concentration	☑	Variable	μM
KD_IP3_IP3R	Global Parameter	☑	0.1	μM
KD_act_Ca_IP3R	Global Parameter	☑	0.2	μM

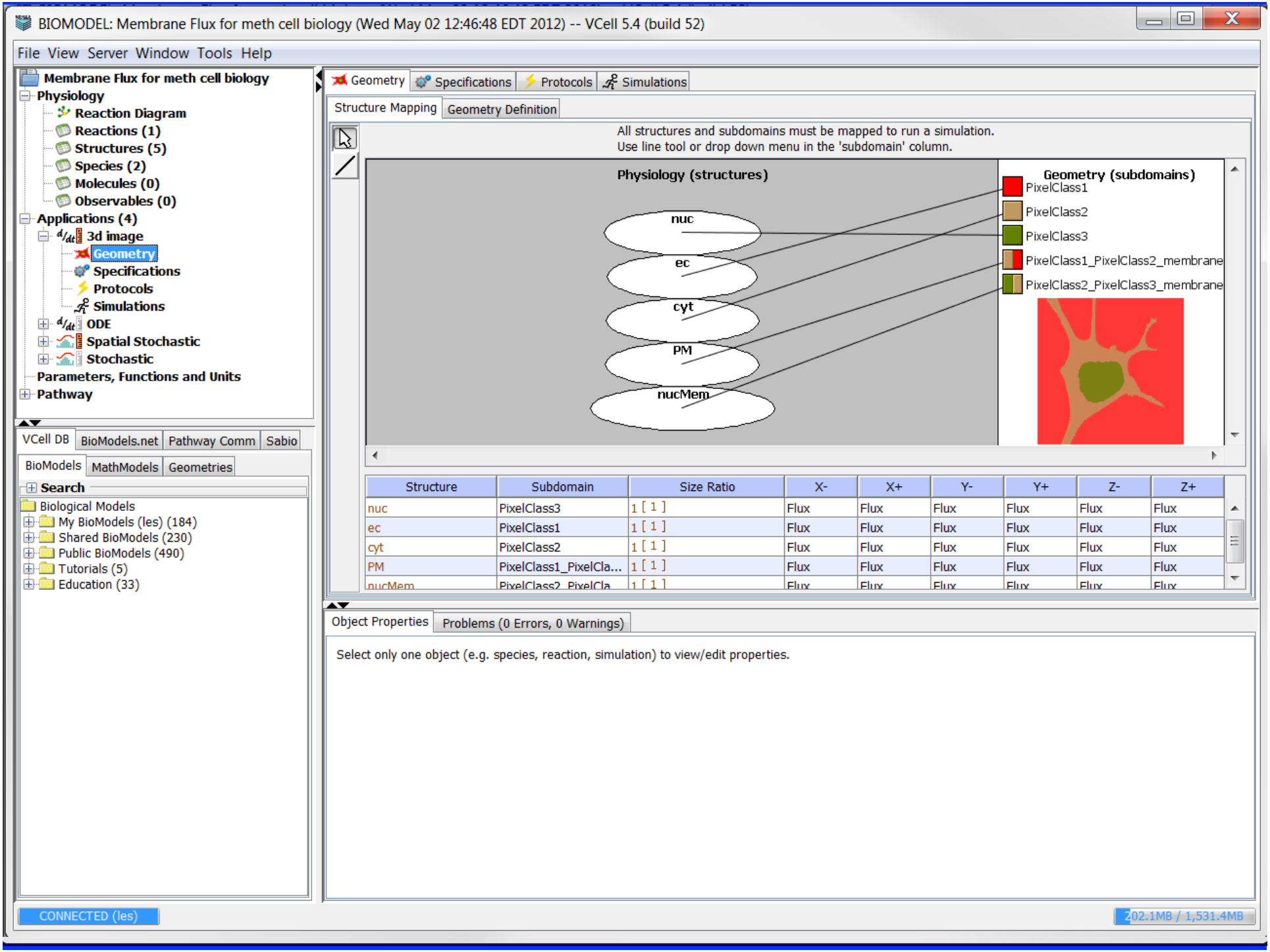


VCELL

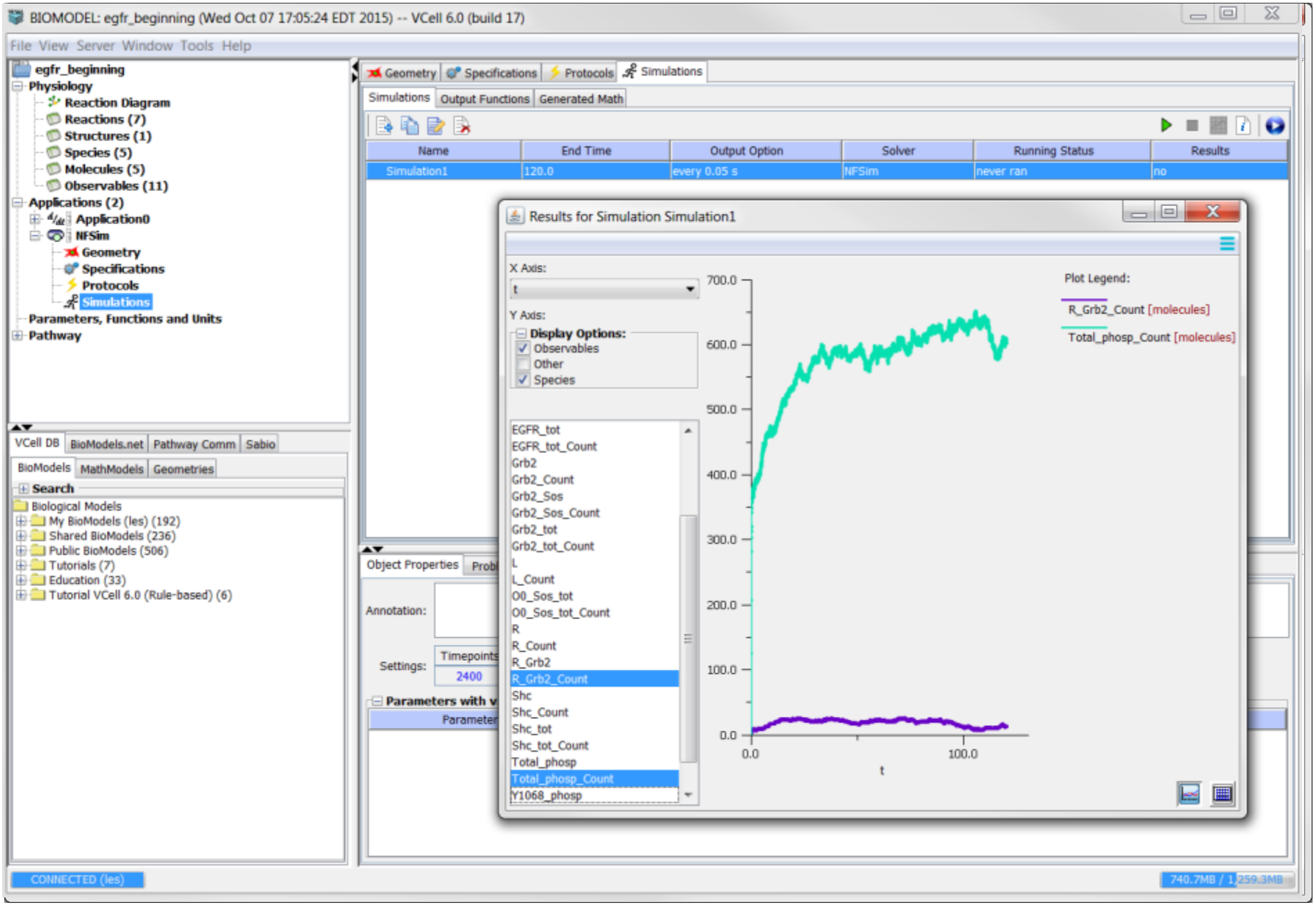
National Resource for Cell Analysis and Modeling

IP3R Ca Flux ModelBrick

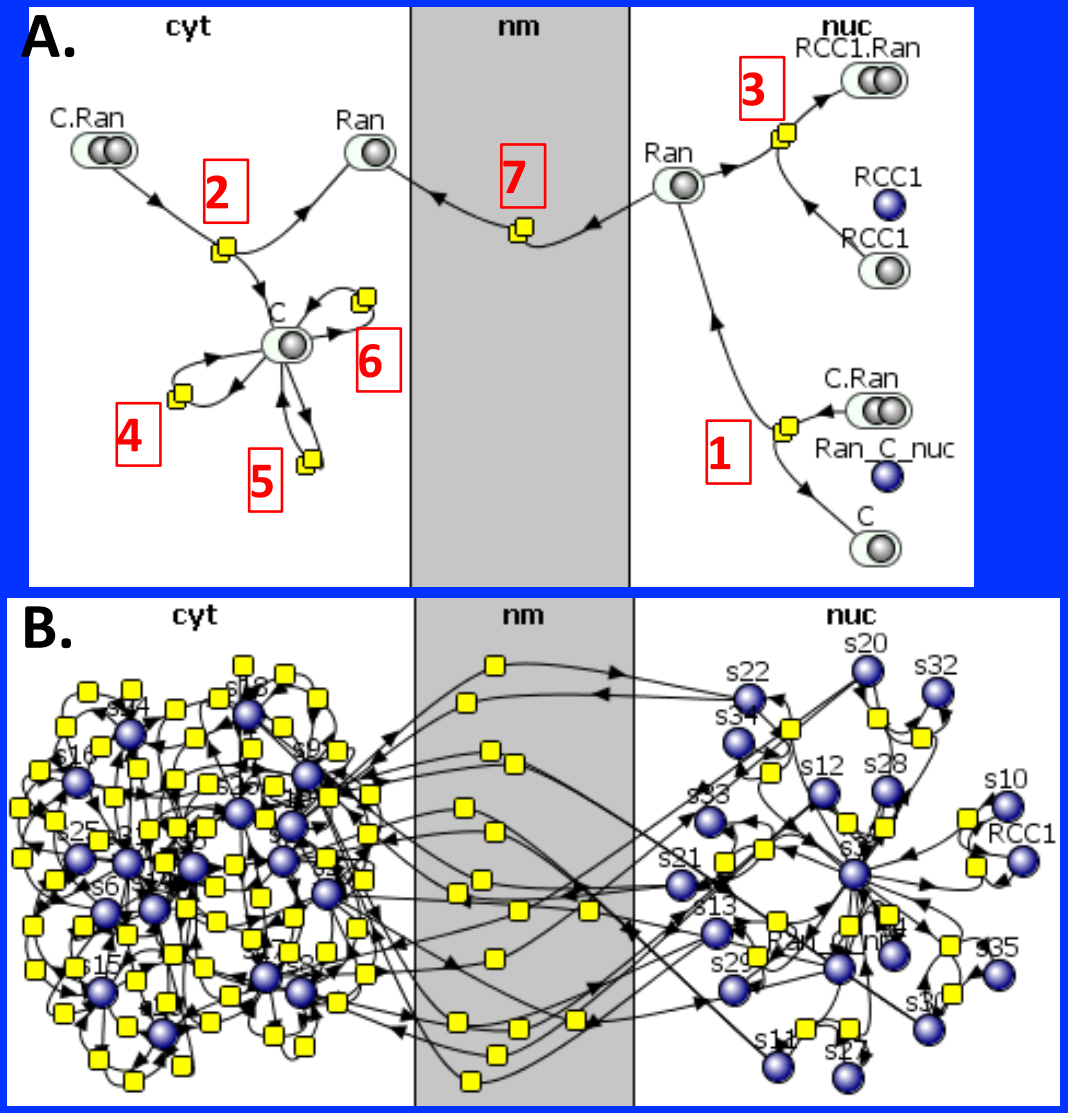



BIOMODEL: Membrane Flux for meth cell biology (Wed May 02 12:46:48 EDT 2012) -- VCell 5.4 (build 52)
File View Server Window Tools Help
Membrane Flux for meth cell biology
Physiology
Reaction Diagram
Reactions (1)
Structures (5)
Species (2)
Molecules (0)
Observables (0)
Applications (4)
3d image
Geometry
Specifications
Protocols
Simulations
ODE
Spatial Stochastic
Stochastic
Parameters, Functions and Units
Pathway
VCell DB
BioModels.net
Pathway Comm
Sabio
BioModels
MathModels
Geometries
Search
Biological Models
My BioModels (les) (184)
Shared BioModels (230)
Public BioModels (490)
Tutorials (5)
Education (33)
Geometry
Specifications
Protocols
Simulations
Structure Mapping
Geometry Definition
All structures and subdomains must be mapped to run a simulation.
Use line tool or drop down menu in the 'subdomain' column.
Physiology (structures)
nuc
ec
cyt
PM
nucMem
Geometry (subdomains)
PixelClass1
PixelClass2
PixelClass3
PixelClass1_PixelClass2_membrane
PixelClass2_PixelClass3_membrane
Structure
Subdomain
Size Ratio
X-
X+
Y-
Y+
Z-
Z+
nuc
PixelClass3
1 [1]
Flux
ec
PixelClass1
cyt
PixelClass2
PM
PixelClass1_PixelCla...
Object Properties
Problems (0 Errors, 0 Warnings)
Select only one object (e.g. species, reaction, simulation) to view/edit properties.
CONNECTED (les)
202.1MB / 1,531.4MB

Demo 1


BIOMODEL: egfr_beginning (Wed Oct 07 17:05:24 EDT 2015) -- VCell 6.0 (build 17)
File View Server Window Tools Help
egfr_beginning
Physiology
Reaction Diagram
Reactions (7)
Structures (1)
Species (5)
Molecules (5)
Observables (11)
Applications (2)
Application0
NFSim
Geometry
Specifications
Protocols
Simulations
Parameters, Functions and Units
Pathway
Geometry
Specifications
Protocols
Simulations
Simulations
Output Functions
Generated Math
Name
End Time
Output Option
Solver
Running Status
Results
Simulation1
120.0
every 0.05 s
NFSim
never ran
no
Results for Simulation Simulation1
X Axis:
t
Y Axis:
Display Options:
Observables
Other
Species
EGFR_tot
EGFR_tot_Count
Grb2
Grb2_Count
Grb2_Sos
Grb2_Sos_Count
Grb2_tot
Grb2_tot_Count
L
L_Count
O0_Sos_tot
O0_Sos_tot_Count
R
R_Count
R_Grb2
R_Grb2_Count
Shc
Shc_Count
Shc_tot
Shc_tot_Count
Total_phosp
Total_phosp_Count
Y1068_phosp
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
0.0
100.0
t
Plot Legend:
R_Grb2_Count [molecules]
Total_phosp_Count [molecules]
VCell DB
BioModels.net
Pathway Comm
Sabio
BioModels
MathModels
Geometries
Search
Biological Models
My BioModels (les) (192)
Shared BioModels (236)
Public BioModels (506)
Tutorials (7)
Education (33)
Tutorial VCell 6.0 (Rule-based) (6)
Object Properties
Annotation:
Settings:
Timepoints
2400
Parameters with v
Parameter
CONNECTED (les)
740.7MB / 1259.3MB

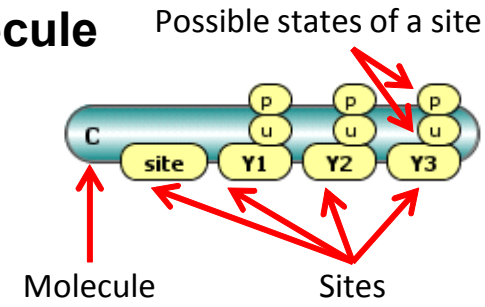
Rule-based vs. Full Reaction Network



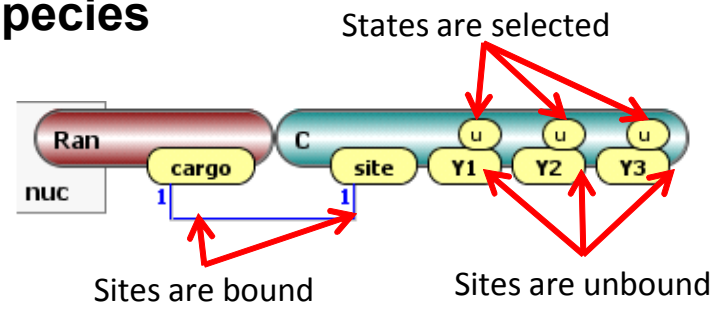
Key Concepts for VCell Rule-based Modeling

Term	Purpose	Composition	Compartmental/Spatial features
Compartment	Cellular structure containing species and reactions	A volume or a surface, corresponding to extracellular regions, cytosol, organelles and their associated membranes. No specification of the relationship between compartments (such as enclosures or adjacency) is required.	For ***Applications*** without explicit geometries, compartmental sizes are specified as surface areas or volumes. For spatial ***Applications***, compartments may be explicitly associated with regions within a geometry.
Molecule	A building block for species.	Comprised of sites that can bind other sites between or within molecules. A site may also have multiple states. In this way, a molecule spawns a collection of chemical species – one per every combination of site occupancy and/or state.	Can be, optionally, ***anchored*** to one or more compartments. A species containing an anchored molecule can be located only in one of these compartments.
Species	An individual chemical species that may occur in the model.	Comprised of molecules that are connected through bonds between binding sites. All modification sites must be explicitly defined. A species can be a ***seed species*** (defined as initial condition and used as a seed for reaction rules application) or a generated species (a result of reaction rule application).	Every species is located in a unique compartment. Seed species are assigned to a compartment by the user. It may not contain molecules that are excluded from that compartment by anchoring to other compartments.
Pattern	Specifies a set of possible states of species to be selected as participants in reaction rules and in observables.	Comprised of molecules. The states of sites may be left unspecified; thus a pattern may select multiple species. Moreover, binding sites may have ***implicit binding status*** (*has external bond* or *may be bound*) where its binding partner is not explicitly defined. Such patterns may be inclusive of species that contain molecules not explicitly specified in a pattern but being possibly bound to molecules within it.	Defined in a single compartment; all molecules that comprise a pattern must be permitted to be located in this compartment.
Observable	Specify simulation outputs of interest.	Consists of one or more patterns that define features of species. The result is the total population (concentration or count) of multiple species.	Defined in a single compartment; all molecules that comprise an observable must be permitted to be located in this compartment.
Reaction rule	Defines transformation of multiple species at once, generating multiple reactions	Species to be transformed are selected by reactant pattern(s). Product pattern(s) define the end result of transformation. Product may differ from reactant by re-assigning molecules, adding or deleting bonds and changing site states. A kinetic expression is also a component of a reaction rule.	Reaction rule is defined in a single compartment. Each reactant pattern and each product pattern are assigned a specific compartment, which may be different from compartment for reactants or products.

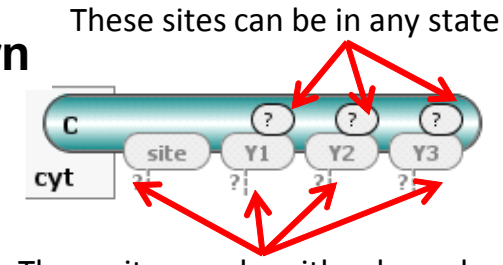
Molecule



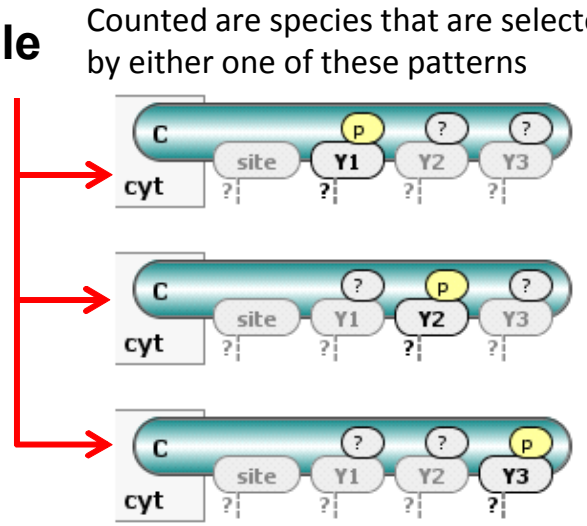
Species



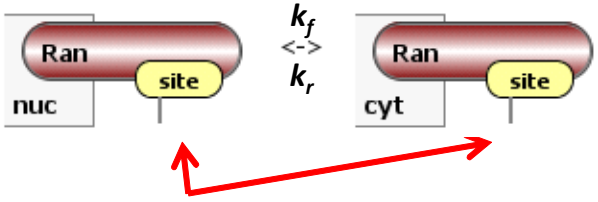
Pattern



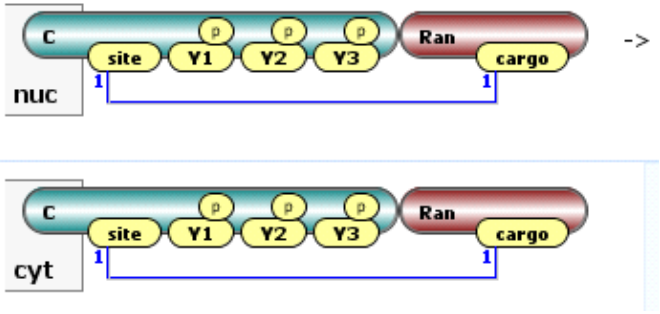
Observable



Reaction rule



Reaction



Demo 2