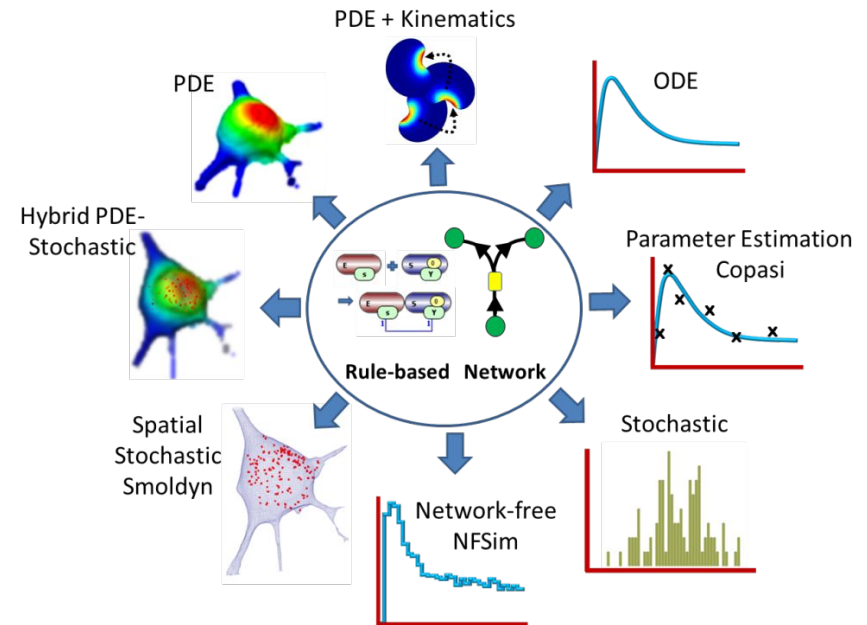




A modeling environment for the simulation of cellular events. Download at vcell.org

Version 7.7 Updated July 2025



Multi Compartment Rule-Based Modeling



Virtual Cell is developed by the Center for Cell Analysis and Modeling at the University of Connecticut Health Center. It is funded by the National Institute of General Medical Sciences (NIGMS)



National Institute of
General Medical Sciences

VCell is funded by the NIGMS



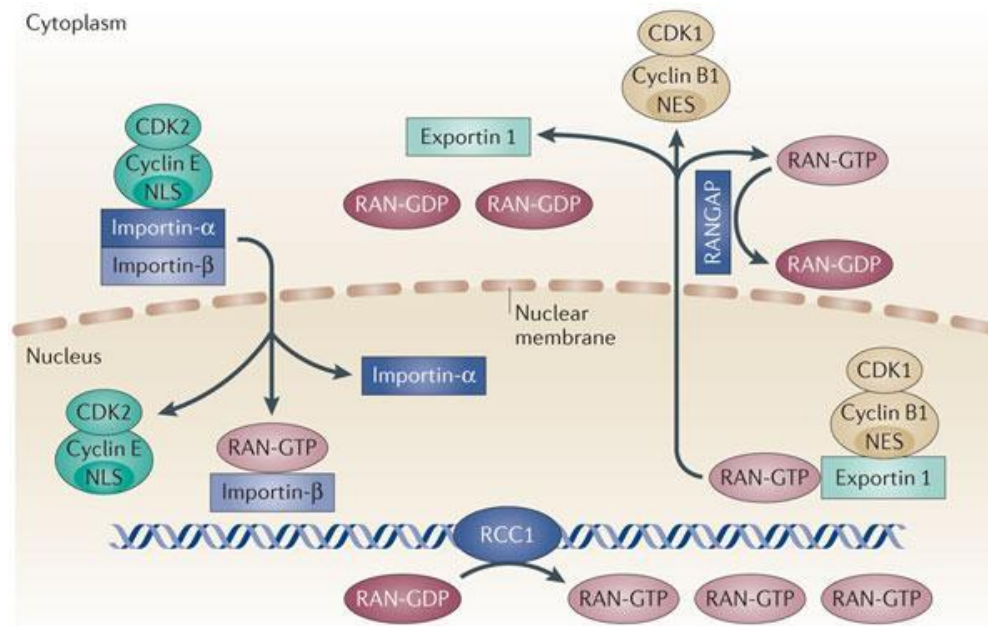
VCell is developed
at CCAM

Center for Cell Analysis & Modeling

VCell Tutorial

Building a Multi-compartment Rule-Based Model

In this tutorial, we will demonstrate how to create a compartmental rule based model of translocation through the nuclear pore of a cargo protein via the GTPase protein Ran. Specifically, this model displays the export part of the cycle. The nuclear Ran is (implicitly) phosphorylated by the shown interaction with its nucleotide exchange factor: the chromatin-associated RCC1 protein. The activated Ran then binds to the cargo molecule, creating a ternary complex with the (not shown) exportin, facilitating translocation into the cytosol. Ran and cargo are then dissociated via the hydrolysis of Ran by the membrane-bound Ran-GAP protein (not shown). The cytosolic cargo molecule may be phosphorylated on any of its three tyrosines while in cytosol.



In this tutorial you will learn how to:

- Create a compartmental rule-based **Physiology** with Molecules, Species, Rules and Observables.
- Simulate a model using **Deterministic application** that expands rules into a reaction network using the **BioNetGen** engine.
- Simulate a model using a **Stochastic application** that simulates the reaction network generated by **BioNetGen**.
- Simulate a model using **Network-Free** application that skips network generation and directly computes Observables using **NFSim** engine.
- Create a 3-D model in **VCell** using existing 3-D image slices.
- Simulate a 3-D model using **Deterministic application** that expands rules into a reaction network using **BioNetGen** engine.
- Simulate a 3-D model using a **Stochastic application** that simulates the reaction network generated by **BioNetGen**.

General familiarity with VCell software is recommended. Although this tutorial can be followed by a VCell novice, it is recommended that novice users first look through the VCell tutorials available at <https://vcell.org/support>.

Model building can be matched to the BioModel [Rule-based_Ran_transport](#) in the Tutorial folder in the VCell Database.

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The image shows a 'Virtual Cell login' dialog box. It has a title bar with the VCell logo and a close button. Below the title bar is a menu icon. The main area contains two input fields: 'User Name' and 'Password'. Below these are three buttons: 'Login', 'Cancel', and 'Forgot Login Password...'. At the bottom is a button labeled 'New User Registration...'. Below the buttons is a paragraph of text: 'Use [this link](#) for details on how to acknowledge Virtual Cell in your publication and how to share your published research through the VCell database.'

Virtual Cell login

User Name

Password

Login Cancel

Forgot Login Password...

New User Registration...

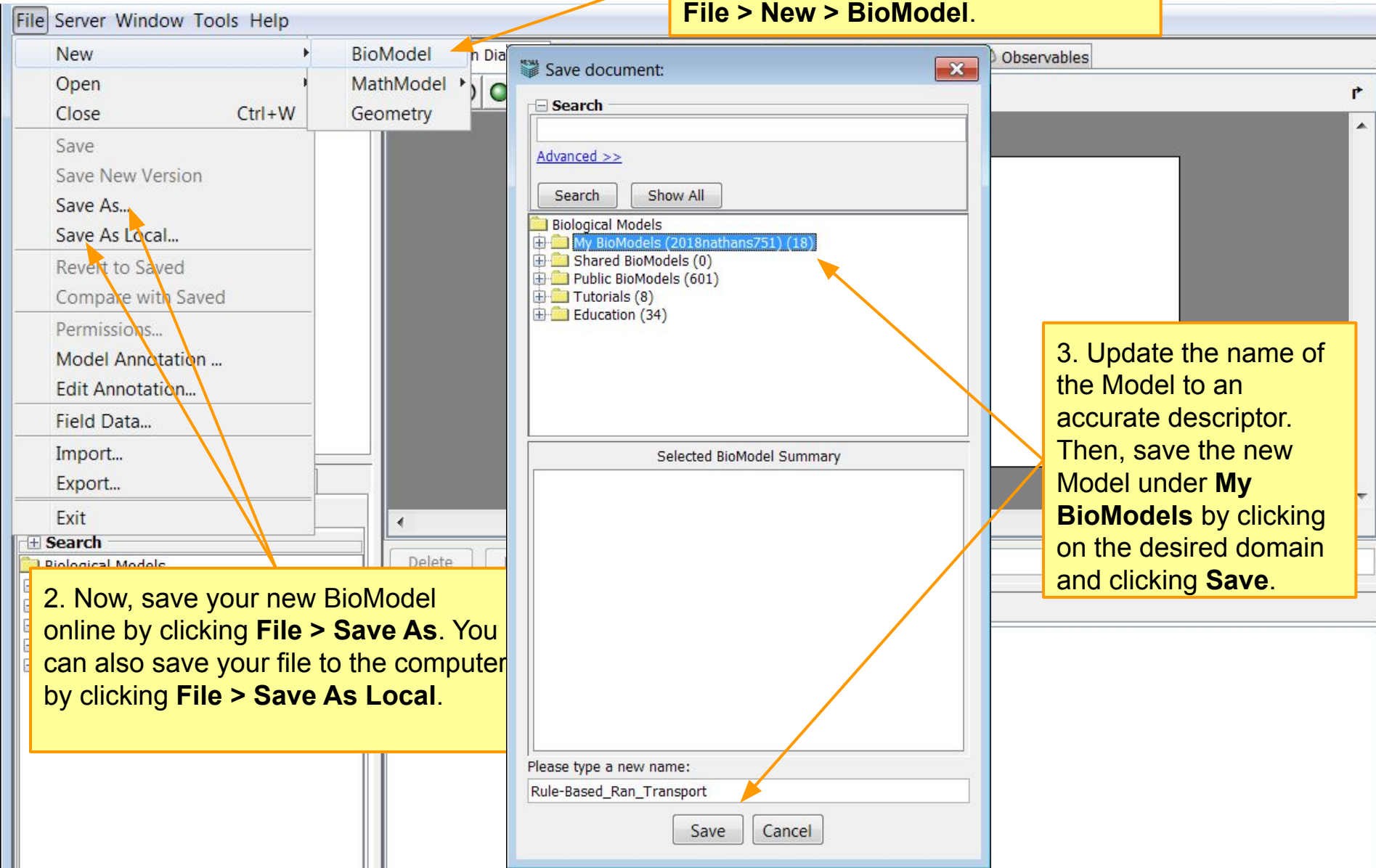
Use [this link](#) for details on how to acknowledge Virtual Cell in your publication and how to share your published research through the VCell database.

The first step to any VCell project is signing in. It is important to do so because only those that are signed in will be able to run simulations using VCell high-performance computers remotely, use the VCell database, and save work. If you are new to VCell, create an account by clicking the **New User Registration** button.

1. Start By creating a new BioModel in which to do your work. Click on **File > New > BioModel**.

2. Now, save your new BioModel online by clicking **File > Save As**. You can also save your file to the computer by clicking **File > Save As Local**.

3. Update the name of the Model to an accurate descriptor. Then, save the new Model under **My BioModels** by clicking on the desired domain and clicking **Save**.



TIP: You can also create new structures using a non-visual format by clicking on the **Structures** tab and pressing either **New Compartment** or **New Membrane**.

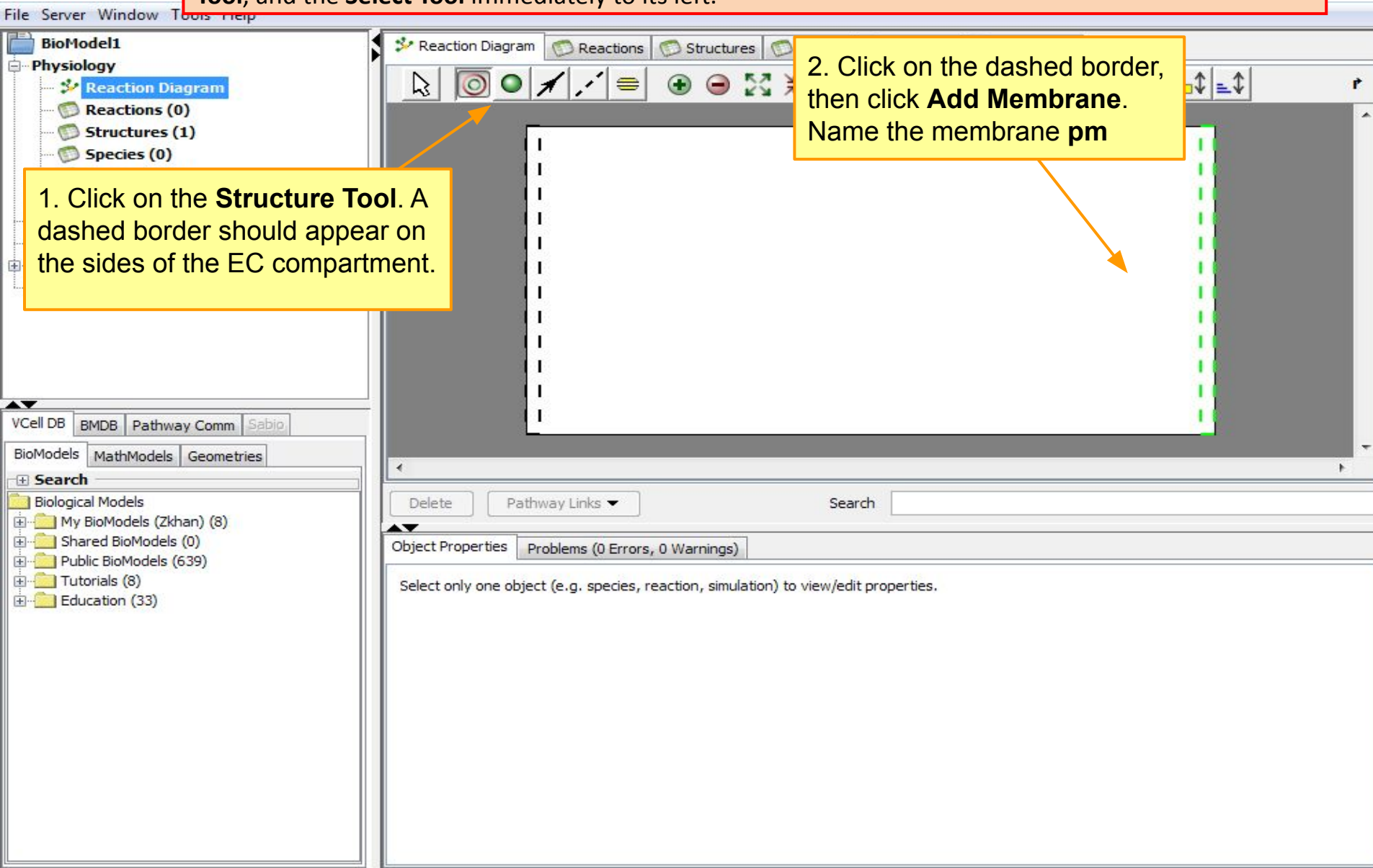
1. To create and edit structures, click on **Reaction Diagram**. Double click on the title of the compartment (**c0**), and rename it **EC**. Press **Enter** to confirm. Alternatively, you can alter the name of the compartment in the box labeled **Structure Name**.

The screenshot displays the VCell software interface. On the left, a tree view shows the project structure under 'BioModel1', with 'Physiology' expanded to show 'Reaction Diagram' (selected), 'Reactions (0)', 'Structures (1)', 'Species (0)', 'Molecules (0)', and 'Observables (0)'. The main workspace is titled 'Reaction Diagram' and contains a single compartment labeled 'EC', which is highlighted with a red rectangular border. An orange arrow points from the 'EC' label in the workspace to the 'Structure Name' field in the 'Object Properties' panel at the bottom. The 'Object Properties' panel has tabs for 'Object Properties' and 'Problems (0 Errors, 0 Warnings)'. The 'Object Properties' tab is active, showing fields for 'Structure Name' (containing 'EC'), 'Size Variable Name' (containing 'EC [μm³]'), and 'Annotation'. A search bar is located above the 'Object Properties' panel. The top menu bar includes 'File', 'Server', 'Window', 'Tools', and 'Help'.

TIP: You can not edit a structure's name or its components while using the **Structure Tool**. Therefore, when creating and naming structures, you have to switch back and forth between said **Construction Tool**, and the **Select Tool** immediately to its left.

1. Click on the **Structure Tool**. A dashed border should appear on the sides of the EC compartment.

2. Click on the dashed border, then click **Add Membrane**. Name the membrane **pm**



TIP: Compartments have a white background, while membranes have a grey background.

TIP: The goal of these structures is to roughly mimic the basic structure of the cell so as to create an environment for reactions to take place.

The screenshot shows the VCell software interface. The main window is titled 'Reaction Diagram' and displays a compartment layout with five columns: EC (white), pm (grey), Cyt (white), nm (grey), and Nuc (white). A yellow text box is overlaid on the EC and pm compartments, containing the text: '1. Continue to make alternating compartments and membranes until you have, starting with a compartment: **EC, pm, Cyt, nm, Nuc.** (Also illustrated in the image.)' The left sidebar shows a tree view of the model structure, including 'Rule-Based_Ran_Transport', 'Physiology', 'Reaction Diagram', 'Reactions (0)', 'Structures (5)', 'Species (0)', 'Molecules (0)', 'Observables (0)', 'Applications (0)', 'Parameters, Functions and Units', and 'Pathway'. The bottom left shows a search bar and a list of BioModels, including 'My BioModels (2018nathans751) (18)', 'Shared BioModels (0)', 'Public BioModels (601)', 'Tutorials (8)', and 'Education (34)'. The bottom right shows the 'Object Properties' panel with the text: 'Select only one object (e.g. species, reaction, simulation) to view/edit properties.'

TIP: For some reactions, like a neuron firing, adjusting the membrane potential can be very important in correct simulation. In this case, the membrane potential is not very important.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (0)
- Structures (5)**
- Species (0)
- Molecules (0)
- Observables (0)
- Applications (0)
- Parameters, Functions and Units
- Pathway

Reaction Diagram Reactions **Structures** Species Molecules Observables

Name	Type	Electrical (Membrane Polarity)
Cyt	Compartment	
EC	Compartment	
Nuc	Compartment	
pm	Membrane	Cyt (+) EC (-)
nm	Membrane	Nuc (+) Cyt (-)

1. Click on nm. At the bottom of the screen, the properties of this membrane will appear.

2. Change the Positive dropdown to nuc and the Negative to cyt (optional, necessary only if voltages across membrane will be considered).

3. Do steps 1-2 for the pm membrane as well. Note that pm separates EC and Cyt.

VCe

BioModels MathModels Geometries

Search

- Biological Models
- My BioModels (2018nathans751) (18)
- Shared BioModels (1)
- Public BioModels (601)
- Tutorials (8)
- Education (34)

New Compartment New Membrane Delete Pathway Links Search

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

Select only one structure to edit properties

Structure Name nm

Size Variable Name nm [μm^2]

Electrophysiology

Voltage Variable Name Voltage_nm [mV]

Positive (inside feature) **Nuc**

Negative (outside feature) **Cyt**

membrane voltage: "Voltage_nm" = voltage(Nuc) - voltage(Cyt)
inward currents: from compartment "Cyt" into compartment "Nuc"
Note: VCell reactions and fluxes specify inward currents (- to +) rather than conventional currents (+ to -).

Annotation

TIP: The color of a molecule is assigned based on the order in which it was created. It is not possible to customize or change the colors of molecules.

The screenshot shows the VCell software interface. The 'Molecules' tab is selected, displaying a table with columns: Name, Depiction, and BioNetGen Definition. The table contains one entry: MT0, with a depiction of a small circle and the definition MT0().

Four numbered instructions are overlaid on the interface:

1. To create molecules that will be involved in the model, click on **New Molecule**. A new, generically named molecule will appear.
2. To change the name, right click on the molecule, and click **Rename**.
3. Change the name to Ran.
4. Right click on the molecule and select **Add Site**.

The interface also shows a left sidebar with a tree view of the model structure, including 'Physiology', 'Reaction Diagram', 'Reactions (0)', 'Structures (5)', 'Species (0)', 'Molecules (1)', and 'Observables (1)'. The 'Molecules (1)' item is selected. Below the tree view is a search bar and a list of biological models. The bottom of the interface shows the 'Object Properties' panel with 'Anchor Molecule' options and a list of compartments (EC, pm, Cyt, nm).

TIP: You can not delete a molecule until all observables, species, and reactions containing said molecule are either altered to not include the molecule or deleted.

The screenshot displays the VCell software interface. The left sidebar shows a tree view under 'Rule-Based_Ran_Transport' with 'Physiology' expanded, listing 'Reaction Diagram', 'Reactions (0)', 'Structures (5)', 'Species (0)', 'Molecules (1)', and 'Observables (1)'. Below this is a 'VCell DB' section with tabs for 'BioModels', 'MathModels', and 'Geometries', and a 'Search' field. The main window has tabs for 'Reaction Diagram', 'Reactions', 'Structures', 'Species', 'Molecules', and 'Observables'. The 'Molecules' tab is active, showing a table with columns 'Name', 'Depiction', and 'BioNetGen Definition'. The table contains one entry: 'Ran' with a depiction of a yellow oval and the definition 'Ran(Cargo)'. Below the table are buttons for 'New Molecule', 'Delete', and 'Pathway Links'. The 'Object Properties' panel is open, showing 'Anchor Molecule' with 'No restrictions' selected. A context menu is open over the 'Cargo' site of the 'Ran' molecule, with options: 'Move right', 'Move left', 'Rename', 'Delete', and 'Add State'. An arrow points from the 'Rename' option to a yellow callout box. Another yellow callout box points to the 'Cargo' site.

1. Right click on the site and select **Rename**.

2. Name the site **cargo**.

TIP: A molecule can also be renamed by double clicking on it in the name column.

The screenshot displays the VCell software interface. The main window is titled 'Rule-Based_Ran_Transport' and shows a tree view on the left with 'Physiology' expanded, containing 'Reaction Diagram', 'Reactions (0)', 'Structures (5)', 'Species (0)', 'Molecules (2)', and 'Observables (2)'. The 'Molecules' tab is selected, showing a table with columns 'Name', 'Depiction', and 'BioNetGen Definition'. The table lists 'Ran' and 'RCC1'. The 'RCC1' molecule is highlighted. Below the table, there are buttons for 'New Molecule', 'Delete', and 'Pathway Links'. The 'Object Properties' panel is open, showing 'Anchor Molecule' with 'RCC1' selected. The 'Site' label is visible. Two yellow callout boxes provide instructions: '1. Create new molecule RCC1.' and '2. Rename Site0 to Site'.

Name	Depiction	BioNetGen Definition
Ran		Ran(Cargo)
RCC1		RCC1(Site)

1. Create new molecule **RCC1**.

2. Rename Site0 to **Site**

File Server Window Tools Help

Rule-Based_Ran_Transport

- Physiology
 - Reaction Diagram
 - Reactions (0)
 - Structures (5)
 - Species (0)
 - Molecules (3)**
 - Observables (3)
- Applications (0)
- Parameters, Functions and Units
- Pathway




VCeCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
 - My BioModels (2018nathans751) (18)
 - Shared BioModels (1)
 - Public BioModels (601)
 - Tutorials (8)
 - Education (34)

Reaction Diagram Reactions Structures Species **Molecules** Observables

Name	Depiction	BioNetGen Definition
Ran		Ran(Cargo)
RCC1		RCC1(Site)
C		C(site,Y1,Y2,Y3)

New Molecule ▼ Delete Pathway Links ▼

Object Properties Problems (0 Errors, 0 Warnings)

Anchor Molecule

☒ No restrictions

☐ Only these:

- ☐ EC
- ☐ pm
- ☐ Cyt
- ☐ nm

Annotation

1. Create new molecule **C**.

2. Add sites **Site**, **Y1**, **Y2**, and **Y3**.

3. Right click on site **Y1** and press add state. Do this for sites **Y2** and **Y3** as well (2x for each site).

Move right
Move left
Rename
Delete
Add State

TIP: The BioNetGen Definition is another way of describing a molecule. The format is the name of the molecule followed by closed parentheses, containing the names of sites, separated by commas. States are indicated by adding a tilde to the end of the site, followed by the name of the state. Multiple states can be created per site.

File Server window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (0)
- Structures (5)
- Species (0)
- Molecules (3)**
- Observables (3)

Applications (0)

Parameters, Functions and Units

Pathway




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BioModels MathModels Geometries

Search

- Biological Models
- My BioModels (2018nathans751) (18)
- Shared BioModels (1)
- Public BioModels (601)
- Tutorials (8)
- Education (34)

Reaction Diagram Reactions Structures Species **Molecules** Observables

Name	Depiction	BioNetGen Definition
Ran		Ran(Cargo)
RCC1		RCC1(Site)
C		C(site,Y1~u~p,Y2~u~p,Y3~state0~p)

1. To rename the state, right click on it and select **Rename**.

2. Rename the states so that each site has two states; **p** on the top and **u** on the bottom.

New Molecule

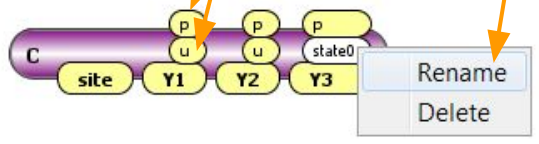
Object Properties Problems (0 Errors, 0 Warnings) Database File Info

Anchor Molecule

☒ No restrictions

☐ Only these:

- ☐ EC
- ☐ pm
- ☐ Cyt
- ☐ nm



Rename

Delete

Annotation

TIP: Each Observable corresponds to a sum of species selected by species patterns. Specific species are identified the network is generated using reaction rules. An observable corresponding to the total amount of all species that include this molecule is automatically generated for every molecule.

Rule-Based_Ran_Transport Physiology

- Reaction Diagram
- Reactions (0)
- Structures (5)
- Species (0)
- Molecules (3)
- Observables (3)**
- Applications (0)
- Parameters, Functions and Units
- Pathway

Name	Structure	Depiction	BioNetGen Definition	Count
O0_Ran_tot	Cyt		Ran()	Molecules
O0_RCC1_tot	Cyt		RCC1()	Molecules
O0_c_tot	Cyt		c()	Molecules

To view, edit, and add observables, Click on the **Observables** tab.

When a molecule is created, an observable for that molecule should also automatically be created. Therefore, there should already be three observables.

Observables are defined in the default compartment, we will explain how to change the compartment later.

VCeCell DB BMDb Pathway Comm Sa

BioModels MathModels Geometries

Search

- Biological Models
- My BioModels (2018nathans751) (18)
- Shared BioModels (1)
- Public BioModels (601)
- Tutorials (8)
- Education (34)

New Observable Duplicate Delete Pathway Links Search

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

Select only one object (e.g. species, reaction, simulation) to view/edit properties.

TIP: Not all of the observables were automatically created in the correct structure.

The screenshot displays the VCell software interface. On the left is a tree view of the model hierarchy, including 'Rule-Based_Ran_Transport', 'Physiology', and 'Observables (3)'. The main window shows a table of observables. Below the table is a toolbar with buttons like 'New Observable', 'Duplicate', and 'Delete'. At the bottom, the 'Object Properties' panel shows a diagram of a 'Ran' molecule with a 'Cyt' site and a 'cargo' site. A question mark is present under the 'Cyt' site.

Name	Structure	Depiction	BioNetGen Definition	Count
Ran_cyt	Cyt		Ran()	Molecules
00_RCC1_tot	Cyt		RCC1()	Molecules
00_c_tot	Cyt		c()	Molecules

1. Rename **00_Ran_tot** to **Ran_Cyt**

You can rename observable by double clicking on their name.

To better identify the observables, their names can be changed.

? underneath the site means that other molecules can be bound to Ran at this site.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (0)
- Structures (5)
- Species (0)
- Molecules (3)
- Observables (3)**
- Applications (0)
- Parameters, Functions and Units
- Pathway

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
 - My BioModels (2018nathans751) (18)
 - Shared BioModels (1)
 - Public BioModels (601)
 - Tutorials (8)
 - Education (34)

Reaction Diagram Reactions Structures Species Molecules **Observables**

Name	Structure	Depiction	BioNetGen Definition	Count
Ran_cyt	Cyt		Ran()	Molecules
Cargo_Nuc	Cyt		C()	Molecules
RCC1_Nuc	Cyt		RCC1()	Molecules

1. Change names as indicated.

2. Change the structure for both **Cargo_Nuc**, and **RCC1_Nuc** observables to **Nuc**. Select observable. In the bottom of the screen, the observable will be visually displayed.

3. Right click on the grey box that says the name of the observables current structure. Then, select **Specify Structure**, and a list of all the structures will appear. Clicking on one changes the Structure where the selected observable is present.

New Observable Duplicate Delete Pathway Links

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

Add Pattern

Multimolecular

Polymer of

length = 2

length > 1

cyt

site Y1 Y2 Y3

Delete Species Pattern

Add Molecule

Specify structure (for all)

Cyt

EC

Nuc

pm

nm

Annotation

TIP: A duplicate observable can be created by selecting the desired observable and clicking Duplicate.

The screenshot shows the VCell software interface with the 'Observables' tab selected. The left sidebar displays a tree view of the model structure, including 'Physiology', 'Reaction Diagram', 'Reactions (0)', 'Structures (5)', 'Species (0)', 'Molecules (3)', 'Observables (3)', 'Applications (0)', 'Parameters, Functions and Units', and 'Pathway'. The main workspace shows a table of existing observables:

Name	Structure	Depiction	BioNetGen Definition	Count
Ran_cyt	Cyt		Ran()	Molecules
RCC1_Nuc	Nuc		RCC1()	Molecules
Cargo_Nuc	Nuc		C()	Molecules

Below the table, there is a 'New Observable' button and a dropdown menu. The dropdown menu is open, showing options: 'In Compartment EC', 'In Compartment Nuc', 'In Compartment Cyt', 'In Membrane pm', and 'In Membrane nm'. A yellow callout box points to the 'New Observable' button with the text: 'To create a new observable, click on **New Observable**, then specify the structure where it should be.' Another yellow callout box points to the 'In Compartment Cyt' option with the text: '1. Create a new observable in the **Cyt** compartment.'

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (0)
- Structures (5)
- Species (0)
- Molecules (3)
- Observables (4)

Applications (0)

Parameters, Functions and Units

Pathway

Reaction Diagram Reactions Structures Species Molecules Observables

Name	Structure	Depiction	BioNetGen Definition	Count
Ran_cyt	Cyt		Ran()	Molecules
RCC1_Nuc	Nuc		RCC1()	Molecules
Cargo_Nuc	Nuc		C()	Molecules
Cargo_Cyt	Cyt			Molecules

1. Rename the new observable to **Cargo_Cyt**. It will count all molecules of cargo in cytosol.

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
- My BioModels (2018nathans751) (18)
- Shared BioModels (1)
- Public BioModels (602)
- Tutorials (8)
- Education (34)

New Observable Duplicate Delete

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

Add Pattern

Multimolecular

Polymer of

length = 2

length > 1

Delete Species Pattern

Add Molecule

Specify structure (for all)

Ran

RCC1

C

2. Right click on the grey area. Select **Add Molecule -> C**.

3. The generated observable will have all sites of cargo molecule in grey with question marks, meaning that all tyrosines can be either phosphorylated or not, and other molecules can be bound or not.

TIP: For some observables it is important to specify certain sites being bound or unbound, phosphorylated, or unphosphorylated.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (0)
- Structures (5)
- Species (0)
- Molecules (3)
- Observables (5)**
- Applications (0)
- Parameters, Functions and Units
- Pathway

Reaction Diagram Reactions Structures Species Molecules **Observables**

Name	Structure	Depiction	BioNetGen Definition	Count
Ran_cyt	Cyt		Ran()	Molecules
RCC1_Nuc	Nuc		RCC1()	Molecules
Cargo_Nuc	Nuc		C()	Molecules
Cargo_Cyt	Cyt		C()	Molecules
Ran_Bound_Cyt	Cyt		Ran()	Molecules

1. Create a new observable named **Ran_Bound_Cyt** in the **Cyt** compartment.

2. Assign the observable the **Ran** molecule.

2. Right click on the site **Cargo**, and click **Site Has External Bond**. This specifies that there is an observable that selects all Ran molecules that are bound to something (and this “something” can be only cargo molecule), and located in the Cytosol.

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
- My BioModels (2018nathans751) (18)
- Shared BioModels (1)
- Public BioModels (602)
- Tutorials (8)
- Education (34)

Object Properties Problems (0 Errors, 0 Warnings) Database

Add Pattern

Multimolecular

Polymer of

length = 2

length > 1

Ran

Cyt

cargo

Site is unbound

Site has external bond

Site may be bound

Site bond specified

Annotation

TIP: A state of "p" means phosphorylated, while a "u" state means unphosphorylated.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (0)
- Structures (5)
- Species (0)
- Molecules (3)
- Observables (6)**
- Applications (0)
- Parameters, Functions and Units
- Pathway

Reaction Diagram Reactions Structures Species Molecules **Observables**

Name	Structure	Depiction	BioNetGen Definition	Count
Ran_cyt	Cyt		Ran()	Molecules
RCC1_Nuc	Nuc		RCC1()	Molecules
Cargo_Nuc	Nuc		C()	Molecules
Cargo_Cyt	Cyt		C()	Molecules
Ran_Bound_Cyt	Cyt		Ran(cargo!+)	Molecules
Cargo_Phosp_Cyt	Cyt		C(Y1~p!,Y2~p!?)	Molecules

1. Create a new observable named **Cargo_Phosp_Cyt** in the **Cyt** compartment. Assign the observable the **C** molecule.

2. Right click on the states above the **Y** sites. Set all three states to **p**. This creates an observable selecting all species that contain C molecule phosphorylated at all **Y** sites.

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
- My BioModels (2018nathans751) (18)
- Shared BioModels (1)
- Public BioModels (602)
- Tutorials (8)
- Education (34)

New Observable Duplicate Delete Pathway Links

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

Add Pattern

Multimolecular

Polymer of

length = 2

length > 1

C

Cyt

site

Y1 Y2 Y3

State: not specified

State: u

State: p

Annotation

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (0)
- Structures (5)
- Species (0)
- Molecules (3)
- Observables (7)

Applications (0)

Parameters, Functions and Units

Pathway

Reaction Diagram Reactions Structures Species Molecules Observables

Name	Structure	Depiction	BioNetGen Definition	Count
Ran_cyt	Cyt		Ran()	Molecules
RCC1_Nuc	Nuc		RCC1()	Molecules
Cargo_Nuc	Nuc		C()	Molecules
Cargo_Cyt	Cyt		C()	Molecules
Ran_Bound_Cyt	Cyt		Ran(cargo!+)	Molecules
Cargo_Phosp_Cyt	Cyt		C(Y1~p!?,Y2~p!?,Y3~p!?)	Molecules
Cargo_Phosp_Cyt_Tot	Cyt		C()	Molecules

1. Create a new observable named **Cargo_Phosp_Cyt_Tot** in the **Cyt** compartment. Assign the observable the **C** molecule.

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
 - My BioModels (2018nathans751) (19)
 - Shared BioModels (1)
 - Public BioModels (602)
 - Tutorials (8)
 - Education (34)

New Observable Duplicate Delete Pathway Links Search

Object Properties Problems (0 Errors, 2 Warnings)

Add Pattern

Multimolecular

Polymer of

2

1

3. Specify the new pattern as the **C** molecule.

4. Specify the third pattern as molecule **C** as well.

2. Add a new species pattern into the existing observable by selecting the **Add Pattern** button (2X).

Delete Species Pattern

Add Molecule

Specify structure (for all)

Ran

RCC1

C

TIP: A grey site with a question mark at the bottom means that the site may or may not be bound.

File Server Window Tools Help

Rule-Based_Ran_Transport

- Physiology
 - Reaction Diagram
 - Reactions (0)
 - Structures (5)
 - Species (0)
 - Molecules (3)
 - Observables (7)**
- Applications (0)
- Parameters, Functions and Units
- Pathway

VCeDB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
 - My BioModels (2018nathans751) (19)
 - Shared BioModels (1)
 - Public BioModels (602)
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 - Education (34)

Reaction Diagram Reactions Structures Species Molecules **Observables**

Name	Structure	Depiction	BioNetGen Definition	Count
Ran_cyt	Cyt		Ran()	Molecules
RCC1_Nuc	Nuc		RCC1()	Molecules
Cargo_Nuc	Nuc		C()	Molecules
Cargo_Cyt	Cyt		C()	Molecules
Ran_Bound_Cyt	Cyt		Ran(cargo!+)	Molecules
Cargo_Phosp_Cyt	Cyt		C(Y1~p!?,Y2~p!?,Y3~p!?)	Molecules
Cargo_Phosp_Cyt_Tot	Cyt		C(Y1~p!?) C(Y2~p!?) C(Y3~p!?)	Molecules

New Observable Duplicate Delete Pathway Links

Object Properties Problems (0 Errors, 0 Warnings)

Add Pattern

☒ Multimolecular

Polymer of

☐ length = 2

☐ length > 1

1. Set Y1 as phosphorylated on the first molecular structure.

2. Set Y2 as phosphorylated on the second molecular structure.

3. Set Y3 as phosphorylated on the third molecular structure.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (0)
- Structures (5)
- Species (0)
- Molecules (3)
- Observables (7)

Applications (0)

Parameters, Functions and Units

Pathway

Reaction Diagram Reactions Structures Species Molecules Observables

Name	Structure	Depiction	Link	BioNetGen Definition
------	-----------	-----------	------	----------------------

1. To make a new species, click the **New Species** button, then specify the structure in which the species will exist.

2. Create the new species in compartment **Nuc**.

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

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New Species Duplicate Delete Pathway Links

- In Compartment EC
- In Compartment Nuc
- In Compartment Cyt
- In Membrane pm
- In Membrane nm

Errors, 0 Warnings Database File Info

Species, reaction, simulation) to view/edit properties.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology


- Reaction Diagram
- Reactions (0)
- Structures (5)
- Species (1)
- Molecules (3)
- Observables (7)

Applications (0)

Parameters, Functions and Units

Pathway

Reaction Diagram Reactions Structures Species Molecules Observables

Name	Structure	Depiction	Link	BioNetGen Definition
Ran_C_Nuc	Nuc			

1. Rename the species to **Ran_C_Nuc** by either double clicking in the name column, or typing it in the **Species Name** box in the **Object Properties** tab.

VCeDB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
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New Species Duplicate Delete Pathway Links Search

Object Properties Problems (0 Errors, 0 Warnings)

Species Name Ran_C_Nuc

Linked Pathway Object(s)

Annotation

Specify Molecule

- Ran
- RCC1
- C

2. To assign a molecule to the blank species, right click on the green ball, and click **Specify Molecule**. Assign the blank species to the **Ran** molecule.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (0)
- Structures (5)
- Species (1)
- Molecules (3)
- Observables (7)

Applications (0)

Parameters, Functions and Units

Pathway


VCell DB BMDB Pathway Comm Sabio

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Reaction Diagram Reactions Structures **Species** Molecules Observables

Name	Structure	Depiction	Link	BioNetGen Definition
Ran_C_Nuc	Nuc			Ran(cargo)

New Species Duplicate Delete

Object Properties Problems (0 Errors, 0 Warning)




Species Name Ran_C_Nuc

Linked Pathway Object(s)

Annotation

Ran cargo Nuc

Specify Molecule

-  Ran
-  RCC1
-  C

1. To add another molecule into the specie, right click on the white space next to the molecule, and select **Specify Molecule**. Select the **C** molecule.

File Server Window Tools Help

Rule-Based_Ran_Transport

- Physiology
 - Reaction Diagram
 - Reactions (0)
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VCeDB BMDB Pathway Comm **Sabio**

BioModels MathModels Geometries

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Reaction Diagram Reactions Structures **Species** Molecules Observables

Name	Structure	Depiction	Link	BioNetGen Definition
Ran_C_Nuc	Nuc			Ran(cargo).C(site,Y1~u,Y2~u,Y3~u)

New Species ▾ Duplicate ▾ Delete Pathway Links ▾ Search

Object Properties Problems (1 Errors, 0 Warnings)

Species Name Ran_C_Nuc

Linked Pathway Object(s)

Annotation

Nuc cargo = Site is unbound
Site bond specified

- Ran(cargo!1).C(site!1)
- Ran(cargo!1).C(Y1!1)
- Ran(cargo!1).C(Y2!1)
- Ran(cargo!1).C(Y3!1)

CONNECTED (2018nathans751) 777.2MB / 899.2MB

TIP: A yellow site with no line out the bottom is an unbound site.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (0)
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- Species (2)
- Molecules (3)
- Observables (7)
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- Parameters, Functions and Units
- Pathway

Reaction Diagram Reactions Structures Species Molecules Observables

Name	Structure	Depiction	Link	BioNetGen Definition
Ran_C_Nuc	Nuc			Ran(cargo!1).C(site!1,Y1~u,Y2~u,Y3
RCC1	Nuc			RCC1(site)

1. Create new species **RCC1** in the **Nuc** compartment.

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

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New Species Duplicate Delete Pathway Links Search

Object Properties Problems (0 Errors, 0 Warnings)

Species Name RCC1

Linked Pathway Object(s)

Annotation

2. Specify the molecule to **RCC1**.

RCC1 site

Nuc

1. Select the **Reactions** tab.

3. Rename the reaction rule by double clicking in the **Name** column. Name this rule **C_p1**.

2. To create a new reaction rule, click on the **New Rule** button, and specify which structure the reaction should take place. In this case, create the new rule in the **Cyt** compartment.

The screenshot displays the VCell software interface. The top menu bar includes 'File', 'Server', 'Window', 'Tools', and 'Help'. The left sidebar shows a tree view for 'Rule-Based_Ran_Transport' with a 'Physiology' sub-section containing 'Reaction Diagram', 'Reactions (1)', 'Structures (5)', 'Species (2)', 'Molecules (3)', and 'Observables (7)'. The main window has a tabbed interface with 'Reaction Diagram', 'Reactions', 'Structures', 'Species', 'Molecules', and 'Observables'. The 'Reactions' tab is active, showing a table with columns: Reaction, Name, Structure, Depiction, Kinetics, Link, and BioNetGen Definition. A single row is visible: 'Reaction Rule', 'C_p1', 'Cyt', a reaction depiction, 'MassAction', and '->'. Below the table, there are buttons for 'New Reaction', 'New Rule', 'Duplicate', 'Delete', and 'Pathway Links'. The 'New Rule' button is clicked, opening a dropdown menu with options: 'In Compartment Cyt', 'In Compartment EC', 'In Compartment Nuc', 'In Membrane pm', and 'In Membrane nm'. The 'In Compartment Cyt' option is selected. At the bottom, there are checkboxes for 'Single Row Viewer', 'Show Molecule Color', 'Show Non-trivial', and 'Show Differe...'. A search bar is located at the bottom right of the main window.

Reaction	Name	Structure	Depiction	Kinetics	Link	BioNetGen Definition
Reaction Rule	C_p1	Cyt		MassAction		->

Buttons: New Reaction, New Rule, Duplicate, Delete, Pathway Links

Object Properties: Kinetics, Reversible, Add Reactant, Add Product

Options: ☐ Single Row Viewer, ☒ Show Molecule Color, ☒ Show Non-trivial, ☐ Show Differe...

Search:

TIP: To make the reaction larger or smaller, use the respectively green and red plus and minus button. Checking the **Single Row Viewer** box aligns the entire reaction in one row. You can not edit the reaction in this mode.

File Server Window Tools Help

Rule-Based_Ran_Transport

- Physiology
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VCeL DB BMDB Pathway Comm Sabio

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Reaction Diagram Reactions Structures Species Molecules Observables

Reaction	Name	Structure	Depiction	Kinetics	Link	BioNetGen Definition
Reaction Rule	C_p1	Cyt		MassAction		@Cyt:C() ->

1. Like in the observables tab, you add molecules by right clicking on the dashed blank molecule, and select **Specify Molecule**. Specify to the **C** molecule.

2. You will see that there is an arrow. This arrow separates the products from the reactants. You have already specified the molecule of the reactant as **C**. Now specify the product as **C** as well.

New Reaction New Rule Duplicate Delete Pa

Object Properties Problems (1 Errors, 1 Warnings)

Kinetics Editor

Reversible ☐

Add Reactant

Add Product

site Y1 Y2 Y3

Cyt

Single Row Viewer ☐

Show Molecule Color ☒

Show Non-trivial ☒

Show Differ...

Delete

Specify Molecule

Specify structure

Ran

RCC1

C

TIP: With no boxes checked, the reaction is shown in black and white, with only the site specific bonds indicated in color. Checking the **Show Molecule Color** box adds an ordered color to the molecule to help with visual differentiation. The specific color can not be changed.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

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VCell DB BMDB Pathway Comm Sabio

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Reaction Diagram Reactions Structures Species Molecules Observables

Reaction	Name	Structure	Depiction	Kinetics	Link	BioNetGen Definition
Reaction Rule	C_p1	Cyt		MassAction		@Cyt:C(Y3~u!?) -> @Cyt:C(Y3~p!?)

New Reaction New Rule Duplicate Delete

Object Properties Problems (0 Errors, 0 Warnings)

Kinetics Editor

Reversible ☐

Add Reactant

Add Product

☐ Single Row Viewer

☒ Show Molecule Color

☒ Show Non-trivial

☐ Show Differe...

1. This reaction rule is for phosphorylation, so set the Y3 site as u in the reactants, and p in the products.

TIP: Checking the **Show Non-trivial** box highlights assigned sites and states in yellow. Checking the **Show Differe...** box highlights in orange the differences in bonds, sites, and states between the reactants and the products.

File Server Window Tools Help

Rule-Based_Ran_Transport

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VCeL DB BMDb Pathway Comm Sabio

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Reaction Diagram Reactions Structures Species Molecules Observables

Reaction	Name	Structure	Depiction	Kinetics	Link	BioNetGen Definition
Reaction Rule	C_p1	Cyt		MassAction		@Cyt:C(Y3~u!?) -> @Cyt:C(Y3~p!?)
Reaction Rule	C_p2	Cyt		MassAction		@Cyt:C(Y2~u!?) -> @Cyt:C(Y2~p!?)

1. Create a duplicate reaction rule by pressing **Duplicate**. Specify the location as being in the **Cyt** compartment.

2. Rename the rule **C_p2**.

3. Change the **Y3** sites to a non-specified state.

4. Switch the **Y2** site in the reactants to a **u** state, and in the products to a **p** state.

Object Properties Problems (0 Errors, 0 Warnings)

Kinetics Editor

Reversible ☐

Add Reactant

Add Product

☐ Single Row Viewer

☒ Show Molecule Color

☒ Show Non-trivial

☐ Show Differe...

1. Select the reaction rule **C_p1**.

2. Select the **Kinetics** tab.

3. Check the **Reversible** box to allow for a bidirectional reaction rule (Not all rules are reversible).

4. Enter the value 10.0 in the **Expression** column for Kf, and 1.0 for Kr (Forward and reverse rate constants).

Reaction	Name	Structure	Depiction	Kinetics	Link	BioNetGen Definition
Reaction Rule	C_p1	Cyt		MassAction		@Cyt:C(Y3~u!?) <-> @Cyt:C(Y3~p!?)
Reaction Rule	C_p2	Cyt		MassAction		@Cyt:C(Y2~u!?) -> @Cyt:C(Y2~p!?)

Name	Description	Global	Expression	Units
ruleRate	rate of reactions generated by rule	<input type="checkbox"/>	Variable	$\mu\text{M} \cdot \text{s}^{-1}$
Kf	microscopic forward rate	<input type="checkbox"/>	10.0	s^{-1}
Kr	microscopic reverse rate	<input type="checkbox"/>	1.0	s^{-1}

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (2)**
- Structures (5)
- Species (2)
- Molecules (3)
- Observables (7)
- Applications (0)
- Parameters, Functions and Units
- Pathway

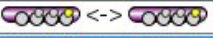

VCell DB BMDB Pathway Comm Sabio

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Reaction Diagram Reactions Structures Species Molecules Observables

Reaction	Name	Structure	Depiction	Kinetics	Link	BioNetGen Definition
Reaction Rule	C_p1	Cyt		MassAction		@Cyt:C(Y3~u!?) <-> @Cyt:C(Y3~p!?)
Reaction Rule	C_p2	Cyt		MassAction		@Cyt:C(Y2~u!?) <-> @Cyt:C(Y2~p!?)

1. Select the reaction rule **C_p2**.

2. Click on **Kinetics** and check **Reversible**.

3. Set forward and reverse rates **Kf** to be 10.0 and a **Kr** to be 1.0

New Reaction New Rule Duplicate Delete Pathway Links Search

Object Properties Problems (0 Errors, 0 Warnings)

Kinetics Editor

Reaction Name C_p2

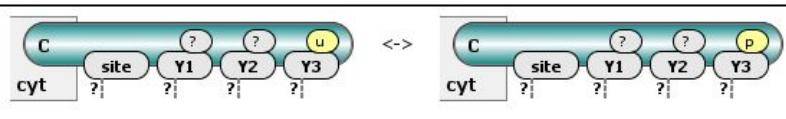
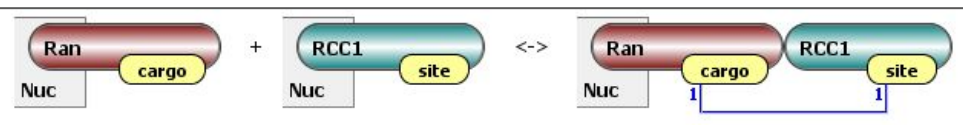
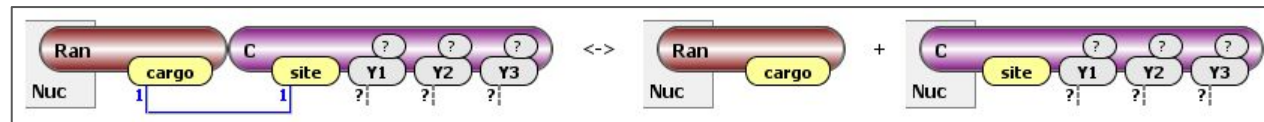
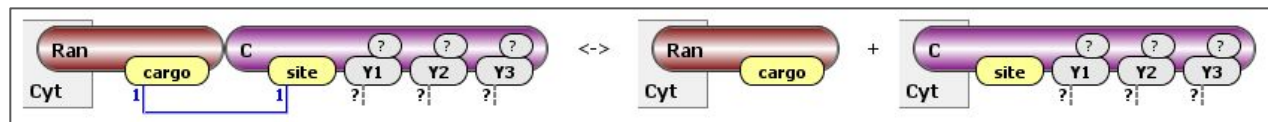
Reversible ☒ Kinetic Type Mass Action (for each reaction: $K_f \cdot \prod \text{reactants} - K_r \cdot \prod \text{products}$) Convert units

Name	Description	Global	Expression	Units
ruleRate	rate of reactions generated by rule	<input type="checkbox"/>	Variable	$\mu\text{M} \cdot \text{s}^{-1}$
Kf	microscopic forward rate	<input type="checkbox"/>	10.0	s^{-1}
Kr	microscopic reverse rate	<input type="checkbox"/>	1.0	s^{-1}

Annotation and Pathway Links

Linked Pathway Object(s):

Finish inputting the rest of the reactions pictured below. (You already did the first two)

**C_p1****C_p2****Ran_RCC1_Bind****C_p3****Transfer****Ran_C_Bind_Nuc****Ran_C_Bind_Cyt**

Finish inputting the rest of the Kinetics shown below (you already did the first two).

Reaction	Structure	Reversible?	Kf	Kr
C_p1	Cyt	yes	10.0	1.0
C_p2	Cyt	yes	10.0	1.0
C_p3	Cyt	yes	10.0	1.0
Ran_C_Bind_Cyt	Cyt	yes	1.0	100.0
Ran_C_Bind_Nuc	Nuc	yes	1.0	100.0
Ran_RCC1_Bind	Nuc	yes	1.0	100.0
Transport	nm	yes	(2.0 * 602.0)	0.0

The screenshot shows the VCell software interface. The top menu bar includes 'File', 'Server', 'Window', 'Tools', and 'Help'. The left sidebar contains a tree view with the following structure:

- Rule-Based_Ran_Transport
 - Physiology
 - Reaction Diagram
 - Reactions (7)
 - Structures (5)
 - Species (2)
 - Molecules (3)
 - Observables (7)
 - Applications (0)**
 - Parameters, Fur
 - Pathway

The 'Applications (0)' folder is selected, and a context menu is open with the following options:

- New Application ▸
 - Deterministic
 - Stochastic
 - Network-Free
- Expand All
- Collapse All

Two yellow callout boxes provide instructions:

1. Right Click on **Applications**.
2. Select **New Application>Deterministic**. A **Deterministic application** uses the BioNetGen engine to generate a reaction network that is solved as a system of ODEs.

The bottom of the interface shows a 'VCell DB' tab with 'BMDDB' and 'Pat' sub-tabs. Below this is a 'Search' bar and a list of biological models:

- Biological Models
 - My BioModels (2018nathans751) (19)
 - Shared BioModels (1)
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 - Education (34)

The bottom right section contains a 'New Application' dropdown, 'Delete', 'More Copy Actions', and 'Compare...' buttons. Below these are tabs for 'Object Properties', 'Problems (0 Errors, 0 Warnings)', and 'Database File Info'. The 'Object Properties' tab is active, displaying the text: 'Select only one object (e.g. species, reaction, simulation) to view/edit properties.'

File Server Window Tools Help

Rule-Based_Ran_Transport

- Physiology
 - Reaction Diagram
 - Reactions (7)
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- Applications (1)**
 - Non-Spatial Deterministic**
- Parameters, Functions and Units
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VCeL DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
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Name	Math Type	Annotation
Non-Spatial Deterministic	explicit network model, compartmental, determi...	

1. Rename the application to **Non-Spatial Deterministic** by double clicking in the name box.

New Application ▼ Delete More Copy Actions ▼ Compare... Search

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

Application Name Application0

Annotation

Summary

- Deterministic
- ✖ Compartmental
- math not generated

TIP: The size values for this geometry are taken from the size of a real cell model that you will use later on. For deterministic applications the sizes are not that important. However, for stochastic applications, where values of species are specified with particle numbers, these sizes will be very important. They will be used to convert concentrations into particle numbers in a particular 3D geometry.

File Server Window Tools Help

Rule-Based Ran Transport

1. Click on the **Non-Spatial Deterministic** application.

- Species (2)
- Molecules (3)
- Observables (7)
- Applications (1)
 - Non-Spatial Deterministic**
- Parameters, Functions and Units
- Pathway

Geometry Specifications Protocols Simulations Parameter Estimation

Structure Mapping Geometry Definition

Physiology (structures)

EC Nuc Cyt pm nm

Geometry (subd) Compartment

2. Select **Geometry -> Structure Mapping**. Change the size of the structure by double clicking on the old value, and typing in the new one in the **Size** Column.

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

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Volume/Surface Calculator

Structure	Size
EC	14891.899581611733
Nuc	124712.1 [μm^3]
Cyt	3697.0137 [μm^3]
pm	4738.6406 [μm^2]
nm	1406.7734 [μm^2]

3. Change **EC** to **14891.9**, **Nuc** to **124712.1**, **Cyt** to **3697.0137**, **pm** to **4738.6406**, and **nm** to **1406.7734**.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (7)
- Structures (5)
- Species (2)
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Applications (1)



- Non-Spatial Deterministic
 - Geometry
 - Specifications**
 - Protocols
 - Simulations
 - Parameter Estimation

Parameters, Functions and Units

Pathway

Specifications

Species Reaction Network

Species	Structure	Depiction	Clamped	Initial Condition
Ran_C_Nuc	Nuc		<input type="checkbox"/>	4.493165893949507E-4 [μM]
RCC1	Nuc		<input type="checkbox"/>	4.493165893949507E-4 [μM]

1. Click on the **Specifications** tab, then make sure you are in the **Species** section.

2. Change the initial concentration for both species to 4.5E-4

VCell DB BMBD Pathway Comm Sabio

BioModels MathModels Geometries

Search

Biological Models

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- Education (34)

Object Properties Problems (0 Errors, 0 Warnings) Database File Info Network Generation Status

Description	Parameter	Expression	Units
initial concentration for RCC1	initConc	4.493165893949507E-4	μM

RCC1 site

Nuc

TIP: Creating a reaction network lets the computer do find all the possible permutations of reactions and species that are allowed by the reaction rules.

The screenshot shows the VCell software interface. On the left is a tree view with categories like Physiology, Applications (1), and Pathway. Under Applications, 'Non-Spatial Deterministic' is selected, and its sub-items are Geometry, Specifications (highlighted), Protocols, Simulations, and Parameter Estimation. Below this is a 'BioModels' search section with tabs for BioModels, MathModels, and Geometries. The main window has tabs for Geometry, Specifications, Protocols, and Simulation. The 'Specifications' tab is active, showing 'Species', 'Reaction', and 'Network' sub-tabs. The 'Network' sub-tab is selected, displaying a table of network constraints. An arrow points from a yellow callout box to the 'Network' sub-tab. Another yellow callout box points to the 'Edit / Test Constraints' button in the bottom right. A third yellow callout box points to the 'Test / Run' button in the 'Edit / Test Constraints' dialog box, which is open in the center. The dialog box shows 'Max. Iterations' set to 3 and 'Max. Molecules / Species' set to 10. A fourth yellow callout box points to the 'Test / Run' button in the dialog box.

1. Select the **Network** tab.

Name	Type	Value
Max Iterations	value	3
Max Molecules / Species	value	10

Note the constraints on the network

2. Click on **Edit/Test Constraints**.

3. To test if the current constraints are adequate for the reaction simulation, click on **Test/Run**

The screenshot shows the VCell software interface. The left sidebar contains a tree view with the following structure:

- Rule-Based_Ran_Transport
 - Physiology
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 - Structures (5)
 - Species (2)
 - Molecules (3)
 - Observables (7)
 - Applications (1)
 - Non-Spatial Deterministic
 - Geometry
 - Specifications**
 - Protocols
 - Simulations
 - Parameter Estimation
 - Parameters, Functions and Units
 - Pathway

The main window has tabs for File, Server, Window, Tools, and Help. Below these are tabs for Geometry, Specifications (selected), Protocols, Simulations, and Parameter Estimation. The Specifications panel has sub-tabs for Species, Reaction, and Network (selected). The Network Constraints table is shown below:

Name	Type	Value
Max Iterations	value	3
Max Molecules / Species	value	10

Below the table, the Generated Network section shows:

- Species: 21
- Reactions: 30
- Warning: Max Iterations number may be insufficient.

Buttons for View, Edit / Test Constraints, and Create new VCell BioModel from Network are visible.

The bottom panel shows the Object Properties tab with the following text:

```
Running BioNetGen ...
Iteration 0: 2 species
Iteration 1: 5 species
Iteration 2: 11 species
Iteration 3: 21 species
Creating BNG output spec ...
Return BioNetGen output to requester...
Total run time: 2.7 s.
Warning: Max Iterations number may be insufficient.
Please go to the Specifications / Network panel and adjust the number of Iterations.
The Network constraints are unchanged.
```

A yellow callout box with an arrow pointing to the warning message contains the text:

If the network is too small, after running BioNetGen, a red warning text will appear and specify the possible problems with the network constraints. In this case, the max number of iterations is too small.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (7)
- Structures (5)
- Species (2)
- Molecules (3)
- Observables (7)

Applications (1)

- Non-Spatial Deterministic
 - Geometry
 - Specifications**
 - Protocols
 - Simulations
 - Parameter Estimation

Parameters, Functions and Units

Pathway

VCell DB BMDB Pathway Comm Sabio

BioModel

Search

- Biologi
- My
- Sha
- Public BioModels (602)
- Tutorials (8)
- Education (34)

Geometry Specifications Protocols Simulations Parameter Estimation

Species Reaction Network

Network Constraints

Name	Type	Value
Max Iterations	value	3
Max Molecules / Species	value	10

Generated Network

Species: unavailable

Reactions: unavailable

Max. Iterations 10

Max. Molecules / Species 10

Test / Run Apply Cancel

Edit / Test Constraints

Create new VCell BioModel from Network

2. Click **Test/Run** to test the new network.

1. Change the max iterations to ten by clicking on **Edit/Test Constraints**, and replacing the current **Max Iterations** value with ten.

3. If there is no error shown after generating the network, then it is of adequate size. After this, click **Apply** to apply the new network constraints.

Running BioNetGen ...

```
Iteration 0: 2 species
Iteration 1: 6 species
Iteration 2: 11 species
Iteration 3: 21 species
Iteration 4: 31 species
Iteration 5: 36 species
Iteration 6: 37 species
Iteration 7: 37 species
Creating BNG output spec ...
Return BioNetGen output to requester...
Total run time: 5.7 s.
```


File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (7)
- Structures (5)
- Species (2)
- Molecules (3)
- Observables (7)

Applications (1)

- Non-Spatial Deterministic
 - Geometry
 - Specifications**
 - Protocols
 - Simulations
 - Parameter Estimation

Parameters, Functions and Units

Pathway

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
- My BioModels (2018nathans751) (19)
- Shared BioModels (1)
- Public BioModels (602)
- Tutorials (8)
- Education (34)

Geometry Specifications Protocols Simulations Parameter Estimation

Species Reaction Network

Network Constraints

Name	Type	Value
Max Iterations	value	10
Max Molecules / Species	value	10

Generated Network

Species: 37

Reactions: 100

Warning: none

1. Click to see all species in a separate pop-up window.

View

Edit / Test Constraints

View

Create new VCell BioModel from Network

Search

Object Properties Problems (0 Errors, 0 Warnings) Database File Info Network Generation Status

Running BioNetGen ...

```
Iteration 0: 2 species
Iteration 1: 5 species
Iteration 2: 11 species
Iteration 3: 21 species
Iteration 4: 31 species
Iteration 5: 36 species
Iteration 6: 37 species
Iteration 7: 37 species
```

Creating BNG output spec ...

Return BioNetGen output to requester...

Total run time: 5.7 s.

Updating the network constraints with the test values.

2. Click to see all reactions in a separate pop-up window.

3. See a reaction network in a separate window (may take a long time).

TIP: Filtering is very useful to verify the model. If you see that names of Molecules and Sites are too generic for efficient filtering – go back and change them. This is an easy and safe procedure, but you will need to rerun network generation. After the network is verified, it can be simulated.

View Generated Species

Index	Name	Structure	Depiction	Expression
1	Ran_C_...	Nuc		@Nuc:C(Y1~u,Y2~u,Y3~u,site!1).Ran(c...
2	RCC1	Nuc		@Nuc:RCC1(site)
3	s2	Nuc		@Nuc:Ran(cargo)
4	s3	Nuc		@Nuc:C(Y1~u,Y2~u,Y3~u,site)
5	s4	Cyt		@Cyt:C(Y1~u,Y2~u,Y3~u,site!1).Ran(c...
6	s5	Cyt		@Cyt:C(Y1~u,Y2~u,Y3~p,site!1).Ran(c...
7	s6	Cyt		@Cyt:C(Y1~u,Y2~p,Y3~u,site!1).Ran(c...
8	s7	Cyt		@Cyt:C(Y1~p,Y2~u,Y3~u,site!1).Ran(c...
9	s8	Cyt		@Cyt:Ran(cargo)
10	s9	Cyt		@Cyt:C(Y1~u,Y2~u,Y3~u,site)
11	s10	Nuc		@Nuc:RCC1(site!1).Ran(cargo!1)
12	s11	Cyt		@Cyt:C(Y1~u,Y2~p,Y3~p,site!1).Ran(c...
13	s12	Cyt		@Cyt:C(Y1~p,Y2~u,Y3~p,site!1).Ran(c...
14	s13	Cyt		@Cyt:C(Y1~u,Y2~u,Y3~p,site)
15	s14	Cyt		@Cyt:C(Y1~p,Y2~p,Y3~u,site!1).Ran(c...
16	s15	Cyt		@Cyt:C(Y1~u,Y2~p,Y3~u,site)
17	s16	Cyt		@Cyt:C(Y1~p,Y2~u,Y3~u,site)

Search

Nuc 1

Different bonds are shown in different colors.

Species and reactions can be filtered by entering a string, e.g. Molecule or Site name, in the Search box.

Close

View Generated Reactions

Index	Rule	Structure	Depiction	Expression
1	C_p1	Cyt		@Cyt:C(Y1~u,Y2~u,Y3~u,site!1).Ran(cargo!1) -> @Cyt:C(Y1~u,Y...
2	C_p1	Cyt		@Cyt:C(Y1~u,Y2~p,Y3~u,site!1).Ran(cargo!1) -> @Cyt:C(Y1~u,Y...
3	C_p1	Cyt		@Cyt:C(Y1~p,Y2~u,Y3~u,site!1).Ran(cargo!1) -> @Cyt:C(Y1~p,Y...
4	C_p1	Cyt		@Cyt:C(Y1~u,Y2~u,Y3~u,site) -> @Cyt:C(Y1~u,Y2~u,Y3~p,site)
5	C_p1	Cyt		@Cyt:C(Y1~p,Y2~p,Y3~u,site!1).Ran(cargo!1) -> @Cyt:C(Y1~p,Y...
6	C_p1	Cyt		@Cyt:C(Y1~u,Y2~p,Y3~u,site) -> @Cyt:C(Y1~u,Y2~p,Y3~p,site)
7	C_p1	Cyt		@Cyt:C(Y1~p,Y2~u,Y3~u,site) -> @Cyt:C(Y1~p,Y2~u,Y3~p,site)
8	C_p1	Cyt		@Cyt:C(Y1~p,Y2~p,Y3~u,site) -> @Cyt:C(Y1~p,Y2~p,Y3~p,site)
9	C_p1 (rev)	Cyt		@Cyt:C(Y1~u,Y2~u,Y3~p,site!1).Ran(cargo!1) -> @Cyt:C(Y1~u,Y...
10	C_p1 (rev)	Cyt		@Cyt:C(Y1~u,Y2~p,Y3~p,site!1).Ran(cargo!1) -> @Cyt:C(Y1~u,Y...
11	C_p1 (rev)	Cyt		@Cyt:C(Y1~p,Y2~u,Y3~p,site!1).Ran(cargo!1) -> @Cyt:C(Y1~p,Y...
12	C_p1 (rev)	Cyt		@Cyt:C(Y1~u,Y2~u,Y3~p,site) -> @Cyt:C(Y1~u,Y2~u,Y3~u,site)
13	C_p1 (rev)	Cyt		@Cyt:C(Y1~p,Y2~p,Y3~p,site!1).Ran(cargo!1) -> @Cyt:C(Y1~p,Y...
14	C_p1 (rev)	Cyt		@Cyt:C(Y1~u,Y2~p,Y3~p,site) -> @Cyt:C(Y1~u,Y2~p,Y3~u,site)
15	C_p1 (rev)	Cyt		@Cyt:C(Y1~p,Y2~u,Y3~p,site) -> @Cyt:C(Y1~p,Y2~u,Y3~u,site)
16	C_p1 (rev)	Cyt		@Cyt:C(Y1~p,Y2~p,Y3~p,site) -> @Cyt:C(Y1~p,Y2~p,Y3~u,site)
17	C_p2	Cyt		@Cyt:C(Y1~u,Y2~u,Y3~u,site!1).Ran(cargo!1) -> @Cyt:C(Y1~u,Y...
18	C_p2	Cyt		@Cyt:C(Y1~u,Y2~u,Y3~p,site!1).Ran(cargo!1) -> @Cyt:C(Y1~u,Y...
19	C_p2	Cyt		@Cyt:C(Y1~p,Y2~u,Y3~u,site!1).Ran(cargo!1) -> @Cyt:C(Y1~p,Y...
20	C_p2	Cyt		@Cyt:C(Y1~u,Y2~u,Y3~u,site) -> @Cyt:C(Y1~u,Y2~p,Y3~u,site)
21	C_p2	Cyt		@Cyt:C(Y1~p,Y2~u,Y3~p,site!1).Ran(cargo!1) -> @Cyt:C(Y1~p,Y...
22	C_p2	Cyt		@Cyt:C(Y1~u,Y2~u,Y3~p,site) -> @Cyt:C(Y1~u,Y2~p,Y3~p,site)
23	C_p2	Cyt		@Cyt:C(Y1~p,Y2~u,Y3~u,site) -> @Cyt:C(Y1~p,Y2~p,Y3~u,site)
24	C_p2	Cyt		@Cyt:C(Y1~p,Y2~u,Y3~p,site) -> @Cyt:C(Y1~p,Y2~p,Y3~p,site)

Search

Use this button if a reaction is too long and does not fit on the screen.

Close

1. Click on **Simulations**.

2. Click to add **New Simulation**.

3. Rename the simulation to **ODE** by double clicking its name to edit.

4. Set end time. In this case it is 10 seconds.

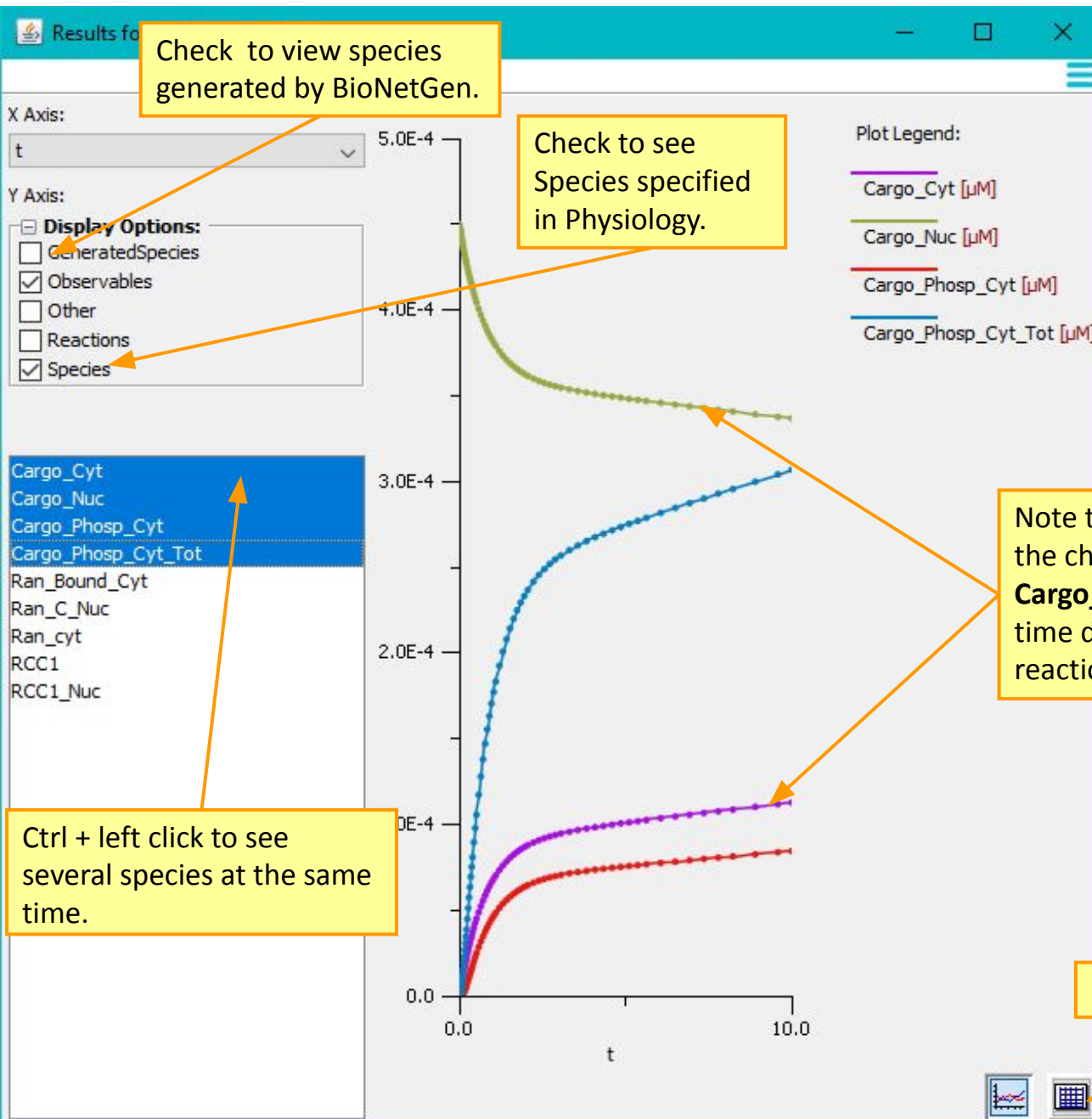
5. For advanced options; i.e. different solvers and outputs, click **Edit**.

6. Click blue button to run locally (on user's computer). You can also click the green arrow to run on a VCell server (will store simulation results).

Name	End Time	Output Option	Solver	Running Status	Results
ODE	10.0	keep every 1 sample	Combined IDA/CVODE	not saved	no

Max timestep	Output	Rel tol	Abs tol	Sensitivity Analysis
1.0s	keep every 1 sample, at most 1000	1.0E-9	1.0E-9	no

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



TIP1: Generated species are listed by index (s10, s11, ...). The molecular composition of species can be seen under **Specification > Network > View Species**.

TIP2: **Reactions** show fluxes through individual reactions generated by each rule.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (7)
- Structures (5)
- Species (2)
- Molecules (3)
- Observables (7)

Applications (1)

- Non-Spatial Deterministic**

Parameters, Functions and Units

Pathway

TIP: Clamped means that the value of species is kept constant during the simulation.

Name	Type	Value
Max Iterations	value	10
Max Molecules / Species	value	10

Network Constraints

Reactions: 100
Warning: none

View Edit / Test Constraints
View Create new VCell BioModel from Network

Search

Object Selection

Database File Info Network Generation Status

to view/edit properties.

1. To create a stochastic application from existing deterministic, Right click on the **Non-Spatial Deterministic** app, and select **Copy As > Stochastic**.

2. To rename the new application, right click on it and select **Rename**. Change the name to **Non-Spatial Stochastic**.

File Server Window Tools Help

1. Switch to **Species** tab

2. Select the **Non-Spatial Stochastic** application, and go to **Specifications**.

3. Set the initial condition to **Number Of Particles**.

4. Change the initial condition to one thousand molecules for both species.

The screenshot shows the VCell software interface. The left sidebar contains a tree view with categories: Physiology (Reaction Diagram, Reactions (7), Structures (5), Species (2), Molecules (3), Observables (7)), Applications (2) (Non-Spatial Deterministic, Non-Spatial Stochastic), Parameters, Functions and Units, and Pathway. The 'Non-Spatial Stochastic' application is selected. The main window has tabs for Geometry, Specifications, Protocols, and Simulations. The 'Specifications' tab is active, showing a table of species with their initial conditions. The 'Initial Condition' is set to 'Number of Particles' for both species. The 'Initial Condition' column shows '1000.0 [molecules]' for both species.

Species	Structure	Depiction	Clamped	Initial Condition	Force Continuous
Ran_C_Nuc	Nuc		<input type="checkbox"/>	1000.0 [molecules]	<input type="checkbox"/>
RCC1	Nuc		<input type="checkbox"/>	1000.0 [molecules]	<input type="checkbox"/>

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

Select only one object (e.g. species, reaction, simulation) to view/edit properties.

The screenshot displays the VCell software interface with the following components:

- Left Panel:** A tree view showing the project structure. The 'Simulations' folder is selected under 'Applications (2)'. Other folders include 'Physiology', 'Parameters, Functions and Units', and 'Pathway'.
- Top Panel:** Tabs for 'Geometry', 'Specifications', 'Protocols', and 'Simulations'. The 'Simulations' tab is active, showing a table of simulations.
- Simulation Table:** A table with columns: Name, End Time, Output Option, Solver, Running Status, and Results. The first row is 'SSA' with an end time of '10.0' and an output option of 'every 0.1 s'.
- Bottom Panel:** Tabs for 'Object Properties', 'Problems (0 Errors, 0 Warnings)', 'Database File Info', and 'Network Generation Status'. The 'Object Properties' tab is active, showing settings for the selected simulation.

Three numbered instructions are overlaid on the image:

1. Create a new simulation entitled **SSA**.
2. Set end time to 10 seconds, and an output option of **every 0.1 seconds**.
3. Run the simulation.

The 'Object Properties' tab shows the following settings:

- Annotation: (empty)
- Settings: Timestep (empty), Output (every 0.1 sec)
- Parameters with values changed from defaults: (empty table)

Results for

Species defined initially.

X Axis: t

Y Axis: t

Display Options:

- ☐ GeneratedSpecies
- ☒ Observables
- ☐ Other
- ☐ Reactions
- ☒ Species

Plot Legend:

- Cargo_Cyt [μM]
- Cargo_Nuc [μM]
- Ran_Bound_Cyt [μM]
- Ran_C_Nuc [μM]

Cargo_Cyt

Cargo_Cyt_Count

Cargo_Nuc

Cargo_Nuc_Count

Cargo_Phosp_Cyt

Cargo_Phosp_Cyt_Count

Cargo_Phosp_Cyt_Tot

Cargo_Phosp_Cyt_Tot_Count

Ran_Bound_Cyt

Ran_Bound_Cyt_Count

Ran_C_Nuc

Ran_C_Nuc_Count

Ran_cyt

Ran_cyt_Count

RCC1

RCC1_Count

RCC1_Nuc

RCC1_Nuc_Count

Ctrl + left click to see several species at once.

Click to see numerical values

File Server Window Tools Help

Rule-Based_Ran_Transport

- Physiology
 - Reaction Diagram
 - Species (2)
 - Molecules (3)
 - Observables (7)
 - Applications (3)**
 - NFSim
 - Non-Spatial Deterministic
 - Non-Spatial Stochastic
 - Parameters, Functions and Units
 - Pathway

1. Click on Applications.

Name	Math Type	Annotation
Non-Spatial Deterministic	explicit network model, compartmental, determi...	
Non-Spatial Stochastic	explicit network model, compartmental, stochas...	(copied from Non-Spatial Deterministic)
NFSim	Agent-based model, compartmental, stochastic ...	(copied from Non-Spatial Stochastic) (copied fro...

2. Select Non-Spatial Stochastic.

3. Click on More Copy Actions > Copy As > Network-Free.

4. Rename the application to NFSim.

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
 - My BioModels (2018nathans751) (19)
 - Shared BioModels (1)
 - Public BioModels (602)
 - Tutorials (8)
 - Education (34)

New Application ▼ Delete More Copy Actions ▼ Compare... Search

Object Properties Problems (0 Error)

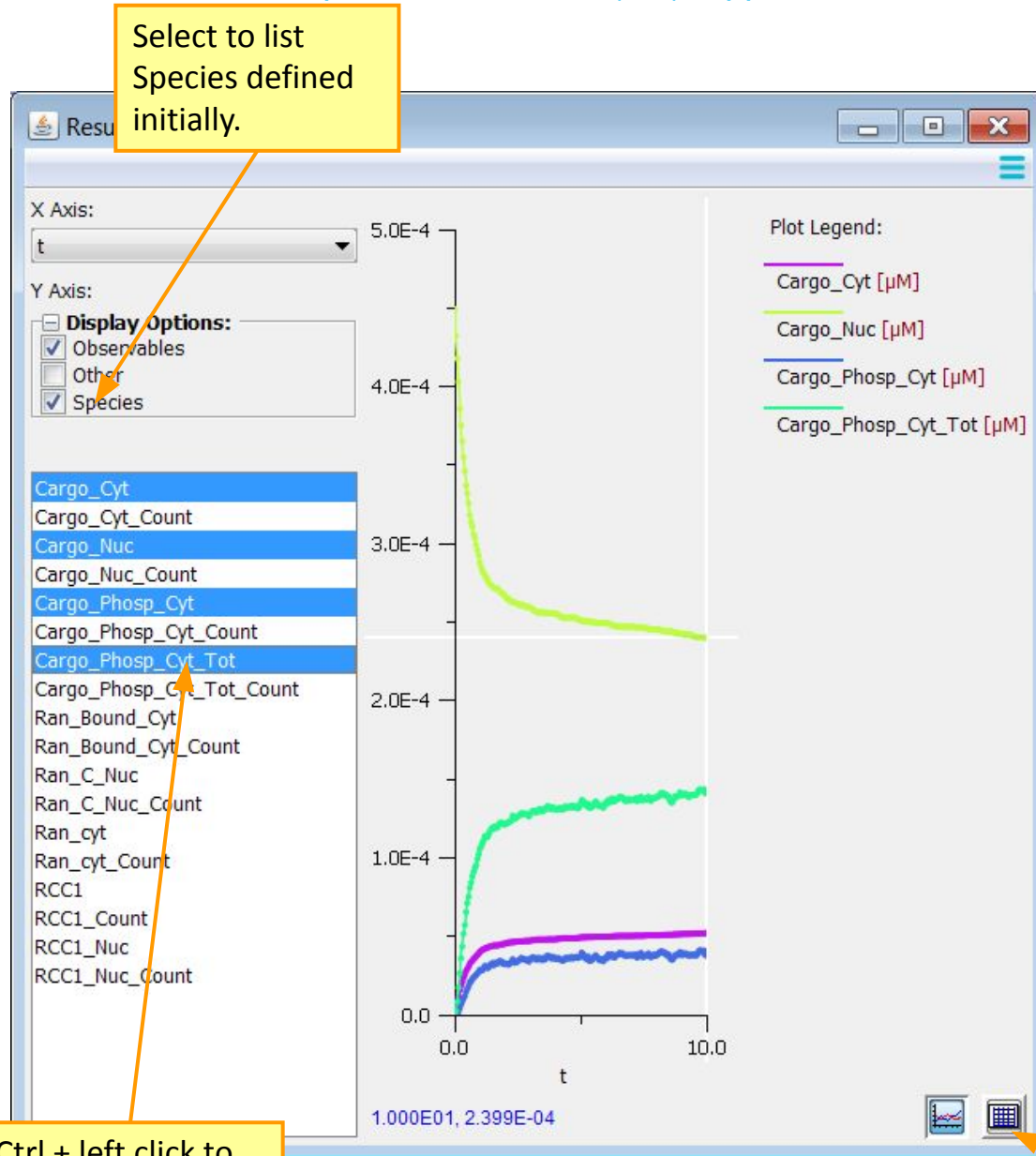
Application Name Non-Spatial Stochastic

Annotation (copied from Non-Spatial D

Copy As ▸

- Deterministic
- Stochastic
- Network-Free

5. Using NFSim, create and run a new simulation with an end time of 10.0, and and 0.05 output option.



File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

Reaction Diagram

1. Click on **Applications**.

Species (2)

Molecules (3)

Observable (7)

Applications (4)

- PDE_3D
- NFSim
- Non-Spatial Deterministic
- Non-Spatial Stochastic

Parameters, Functions and Units

Pathway

Name	Math Type	Annotation
Non-Spatial Deterministic	explicit network model, compartmental, determi...	
Non-Spatial Stochastic	explicit network model, compartmental, stochast...	(copied from Non-Spatial Deterministic)
NFSim	Agent-based model, compartmental, stochastic ...	(copied from Non-Spatial Stochastic) (copied fro...
PDE_3D	explicit network model, compartmental, determi...	

2. Rename the application to **PDE_3D**.

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
- My BioModels (2018nathans751) (19)
- Shared BioModels (1)
- Public BioModels (602)
- Tutorials (8)
- Education (34)

3. Select **New Application > Deterministic**.

New Application ▼ Delete More Copy Actions ▼ Compare... Search

Deterministic

Stochastic

Network-Free

Annotation

Summary

- Deterministic
- ✖ Compartmental

1. Go to <http://vcell.org/support-2>, and click **(3D Images for Tutorial)** to download the necessary geometry for this application.

Tutorial Guides (pdf) for VCell

Multiple Application of a Nuclear Transport Part 1 (3D images for Tutorial) (ver 6.1)

Multiple Application of a Nuclear Transport Part 2 (see image link above for the 3D images) (ver 6.1)

Rule-Based Modeling (single compartment) EGFR model (ver 6.0)

simple FRAP (ver 6.0)

FRAP with binding (ver 6.0)

PH-GFP Translocation (ver 6.0)

Using Pathway Commons (ver 6.0)

2. Save the file wherever is easiest for you to remember and access.

3. Use this tutorial to create a spatial geometry. Don't worry if your numbers for volumes and membrane sizes will be a bit off. Alternatively, use the existing Geometry (see the next slide).

1. Select the **Structure Mapping** tab.

TIP: If not interested in creating image-based geometry, save time by uploading the geometry to PDE_3D by clicking **Geometry Definition** -> **New Geometry** → **Open From** and navigating to **MultiApp_Tutorial** model.

2. Use the **Line Tool** to drag a line from the Physiology you created, to the color that represents that structure in the picture. After the lines are drawn, they should correspond to the above image.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (7)
- Structures (5)
- Species (2)

Structure Mapping Geometry Definition

All structures and subdomains must be mapped to run a simulation.

EC

Nuc

Cyt

pm

nm

Geometry (subdomains)

- background
- Nuc
- Cyt
- Cyt_background_membrane
- Cyt_Nuc_membrane

Membrane boundary conditions are chosen alphabetically among the adjacent subdomains.

Structure	Subdomain	Size Ratio	X-	X+	Y-	Y+	Z-	Z+
EC	background	1 [1]	Flux	Flux	Flux	Flux	Flux	Flux
Nuc	Nuc	1 [1]	Flux	Flux	Flux	Flux	Flux	Flux
Cyt	Cyt	1 [1]	Flux	Flux	Flux	Flux	Flux	Flux
pm	Cyt	1 [1]	Flux	Flux	Flux	Flux	Flux	Flux
nm	Cyt	1 [1]	Flux	Flux	Flux	Flux	Flux	Flux

Object Properties Problems (0 Errors, 0 Warnings)

Select only one object (e.g. species, reaction, structure, etc.)

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (7)
- Structures (5)
- Species (2)
- Molecules (3)
- Observables (7)

Applications (4)



- NFSim
- Non-Spatial Deterministic
- Non-Spatial Stochastic
- PDE_3D
 - Geometry
 - Specifications**
 - Protocols
 - Simulations

Parameters, Functions and Units

Pathway

Geometry Specifications Protocols Simulations

Species Reaction Network

Species	Structure	Depiction	Clamped	Initial Condition	Well Mixed	Diffusion Constant
Ran_C_Nuc	Nuc		<input type="checkbox"/>	4.5E-4 [μM]	<input type="checkbox"/>	10.0 [μm ² .s ⁻¹]
RCC1	Nuc		<input type="checkbox"/>	4.5E-4 [μM]	<input type="checkbox"/>	10.0 [μm ² .s ⁻¹]

1. Go to the **Specifications** tab, click on **Species**, and change the initial condition for both species to 4.5E-4.

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
- My BioModels (2018nathans751) (19)
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- Tutorials (8)
- Education (34)

Search

Object Properties Problems (3 Errors, 0 Warnings) Database File Info Network Generation Status

Description	Parameter	Expression	Units
initial concentration for RCC1	initConc	4.5E-4	μM
diffusion constant for RCC1	diff	10.0	μm ² .s ⁻¹
Boundary Condition X- for RCC1	BC_Xm	<zero flux>	μM.μm.s ⁻¹
Boundary Condition X+ for RCC1	BC_Xp	<zero flux>	μM.μm.s ⁻¹
Boundary Condition Y- for RCC1	BC_Ym	<zero flux>	μM.μm.s ⁻¹
Boundary Condition Y+ for RCC1	BC_Yp	<zero flux>	μM.μm.s ⁻¹
Boundary Condition Z- for RCC1	BC_Zm	<zero flux>	μM.μm.s ⁻¹

The screenshot shows the VCell software interface with several components:

- Left Panel:** A tree view showing the project structure. The 'Simulations' tab is selected, and a new simulation named 'Simulation_PDE' has been created.
- Top Panel:** A table listing the simulation. The 'Name' column shows 'Simulation_PDE', 'End Time' is '1.0', and 'Output Op' is 'every 0.05 s'.
- Right Panel:** A table showing the 'Running Status' and 'Results'.
- Bottom Panel:** A dialog box titled 'Edit: Simulation_PDE' with tabs for 'Parameters', 'Mesh', and 'Solver'. The 'Solver' tab is active, showing options for the solver algorithm and time conditions.

Four numbered instructions are overlaid on the image:

1. Make sure your reaction network is big enough. Then, go to the **Simulations** tab
2. Create a new simulation entitled **Simulation_PDE**.
3. Click on the **Edit Simulation** button. Select the **Solver** tab.
4. Change the parameters so that the simulation has an ending at 10.0 seconds a maximum of 0.1, and an output interval of 0.1. Click **OK** to save the changes.

The 'Edit: Simulation_PDE' dialog box shows the following settings:

- Integr...**: Fully-Implicit Finite Volume, Regular Grid (Variable Time Step)
- General**:
 - Time Bounds**: Starting 0.0, Ending 10.0
 - Time Step**: Minimum, Default, Maximum 0.1
 - Error Tolerance**: Absolute 1.0E-9, Relative 1.0E-7
- Output Options**:
 - ☒ **Output Interval**: 0.1 s
- Miscellaneous**: (Empty)

Buttons at the bottom of the dialog are 'OK' and 'Cancel'.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (7)
- Structures (5)

Geometry Specifications Protocols Simulations

Simulations Output Functions Generated Math

Name	End Time	Output Option	Solver	Running Status	Results
Simulation_PDE	1.0	every 0.05 s	Fully-Implicit	not saved	no

1. Re-open the **Simulation Editor**, and go to the **Mesh** tab.

2. Make sure that the **Lock Aspect Ratio** box is checked, and change the **X** value to **101**. The **Y** and **Z** values should also automatically change to preserve the aspect ratio.

3. Hit **OK** to save these changes.

Object Properties

Annotation:

Settings: Max time 0.1

Mesh: 71x71x25

Parameters with

Param

OK Cancel

Scan

1. An warning message will appear. Just click OK.

2. Run the simulation. Be patient, it may take a while.

Warnings from Simulation: 'Simulation_PDE'!
The simulation has large result dataset (10870MB), suggested size limits are:
5 MB for compartmental ODE simulations
200 MB for spatial simulations
100 MB for compartmental stochastic simulations
Try saving fewer timepoints or using a coarser mesh if spatial.
Do you want to continue anyway?

Simulation Parameters Table:

Name	End Time	Output Option	Solver	Running Status	Results
Simulation_PDE	10.0	every 0.1 s	Fully-Implicit	not saved	no

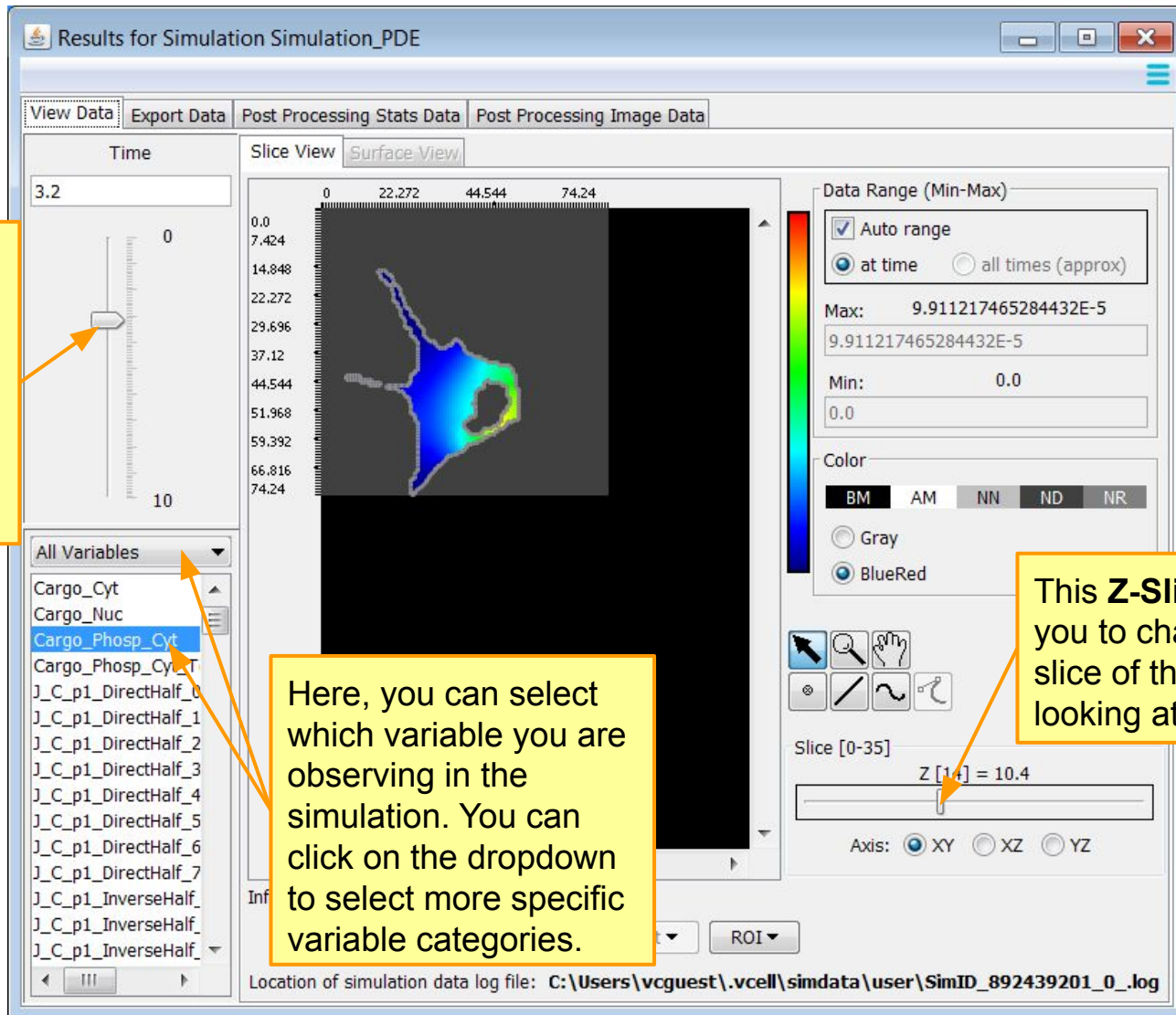
Settings:

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

Mesh: 71x71x25 = 126025 elements
Geometry size: (74.24,74.24,26.0) microns

Parameters with values changed from defaults

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



File Server Window Tools Help

Physiology

- Reaction Diagram
- Reactions (7)
- Structures (5)
- Species (2)
- Molecules (3)
- Observables (7)

Applications (4)

- NFSim
- Geometry
- Specifications
- Protocols
- Simulations

Non-Spatial Deterministic

Non-Spatial Stochastic

PDE_3D

Parameters, Functions

Pathway

VCell DB BMDB Pathway

BioModels MathModels Geometries

Search

- Biological Models
- My BioModels (20)
- Shared BioModels
- Public BioModels
- Tutorials (8)
- Education (34)

Species Reaction Network

Species	Structure	Depiction	Clamped	Initial Condition	Well Mixed	Diffusion Constant
Ran_C_Nuc	Nuc		<input type="checkbox"/>	4.5E-4 [μM]	<input type="checkbox"/>	10.0 [μm².s⁻¹]
RCC1	Nuc		<input type="checkbox"/>	4.5E-4 [μM]	<input type="checkbox"/>	10.0 [μm².s⁻¹]

Object Properties Problems (0 Errors, 0 Warnings) Database File Info Network Generation Status

Select only one object (e.g. species, reaction, simulation) to view/edit properties.

1. Right click on **PDE_3D**.
Select **Copy As > Spatial > Stochastic**.

File Server Window Tools Help

Rule-Based_Ran_Transport

Physiology

- Reaction Diagram
- Reactions (7)
- Structures (5)
- Species (2)
- Molecules (3)
- Observables (7)

Applications (5)

- Copy of PDE_3D
- NFSim
- Non-Spatial Det
- Non-Spatial Sto
- PDE_3D

Parameters, Functions

Pathway

Geometry Specifications Protocols Simulations

Species Reaction Network

Initial Condition: ☒ Concentration ☐ Number of Parties

Species	Structure	Depiction	Clamped	Initial Condition	Well Mixed	Diffusion Constant	Force Continuous
Ran_C_Nuc	Nuc		<input type="checkbox"/>	4.5E-4 [μM]	<input type="checkbox"/>	10.0 [μm².s⁻¹]	<input type="checkbox"/>
RCC1	Nuc		<input type="checkbox"/>	4.5E-4 [μM]	<input type="checkbox"/>	10.0 [μm².s⁻¹]	<input type="checkbox"/>

1. Right click on the copy, and select **Rename**. Change the name to **Stoch Spatial**.

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

Biological Models

- My BioModels (2018nathans751) (19)
- Shared BioModels (1)
- Public BioModels (602)
- Tutorials (8)
- Education (34)

Object Properties Problems (0 Errors, 0 Warnings) Database File Info Network Generation Status

Select only one object (e.g. species, reaction, simulation) to view/edit properties.

1. Go to the **Simulations** tab and create a new simulation.

2. Rename the new simulation **100 Particles**.

Because this Application is a copy, the specifications and geometry are already input.

3. Open the **Simulation Editor**, and select the **Mesh** tab. Make sure that the **Lock Aspect Ratio** box is checked, and change the **X** value to **101**.

4. Hit **OK** to save these changes.

The screenshot displays the VCell software interface. The main window has tabs for Geometry, Specifications, Protocols, and Simulations. The Simulations tab is active, showing a table with one simulation named '100 Particles'. An arrow points from the first instruction to the 'Simulations' tab. Another arrow points from the second instruction to the '100 Particles' simulation entry. A third arrow points from the third instruction to the 'Mesh' tab in the 'Edit: 100 Particles' dialog box. A fourth arrow points from the fourth instruction to the 'OK' button in the same dialog box.

The 'Edit: 100 Particles' dialog box has three tabs: Parameters, Mesh, and Solver. The Mesh tab is selected, showing the following settings:

- Geometry Size (um): (74.24, 74.24, 26.0)
- Mesh Size (elements): ☒ Lock aspect ratio
- X: 101
- Y: 101
- Z: 36
- Total Size (elements): 101 x 101 x 36 = 367236
- Spatial Step (um) Δx : 0.7424
- Δy : 0.7424
- Δz : 0.7428571428571429

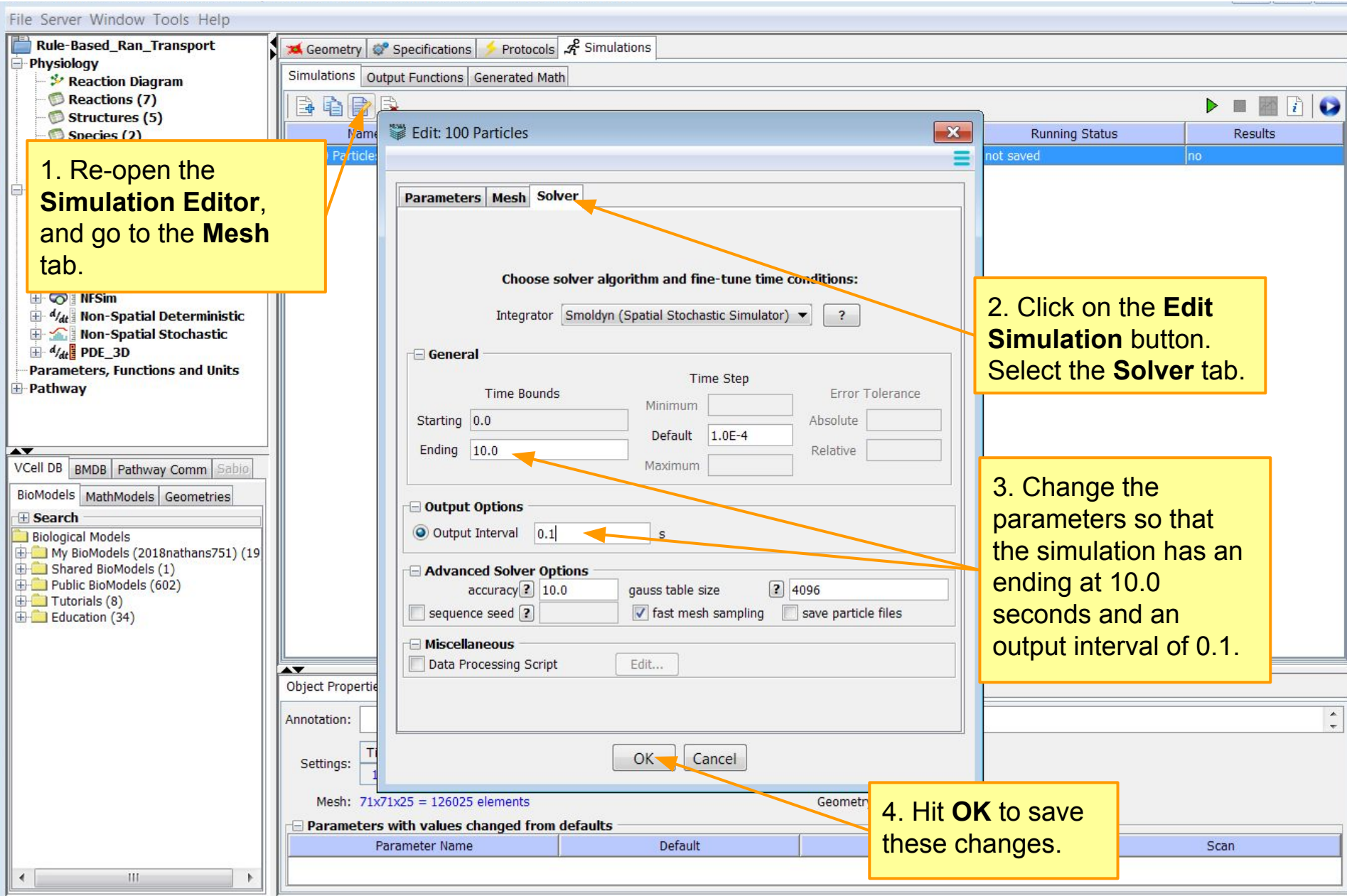
The 'OK' button is located at the bottom of the dialog box.

1. Re-open the **Simulation Editor**, and go to the **Mesh** tab.

2. Click on the **Edit Simulation** button. Select the **Solver** tab.

3. Change the parameters so that the simulation has an ending at 10.0 seconds and an output interval of 0.1.

4. Hit **OK** to save these changes.



File Server Window Tools Help

Rule-Based_Ran_Transport

- Physiology
 - Reaction Diagram
 - Reactions (7)
 - Structures (5)
 - Species (2)
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- Applications (5)
 - Stoch Spatial
 - Geometry
 - Specifications
 - Protocols
 - Simulations**
 - NFSim
 - Non-Spatial Deterministic
 - Non-Spatial Stochastic
 - PDE_3D
- Parameters, Functions and Units
- Pathway

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

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Simulations Output Functions Generated Math

Name	End Time	Output Option	Solver	Running Status	Results
100 Particles	10.0	every 0.1 s	Smoldyn	not saved	no

1. Run the simulation

Object Properties Problems (0 Errors, 0 Warnings) Database File Info Network Generation Status

```
Iteration 0: 2 species
Iteration 1: 5 species
Iteration 2: 11 species
Iteration 3: 21 species
Iteration 4: 31 species
Iteration 5: 36 species
Iteration 6: 37 species
Iteration 7: 37 species
Canceled by user.
```


Acknowledgements

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