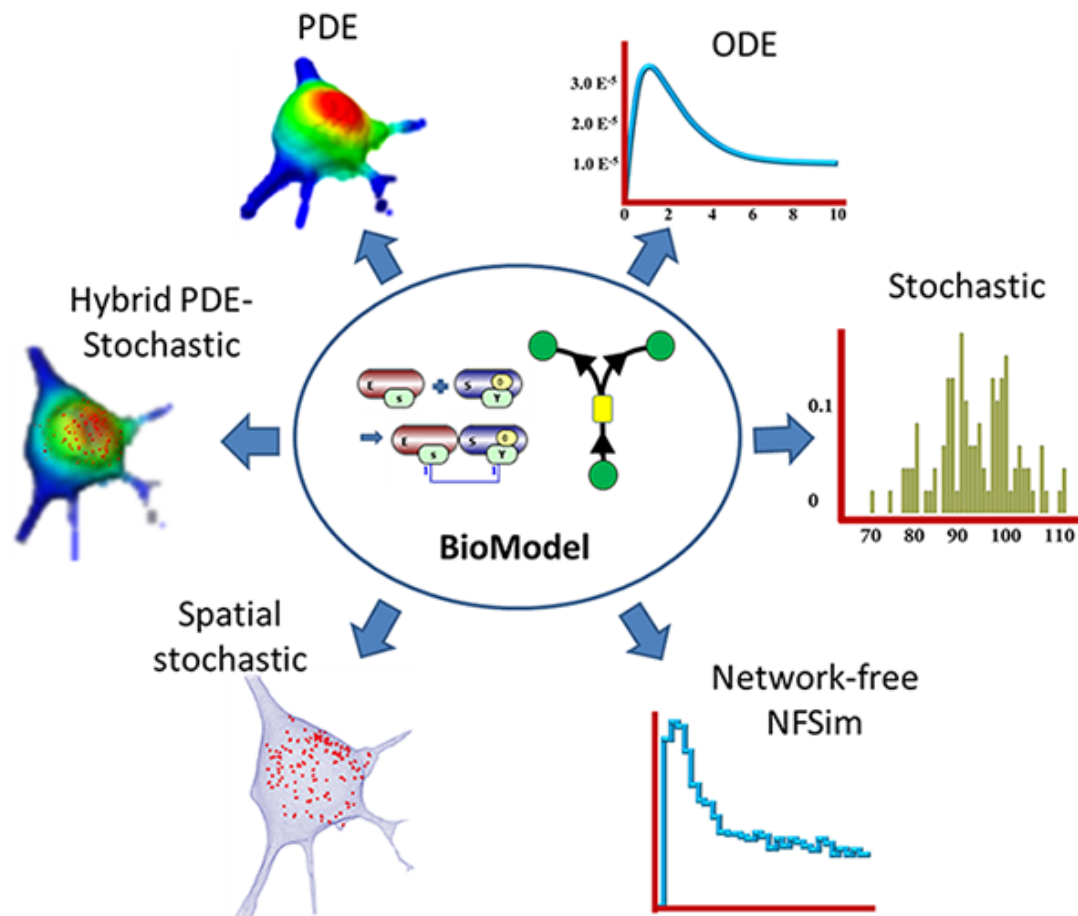


# VCell

To run VCell go to:  
[vcell.org](http://vcell.org)



VCell is developed  
at CCAM

Center for Cell Analysis & Modeling



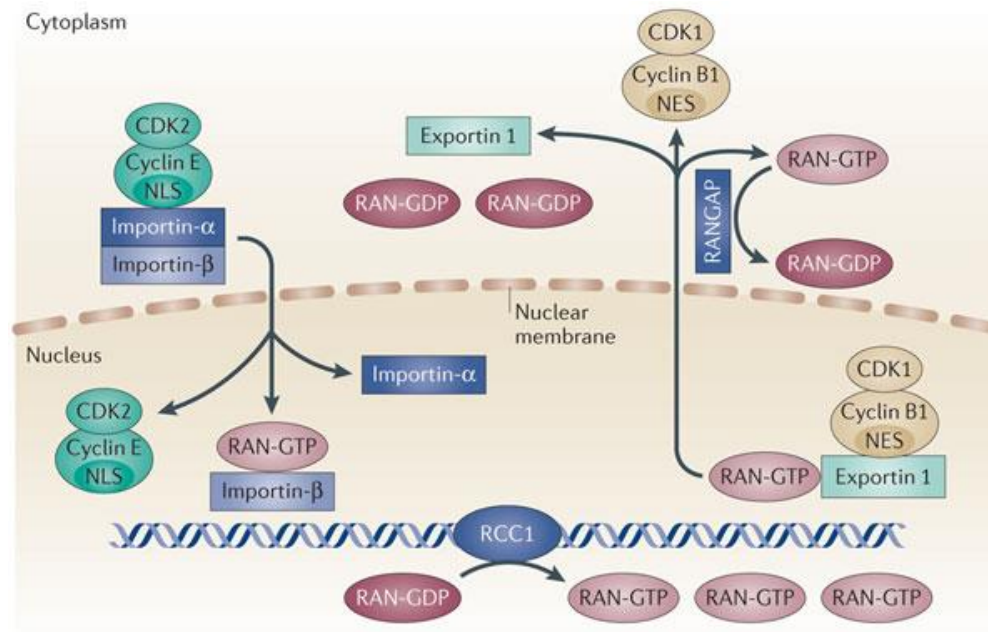
National Institute of  
General Medical Sciences

VCell is funded by the NIGMS

# 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**.

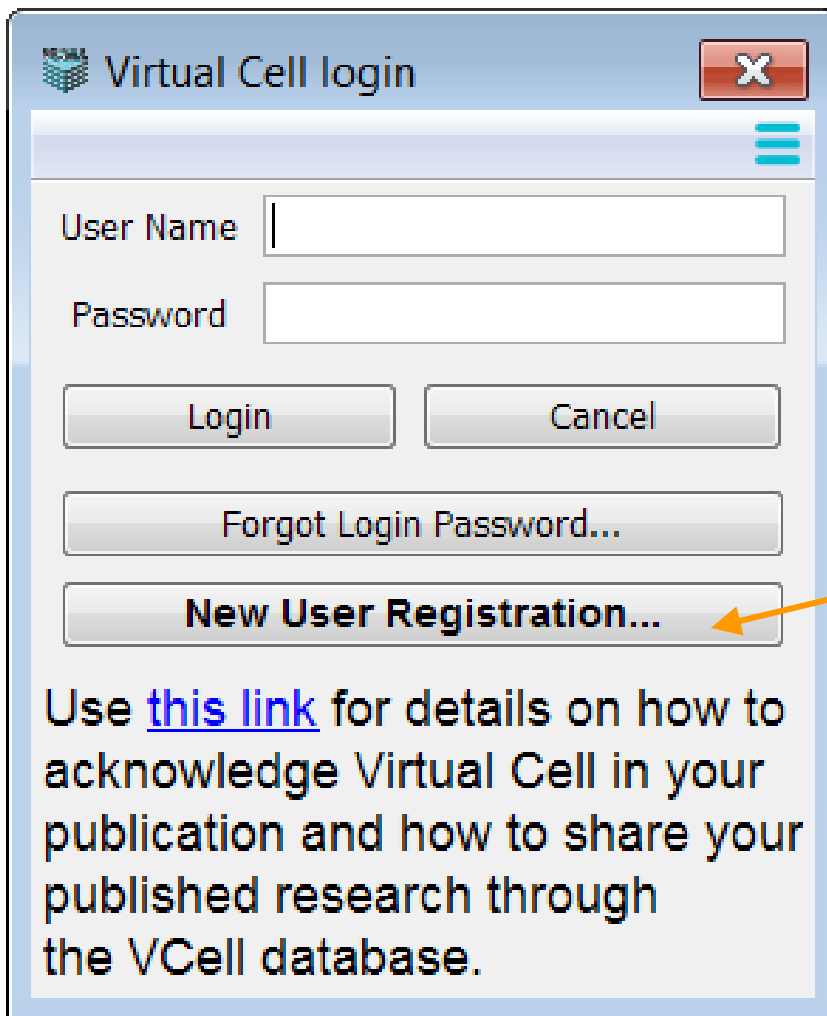
General familiarity with VCell software is recommended. Although this tutorial can be followed by a VCell novice, it is recommended that novice users first look through the VCell tutorials available at [http://vcell.org/vcell\\_software/user\\_guide.html](http://vcell.org/vcell_software/user_guide.html) .

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

# Contents

- [Opening VCell](#)
- [Saving a VCell model](#)
- [Physiology](#)
  - [Structures](#)
  - [Molecules](#)
  - [Observables](#)
  - [Species](#)
  - [Reactions](#)
- [Applications](#)
  - [Non-Spatial Deterministic](#)
  - [Non-Spatial Stochastic](#)
  - [NFSim](#)
  - [PDE 3D](#)
    - [Creating a Geometry](#)
  - [Stoch Spatial](#)





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 text block that reads: '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...**

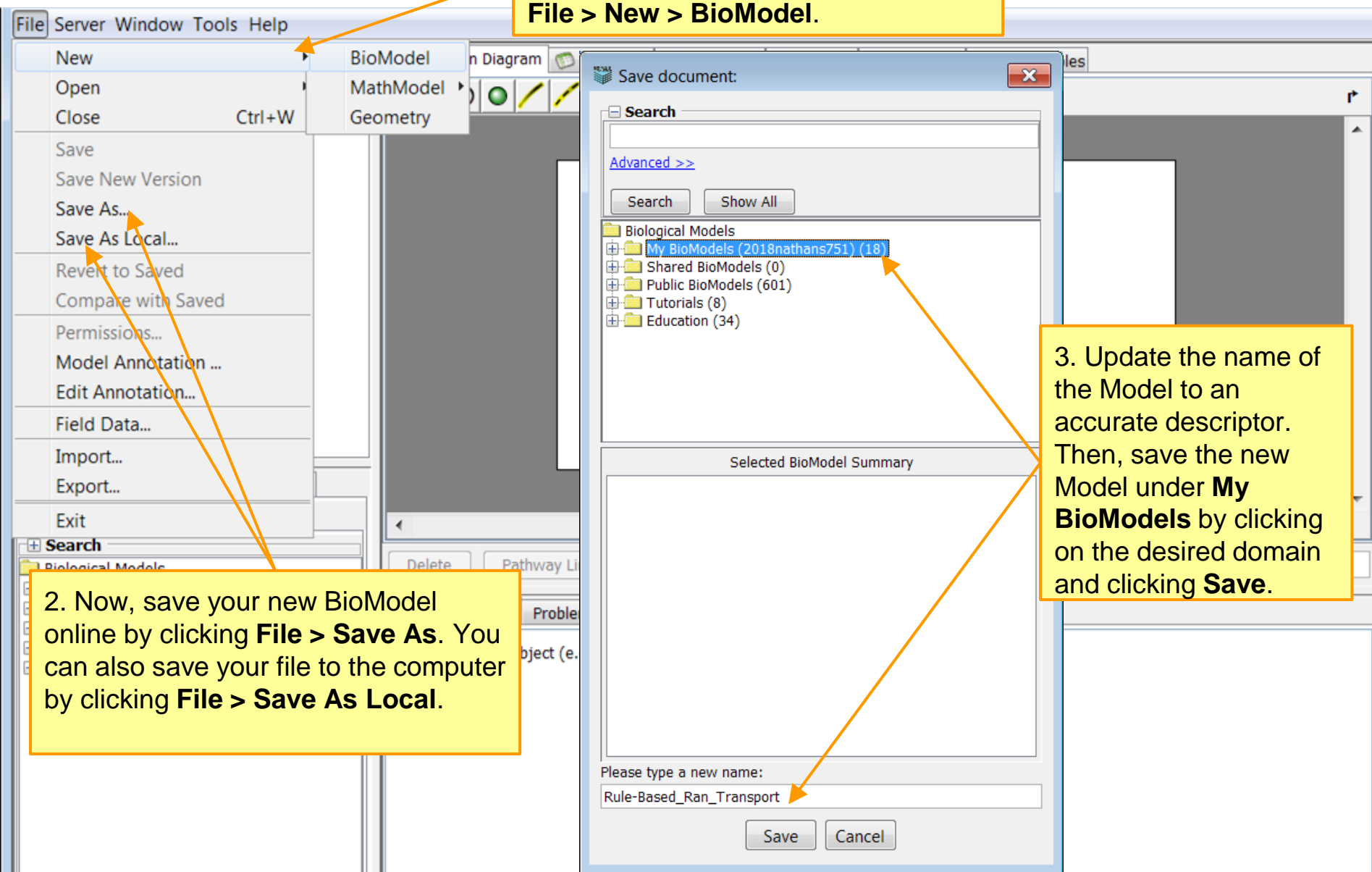
Use [this link](#) for details on how to acknowledge Virtual Cell in your publication and how to share your published research through the VCell database.

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**.

**Select only one structure to edit properties**

Structure Name

Size Variable Name

Annotation

**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**

Add Compartment  
Add Membrane

Object Properties Problems (0 Errors, 0 Warnings)

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

**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 left sidebar contains a tree view with 'Rule-Based\_Ran\_Transport' expanded, showing 'Physiology' with sub-items: 'Reaction Diagram' (selected), 'Reactions (0)', 'Structures (5)', 'Species (0)', 'Molecules (0)', 'Observables (0)', 'Applications (0)', 'Parameters, Functions and Units', and 'Pathway'. Below this is a 'BioModels' section with tabs for 'BioModels', 'MathModels', and 'Geometries', and a 'Search' field. The main window is titled 'Reaction Diagram' and has tabs for 'Reactions', 'Structures', 'Species', 'Molecules', and 'Observables'. The 'Structures' tab is active, showing a diagram of compartments: 'EC' (white), 'pm' (grey), 'Cyt' (white), 'nm' (grey), and 'Nuc' (white). A yellow text box is overlaid on the diagram with the text: '1. Continue to make compartments and membranes until you have, starting with a compartment, and alternating: **EC, pm, Cyt, nm, Nuc.** (Also illustrated in the image.)'. The bottom of the interface has a 'Delete' button, a 'Pathway Links' dropdown, a 'Search' field, and an 'Object Properties' section with a tab for 'Problems (0 Errors, 0 Warnings)' and a message: '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 (0)
- Structures (5)
- Species (0)
- Molecules (0)
- Observables (0)
- Applications (0)
- Parameters, Functions and Units
- Pathway

VCeDB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
- My BioModels (2018nathans751) (18)
- Shared BioModels (0)
- Public BioModels (601)
- Tutorials (8)
- Education (34)

Reaction Diagram Reactions Structures Species Molecules Observables

EC pm Cyt nm Nuc

1. Continue to make compartments and membranes until you have, starting with a compartment, and alternating: **EC, pm, Cyt, nm, Nuc.** (Also illustrated in the image.)

Delete Pathway Links Search

Object Properties Problems (0 Errors, 0 Warnings)

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.

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)

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 [ $\mu\text{m}^2$ ]

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.

File Server Window Tools Help

Rule-Based\_Ran\_Transport

Physiology

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

Applications (0)

Parameters, Functions and Units

Pathway

Reaction Diagram Reactions Structures Species **Molecules** Observables

Name	Depiction	BioNetGen Definition
MT0		MT0()

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**.

VCeL DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
- My BioModels (2018nathans751) (18)
- Shared BioModels (0)
- Public BioModels (601)
- Tutorials (8)
- Education (34)

New Molecule Delete Pathway Links Search

Object Properties Problems (0 Errors, 0 Warnings)

**Anchor Molecule**

☒ No restrictions

☐ Only these:

- ☐ EC
- ☐ pm
- ☐ Cyt
- ☐ nm

MT0

Rename

Add Site

Annotation

**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 project tree for 'Rule-Based\_Ran\_Transport' under 'Physiology', with 'Molecules (1)' selected. The main window has tabs for 'Reaction Diagram', 'Reactions', 'Structures', 'Species', 'Molecules', and 'Observables'. The 'Molecules' tab is active, showing a table with one molecule, 'Ran', depicted as a yellow circle with a black dot, and its BioNetGen definition 'Ran(Cargo)'. Below the table are buttons for 'New Molecule', 'Delete', and 'Pathway Links'. The 'Object Properties' panel at the bottom left shows 'Anchor Molecule' settings. 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 label.

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 shows the VCell software interface. The 'Molecules' tab is selected, displaying a table with the following data:

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

Below the table, the 'Anchor Molecule' section shows 'RCC1' with a 'Site' label. Two callouts provide instructions:

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




VCeL 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




VCeL 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~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

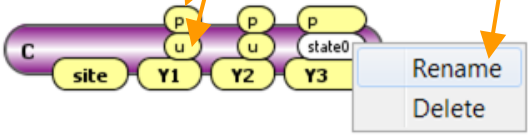
Object Properties Problems (0 Errors, 0 Warnings) Database File Info

**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

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)

Name	Structure	Depiction	BioNetGen Definition	Count
O0_Ran_tot	Cyt		Ran()	Molecules
O0_RCC1_tot	Cyt		RCC1()	Molecules
O0_tot	Cyt		c()	Molecules

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

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

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.

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

Reaction Diagram Reactions Structures Species Molecules **Observables**

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.

VCeDB BMDb Pathway Comm Sabio

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

Add Pattern

Multimolecular

Polymer of

☐ length = 2

☐ length > 1

Ran

Cyt

cargo

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

Annotation

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

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

2. 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.

3. Change names as indicated. Change the structure for both **Cargo\_Nuc**, and **RCC1\_Nuc** observables to **Nuc**.

1. To change the assigned structure of an observable, start by selecting said observable. In the bottom of the screen, the observable will be visually displayed.

new Observable ▾ Duplicate ▾ Delete Pathway Links ▾ Search

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

Add Pattern

☒ Multimeric

Polymer of

☐ length = 2

☐ length > 1

**Cyt**

- 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.

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

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

To create a new observable, click on **New Observable**, then specify the structure where it should be.

VCe ll DB BMD B 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 Search

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

Errors, 0 Warnings) Database File Info

cies, reaction, simulation) to view/edit properties

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

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)

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
<b>Cargo_Phosp_Cyt</b>	<b>Cyt</b>		<b>C(Y1~p!?,Y2~p!?)</b>	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.

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

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

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

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

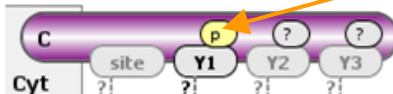
Object Properties

Problems (0 Errors, 0 Warnings)

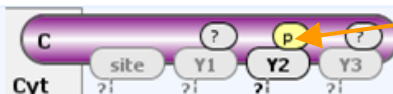
Add Pattern

☒ Multimolecular

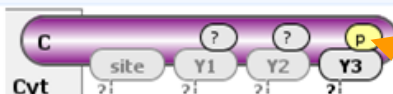
Polymer of

☐ 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.

The screenshot shows the VCell software interface. On the left is a tree view of the model hierarchy. The top menu bar includes 'File', 'Server', 'Window', 'Tools', and 'Help'. Below the menu bar is a toolbar with icons for 'Reaction Diagram', 'Reactions', 'Structures', 'Species', 'Molecules', and 'Observables'. The 'Species' tab is selected, displaying a table with columns: 'Name', 'Structure', 'Depiction', 'Link', and 'BioNetGen Definition'. Below the table is a toolbar with buttons: 'New Species', 'Duplicate', 'Delete', and 'Pathway Links'. A dropdown menu is open for the 'New Species' button, showing options: 'In Compartment EC', 'In Compartment Nuc', 'In Compartment Cyt', 'In Membrane pm', and 'In Membrane nm'. Two yellow callout boxes provide instructions: the first points to the 'New Species' button, and the second points to the 'In Compartment Nuc' option.

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

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)

Reaction Diagram Reactions Structures Species Molecules Observables

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

New Species Duplicate Delete Pathway Links Search

- 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.

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**.

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

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

BioModels MathModels Geometries

Search

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

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 Nuc cargo

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)
- Structures (5)
- Species (1)
- Molecules (3)
- Observables (7)

Applications (0)

Parameters, Functions and Units

Pathway

VCeL 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)

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

Linked Pathways

Annotation

1. Set all three Y sites to U, and make sure that all Y sites are unbound as well.

2. To specify the bond between Ran and C, right click on the Ran site Cargo, select Site bond specified, and select the option that binds the Cargo site on Ran to the Site site on C.

Ran cargo Nuc

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)



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

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

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

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.

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 project tree for 'Rule-Based\_Ran\_Transport' under the 'Physiology' category, with sub-items: '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' (with a red 'x' icon), 'C\_p1', 'Cyt', a depiction of a reaction, 'MassAction', and a link icon. Below the table, there are buttons for 'New Reaction', 'New Rule', 'Duplicate', 'Delete', and 'Pathway Links'. The 'New Rule' button is highlighted, and a dropdown menu is open, showing 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 is an 'Object Properties' panel with tabs for 'Kinetics' and 'Edit'. The 'Kinetics' tab is active, showing a 'Reversible' checkbox (unchecked) and a green plus icon. Below are 'Add Reactant' and 'Add Product' buttons. At the very bottom, there are checkboxes for 'Single Row Viewer' (unchecked), 'Show Molecule Color' (checked), 'Show Non-trivial' (checked), and 'Show Differ...' (unchecked).

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, Edit

Reversible: ☐

Add Reactant, Add Product

Single Row Viewer: ☐  
Show Molecule Color: ☒  
Show Non-trivial: ☒  
Show Differ...: ☐

**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

- Reaction Diagram
- Reactions (1)
- Structures (5)
- Species (2)
- Molecules (3)
- Observables (7)

Applications (0)

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)

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

☐ 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

- Reaction Diagram
- Reactions (1)
- Structures (5)
- Species (2)
- Molecules (3)
- Observables (7)
- Applications (0)
- Parameters, Functions and Units
- Pathway

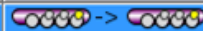
VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

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

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

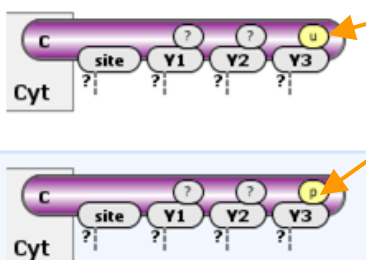
☐ Single Row Viewer

☒ 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

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

BioModels MathModels Geometries

Search

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

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!?)

2. Rename the rule **C\_p2**.

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

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

4. Switch the **Y3** site in the reactants to a **u** state, and in the products to a **p** state.

New Reaction

New Rule

Duplicate

Delete

Pa

Object Properties

Problems (0 Errors, 0 Warnings)

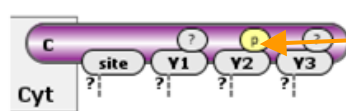
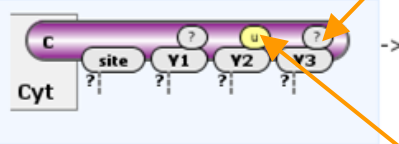
Kinetics

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	$\text{s}^{-1}$
Kr	microscopic reverse rate	<input type="checkbox"/>	1.0	$\text{s}^{-1}$



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

BioModels MathModels Geometries

Search

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

Reaction Diagram Reactions Structures Species Molecules Observables

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

1. Select the reaction rule C\_p2.

2. Edit the **Kinetics** so that the reaction rule is reversible, with a Kf of 10.0 and a Kr of 1.0

New Reaction New Rule

Object Properties Problems (0 Errors, 0 Warnings)

**Kinetics** Editor

Reaction Name C\_p2

Reversible ☒ Kinetic Type Mass Action ( for each reaction:  $K_f \cdot \Pi \text{ reactants} - K_r \cdot \Pi \text{ products}$  ) 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	$\text{s}^{-1}$
Kr	microscopic reverse rate	<input type="checkbox"/>	1.0	$\text{s}^{-1}$

Annotation and Pathway Links

Linked Pathway Object(s):

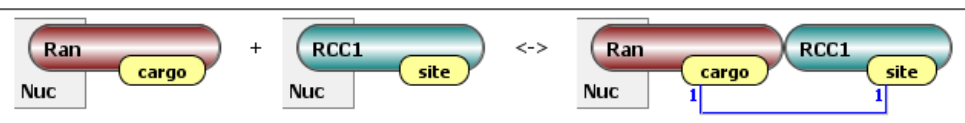
Finish inputting the rest of the reactions pictured below. (You already did the first two)



C\_p1



C\_p2



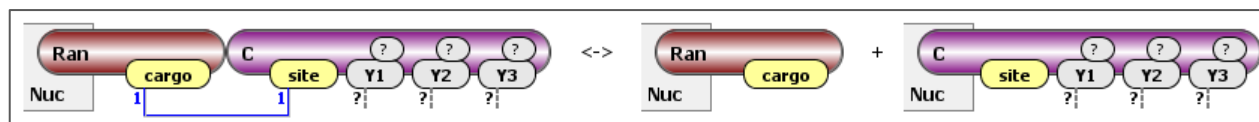
Ran\_RCC1\_Bind



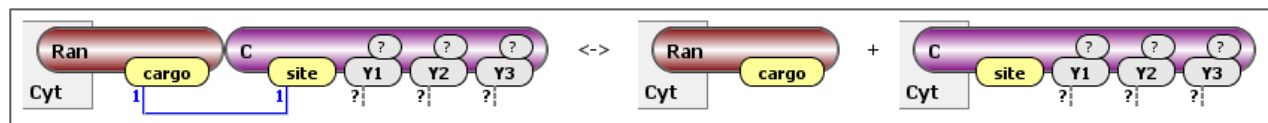
C\_p3



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. On the left is a tree view with categories like Physiology, Reactions (7), Structures (5), Species (2), Molecules (3), Observables (7), Applications (0), Parameters, Fur, and Pathway. The 'Applications (0)' item is selected, and a context menu is open with options: 'New Application', 'Expand All', and 'Collapse All'. The 'New Application' sub-menu is also open, showing 'Deterministic', 'Stochastic', and 'Network-Free'. An orange box with an arrow points to the 'Applications (0)' item, containing the text: '1. Right Click on **Applications**.' Another orange box with an arrow points to the 'Deterministic' option, containing the text: '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.' A third orange box with an arrow points to the 'Single Row Viewer' checkbox, containing the text: 'Checking the **Single Row Viewer** box aligns the entire reaction in one row. You can not edit the reaction in this mode.' The bottom of the interface shows a 'BioModels' search bar, 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.'

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.

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
  - Reaction Diagram
  - Reactions (7)
  - Structures (5)
  - Species (2)
  - Molecules (3)
  - Observables (7)
- Applications (1)**
  - Non-Spatial Deterministic**
- Parameters, Functions and Units
- Pathway

VCeL 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)

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

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

Volume/Surface Calculator

Structure	Size
EC	14891.899581611733
Nuc	124712.1 [ $\mu\text{m}^3$ ]
Cyt	3697.0137 [ $\mu\text{m}^3$ ]
pm	4738.6406 [ $\mu\text{m}^2$ ]
nm	1406.7734 [ $\mu\text{m}^2$ ]

Object P  
Select o

3. Change **Cyt** to 14891.9, **EC** to 124712.1, **Nuc** 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)
- Molecules (3)
- Observables (7)

Applications (1)

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

Parameters, Functions and Units

Pathway

VCell DB BMBDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

Biological Models

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

Geometry Specifications Protocols Simulations Parameter Estimation

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]

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

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

Search

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 'Specifications' is highlighted. The main window has tabs for Geometry, Specifications, Protocols, and Simulation. The 'Network' tab is active, showing a table of Network Constraints. An arrow points to the 'Network' tab with the instruction '1. Select the **Network** tab.' The table lists 'Max Iterations' with a value of 3 and 'Max Molecules / Species' with a value of 10. Another arrow points to this table with the instruction 'Note the constraints on the network'. Below the table, an 'Edit / Test Constraints' dialog box is open, showing the same constraints and a 'Test / Run' button. An arrow points to this button with the instruction '3. To test if the current constraints are adequate for the reaction simulation, click on **Test/Run**'. In the background, another arrow points to the 'Edit / Test Constraints' button in the main window with the instruction '2. Click on **Edit/Test Constraints**'.

1. Select the **Network** tab.

Note the constraints on the network

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

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 displays the VCell software interface. On the left is a hierarchical tree view with categories like 'Rule-Based\_Ran\_Transport', 'Physiology', 'Applications (1)', 'Parameters, Functions and Units', and 'Pathway'. The 'Applications (1)' category is expanded, showing 'Non-Spatial Deterministic' with sub-items: 'Geometry', 'Specifications' (highlighted), 'Protocols', 'Simulations', and 'Parameter Estimation'. Below this is a 'VCell DB' section with tabs for 'BMDB', 'Pathway Comm', and 'Sabio'. A 'Search' section lists various biological models. The main window has tabs for 'Geometry', 'Specifications', 'Protocols', 'Simulations', and 'Parameter Estimation'. The 'Specifications' tab is active, showing 'Network Constraints' and 'Generated Network' sections. The 'Network Constraints' section contains a table with two rows: 'Max Iterations' with a value of 3, and 'Max Molecules / Species' with a value of 10. The 'Generated Network' section shows 'Species: 21' and 'Reactions: 30'. A red warning message states: 'Warning: Max Iterations number may be insufficient.' Below this, a 'Search' bar is visible. At the bottom, the 'Object Properties' panel shows the output of a 'Running BioNetGen' process, including iteration counts and a red warning message: '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.' An orange arrow points from a yellow text box to this warning message.

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	3
Max Molecules / Species	value	10

Generated Network

Species: 21

Reactions: 30

Warning: Max Iterations number may be insufficient.

View Edit / Test Constraints

View Create new VCell BioModel from Network

Search

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

```
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.
```

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
- Sh
- 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: 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.
```

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

VCeDB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

**Search**

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

**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

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.

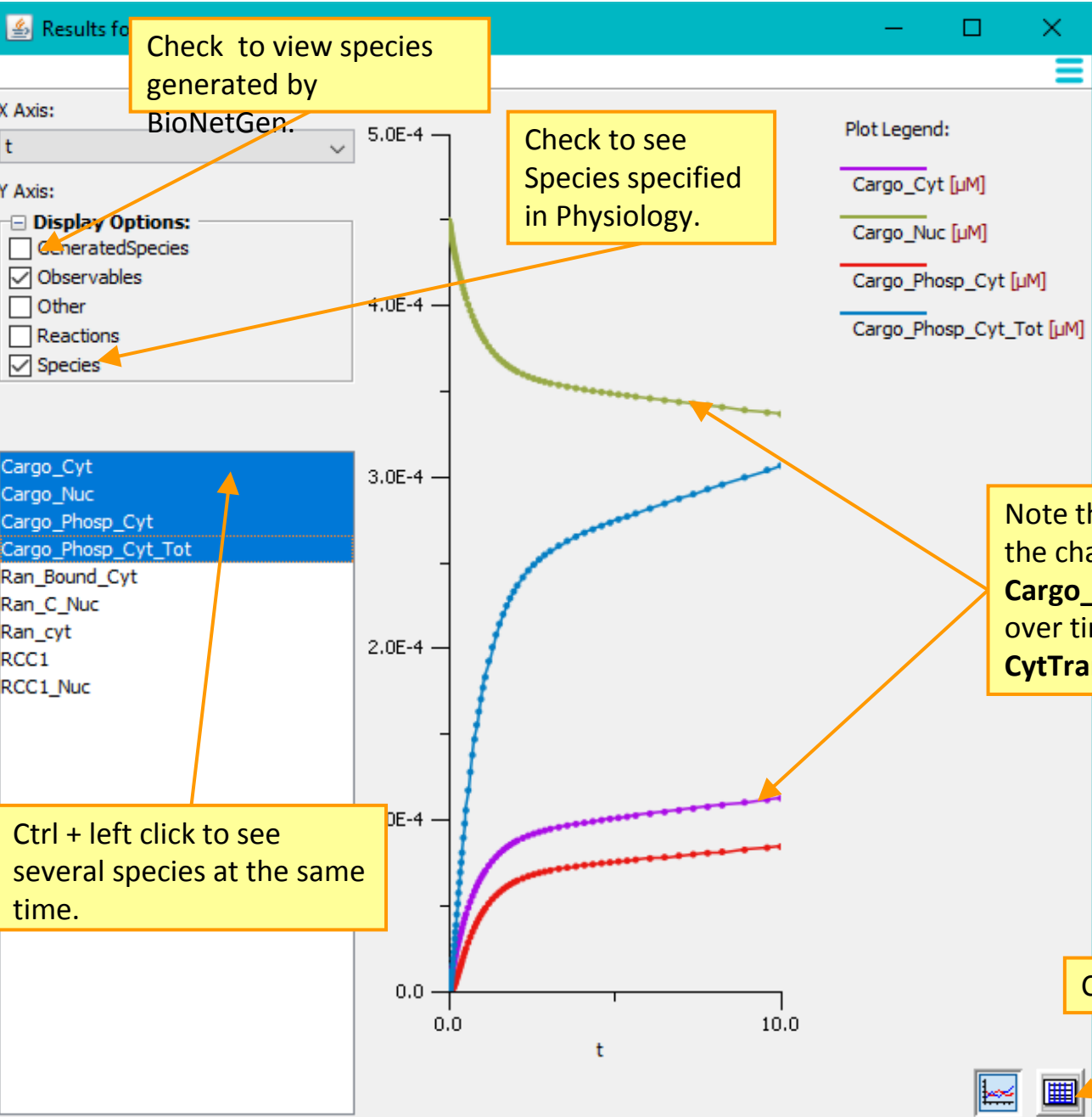
5. For advanced options; i.e. different solvers and outputs, click **Edit**.

6. Click 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

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

Rule Based Ran Transport VCell Tutorial (6.1): [Applications: Non-Spatial Deterministic](#)



**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.



**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

Reactions: 100  
Warning: none

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

**Rule-Based\_Ran\_Transport**

**Physiology**

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

**Applications (2)**

- $d/dt$  Non-Spatial Deterministic
- Non-Spatial Stochastic
  - Geometry
  - Specifications**
  - Protocols
  - Simulations

**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**

**Species** Reaction Network

Initial Condition: ☐ Concentration ☒ Number of Particles ☐ Randomize Initial Condition

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"/>

Search

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

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

1. Select the **Non-Spatial Stochastic** application, and go to **Specifications**.
2. Set the initial condition to **Number Of Particles**.
3. Change the initial condition to one thousand molecules for both species.

The screenshot displays the VCell software interface. On the left, a tree view shows the project structure under 'Rule-Based\_Ran\_Transport', including 'Physiology' (Reaction Diagram, Reactions, Structures, Species, Molecules, Observables) and 'Applications' (Non-Spatial Deterministic, Non-Spatial Stochastic). The 'Simulations' tab is selected under 'Applications'. The main window shows a table of simulations with columns: Name, End Time, Output Option, Solver, Running Status, and Results. A single simulation named 'SSA' is listed with an end time of 10.0 and an output option of 'every 0.1 s'. The 'Running Status' is 'never ran'. Three yellow callout boxes with orange arrows provide instructions: 1. 'Create a new simulation entitled SSA.' (points to the 'SSA' row), 2. 'Set end time to 10 seconds, and an output option of every 0.1 seconds.' (points to the 'End Time' and 'Output Option' columns), and 3. 'Run the simulation.' (points to the 'Run' button in the top right of the simulation table). The bottom panel shows the 'Object Properties' section with tabs for 'Problems (0 Errors, 0 Warnings)', 'Database File Info', and 'Network Generation Status'. The 'Settings' section shows 'Timestep' and 'Output' (set to 'every 0.1 sec'). The 'Parameters with values changed from defaults' section is also visible.

1. Create a new simulation entitled **SSA**.

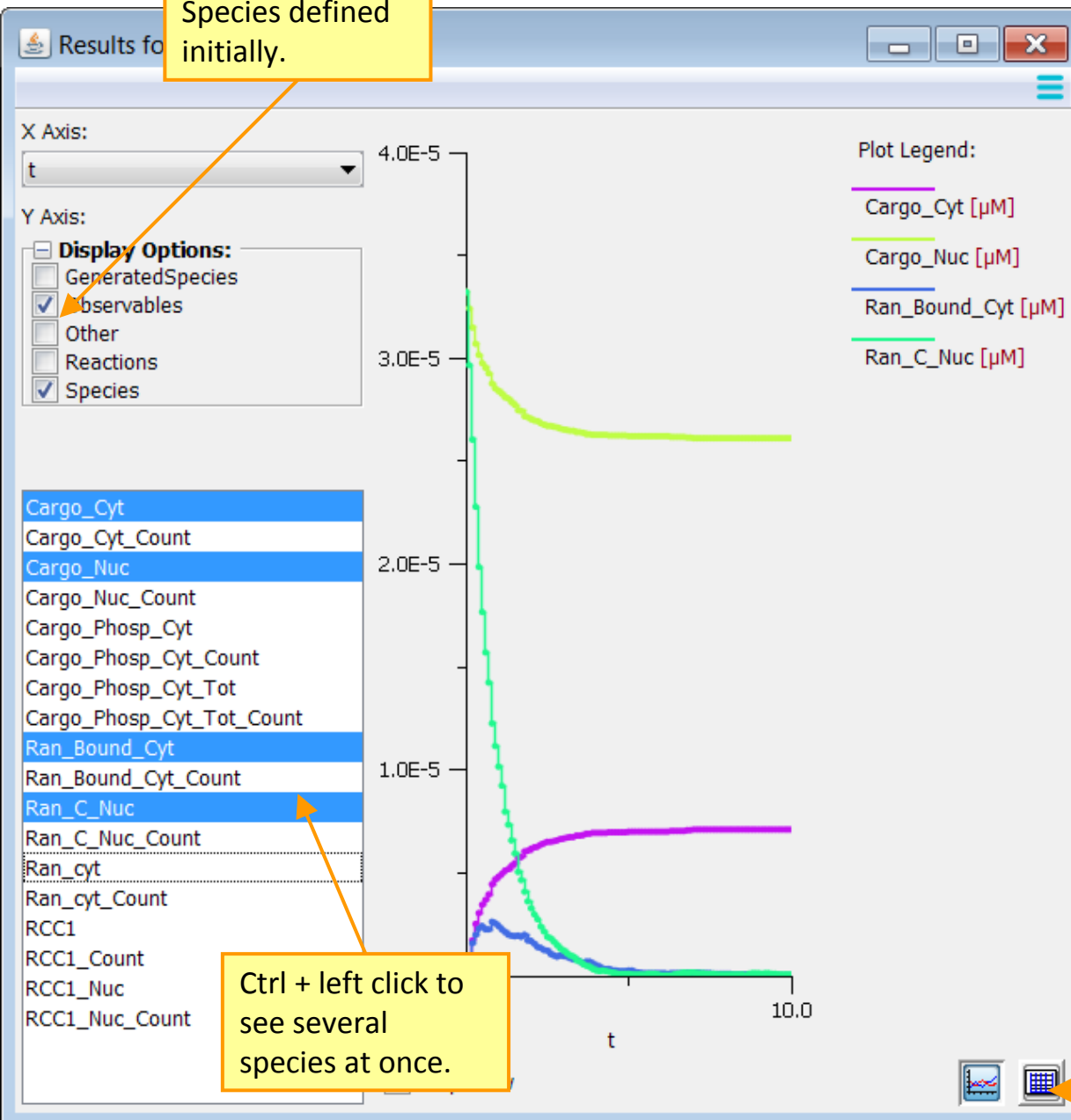
2. Set end time to 10 seconds, and an output option of **every 0.1 seconds**.

3. Run the simulation.

Name	End Time	Output Option	Solver	Running Status	Results
SSA	10.0	every 0.1 s	Gibson	never ran	no

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

Select to list  
Species defined  
initially.



**TIP:** Take into account the scale of the graph. These graphs can sometimes be misleading and make certain plots look much more significant than they are. Additionally, when two or more plots are selected, one may look like a flat line due to scaling. Hover over the plot and check the x and y values to make sure.

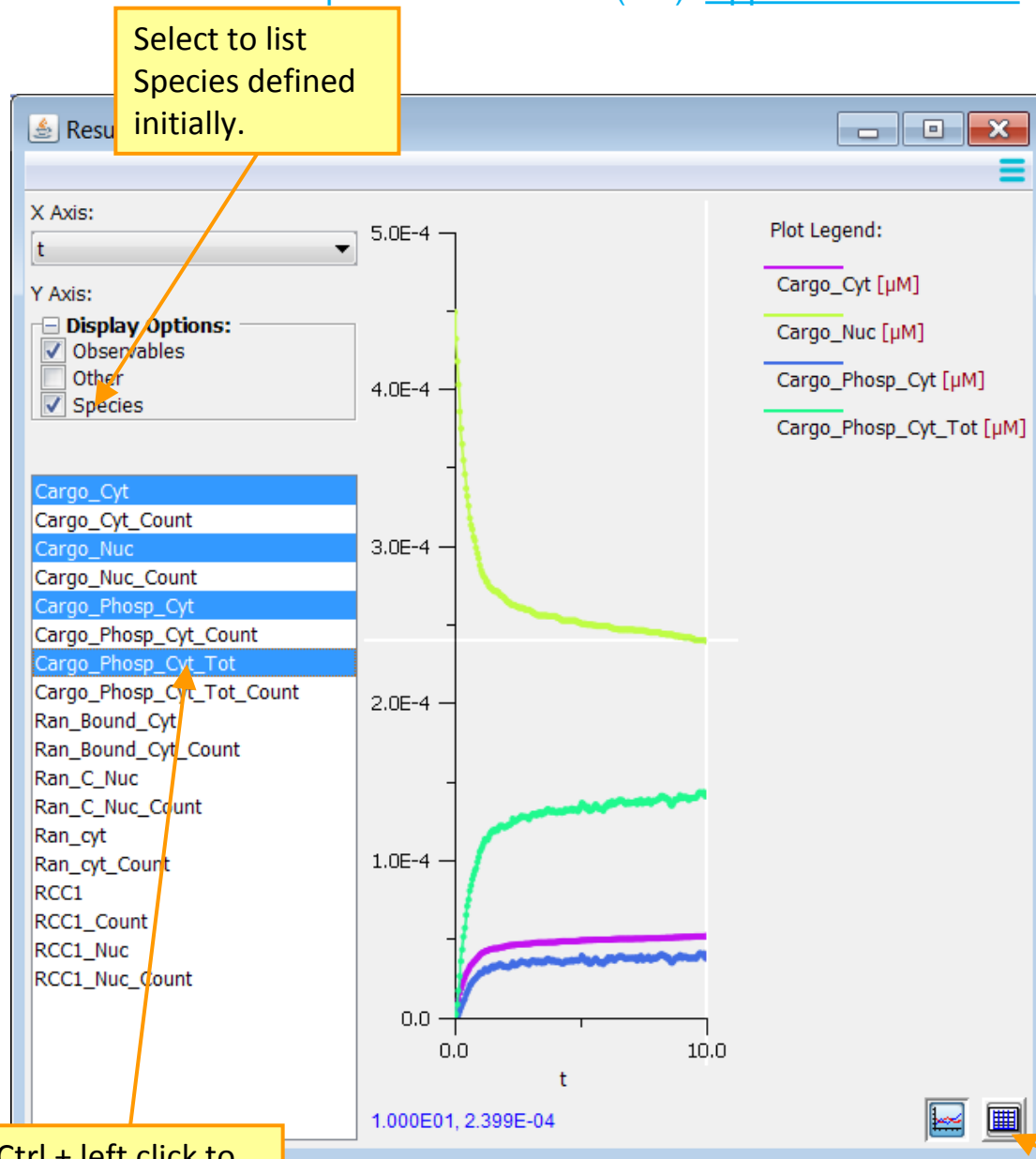
The screenshot displays the VCell software interface with several components:

- Left Panel (Tree View):** Shows a hierarchy under 'Rule-Based\_Ran\_Transport'. The 'Applications (3)' folder is selected, containing 'NFSim', 'Non-Spatial Deterministic', and 'Non-Spatial Stochastic'. Below this is a 'Pathway' section.
- Top Panel (Table):** A table listing applications with columns 'Name', 'Math Type', and 'Annotation'.

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...
- Bottom Left Panel (Search):** A search bar and a list of biological models including 'My BioModels (2018nathans751) (19)', 'Shared BioModels (1)', 'Public BioModels (602)', 'Tutorials (8)', and 'Education (34)'.
- Bottom Right Panel (Object Properties):** Shows the 'Application Name' as 'Non-Spatial Stochastic' and 'Annotation' as '(copied from Non-Spatial Deterministic)'. A 'More Copy Actions' menu is open, showing options: 'Copy', 'Copy As', 'Deterministic', 'Stochastic', and 'Network-Free'.

Five numbered instructions are overlaid on the image:

1. Click on **Applications**.
2. Select **Non-Spatial Stochastic**.
3. Click on **More Copy Actions > Copy As > Network-Free**.
4. Rename the application to **NFSim**.
5. Using NFSim, create and run a new simulation with an end time of 10.0, and and 0.05 output option.



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 (4)**
    - PDE\_3D
    - 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, stochast...	(copied from Non-Spatial Deterministic)
NFSim	Agent-based model, compartmental, stochastic ...	(copied from Non-Spatial Stochastic) (copied fro...
<b>PDE_3D</b>	explicit network model, compartmental, determi...	

**4. 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)

**2. 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.



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

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)

Non-Spatial Stochastic

4/dt PDE\_3D

- Geometry
- Specifications
- Protocols
- Simulations

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

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)

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	5 [ 1 ]	Flux	Flux	Flux	Flux	Flux	Flux
Cyt	Cyt	5 [ 1 ]	Flux	Flux	Flux	Flux	Flux	Flux
pm	Cyt_Nuc_membrane	5 [ 1 ]	from	from	from	from	from	from
nm	Cyt_Nuc_membrane	5 [ 1 ]	from	from	from	from	from	from

Object Properties Problems (0 Errors, 0 Warnings)

Select only one object (e.g. species, reaction, geometry, subdomain, 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



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)

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 <sup>2</sup> .s <sup>-1</sup> ]
RCC1	Nuc		<input type="checkbox"/>	4.5E-4 [μM]	<input type="checkbox"/>	10.0 [μm <sup>2</sup> .s <sup>-1</sup> ]

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

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 <sup>2</sup> .s <sup>-1</sup>
Boundary Condition X- for RCC1	BC_Xm	<zero flux>	μM.μm.s <sup>-1</sup>
Boundary Condition X+ for RCC1	BC_Xp	<zero flux>	μM.μm.s <sup>-1</sup>
Boundary Condition Y- for RCC1	BC_Ym	<zero flux>	μM.μm.s <sup>-1</sup>
Boundary Condition Y+ for RCC1	BC_Yp	<zero flux>	μM.μm.s <sup>-1</sup>
Boundary Condition Z- for RCC1	BC_Zm	<zero flux>	μM.μm.s <sup>-1</sup>

The screenshot displays the VCell software interface. On the left, a tree view shows the project structure under 'Rule-Based\_Ran\_Transport', including 'Physiology', 'Reaction Diagram', and 'Reactions (7)'. The 'Simulations' tab is selected in the top toolbar. A table lists the simulation 'Simulation\_PDE' with an end time of 1.0 and an output interval of every 0.05 s. The 'Edit: Simulation\_PDE' dialog box is open, showing the 'Solver' tab. The 'Integr...' dropdown is set to 'Fully-Implicit Finite Volume, Regular Grid (Variable Time Step)'. The 'General' section shows 'Time Bounds' with 'Starting' at 0.0 and 'Ending' at 10.0. The 'Time Step' section has 'Minimum' at 0.1 and 'Maximum' at 0.1. The 'Error Tolerance' section has 'Absolute' at 1.0E-9 and 'Relative' at 1.0E-7. The 'Output Options' section has 'Output Interval' set to 0.1 s. The 'Miscellaneous' section is empty. The 'OK' and 'Cancel' buttons are at the bottom.

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.

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.

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

**Edit: Simulation\_PDE**

**Parameters Mesh Solver**

**Mesh Size**

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)  $\Delta x$  0.7424

$\Delta y$  0.7424

$\Delta z$  0.7428571428571429

OK Cancel

The screenshot shows the VCell software interface. On the left is a tree view with categories like Physiology, Applications, Parameters, Functions and Units, and Pathway. The 'Applications' section is expanded, showing 'PDE\_3D' selected. The main window has tabs for Geometry, Specifications, Protocols, and Simulations. The 'Simulations' tab is active, displaying a table with simulation details.

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

A warning dialog box is open in the center, titled 'Warnings from Simulation: 'Simulation\_PDE!'. It contains the following text:

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?

Buttons: OK, Cancel

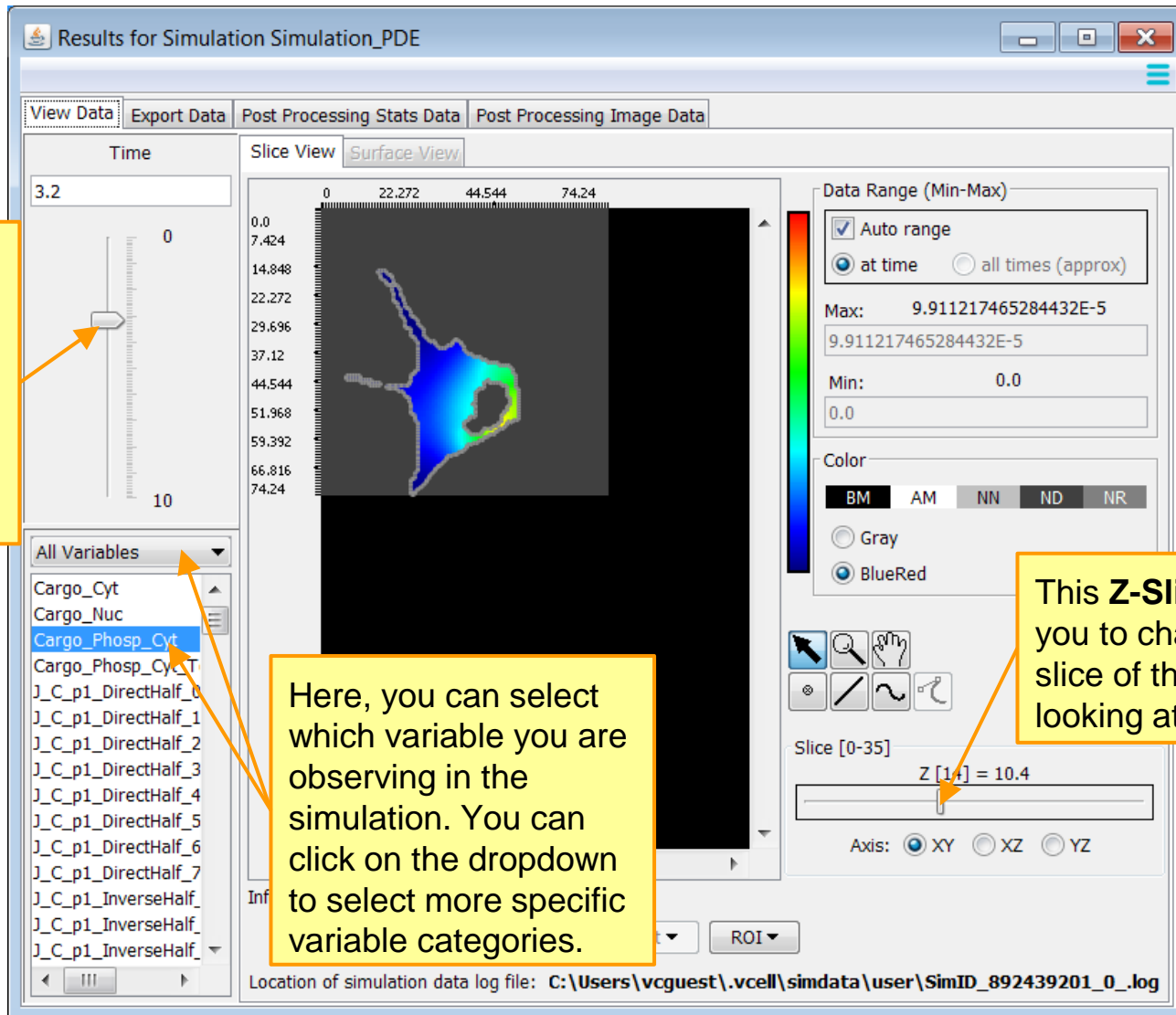
At the bottom of the main window, there is a 'Settings' section with a table:

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

Below the settings, it says 'Mesh: 71x71x25 = 126025 elements' and 'Geometry size: (74.24,74.24,26.0) microns'. At the very bottom, there is a section for 'Parameters with values changed from defaults' with a table with columns: Parameter Name, Default, New Value/Expression, and Scan.

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

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



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**
- Geome
- Specifi
- Protoc
- Simula

Parameters, Fu

Pathway

VCell DB BMDB Pa

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)

Search

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.

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

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

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

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 shows the VCell software interface. The top menu bar includes File, Server, Window, Tools, and Help. Below the menu bar are tabs for Geometry, Specifications, Protocols, and Simulations. The Simulations tab is active, displaying a table of simulations. The table has columns for Name, End Time, Output Option, Solver, Running Status, and Results. A single simulation named '100 Particles' is listed with an end time of 1.0, output every 0.05 s, using the Smoldyn solver, and is currently 'not saved'.

On the left side, there is a tree view showing the project structure. It includes folders for 'Stoch Spatial', 'Geometry', 'Specifications', 'Protocols', and 'Simulations'. The 'Simulations' folder is expanded, showing a sub-folder '100 Particles'.

The 'Edit: 100 Particles' dialog box is open, showing the 'Mesh' tab. The 'Parameters' tab is also visible. The 'Mesh Size' section includes a 'Lock aspect ratio' checkbox, which is checked. The 'Geometry Size (um)' is set to (74.24, 74.24, 26.0). The 'Mesh Size (elements)' is set to X: 101, Y: 101, Z: 36. The 'Total Size (elements)' is calculated as 101 x 101 x 36 = 367236. The 'Spatial Step (um)' is set to Δx: 0.7424, Δy: 0.7424, Δz: 0.7428571428571429.

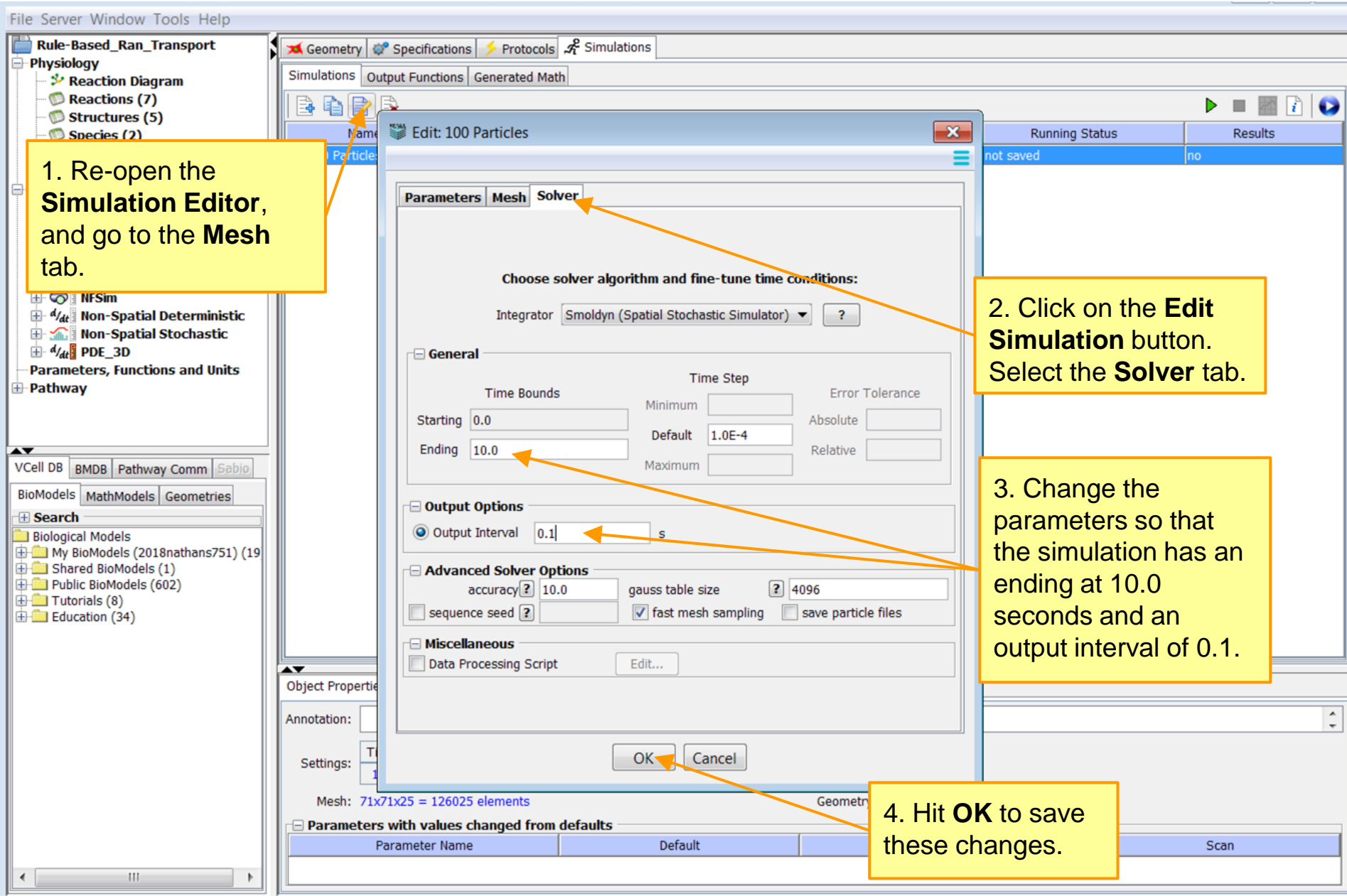
At the bottom of the dialog box, there are 'OK' and 'Cancel' buttons. An arrow points from the 'OK' button to the instruction 'Hit OK to save these changes.'

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)
  - Molecules (3)
  - Observables (7)
- 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**

- Biological Models
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  - Shared BioModels (1)
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  - Tutorials (8)
  - Education (34)

**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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Tanya Miller (2015) – Pomperaug High School

Nathan Schaumburger (2017) – Hall High School, West Hartford

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