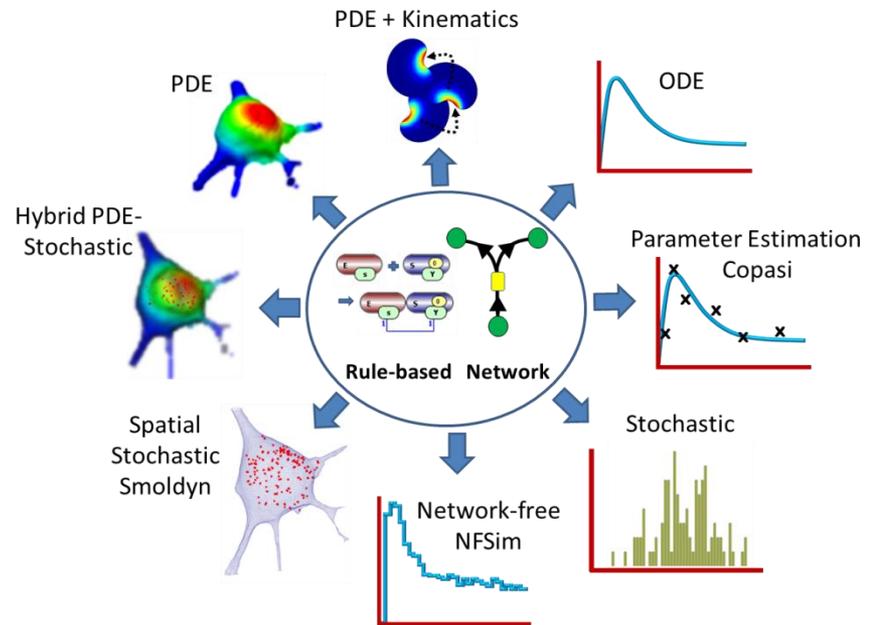


VCell

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



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

VCell BioModel with Multiple Applications

Objective

Create a single Biomodel of RAN nuclear transport then use different modeling strategies to solve simulations.

Goals

- Create a Biomodel Physiology with species, reactions and fluxes
- Create a spatial deterministic application of the Physiology
- Import fluorescence images into VCell and segment a 3D image stack within VCell to create a geometry
- Create a simulation and specify solver, time, and computational mesh.
- Run the simulation, view results and create graphs

Table of contents

- ▶ [Opening VCell](#)
- ▶ [Defining compartments](#)
- ▶ [Creating fluxes, reactions and species](#)
- ▶ [Specifying kinetic laws](#)
- ▶ [Creating applications](#)
- ▶ [Importing images](#)
- ▶ [Segmenting images](#)
- ▶ [Editing computational domain size](#)
- ▶ [Mapping geometry to compartments](#)
- ▶ [Specifying initial conditions](#)
- ▶ [Creating a simulation](#)
- ▶ [Viewing simulation results](#)
- ▶ [Re-Open a model](#)
- ▶ [Copy an application](#)
- ▶ [Create a stochastic simulation](#)
- ▶ [Export results as spreadsheet](#)
- ▶ [Create a non-spatial deterministic application](#)
- ▶ [Using parameter estimation](#)
- ▶ [Create a spatial stochastic application](#)

Your first time opening VCell

You need to register as a New User if you want to run simulations on the VCell compute resources, or use the VCell database to store models that can be shared with collaborators.

this link for details on how to acknowledge Virtual Cell in your publication and how to share your published research through the VCell database.'" data-bbox="521 258 864 798"/>

Virtual Cell login

User Name

Password

Login Cancel

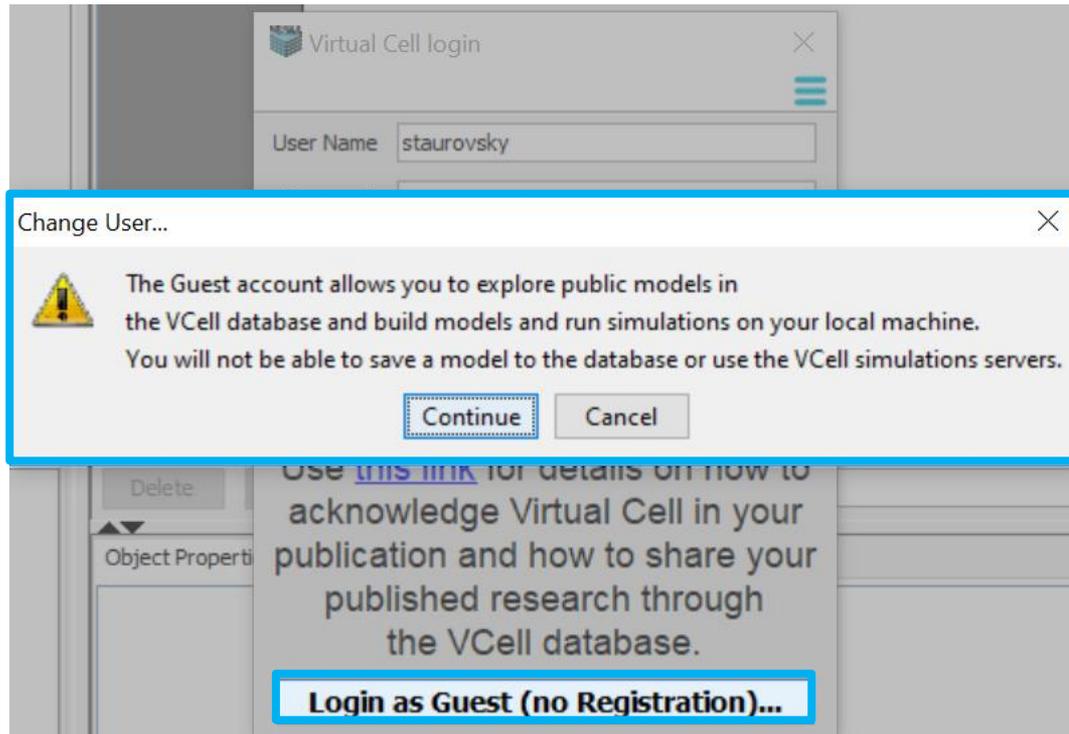
Forgot Login Password...

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.

Your first time opening VCell

Guest Login Option



VCell BioModel Organization

BioModel

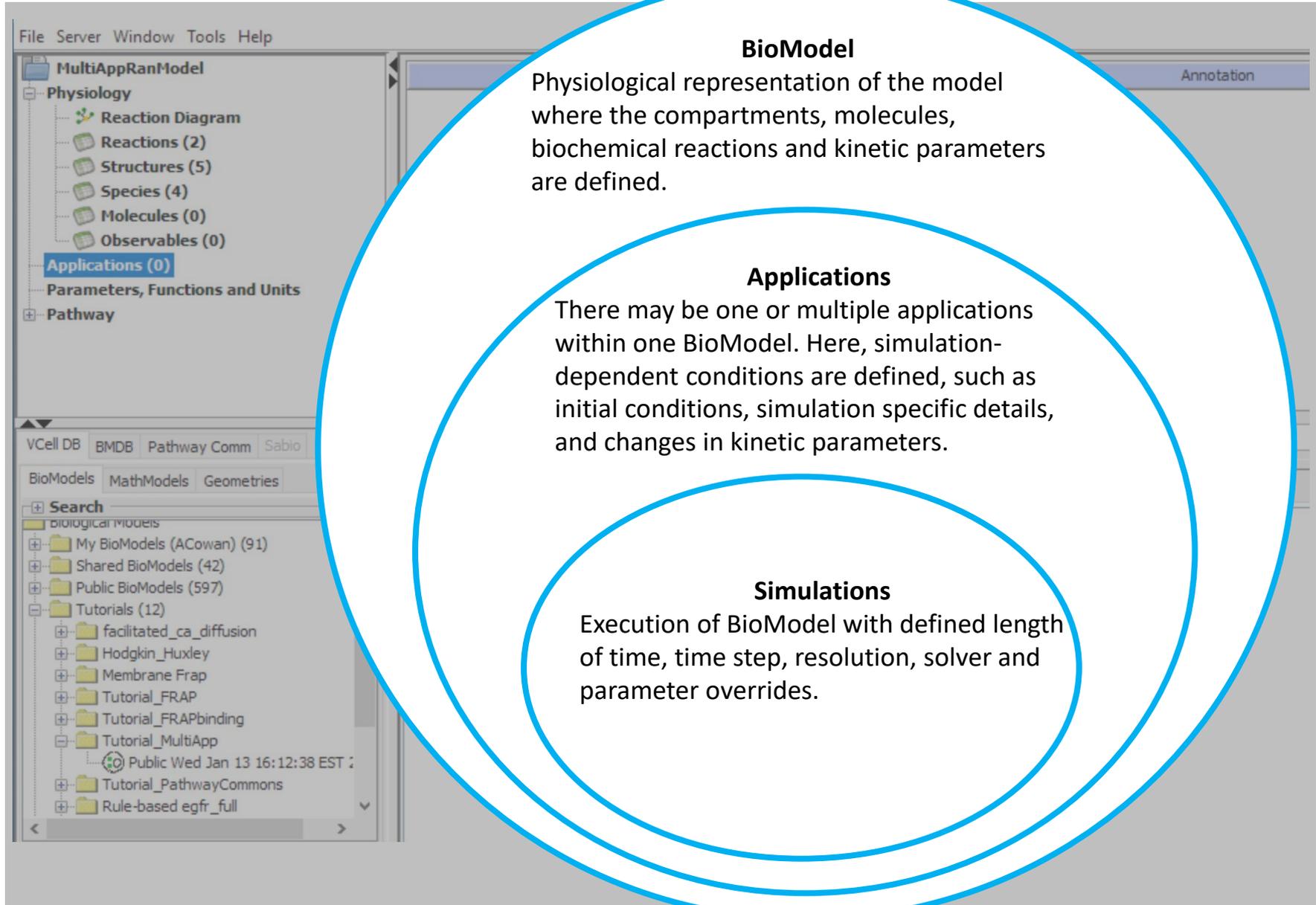
Physiological representation of the model where the compartments, molecules, biochemical reactions and kinetic parameters are defined.

Applications

There may be one or multiple applications within one BioModel. Here, simulation-dependent conditions are defined, such as initial conditions, simulation specific details, and changes in kinetic parameters.

Simulations

Execution of BioModel with defined length of time, time step, resolution, solver and parameter overrides.

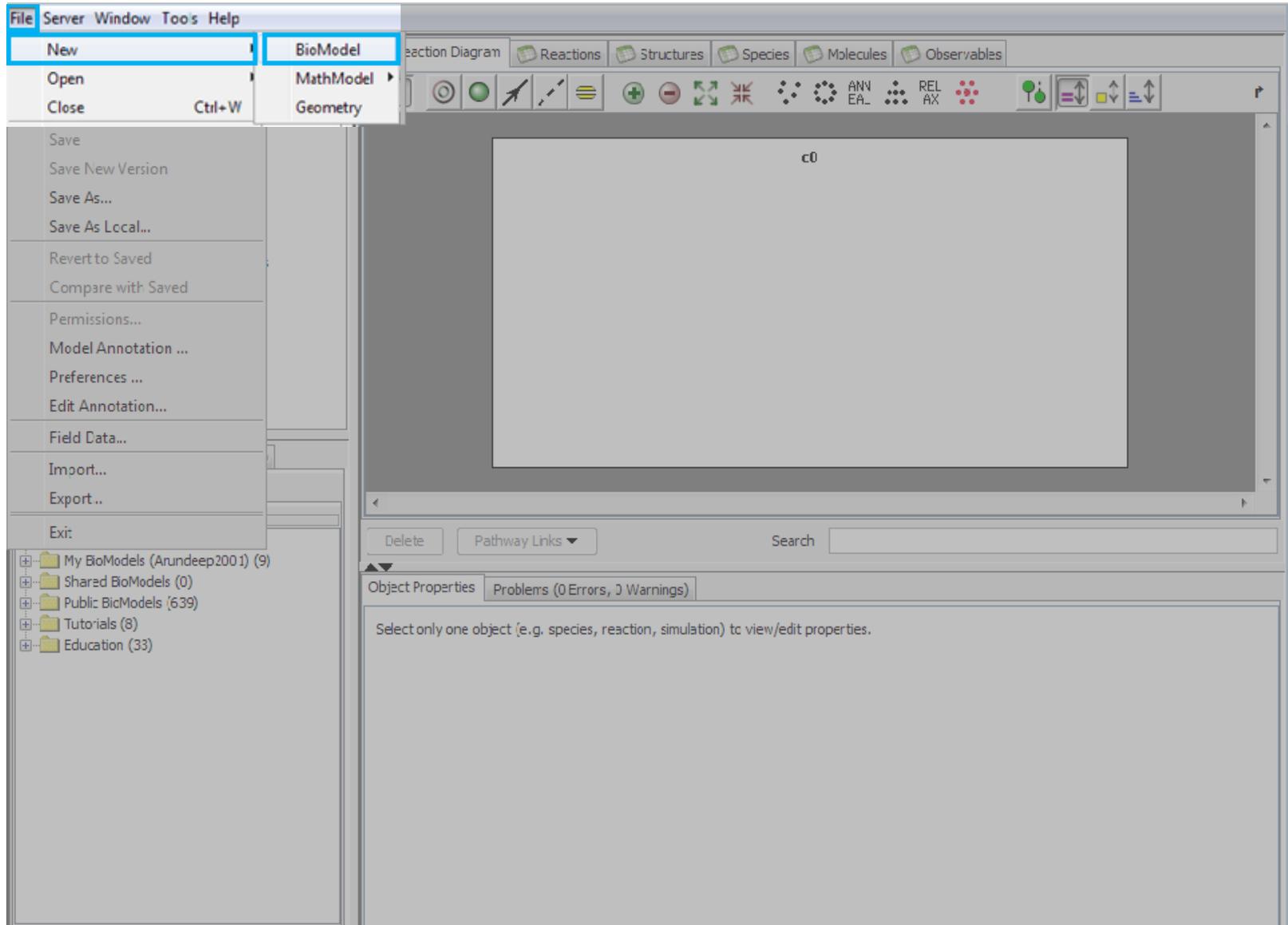


The VCell Interface

The screenshot displays the VCell software interface. At the top, a menu bar includes 'File', 'Server', 'Window', 'Tools', and 'Help'. The main window is divided into several sections:

- Left Panel (BioModel1):** A hierarchical tree view showing the model structure. The 'Physiology' folder is expanded, revealing sub-items: 'Reaction Diagram' (highlighted), 'Reactions (0)', 'Structures (1)', 'Species (0)', 'Molecules (0)', and 'Observables (0)'. Below this are 'Applications (0)', 'Parameters, Functions and Units', 'Pathway', and 'Scripting'.
- Top Panel:** A toolbar with icons for 'Reaction Diagram', 'Reactions', 'Structures', 'Species', 'Molecules', and 'Observables'. Below these are various drawing and editing tools, including a mouse cursor, a target, a green circle, a black arrow, a pencil, a selection tool, a plus sign, a minus sign, a green square, a red square, a black dot, a green dot, and a red dot. There are also buttons for 'ANN EAL' and 'REL AX'.
- Central Workspace:** A large white area containing a single reaction diagram labeled 'c0'.
- Bottom Panel:** A search bar with a 'Delete' button and a 'Pathway Links' dropdown menu. Below this are tabs for 'Object Properties', 'Annotations', and 'Problems (0 Errors, 0 Warnings)'. The 'Object Properties' tab is currently active and empty.
- Bottom Status Bar:** A blue bar at the very bottom shows 'CONNECTED' on the left and '77.9MB / 238MB' on the right.

To create a new VCell model, click “File” > “New” > “BioModel”

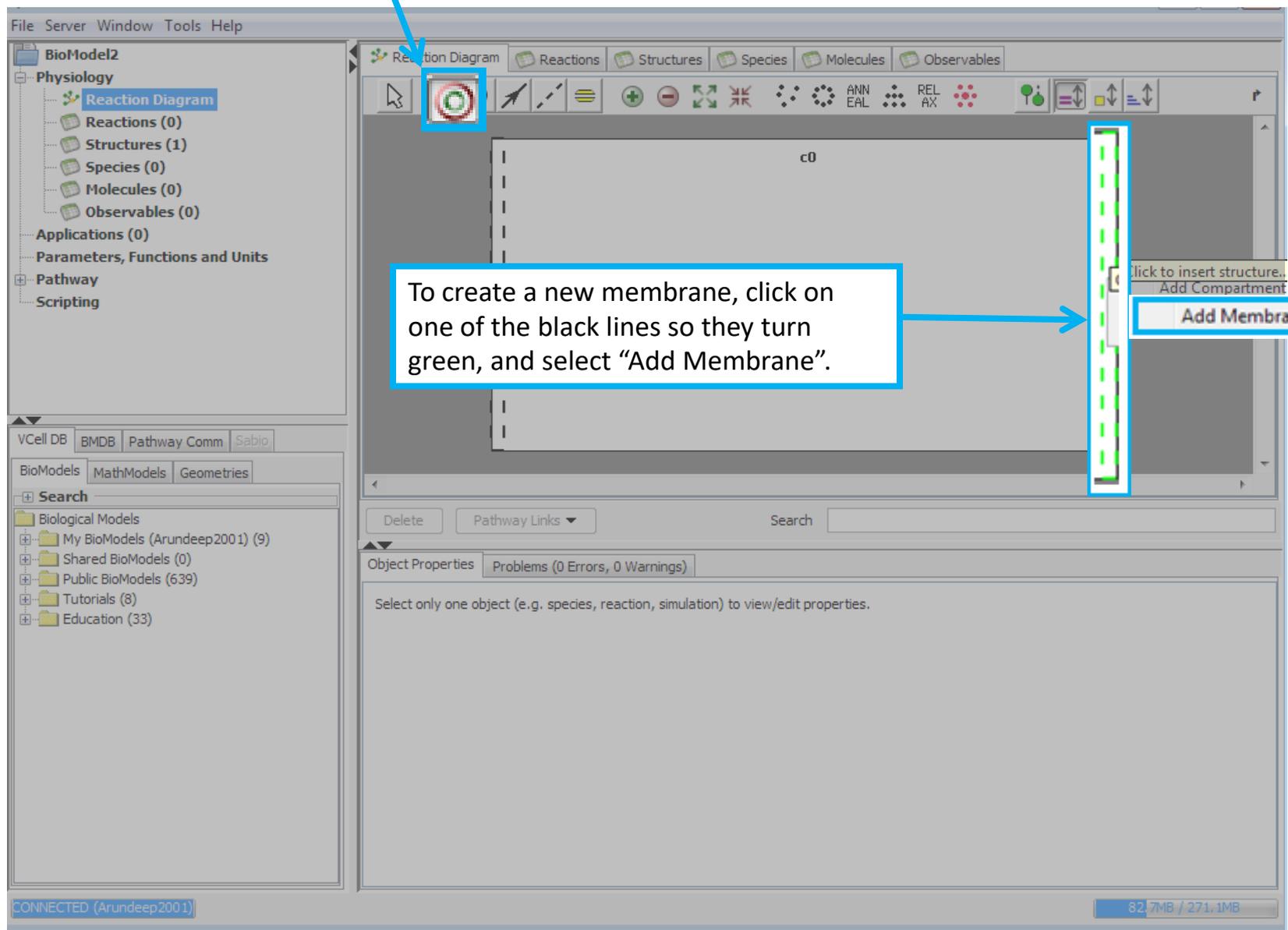


The screenshot displays a software interface with a 'File' menu open on the left. The menu items are: File, Server, Window, Tools, Help. Under 'File', the following options are listed: New, Open, Close (with a keyboard shortcut Ctrl+W), Save, Save New Version, Save As..., Save As Local..., Revert to Saved, and Compare with Saved. The 'Save' option is highlighted in blue. A blue arrow points to the 'Save' option. In the background, a reaction diagram is visible, showing a network of nodes and arrows. The nodes are labeled: C_{cyt}, Ran_{cyt}, RanC_{cyt}, and RanC_{nuc}. The diagram is divided into compartments: C, PM, Cyt, NM, and Nuc. The Cyt compartment contains C_{cyt} and Ran_{cyt}. The NM compartment contains a yellow node. The Nuc compartment contains RanC_{nuc}. Arrows indicate the flow of the reaction: Ran_{cyt} → C_{cyt} → RanC_{cyt} → RanC_{nuc}. The RanC_{cyt} node is connected to a yellow node in the NM compartment, which is then connected to RanC_{nuc} in the Nuc compartment.

To save your model, navigate to “File” and make your selection from the four “Save” options that are available.

The screenshot shows a software interface with a top menu bar (File, Server, Window, Tools, Help) and a toolbar with various icons. On the left is a tree view for 'BioModel2' containing 'Physiology' and its sub-items: 'Reaction Diagram', 'Reactions (2)', 'Structures (5)', 'Species (4)', 'Molecules (0)', and 'Observables (0)'. The main area displays a 'Reaction Diagram' with compartments 'C', 'PM', 'Cyt', 'NM', and 'Nuc'. Species 'C_cyt' and 'Ran_cyt' are shown in the 'Cyt' compartment, and 'nuc' is in the 'Nuc' compartment. A text box with a blue border and white background contains the text: 'To re-open a model, navigate to the folder that the model was saved in and double-click the model name.' A blue arrow points from this text box to a search panel in the bottom-left corner. The search panel has tabs for 'VCell DB', 'BMDB', 'Pathway Comm', and 'Sabio'. Under 'BioModels', there are sub-tabs for 'MathModels' and 'Geometries'. A search bar is present. Below it, a tree view shows 'Biological Models' with sub-folders: 'My BioModels (yourBioModels)', 'Shared BioModels (0)', 'Public BioModels (654)', 'Tutorials (9)', 'Education (33)', and 'Published BioModels (166)'. The 'multiapp tutorial' folder under 'My BioModels' is expanded, and a file named 'Private Fri Dec 14 17:22:00 EST 2018' is highlighted with a blue border. A blue arrow points from the text box to this file.

To create the components to your model, start with creating a volumetric compartment by selecting the Structure Tool. This will automatically create your first compartment.

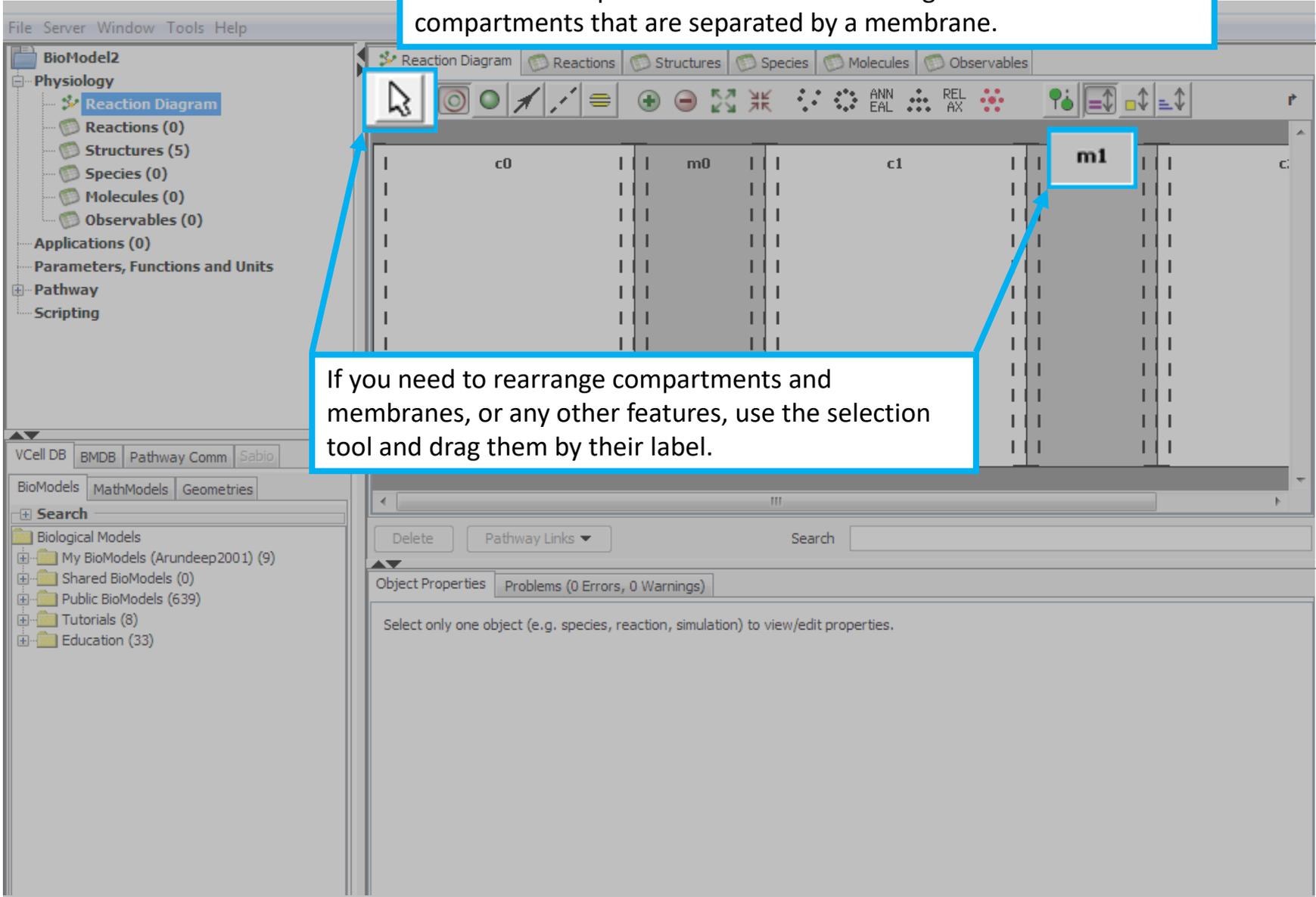


To create a new membrane, click on one of the black lines so they turn green, and select "Add Membrane".

Click to insert structure...
Add Compartment
Add Membrane

The screenshot shows a software interface with a menu bar (File, Server, Window, Tools, Help) and a toolbar with icons for Reaction Diagram, Reactions, Structures, Species, Molecules, and Observables. On the left, a tree view shows a project named 'BioModel2' with a 'Physiology' sub-project containing 'Reaction Diagram', 'Reactions (0)', 'Structures (2)', 'Species (0)', 'Molecules (0)', and 'Observables (0)'. Below this is a 'Search' section with categories like 'Biological Models', 'My BioModels (Arundeeep2001) (9)', 'Shared BioModels (0)', 'Public BioModels (639)', 'Tutorials (8)', and 'Education (33)'. The main workspace displays a reaction diagram with two compartments, 'c0' and 'c1', separated by vertical dashed lines. A blue callout box with white text says: 'To create a new compartment, click on the dotted black lines, which will become green, and select "Add Compartment"'. A blue arrow points from this box to a button labeled 'Add Compartment' in a grey panel at the bottom right of the workspace. Below the workspace is an 'Object Properties' section with a search bar and a message: 'Select only one object (e.g. species, reaction, simulation) to view/edit properties.' The status bar at the bottom shows 'CONNECTED (Arundeeep2001)' and '93.6MB / 271.1MB'.

Your model requires 3 volumetric compartments separated by 2 membrane compartments. Continue creating two additional compartments that are separated by a membrane.



Use the selection tool to name compartments and membranes. The area will turn red upon selection. Double click the structure name you wish to change and enter the new name.

The screenshot shows the software interface with a red box around the 'EC' compartment in the workspace and a blue box around the selection tool icon in the toolbar. The 'Object Properties' panel at the bottom shows the following details:

Object Properties	
Structure Name	EC
Size Variable Name	EC [µm³]
Annotation	

File Server Window Tools Help

BioModel2

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

Reaction Diagram Reactions Structures Species Molecules Observables

EC	PM	c1	NM	c:
----	----	----	----	----

Object Properties Problems (0 Errors, 0 Warnings)

Select only one structure to edit properties

Structure Name EC

Size Variable Name EC [um³]

Annotation

VCCell DB BMBDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
 - My BioModels (Arundeeep2001) (9)
 - Shared BioModels (0)
 - Public BioModels (639)
 - Tutorials (8)
 - Education (33)

You can also change the Structure Name on the Object Properties tab. You can annotate compartments and rename species here as well.

Object Properties Problems (0 Errors, 0 Warnings)

Select only one structure to edit properties

Structure Name EC

Size Variable Name EC [um³]

Annotation

Rename the compartments and membranes to the following:

C0 -> EC (Extracellular)

M0 -> PM (Plasma Membrane)

C1 -> Cyt (Cytosol)

M1 -> NM (Nuclear Membrane)

C2 -> Nuc (Nucleus)

c0

m0

c1

m1

c2

EC

PM

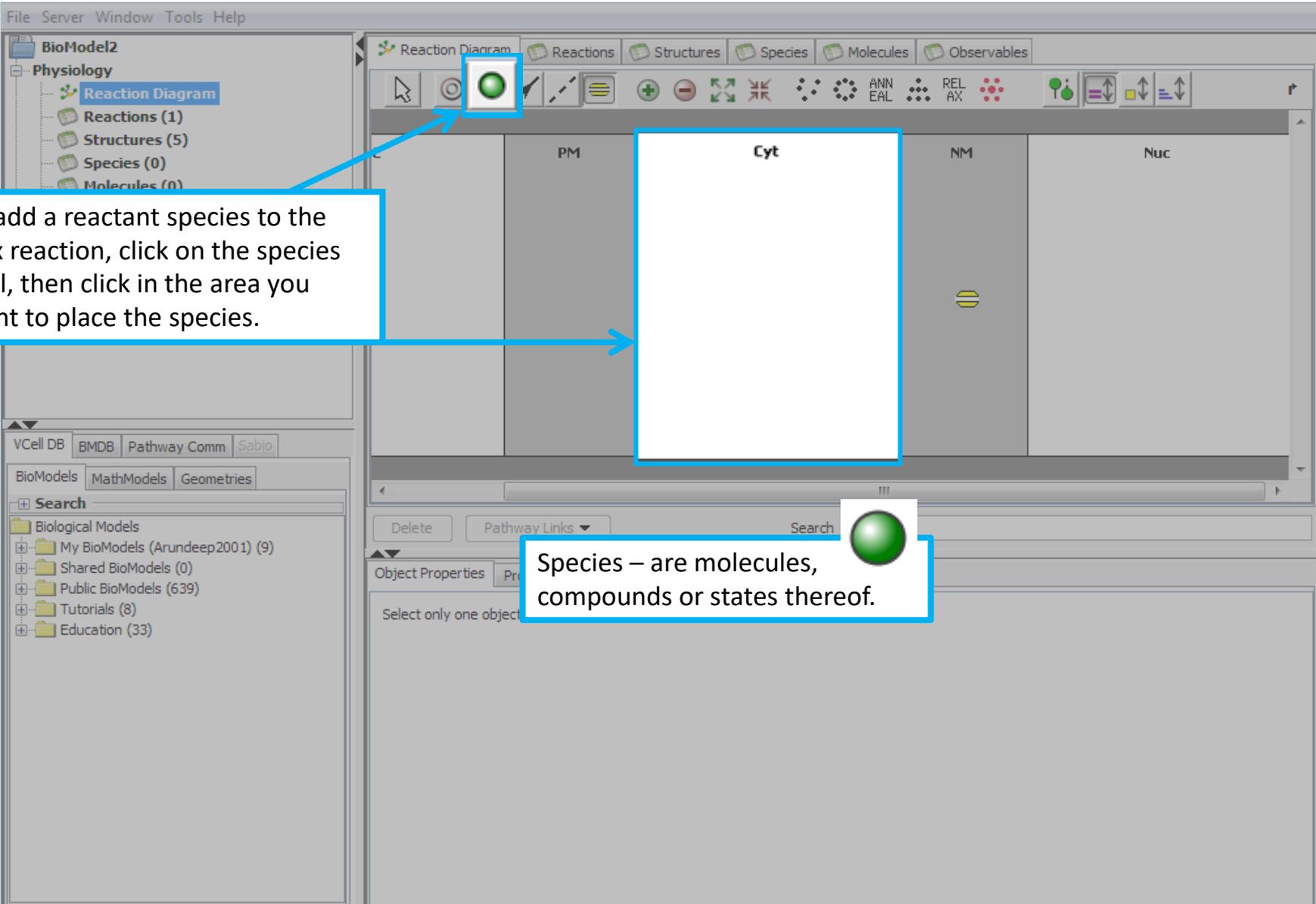
Cyt

NM

Nuc

The screenshot displays the BioModel2 software interface. The top menu bar includes 'File', 'Server', 'Window', 'Tools', and 'Help'. Below the menu is a toolbar with various icons for different model elements: Reaction Diagram, Reactions, Structures, Species, Molecules, and Observables. A specific icon representing a flux reaction (a yellow and black striped cylinder) is highlighted with a blue box and a blue arrow pointing to it. Another blue arrow points from this icon to a similar icon placed within the 'NM' compartment of a reaction diagram. The diagram shows four compartments: PM, Cyt, NM, and Nuc. The bottom left panel shows a search bar and a list of biological models. The bottom right panel shows the 'Object Properties' section with a message: 'Select only one object (e.g. species, reaction, simulation) to view/edit properties.'

To create a flux reaction, click on the FluxReaction tool, then click in the area where you want to place the flux.



To add a reactant species to the flux reaction, click on the species tool, then click in the area you want to place the species.

Species – are molecules, compounds or states thereof.

File Server Window Tools Help

BioModel2

- Physiology
 - Reaction Diagram
 - Reactions (1)
 - Structures (5)
 - Species (2)
 - Molecules (0)
 - Observables (0)
- Applications ()
- Parameters, F
- Pathway
- Scripting

Reaction Diagram

Reactions Structures Species Molecules Observables

EC PM Cyt NM Nuc

sO

Use the reaction tool to connect a reactant species to a flux reaction, by clicking on a species and dragging the line to the flux symbol.

VCCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
 - My BioModels (Arundeeep2001) (9)
 - Shared BioModels (0)
 - Public BioModels (639)
 - Tutorials (8)
 - Education (33)

Delete Pathway Links Search

Object Properties Problems (0 Errors, 0 Warnings)

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

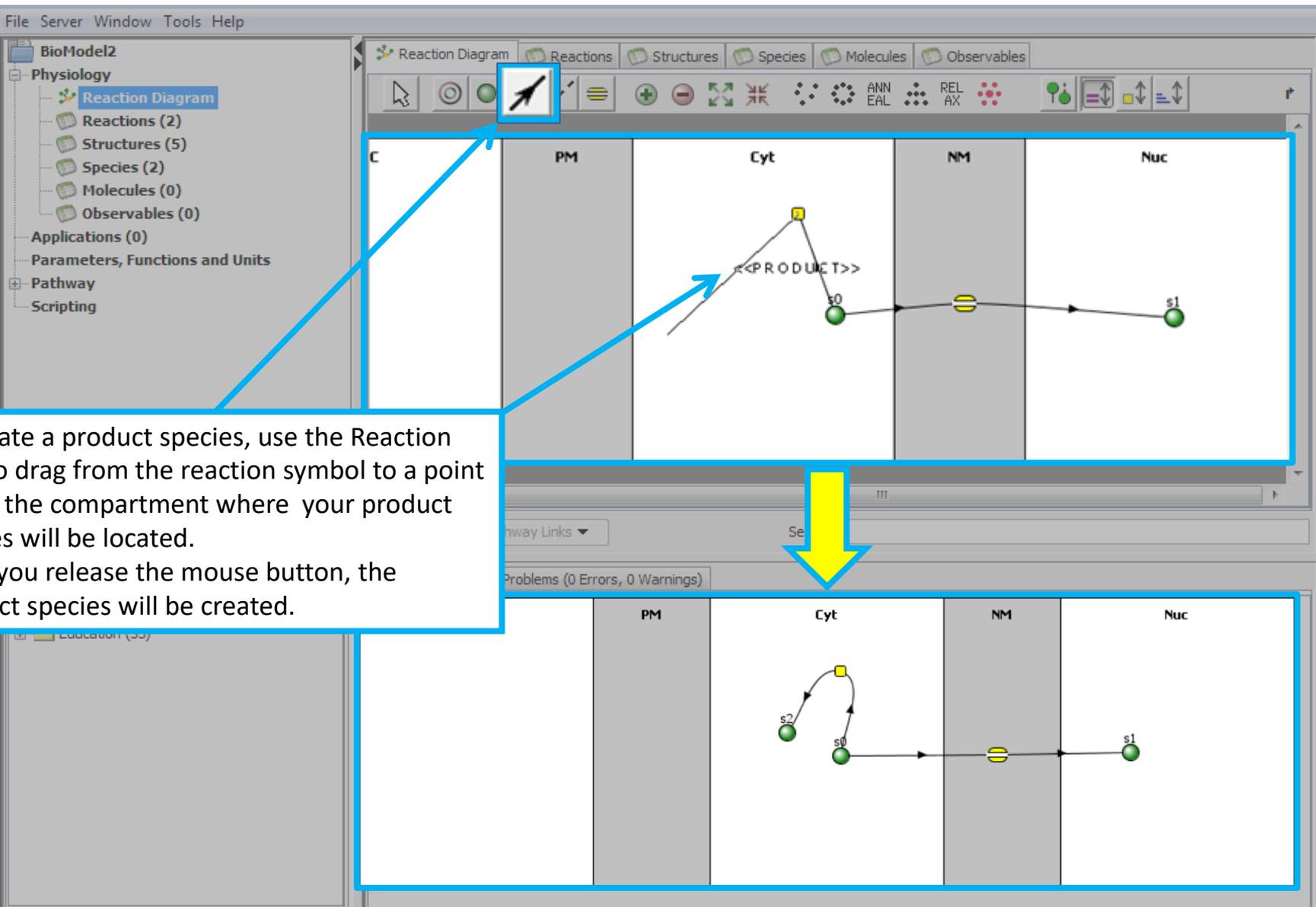
The screenshot shows a software interface for creating a product of flux reaction. The interface is divided into several panels. On the left is a tree view showing a hierarchy of models: BioModel2, Physiology, Reaction Diagram, Reactions (1), Structures (5), Species (2), Molecules (0), Observables (0), Applications (0), Parameters, Functions and Units, Pathway, and Scripting. Below this is a search bar and a list of biological models. The main workspace is titled 'Reaction Diagram' and contains a reaction diagram with five compartments: EC, PM, Cyt, NM, and Nuc. A reaction arrow points from a green sphere labeled 's0' in the EC compartment to a green sphere labeled 's1' in the Nuc compartment. A yellow oval is positioned on the reaction arrow. A blue box highlights the reaction tool in the toolbar, with an arrow pointing to the reaction arrow. Another blue box highlights the yellow oval on the reaction arrow, with an arrow pointing to a text box.

To create a product of flux reaction, use the reaction tool to drag a line from the flux to a point inside the compartment where a product species will be created.

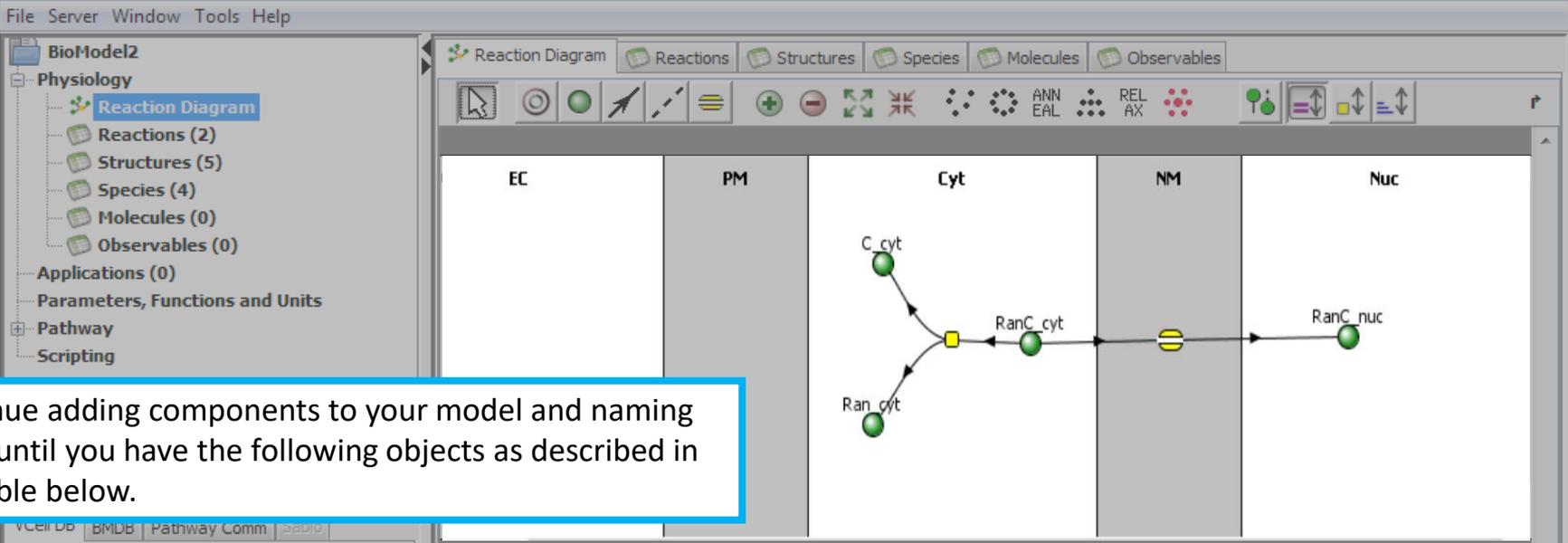
The screenshot displays the BioModel2 software interface. The main window shows a reaction diagram with compartments EC, PM, Cyt, NM, and Nuc. A reaction is shown with a reactant 's0' in the Cyt compartment and a product 's1' in the NM compartment. A yellow box highlights a small square icon above the reaction arrow, and a blue arrow points from a text box to this icon. The 'Delete' button is highlighted in a blue box, with a blue arrow pointing from another text box to it. The interface includes a menu bar (File, Server, Window, Tools, Help), a toolbar with various icons, and a search bar at the bottom.

To create a reaction, using the Reaction Tool, click on a species and drag a line from the species to a point inside the compartment. The active line will read <<REACTANT>>, and a reaction node will be created once you release the mouse button.

To remove a species or reaction from your model, select the species or reaction and click on either the "Delete" button or the backspace button on your keyboard.



To create a product species, use the Reaction Tool to drag from the reaction symbol to a point inside the compartment where your product species will be located. Once you release the mouse button, the product species will be created.



Continue adding components to your model and naming them until you have the following objects as described in the table below.

Name	Description	Location
RanC_nuc	Ran-Cargo Complex	Nucleus
	Flux Reaction Node	Nuclear Membrane
RanC_cyt	Ran-Cargo Complex	Cytoplasm
	Reaction Node	Cytoplasm
C_cyt	Cargo	Cytoplasm
Ran_cyt	Ran- GTPase	Cytoplasm

Note that you cannot move species, reactions, or fluxes from one compartment to another. You must delete a species, flux, or reaction from one compartment and then create it in another compartment.

Reaction Diagram Reactions Structures Species Molecules Observables

EC PM Cyt NM Nuc

C_cyt
RanC_cyt
RanC_nuc

Delete Pathway Links Search

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

Species Name RanC_nuc

If you need to rename a component, select the component, and on the Object Properties tab, use the component's name text field to supply the new name.

Reaction Diagram Reactions Structures Species Molecules Observables

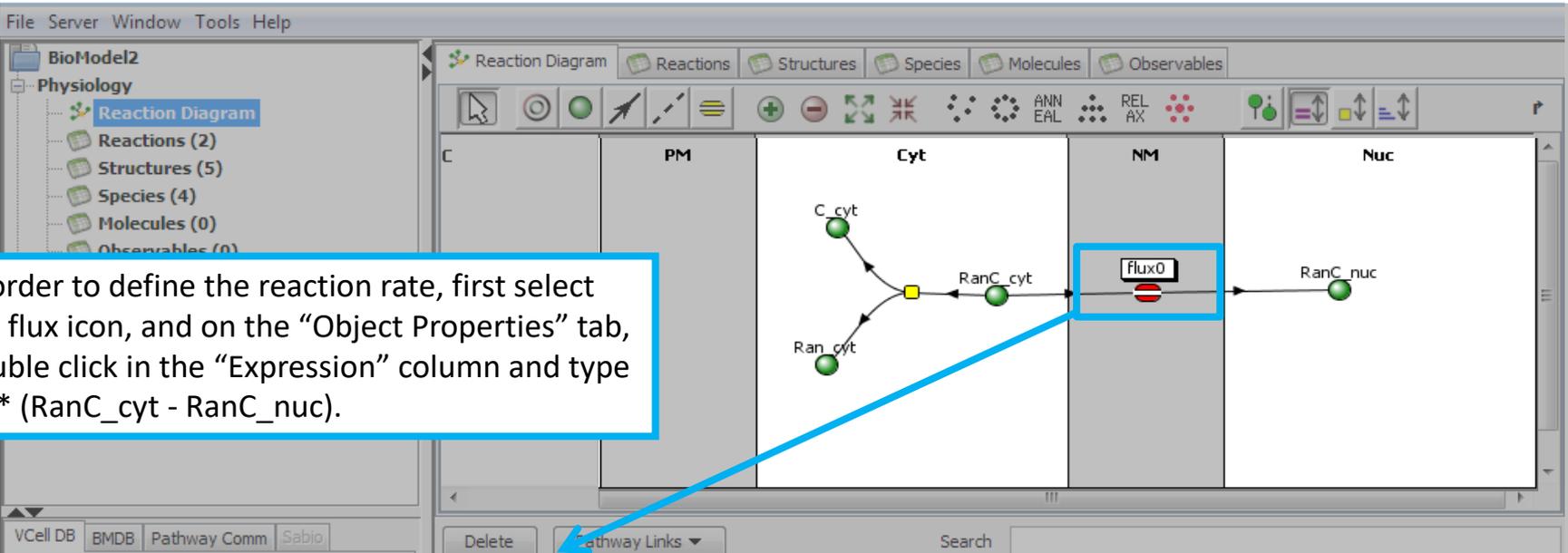
EC PM Cyt NM Nuc

C_cyt
RanC_cyt
flux0
RanC_nuc

Delete Pathway Links Search

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

Reaction Name flux0



In order to define the reaction rate, first select the flux icon, and on the "Object Properties" tab, double click in the "Expression" column and type $kfl * (RanC_cyt - RanC_nuc)$.

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
 - My BioModels (Arundeeep2001) (9)
 - Shared BioModels (0)
 - Public BioModels (639)
 - Tutorials (8)
 - Education (33)

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

Reaction Name flux0

Electrical Properties include molecular flux include electric current (into inside structure "undefined")

Reversible Kinetic Type General Flux Density ($\mu\text{M}\cdot\mu\text{m/s}$) Convert to [molecules.s⁻¹]

Name	Description	Global	Expression	Units
J	reaction rate	<input type="checkbox"/>	$kfl * (RanC_cyt - RanC_nuc)$	$\mu\text{M}\cdot\mu\text{m}\cdot\text{s}^{-1}$
I	inward current density	<input type="checkbox"/>	0.0	$\text{pA}\cdot\mu\text{m}^{-2}$
netValence	net charge valence	<input type="checkbox"/>	1.0	1
kfl	user defined	<input type="checkbox"/>	0.0	$\mu\text{m}\cdot\text{s}^{-1}$
RanC_cyt	Species Concentration	<input checked="" type="checkbox"/>	Variable	μM
RanC_nuc	Species Concentration	<input checked="" type="checkbox"/>	Variable	μM

Annotation and Pathway Links

Linked Pathway Object(s):

The screenshot displays the BioModel2 software interface. On the left is a tree view of the model structure. The main window shows a reaction diagram with compartments Cyt, NM, and Nuc. A reaction labeled 'flux0' is highlighted with a blue box. Below the diagram is the 'Object Properties' panel for the selected reaction, showing its name as 'flux0', kinetic type as 'General Flux Density', and units as $\mu\text{M}\cdot\mu\text{m/s}$. At the bottom, a table lists model parameters, with the 'kfl' parameter highlighted in yellow.

Name	Description	Global	Expression	Units
netValence	net charge valence	<input type="checkbox"/>	1.0	1
kfl	user defined	<input type="checkbox"/>	2.0	$\mu\text{M}\cdot\text{s}^{-1}$
RanC_cyt	Species Concentration	<input checked="" type="checkbox"/>	Variable	μM
RanC_nuc	Species Concentration	<input checked="" type="checkbox"/>	Variable	μM

With the flux icon still selected, on the Object Properties tab locate the user defined parameter "Kfl". Double click and type in the value of 2.0 in the "Expression" column.

The screenshot shows a software interface for modeling biological systems. On the left is a tree view of the model structure. The main area displays a reaction diagram with compartments Cyt, NM, and Nuc. A reaction node 'r0' is highlighted with a blue box. Below the diagram, the 'Object Properties' window is open, showing the reaction name 'r0' and a table of parameters. The 'Kf' parameter is highlighted in yellow, with its value set to 1.0.

Name	Description	Global	Expression	Units
Kf	forward rate constant	<input type="checkbox"/>	1.0	s ⁻¹
Kr	reverse rate constant	<input type="checkbox"/>	0.0	s ⁻¹ .μM ⁻¹

In order to define the forward rate constant, Kf, select the reaction node. On the Object Properties tab, locate the "forward rate constant" parameter and double click the Expression column. Type in the value 1.0 for this tutorial.

The screenshot shows the BioModel2 software interface. On the left is a tree view of the model structure, including 'Physiology', 'Reaction Diagram', 'Reactions (2)', 'Structures (5)', 'Species (4)', 'Molecules (0)', and 'Observables (0)'. The main window displays a reaction diagram with compartments 'Cyt', 'NM', and 'Nuc'. A reaction node 'r0' is highlighted with a blue box. Below the diagram is the 'Object Properties' tab, which is also highlighted with a blue box. It shows the reaction name 'r0', 'Reversible' checked, and 'Kinetic Type' set to 'Mass Action [μM/s]'. A table below lists the reaction parameters:

Name	Description	Global	Expression	Units
Kf	forward rate constant	<input type="checkbox"/>	1.0	s ⁻¹
Kr	reverse rate constant	<input type="checkbox"/>	1000.00	s ⁻¹ ·μM ⁻¹

With the reaction node still selected, define the reverse rate constant, Kr. On the Object Properties tab, locate the “reverse rate constant”. Double click the “Expression” column, and type in the value 1000.0 for this tutorial.

The screenshot shows a software interface with a menu bar (File, Server, Window, Tools, Help) and a left sidebar containing a tree view of a model named 'BioModel2'. The tree view includes 'Physiology' with sub-items: 'Reaction Diagram', 'Reactions (2)', 'Structures (5)', 'Species (4)', 'Molecules (0)', and 'Observables (0)'. Below this is 'Applications (0)'. The main window has a tabbed interface with 'Reaction Diagram' selected. A blue box highlights the tabs: 'Reactions', 'Structures', 'Species', 'Molecules', and 'Observables'. A blue arrow points from the 'Reactions' tab to a table. The table has columns for 'Name', 'Type', and 'Electrical (Membrane Polarity)'. The rows are:

Name	Type	Electrical (Membrane Polarity)
NUC	Compartment	
EC	Compartment	
Cyt	Compartment	
PM	Membrane	unspecified compartment (+) unspecified compartment (-)
NM	Membrane	unspecified compartment (+) unspecified compartment (-)

Below the table are buttons for 'New Compartment', 'New Membrane', 'Delete', and 'Pathway Links', along with a search field. Below that are tabs for 'Object Properties', 'Problems (0 Errors, 0 Warnings)', and 'Database File Info'. The 'Object Properties' tab is active, showing a form for editing the 'NM' structure. The form includes fields for 'Structure Name' (NM), 'Size Variable Name' (NM [μm^2]), and 'Voltage Variable Name' (Voltage_NM [mV]). There are also dropdown menus for 'Positive (inside feature)' and 'Negative (outside feature)'. Below these fields is a section titled 'Electrophysiology' with explanatory text: 'membrane voltage: "Voltage_NM" = voltage(inside (+) compartment) - voltage(outside (-) compartment)' and 'inward currents: from compartment "outside (-) compartment" into compartment "inside (+) compartment"'. A note follows: 'Note: VCell reactions and fluxes specify inward currents (- to +) rather than conventional currents (+ to -)'. At the bottom is an 'Annotation' field.

Use the Reactions, Structures, Species, Molecules or Observables tabs to look up specific details of the physiology shown in a table view as opposed to the Reaction Diagram. The table view is useful when working with large and complicated models.

The screenshot displays the MultiAppRanModel software interface. The left sidebar shows a hierarchical tree view of the model structure, including Physiology, Reaction Diagram, Reactions (2), Structures (5), Species (4), Observables (0), Application (2), Parameters, Pathway, and Scripting. A context menu is open over the 'Application' folder, showing options: 'New Application' (with a submenu), 'Expand All', and 'Collapse All'. The 'New Application' submenu is open, showing 'Deterministic', 'Stochastic', and 'Network-Free'. A blue box highlights this menu, with an arrow pointing to a text box that reads: "To create an 'Application', select Application and then right click and select 'New Application' > Deterministic, Stochastic, or Network-Free."

Below the tree view, there are tabs for 'VCell DB', 'BMBDB', 'Pathway Comm', and 'Sabio'. Under 'BioModels', there are sub-tabs for 'MathModels' and 'Geometries'. A search bar is present, and a list of biological models is shown, including 'My BioModels (ACowan) (91)', 'Shared BioModels (42)', 'Public BioModels (597)', and 'Tutorials (12)'. A 'New Application' dropdown menu is open, showing 'Deterministic', 'Stochastic', and 'Network-Free'. A blue box highlights this menu, with an arrow pointing to a text box that reads: "Alternatively, select New Application from the drop down menu and choose from Deterministic, Stochastic, or Network-Free."

At the bottom of the interface, a text box reads: "For this tutorial, please create a Deterministic Application."

The Virtual Cell

Home Download **Support** Publications

Support

VCell Open Discussion Forum

For all questions related to VCell use.

VCell Help

For all personal user issues relating to connectivity, login credentials, passwords, etc.

In this tutorial, you will need to use an example neuroblastoma stack of images that is provided for you. These images are located on the VCell website (vcell.org). Navigate to Support > Tutorial Guides. Download the Neuroblastoma Stack for Tutorial and extract the files to a folder of your choice.

Tutorial Guides (pdf) for VCell

Multiple Application of a Nuclear Transport Neuroblastoma Stack for Tutorial (ver 7.0)

Rule-Based Modeling (single compartment) EGFR model (ver 6.1)

Rule-Based Modeling (multiple compartments with transport and anchoring) Ran model (ver 6.1)

simple FRAP (ver 6.0)

FRAP with binding (ver 6.0)

PH-GFP Translocation (ver 6.0)

Quick Start Guides

Quick Start Guide (6.0)

Rule-based Modeling Guide VCell 6.1 (single compartment)

Rule-based Modeling Guide VCell 6.1 (compartmental/spatial)



The screenshot shows the BioModel2 software interface. The left sidebar contains a tree view with 'Applications (1)' expanded to show 'Application0' and 'Geometry' selected. The main window has tabs for 'Geometry', 'Specifications', 'Proteins', and 'Parameter Estimation'. The 'Geometry' tab is active, showing a table with columns 'Name' and 'Value'. The table contains one row: 'Compartment'. A blue box highlights the 'Geometry' tab and the 'Geometry Definition' sub-tab. Another blue box highlights the 'Add Geometry' dropdown menu, which is open, showing 'New...' and 'Open from...' options. A third blue box highlights the 'Applications (1)' section in the sidebar. A text box at the bottom right provides instructions on how to create a new geometry.

Name	Value
Compartment	

Once you have created an “Application”, you can expand the submenu and select the Application you are working with. When an “Application” is selected, the “Geometry Definition” tab will be accessible.

From there, navigate to “Add Geometry” and either create a “New” geometry, or “Open from”.

In this instance, please select “New”.

The screenshot shows the BioModel2 software interface. The main window displays the 'Geometry' tab, with a table showing the current domain structure:

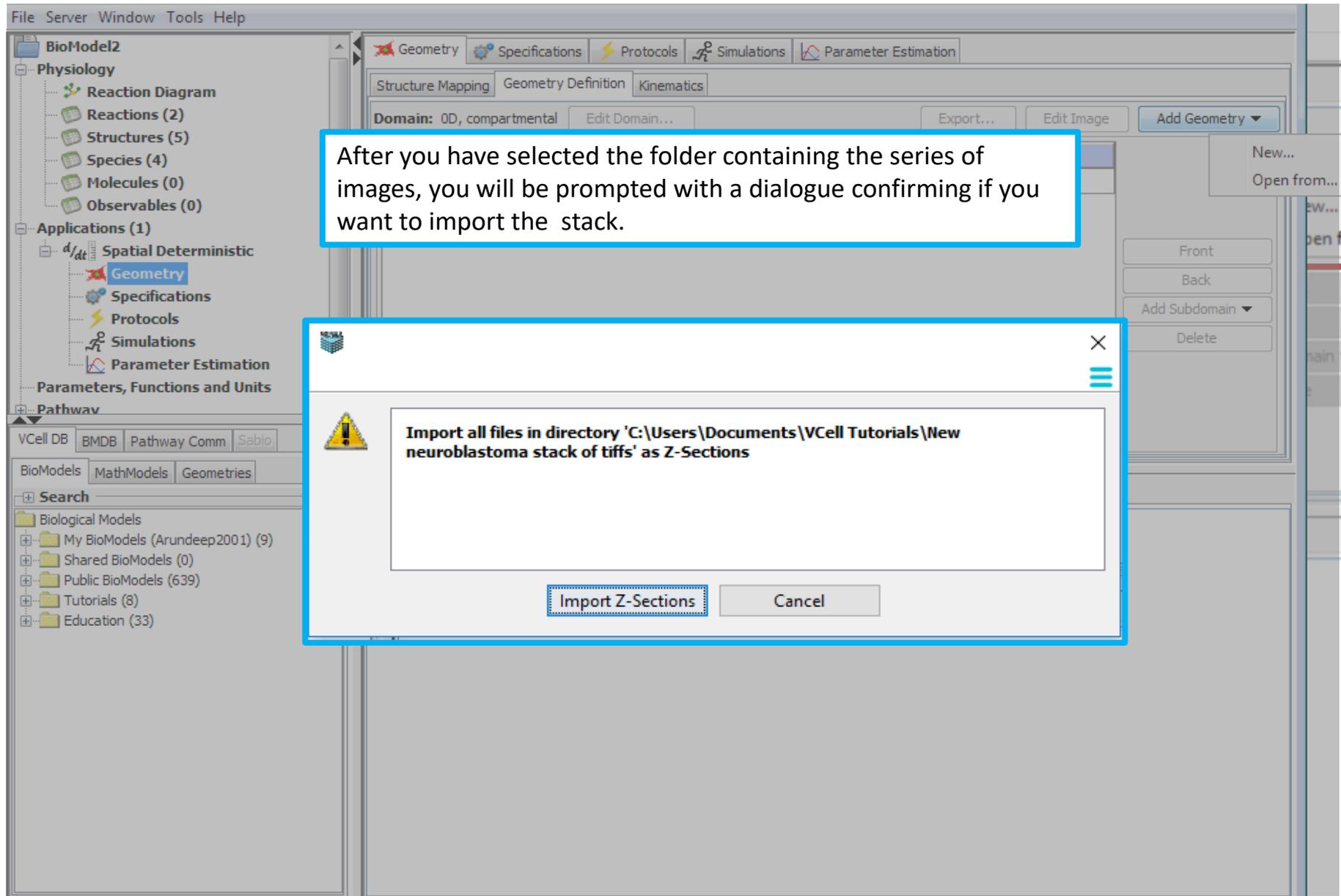
Name	Value
Compartment	

A dialog box titled 'Choose new geometry type to create' is open in the foreground. It contains a list of geometry types:

- Analytic Equations (1D)
- Analytic Equations (2D)
- Analytic Equations (3D)
- Image based (import from file, zip or directory)**
- Mesh based (import from STL file)
- New Blank Image Canvas
- Constructed Solid Geometry (3D)

The 'Image based (import from file, zip or directory)' option is highlighted with a blue box. Below the list are 'OK' and 'Cancel' buttons. An arrow points from a text box at the bottom to the 'OK' button.

Select "Image based (import images from file, zip or directory)" and press "OK", to navigate

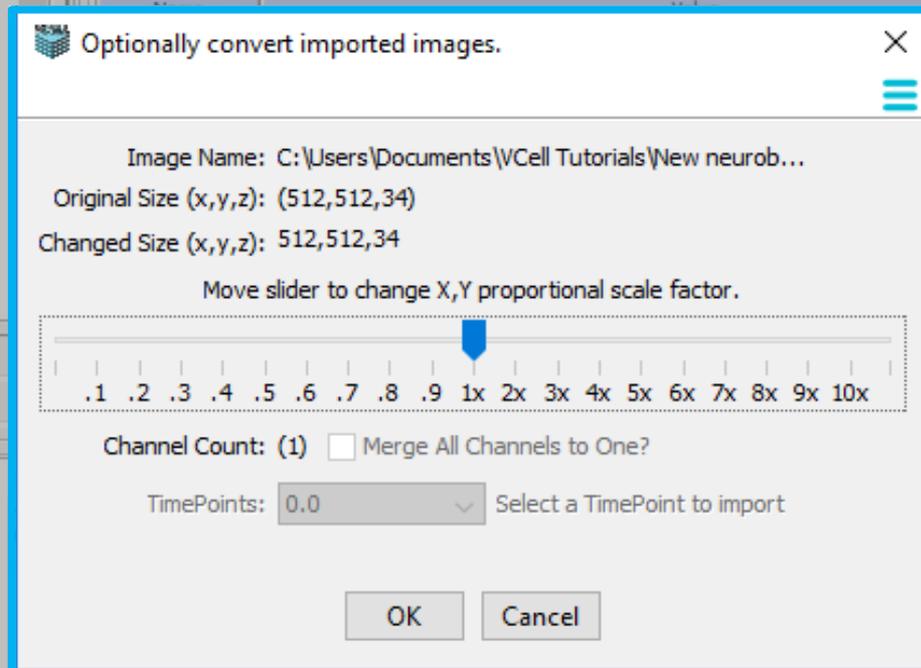


The screenshot shows the VCell software interface. The left sidebar displays a tree view of the model structure, including folders for Physiology, Applications, and Pathway. The main window shows the Geometry tab with various options like Structure Mapping, Geometry Definition, and Kinematics. A dialog box is open in the foreground, prompting the user to import a stack of TIFF files as Z-Sections.

After you have selected the folder containing the series of images, you will be prompted with a dialogue confirming if you want to import the stack.

Import all files in directory 'C:\Users\Documents\VCell Tutorials\New neuroblastoma stack of tiffs' as Z-Sections

To adjust the resolution of imported images, use your cursor to adjust the slider to the desired scale factor of the image sizes, and then click “OK”. Images can either be reduced or enlarged according to the original size.

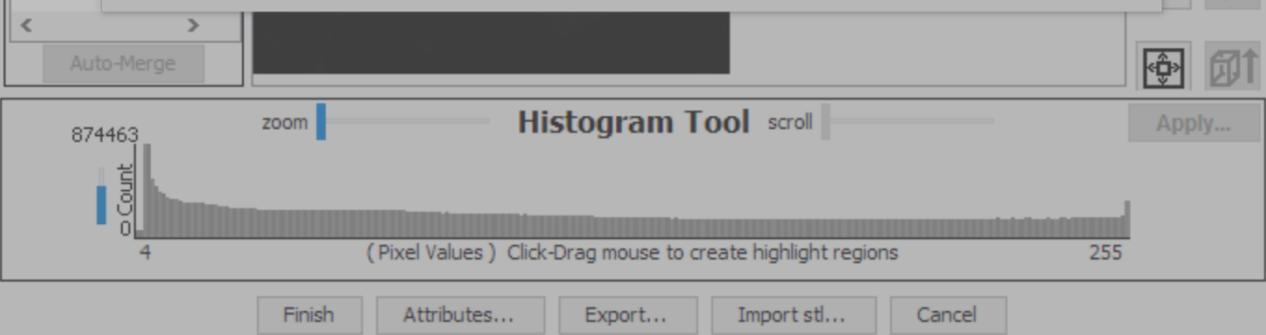


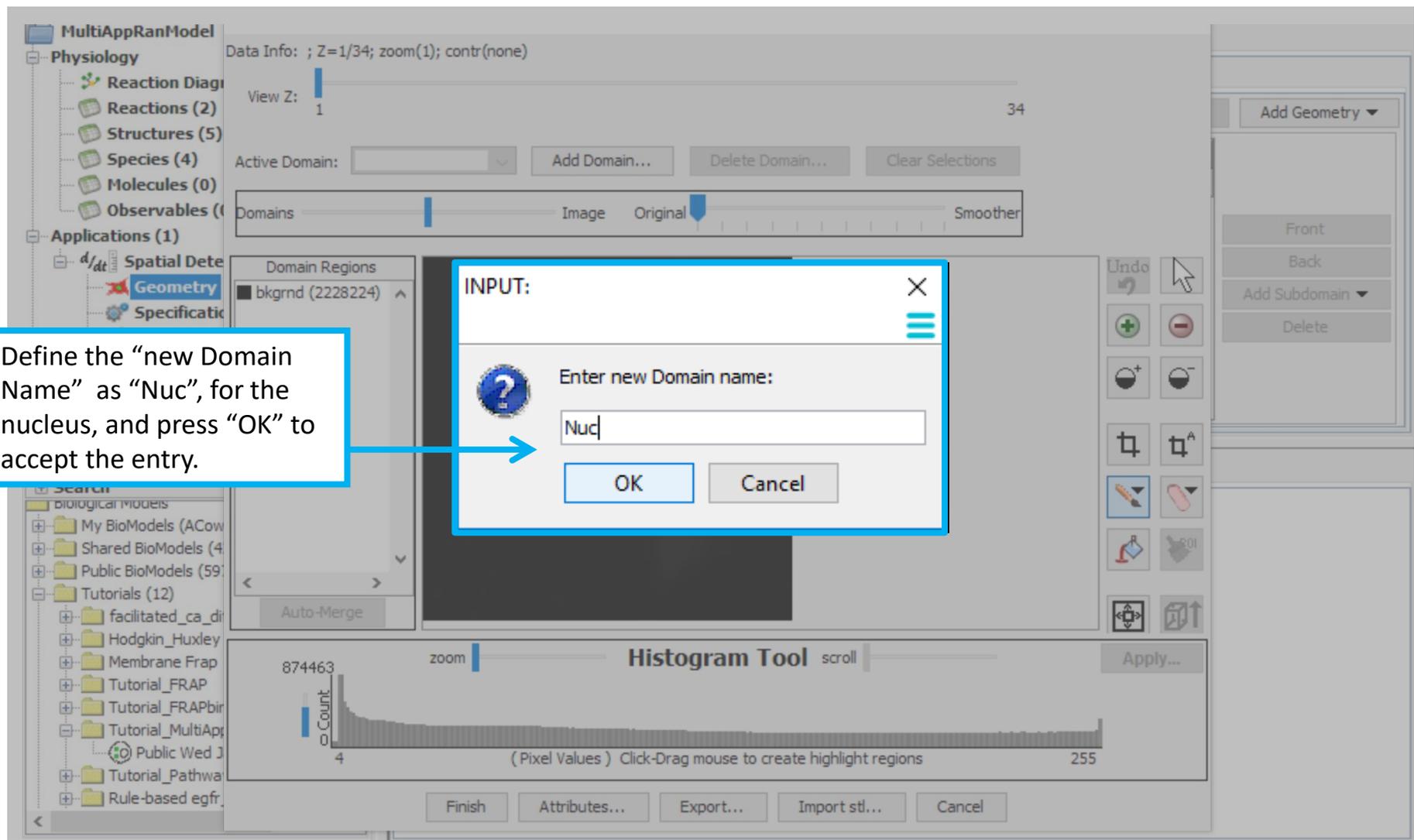
In this tutorial, manually segment the image by selecting "1. Add empty Domain".

Image Editor

 **The current image contains 253 distinct non-zero pixel values. Segmenting an image begins with defining Domain(s) manually or automatically. Editing tools are used to create/edit more Domains. Choose an action:**

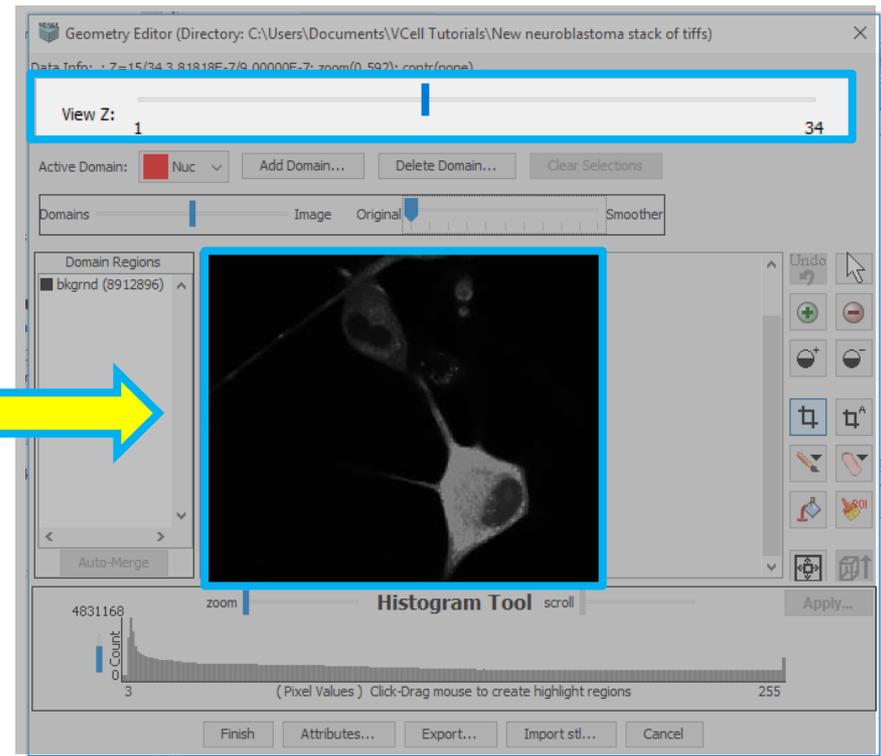
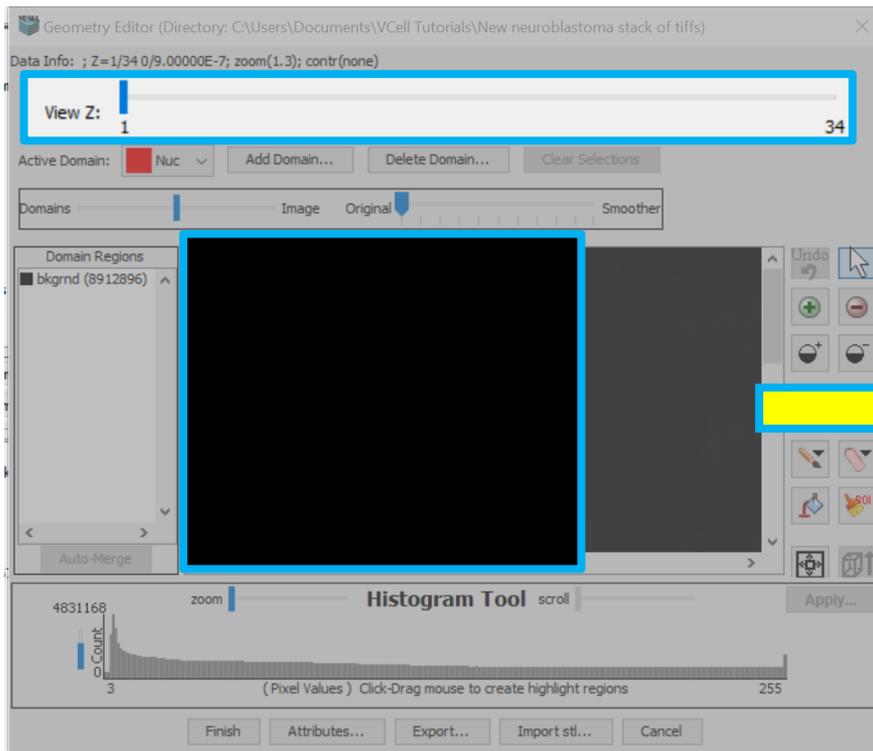
- 1. Add an 'empty' Domain to begin segmenting manually.**
- 2. Pre-Segmented (add Domains for every distinct pixel value).**

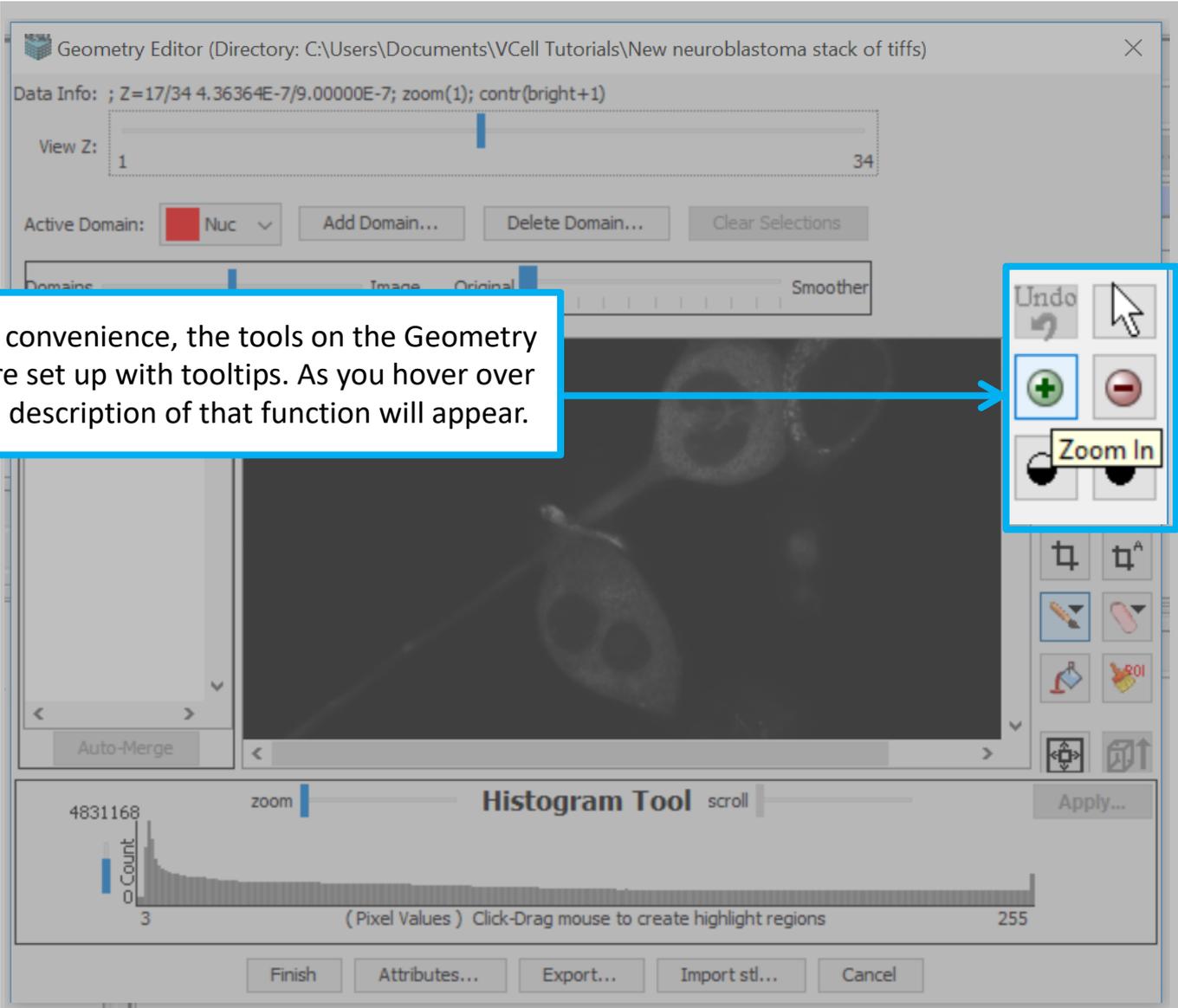




Define the “new Domain Name” as “Nuc”, for the nucleus, and press “OK” to accept the entry.

After importing the images, be sure to adjust the z plane so you can see your cells. The stack defaults to the first z level therefore you may not be able to see your cells until you focus through the stack.





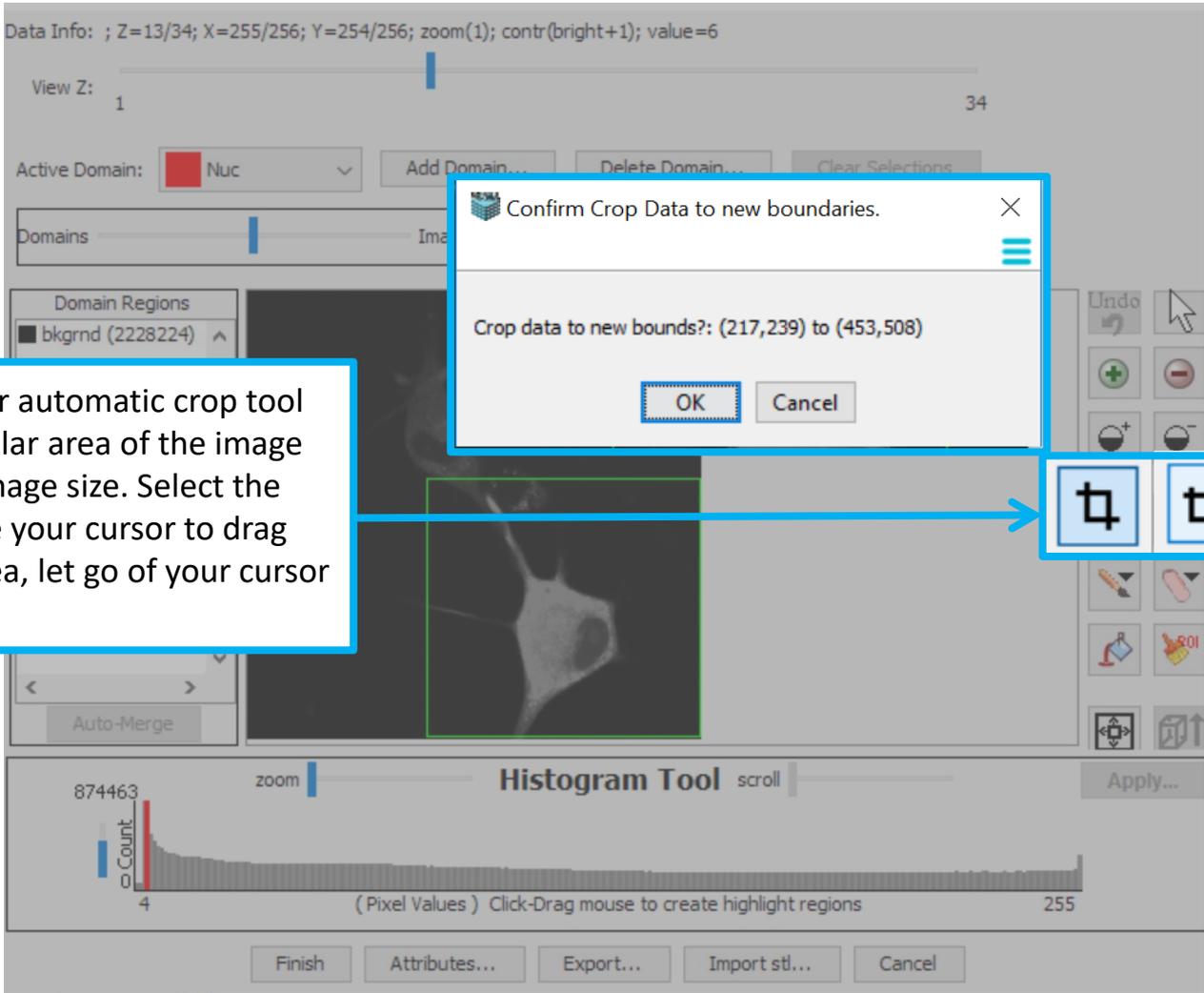
For your convenience, the tools on the Geometry Editor are set up with tooltips. As you hover over a tool, a description of that function will appear.

Undo

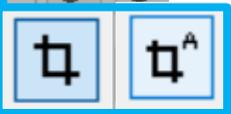
+

-

Zoom In



Use the manual or automatic crop tool to select a particular area of the image and reduce the image size. Select the crop tool, and use your cursor to drag over a specific area, let go of your cursor and click "OK".



Active Domain: Nuc

Domains

Domain Regions

- bkgrnd (769692)

Auto-Merge

Undo

Zoom In

Zoom Out

Zoom In

308492 zoom Histogram Tool scroll 255

o Count

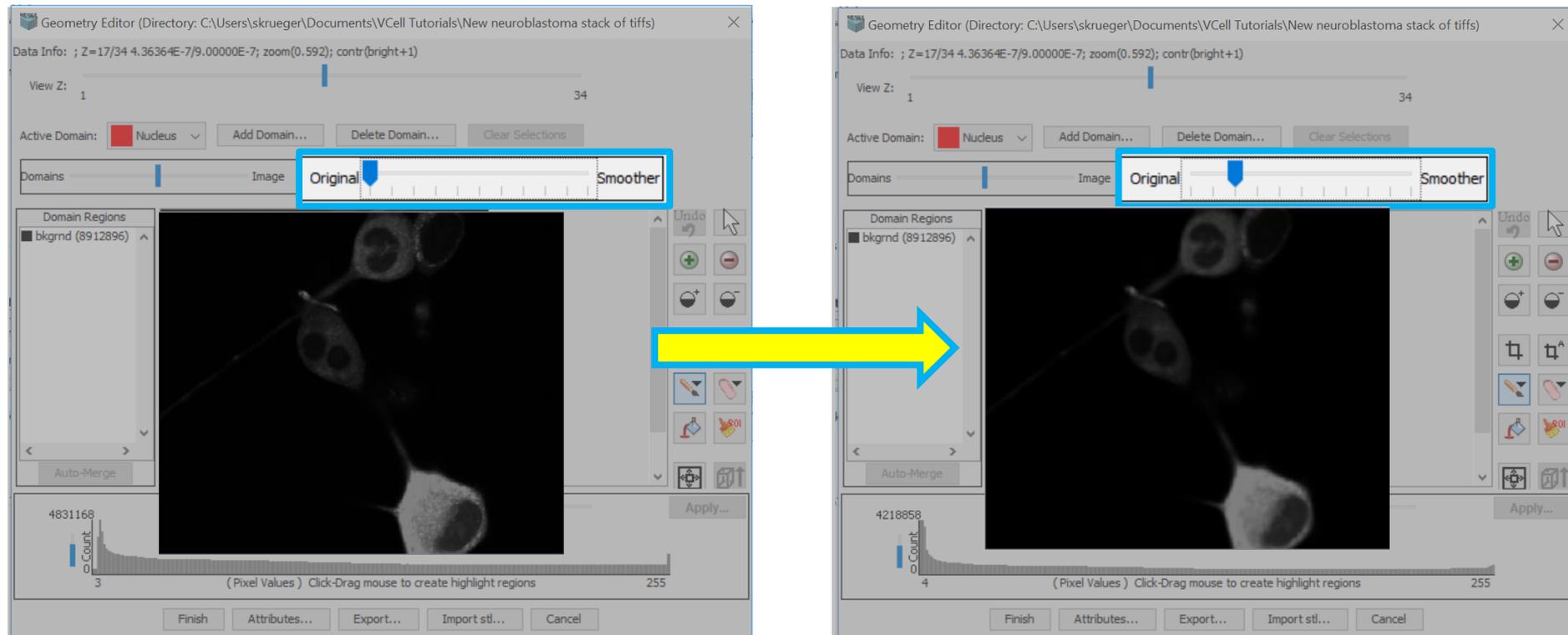
(Pixel Values) Click-Drag mouse to create highlight regions

Finish Attributes... Export... Import st... Cancel

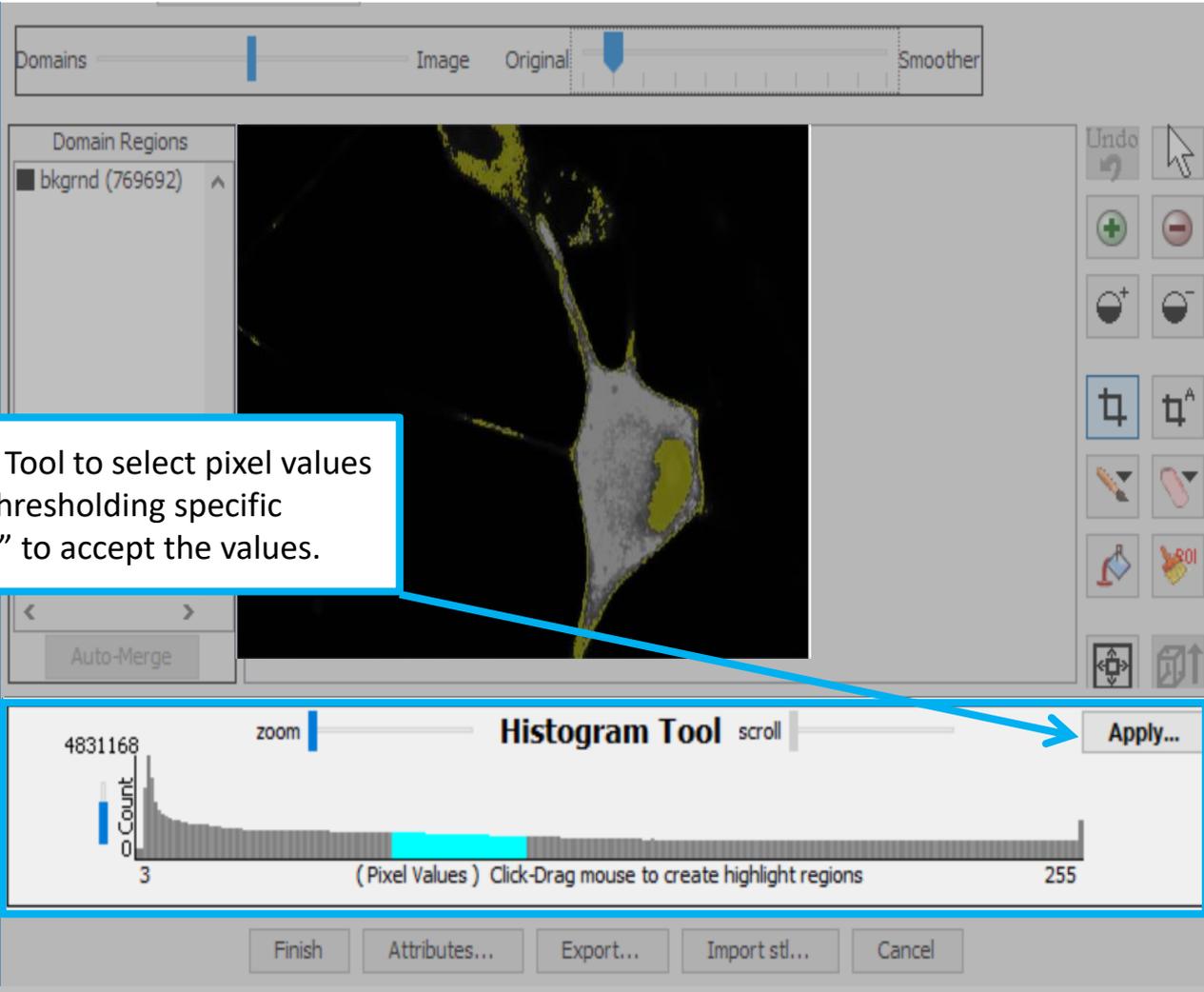
Use the zoom tool to increase, zoom in, or decrease, zoom out, the image magnification.

The image shows a software interface for image processing. At the top, there's a dropdown menu for 'Active Domain' set to 'Nuc'. Below it is a 'Domains' slider. On the left, a 'Domain Regions' panel lists 'bkgrnd (769692)'. The main area contains two grayscale images of a cell, with blue arrows indicating zooming in and out. To the right, a toolbar includes 'Zoom In' (+) and 'Zoom Out' (-) buttons, both highlighted with a blue box and a 'Zoom In' label. Below the images is a 'Histogram Tool' window showing a histogram of pixel values from 5 to 255, with a 'zoom' slider and an 'Apply...' button. At the bottom, there are buttons for 'Finish', 'Attributes...', 'Export...', 'Import st...', and 'Cancel'.

In order to reduce noise in the images, you can apply an averaging filter to the stack.

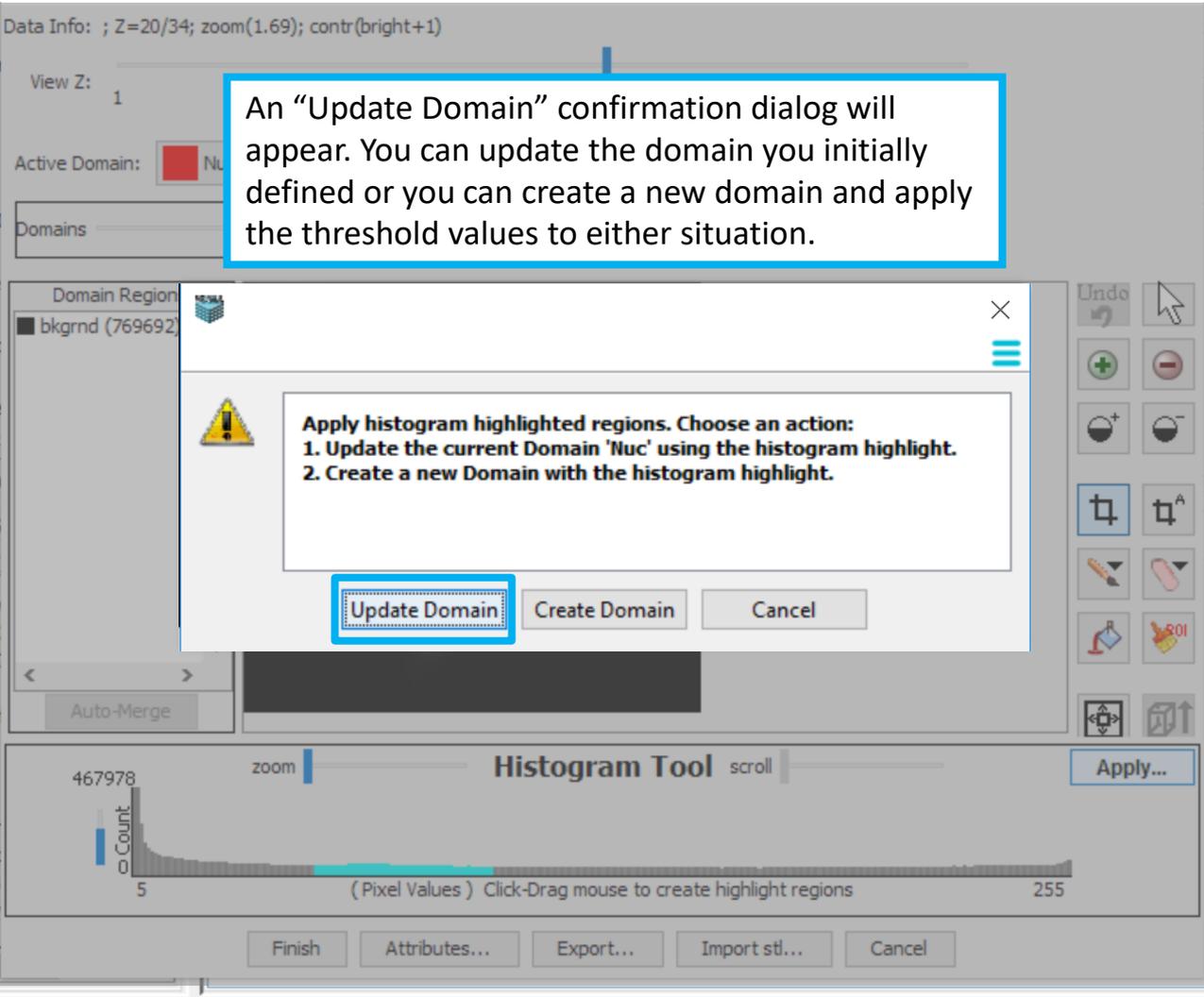


With the Averaging Filter, each pixel and its immediate neighbor's intensity values are added together and the sum is divided by the number of neighbors. For example, in a 2-D image, each pixel has 8 surrounding neighbors. The 9 values are added together and divided by 9 and that value replaces the original pixel value.

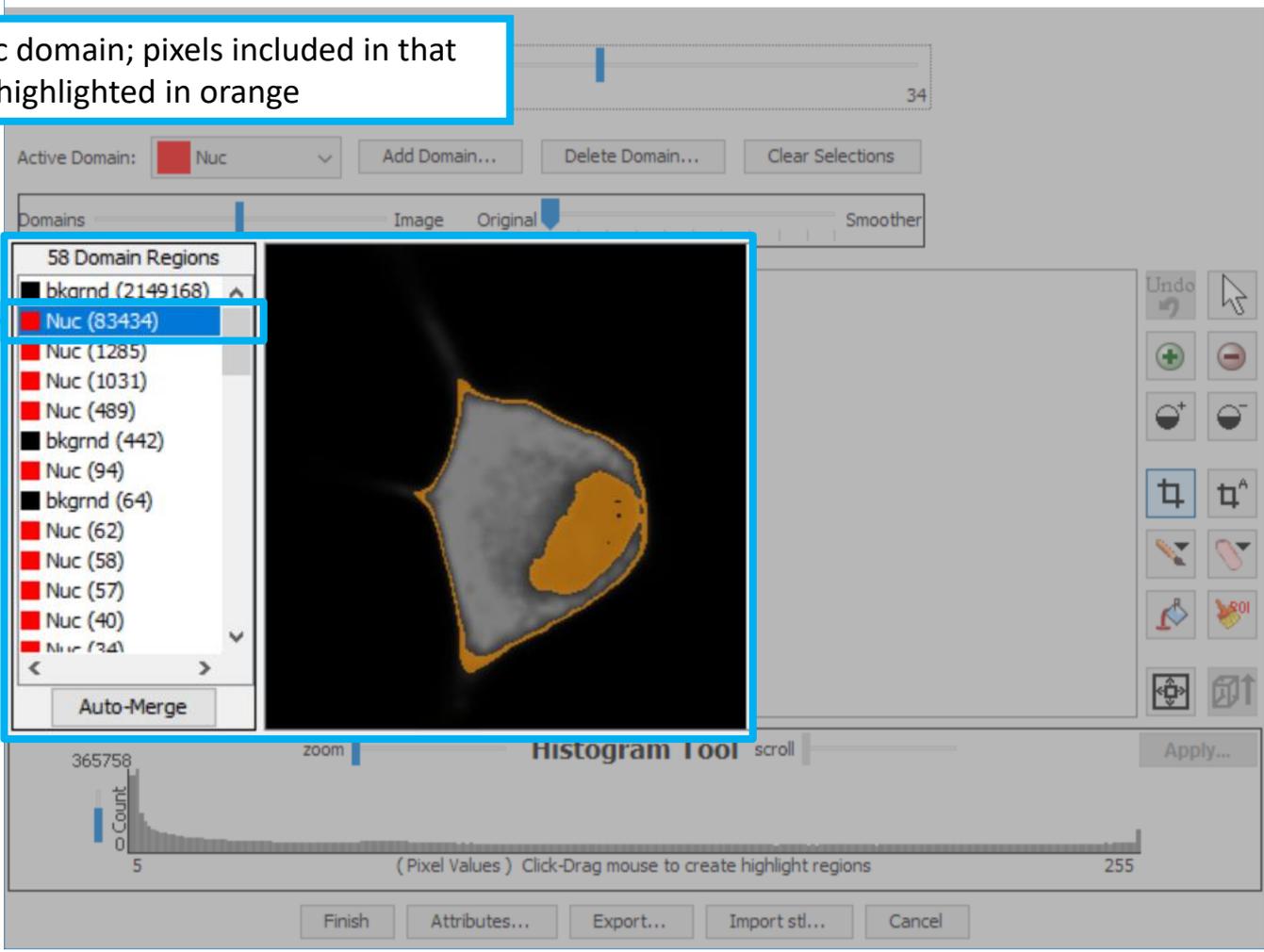


Use the Histogram Tool to select pixel values in your image for thresholding specific regions. Hit "Apply" to accept the values.

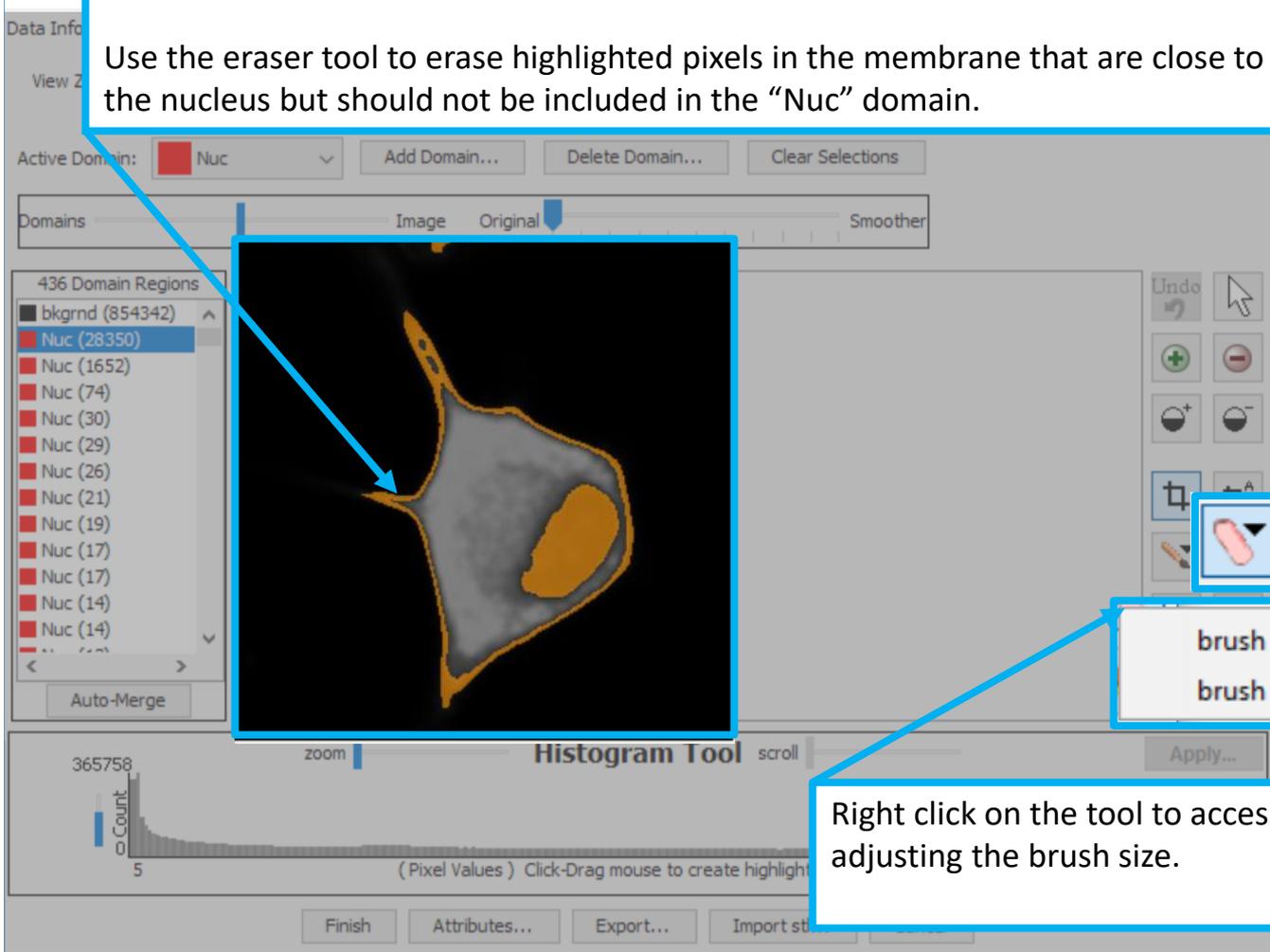




Click on the Nuc domain; pixels included in that domain will be highlighted in orange



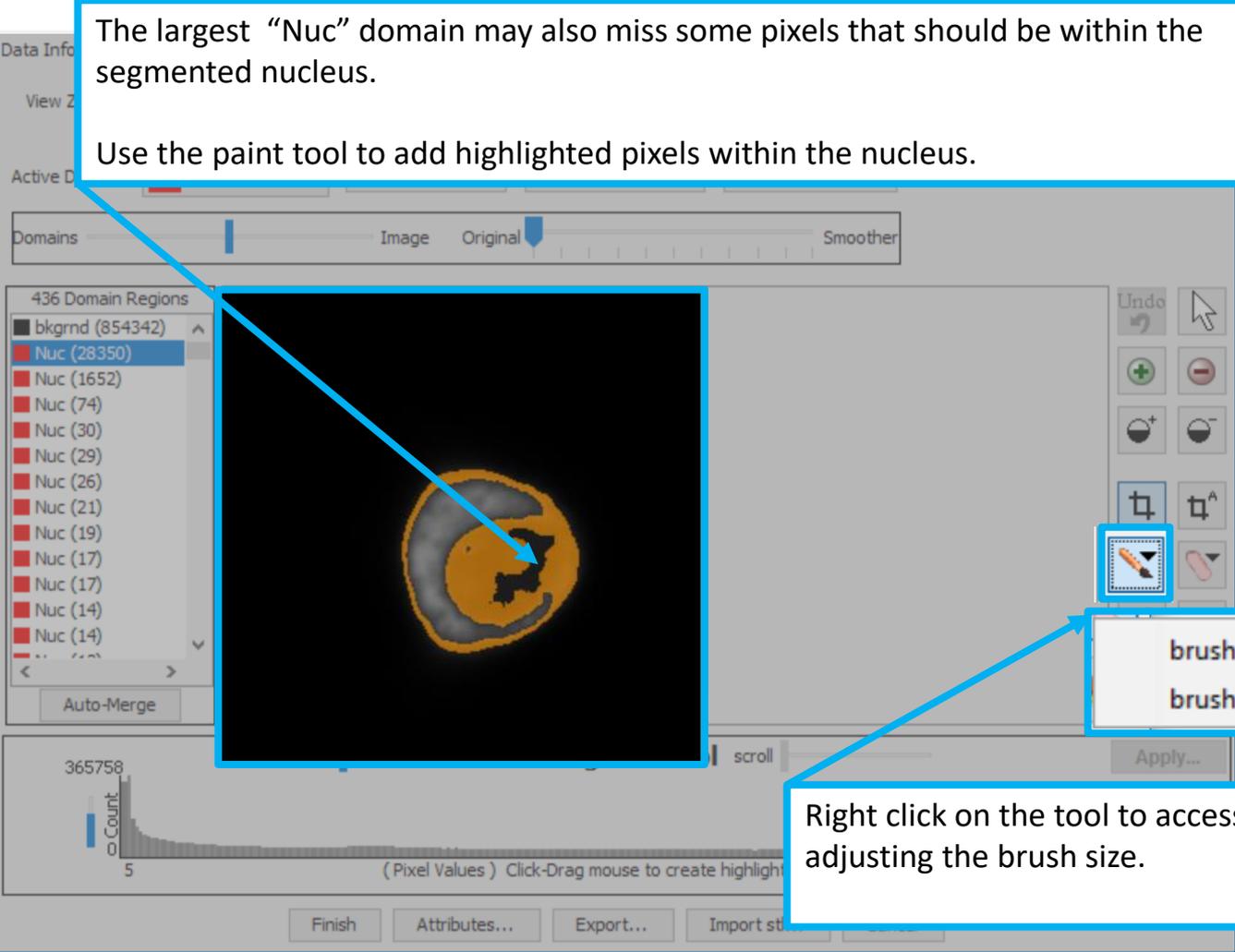
The largest "Nuc" domain includes pixels that are outside of the actual nucleus.
Use the eraser tool to erase highlighted pixels in the membrane that are close to the nucleus but should not be included in the "Nuc" domain.



brush size manual...
brush size click/drag...

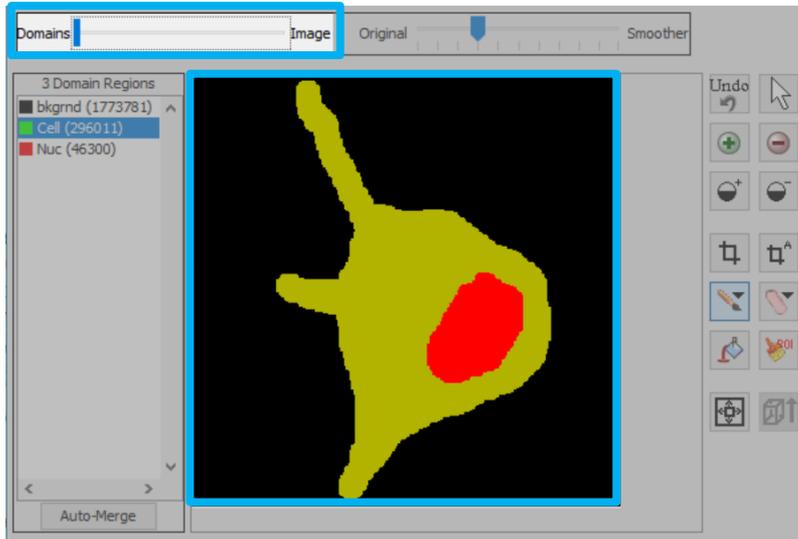
Right click on the tool to access the menu for adjusting the brush size.

The largest “Nuc” domain may also miss some pixels that should be within the segmented nucleus.
Use the paint tool to add highlighted pixels within the nucleus.



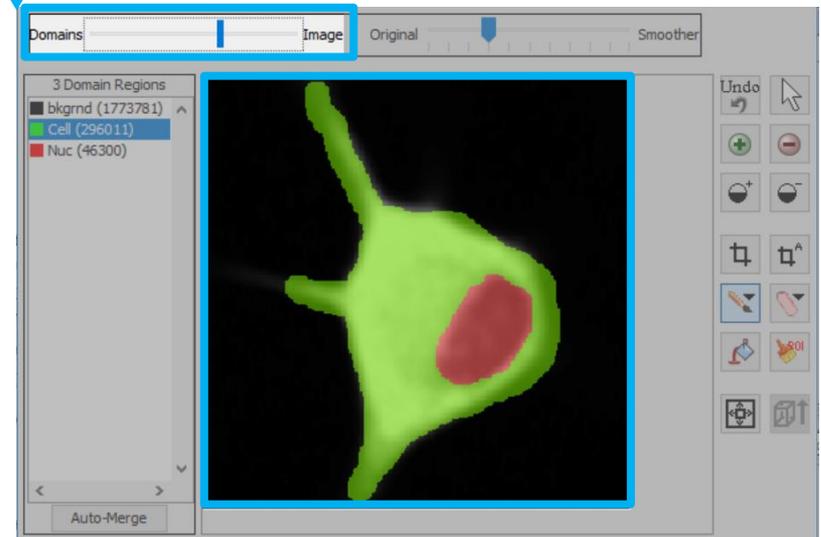
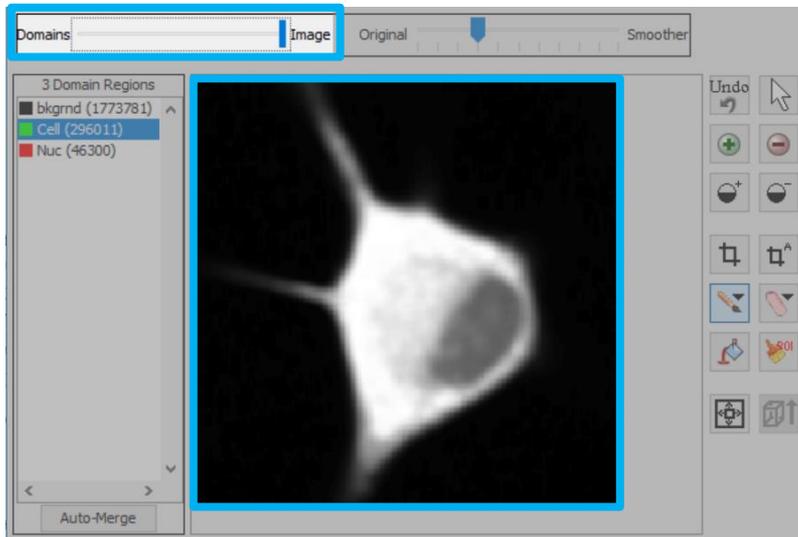
brush size manual...
brush size click/drag...

Right click on the tool to access the menu for adjusting the brush size.

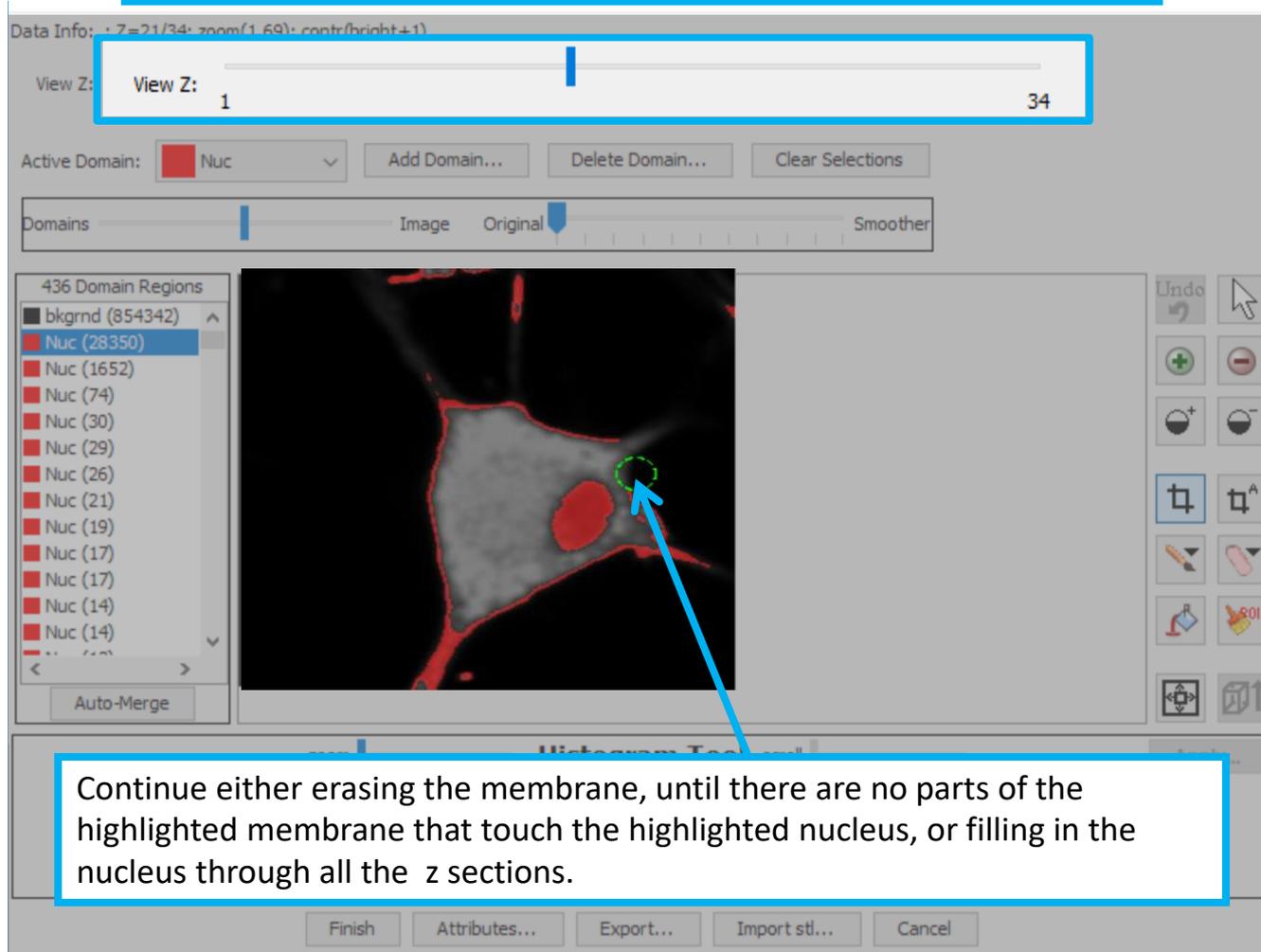


Use the Domains to Image display slider to adjust the way your image is displayed. This can show the image as segmented domains, the image only, or a overlay of the two.

This tool is helpful for visualizing your cell while defining the domains.

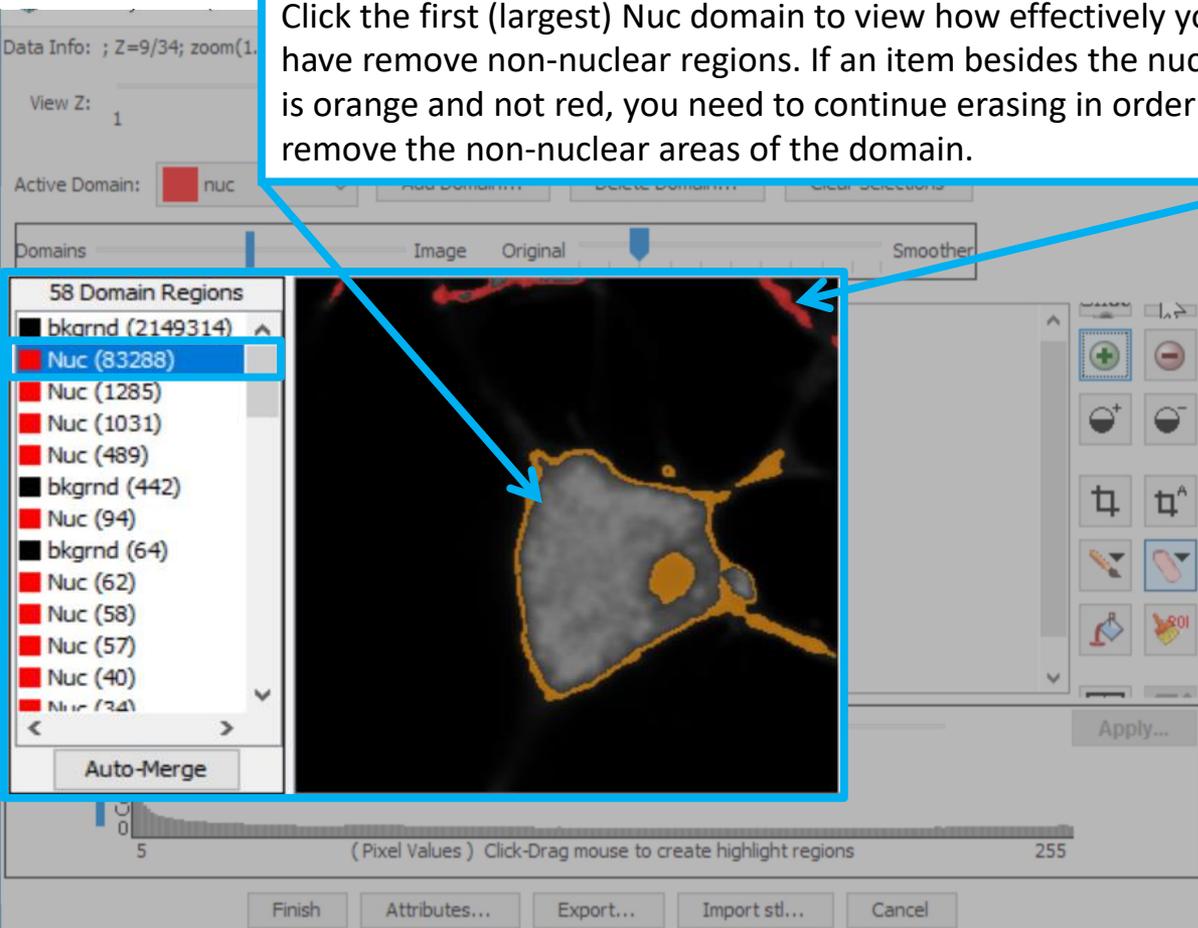


Scroll through the Z slider to view more slices in which the nucleus and membrane are in close proximity or where you need to fill in regions within the nucleus.



Continue either erasing the membrane, until there are no parts of the highlighted membrane that touch the highlighted nucleus, or filling in the nucleus through all the z sections.

Click the first (largest) Nuc domain to view how effectively you have remove non-nuclear regions. If an item besides the nucleus is orange and not red, you need to continue erasing in order to remove the non-nuclear areas of the domain.



The screenshot displays a software interface with a central image showing a cell with a nucleus. The interface includes a 'Domains' panel on the left, a 'Pixel Values' histogram at the bottom, and various tool icons on the right. A blue box highlights the 'Domains' panel, which lists 58 domain regions. The largest region, 'Nuc (83288)', is selected and highlighted in blue. Other regions include 'bkgrnd (2149314)', 'Nuc (1285)', 'Nuc (1031)', 'Nuc (489)', 'bkgrnd (442)', 'Nuc (94)', 'bkgrnd (64)', 'Nuc (62)', 'Nuc (58)', 'Nuc (57)', 'Nuc (40)', and 'Nuc (34)'. The central image shows a cell with a nucleus, where the nucleus is red and the surrounding regions are orange. A blue arrow points from the text box to the largest 'Nuc' domain in the list, and another blue arrow points from the text box to the corresponding region in the central image.

58 Domain Regions

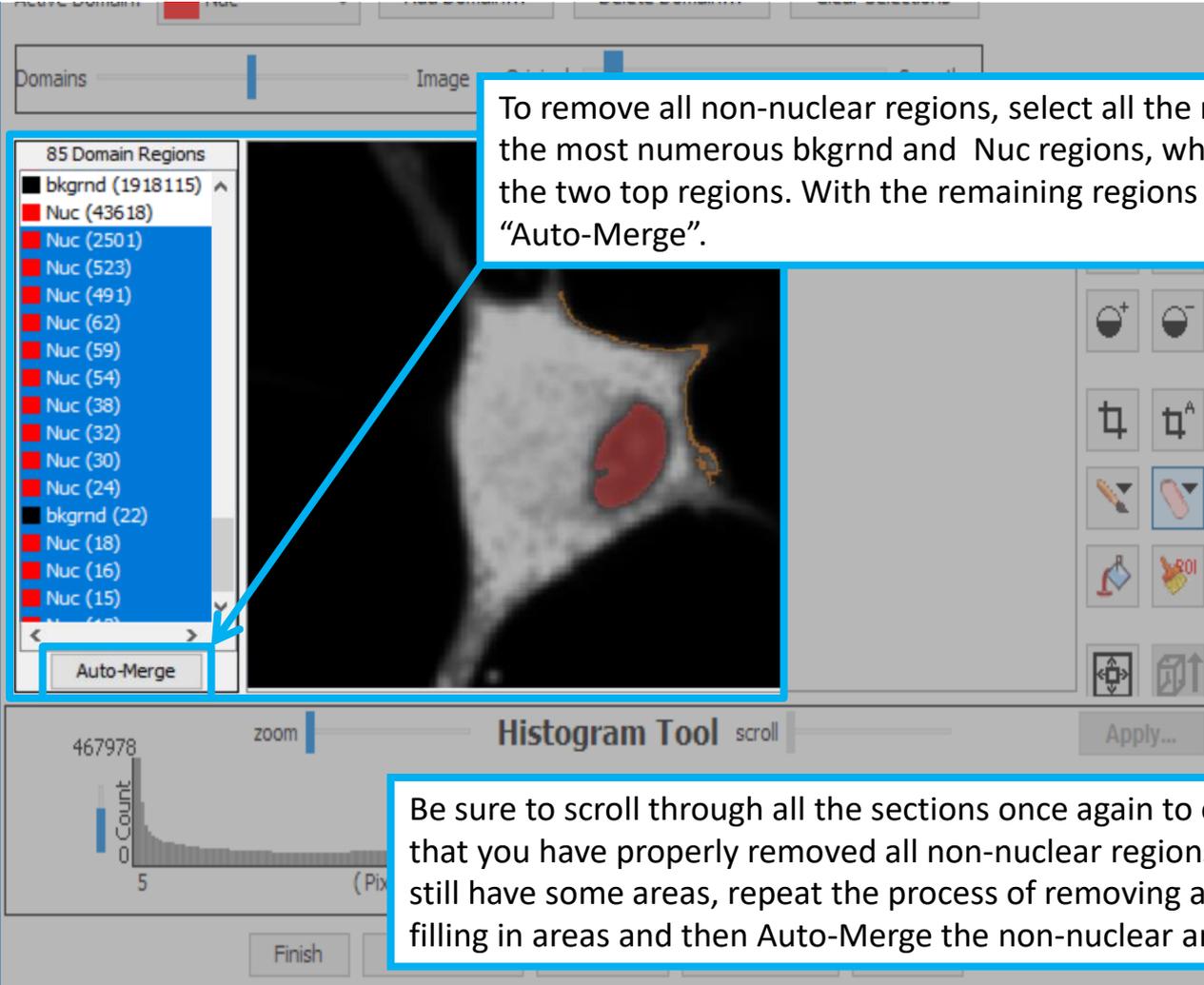
- bkgrnd (2149314)
- Nuc (83288)**
- Nuc (1285)
- Nuc (1031)
- Nuc (489)
- bkgrnd (442)
- Nuc (94)
- bkgrnd (64)
- Nuc (62)
- Nuc (58)
- Nuc (57)
- Nuc (40)
- Nuc (34)

Auto-Merge

(Pixel Values) Click-Drag mouse to create highlight regions

Apply...

Finish Attributes... Export... Import st... Cancel



The screenshot shows a software interface with a central image of a cell. On the left, a list titled "85 Domain Regions" contains entries for "bkgrnd" and "Nuc" with their respective counts. The "Nuc" entries are highlighted in blue. Below the list is an "Auto-Merge" button. On the right, there is a toolbar with various icons. At the bottom, a "Histogram Tool" window is visible, showing a histogram of pixel counts. A blue callout box points to the "Auto-Merge" button.

85 Domain Regions

- bkgrnd (1918115)
- Nuc (43618)
- Nuc (2501)
- Nuc (523)
- Nuc (491)
- Nuc (62)
- Nuc (59)
- Nuc (54)
- Nuc (38)
- Nuc (32)
- Nuc (30)
- Nuc (24)
- bkgrnd (22)
- Nuc (18)
- Nuc (16)
- Nuc (15)

Auto-Merge

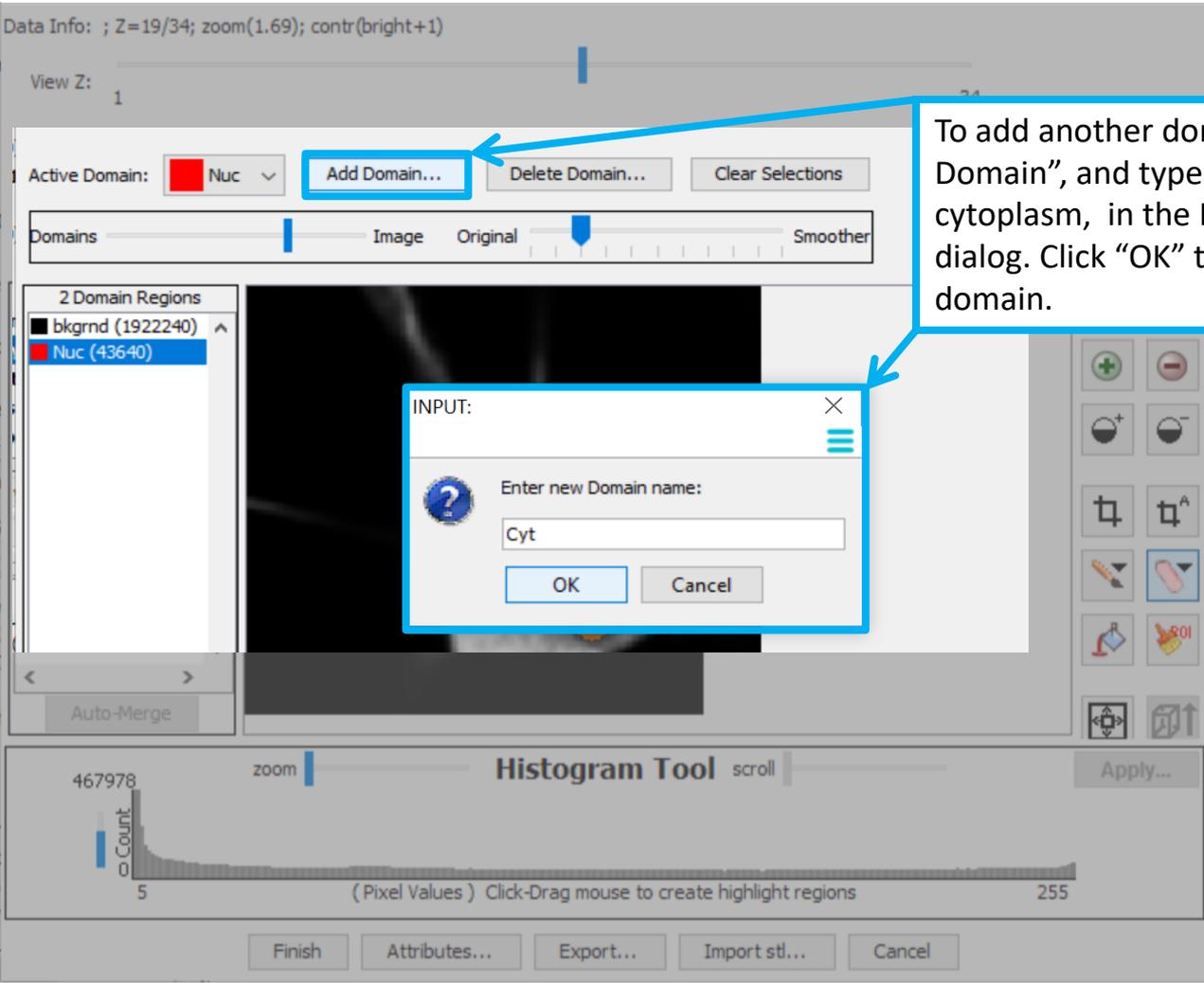
467978 zoom Histogram Tool scroll Apply...

o Count 5 (Pix)

Finish

To remove all non-nuclear regions, select all the regions except the most numerous bkgrnd and Nuc regions, which are usually the two top regions. With the remaining regions selected, click "Auto-Merge".

Be sure to scroll through all the sections once again to ensure that you have properly removed all non-nuclear regions. If you still have some areas, repeat the process of removing and/or filling in areas and then Auto-Merge the non-nuclear areas.



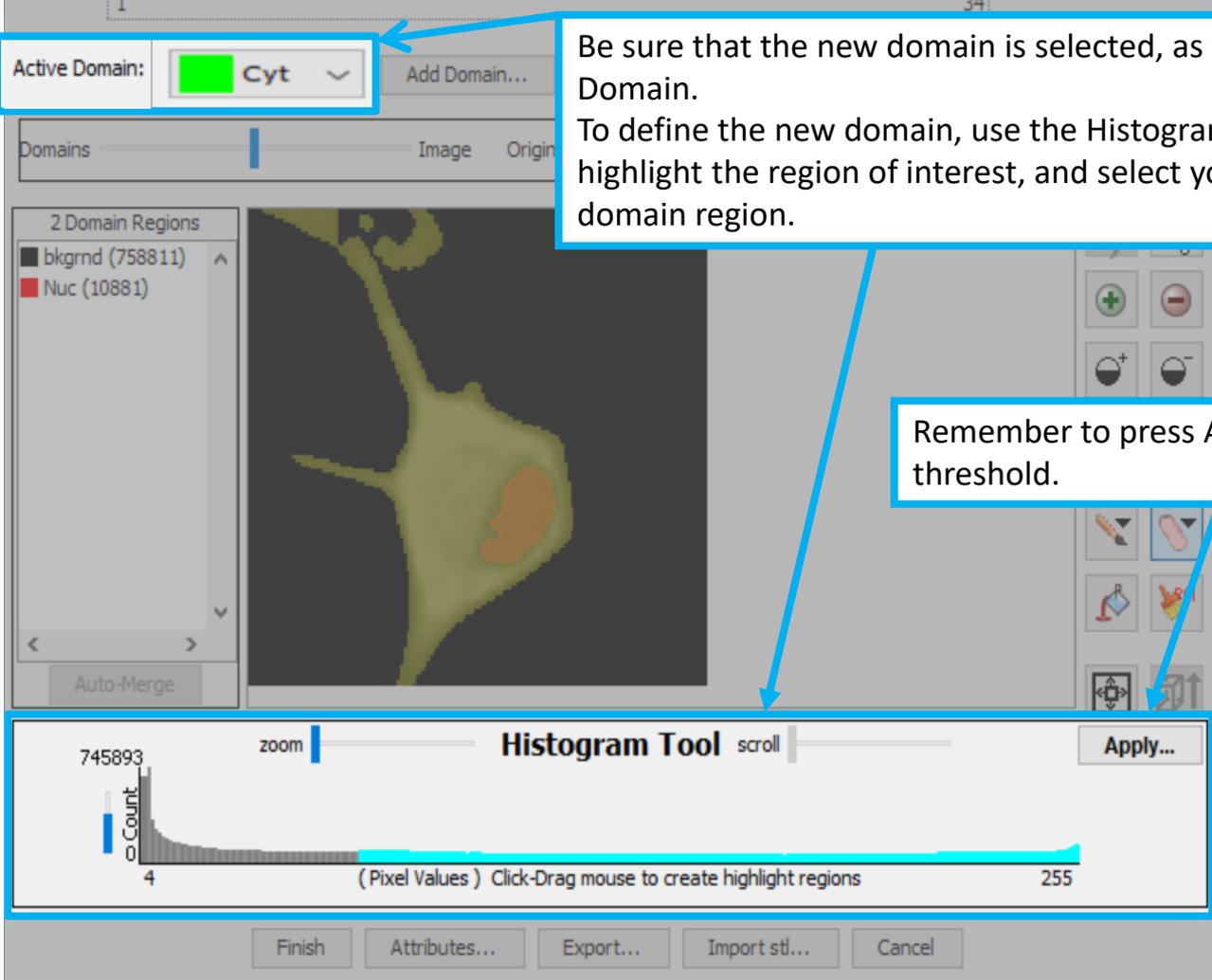
To add another domain, click “Add Domain”, and type in Cyt for cytoplasm, in the New Domain dialog. Click “OK” to accept the new domain.

INPUT: ✕

Enter new Domain name:

Cyt

OK Cancel



Be sure that the new domain is selected, as the Active Domain.
To define the new domain, use the Histogram Tool to highlight the region of interest, and select your desired domain region.

Remember to press Apply to accept the threshold.

Since you have already created the cytoplasmic domain, in the previous steps, confirm the threshold by selecting “Update Domain”.

The screenshot displays a software interface with a central dialog box. The dialog box has a yellow warning icon and contains the following text:

Apply histogram highlighted regions. Choose an action:
1. Update the current Domain 'Nuc' using the histogram highlight.
2. Create a new Domain with the histogram highlight.

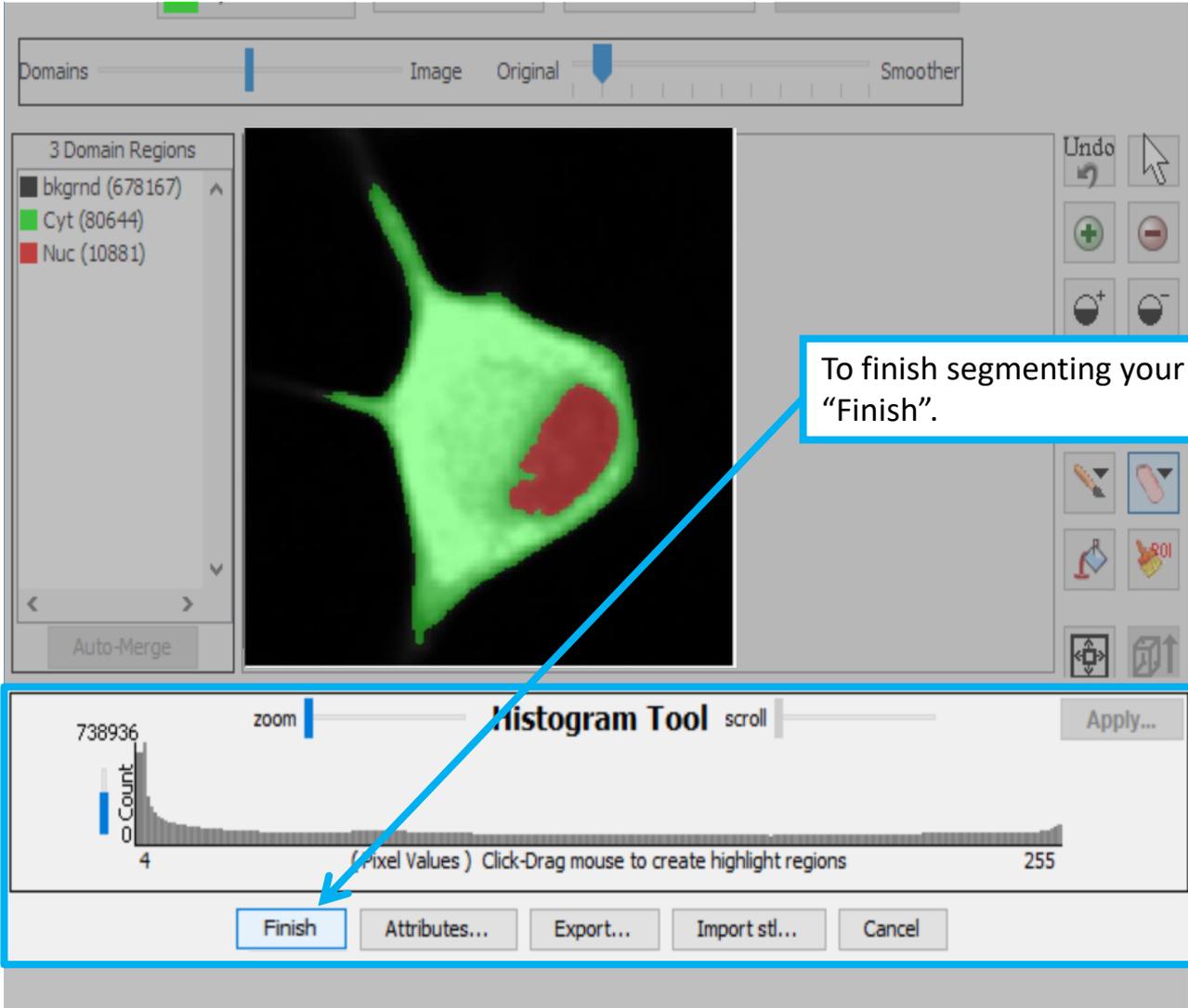
Below the text are three buttons: "Update Domain", "Create Domain", and "Cancel". The "Update Domain" button is highlighted with a blue dashed border. In the background, the software interface shows a "Histogram Tool" window with a histogram plot. The y-axis is labeled "Count" and ranges from 0 to 467978. The x-axis is labeled "(Pixel Values)" and ranges from 5 to 255. A blue highlight is visible on the histogram. The main window shows a 2D image of a cell with a green cytoplasmic domain and an orange nuclear domain. The "Active Domain" is set to "Cyt". The "Domains" list shows "bkgnd (758811)" and "Nuc (10881)".

To prevent the new domain selection from over-writing existing domain regions, click “Keep existing Domain Regions when overlapping”.

The screenshot displays a software interface with a central dialog box. The dialog box has a yellow warning icon and the text: "Some areas of the new Domain Regions overlap with existing Domain Regions." Below the text are three buttons: "Overwrite any existing Domain Regions", "Keep existing Domain Regions when overlapping", and "Cancel". A blue arrow points from the text box above to the "Keep existing Domain Regions when overlapping" button. The background interface includes a top bar with "Active Domain: Cyt", "Add Domain...", "Delete Domain...", and "Clear Selections". Below the dialog is a map view with a zoom slider and an "Auto-Merge" button. At the bottom is a "Histogram Tool" with a histogram showing pixel counts from 5 to 255, and buttons for "Finish", "Attributes...", "Export...", "Import st...", and "Cancel".

To remove all non-cytoplasmic and non-nuclear regions, select all the regions except the most numerous bkgrn, Cyt, and Nuc regions, which are usually the three top regions. With the remaining regions selected, click "Auto-Merge".

The screenshot shows the Geometry Editor interface. At the top, it displays 'Geometry Editor (Directory: C:\Users\...)' and 'Data Info: ; Z=15/34; zoom(1.69); contr(bri...'. Below this, 'View Z: 1' is shown. The 'Active Domain' is set to 'Cyt'. There are buttons for 'Add Domain...', 'Delete Domain...', and 'Clear Selections'. A 'Domains' slider is visible, along with 'Image', 'Original', and 'Smoother' options. The central part of the interface shows a cell image with green cytoplasm and a red nucleus. On the left, a '16 Domain Regions' list is shown with the following items: 'bkgrnd (1708011)', 'Cyt (213613)', 'Nuc (43640)', 'Cyt (255)', 'Cyt (118)', 'Cyt (95)', 'Cyt (62)', 'Cyt (47)', 'Cyt (11)', 'Cyt (7)', 'Cyt (6)', 'Cyt (5)', 'Cyt (4)', 'Cyt (3)', 'bkgrnd (2)', and 'Cyt (1)'. The 'Cyt (255)', 'Cyt (118)', and 'Nuc (43640)' items are highlighted in blue. Below the list is an 'Auto-Merge' button. On the right side, there is a toolbar with icons for 'Undo', 'Zoom In', 'Zoom Out', 'Pan', 'Crop', 'Lasso', 'ROI', and 'Apply...'. At the bottom, there is a histogram showing 'Count' vs '(Pixel Values)' from 5 to 255, and buttons for 'Finish', 'Attributes...', 'Export...', 'Import stl...', and 'Cancel'.



To finish segmenting your images, click "Finish".

738936 zoom | Histogram Tool | scroll | Apply...

o Count

4 (Pixel Values) Click-Drag mouse to create highlight regions 255

Finish | Attributes... | Export... | Import st... | Cancel

The screenshot displays a software interface with a warning dialog box in the foreground. The dialog box contains the following text:

Warning: some areas of image segmentation have not been assigned to a Domain. Choose an action:

1. Leave as is, unassigned areas should be treated as 'background'.
2. Cancel, back to Geometry Editor. (hint: look at 'Domain Regions' list for 'bkgrnd' entries)

At the bottom of the dialog box, there are two buttons: "Assign as default 'background'" and "Cancel". A blue arrow points from the "Assign as default 'background'" button to a text box on the right side of the image.

The background interface shows a 3D view of a segmented image with a color scale. The "Active Domain" is set to "Cyt". Below the dialog box, a "Histogram Tool" is visible, showing a histogram of pixel values with a count of 467978 and a range from 5 to 255. The histogram tool has a "scroll" bar and a "Click-Drag mouse to create highlight regions" instruction. At the bottom of the interface, there are buttons for "Finish", "Attributes...", "Export...", "Import st...", and "Cancel".

To send unassigned pixels to the background, click "Assign as default 'background'".

Data Info: ; Z=17/34; zoom(1.69); contr(bright+1)

View Z: 1

Active Domain: ■

Domains

3 Dom

- bkgnd
- Cyt (8)
- Nuc (1)

One or more Domain Regions touches the outer boundary on the XY and Z border.
Choose an option:

1. Keep as is, do not change.
2. Add empty 'background' border around outer boundary so no Domain Region touches an outer edge.

Keep as is **Add empty border** Cancel

Auto-Merge

467978

Count

5

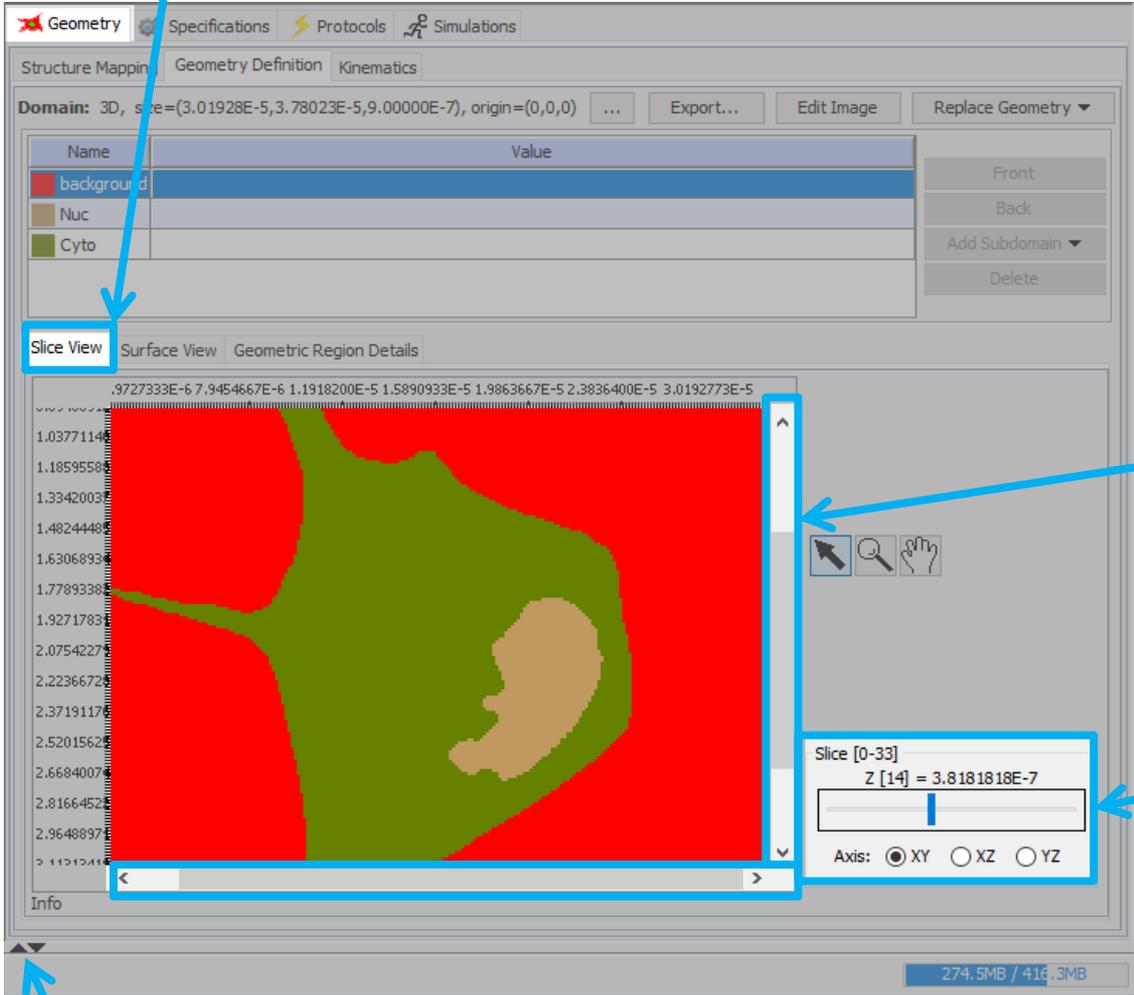
Apply...

Finish Attributes... Export... Import st... Cancel

Click "Add empty border" in order to insert a blank (background) image on top of the 1st image and below the last image in the Z stack and to pad the x,y boundary with a row of background pixels.

This is important to ensure that in your final geometry, a volume compartment intended to be enclosed by a membrane does not reach the edge (boundary) of the simulation space.

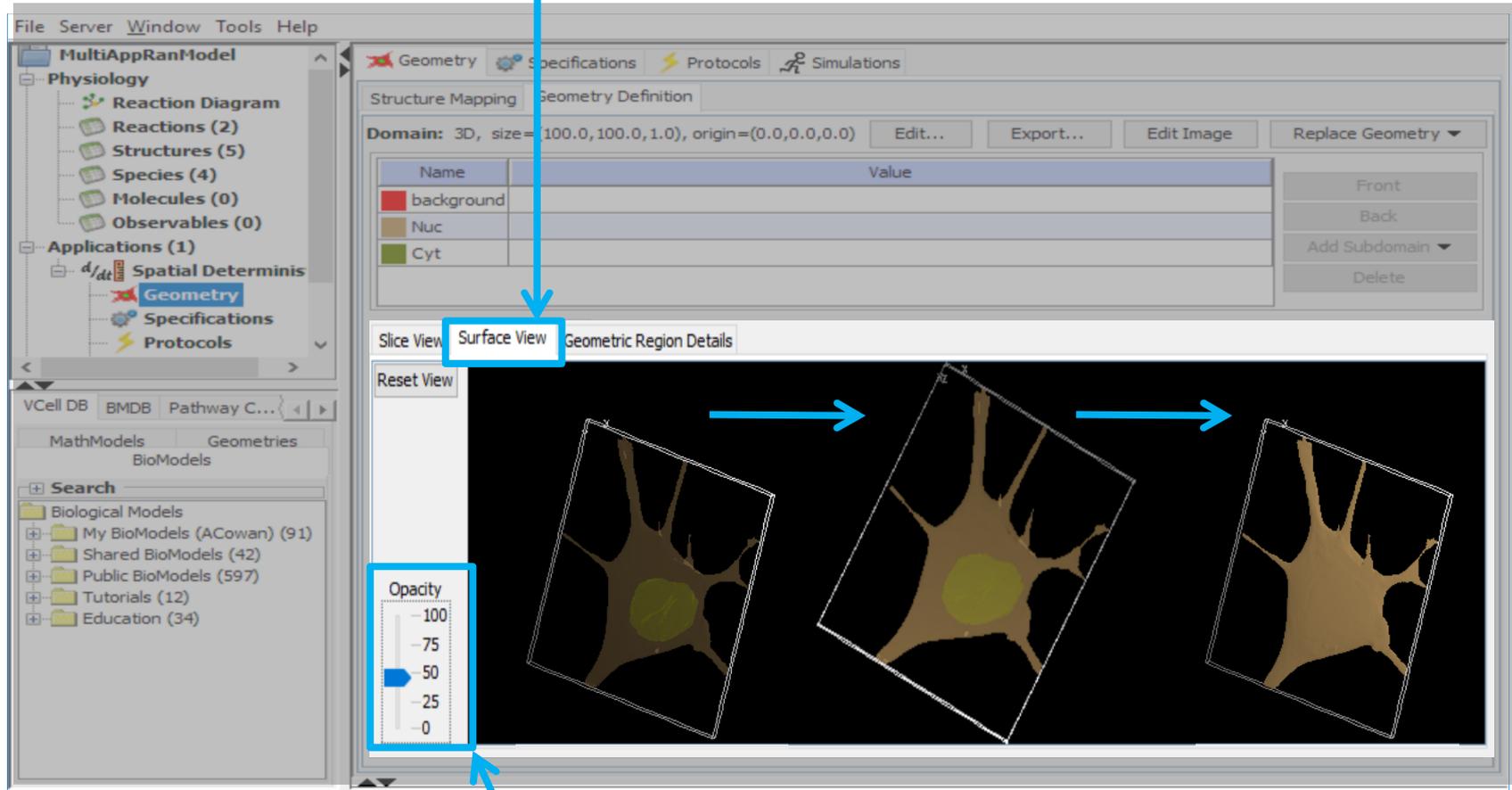
Click "Slice View" in order to view the segmented compartments by individual slices.



Be sure to adjust the scroll bars and Slice indicator to ensure you are able to see the displayed image.

Press the up or down arrow to increase or decrease the window size in order to view more or less of the displayed image.

Click "Surface View" in order to view the volume in 3-D.



Adjust the opacity, from 0 – 100%, to allow for the ease of visualizing the different domains within the volume.

The cell here looks flat because there was no Z step information in the images to use to define the domain size. This will be corrected in the next slide by adjusting the domain size for Z.

Select "Edit Domain" to alter the size of the volume you are working with.

Domain: 3D, size=(100.0,100.0,1.0), origin=(0.0,0.0,0.0)

Name	Value
background	
Nuc	
Cyt	

Geometry Size

Size X 100.0 μm Y 100.0 μm Z 26 μm

Origin X 0.0 μm Y 0.0 μm Z 0.0 μm

OK Cancel

For this tutorial, change the Z value to 26 μm . Press "OK" to accept the changes.

(Note your X and Y values may be slightly different than 100, depending on how you cropped the image).

The screenshot displays the Multi-App software interface. On the left, a sidebar shows a tree view under 'MultiAppRanModel' with categories like 'Physiology' (Reaction Diagram, Reactions (2), Structures (5), Species (4), Molecules (0), Observables (0)) and 'Applications (1)' (Spatial Determinist, Geometry, Specifications, Protocols). Below this is a search section for 'Biological Models' with folders like 'My BioModels (ACowan) (91)', 'Shared BioModels (42)', 'Public BioModels (597)', 'Tutorials (12)', and 'Education (34)'. The main workspace has a menu bar (File, Server, Window, Tools, Help) and tabs for 'Geometry', 'Specifications', 'Protocols', and 'Simulations'. The 'Geometry' tab is active, showing 'Structure Mapping' and 'Geometry Definition' sub-tabs. A 'Domain' section indicates '3D, size=(100.0,100.0,26.0), origin=(0.0,0.0,0.0)' with buttons for 'Edit Domain...', 'Export...', 'Edit Image', and 'Replace Geometry'. A table lists 'Name' and 'Value' for 'background' (red), 'Nuc' (brown), and 'Cyt' (green). To the right of the table are buttons for 'Front', 'Back', 'Add Subdomain', and 'Delete'. Below the table are tabs for 'Slice View', 'Surface View', and 'Geometric Region Details'. The 'Surface View' is selected, showing a 3D model of a cell with a yellowish-green cytoplasm and brown nucleus, enclosed in a white wireframe box. An 'Opacity' slider is on the left of the 3D view, set to 75. A text box in the center of the workspace reads 'The geometry of your model is now complete.'

BIOMODEL: multiapp tutorial (Wed Jan 30 22:39:01 EST 2019) -- VCell 7.1.0 (build 4)

File Server Window Tools Help

multiapp tutorial

- Physiology
 - Reaction Diagram
 - Reactions (2)
 - Structures (5)
 - Species (4)
 - Molecules (0)
 - Observables (0)
 - Applications (1)

Geometry Specifications Protocols Simulations

Species Reaction Network

Species	Structure	Depiction	Clamped	Initial Condition	Well Mixed	Diffusion Constant
RanC_cyt	Cyt	●	<input type="checkbox"/>	0.0 [uM]	<input type="checkbox"/>	10.0 [uM ² ,s ⁻¹]
C_cyt	Cyt	●	<input type="checkbox"/>	0.0 [uM]	<input type="checkbox"/>	10.0 [uM ² ,s ⁻¹]
Ran_cyt	Cyt	●	<input type="checkbox"/>	0.0 [uM]	<input type="checkbox"/>	10.0 [uM ² ,s ⁻¹]
RanC_nuc	Nuc	●	<input type="checkbox"/>	4.5E-4 [uM]	<input type="checkbox"/>	10.0 [uM ² ,s ⁻¹]

Search

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

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

CONNECTED (staurovsky) 20.2MB 4.23.1MB

You will want to change the Initial Conditions concentration for RanC_nuc. Select "Specifications" and type 4.5E-4 in the "Initial Condition" column or in the Expression text field.

The screenshot shows the BIOMODEL software interface. The window title is "BIOMODEL: multiapp tutorial (Wed Jan 30 22:39:01 EST 2019) -- VCell 7.1.0 (build 4)". The "Simulations" tab is active, displaying a table of simulation instances. A blue arrow points from the "New Simulation" icon in the toolbar to the "Simulations" tab. Another blue arrow points from the "Edit Simulation" icon to the "Simulation0" row in the table. A text box on the left explains the first step, and a text box on the right explains the second step.

Click on the "Simulations" tab and click the New Simulation icon to create the instance of a simulation.

To edit a simulation, click the Edit Simulation icon to access the Edit Simulation Dialog with tabs for defining Parameters, the Mesh and the Solver.

Name	Time	Output Option	Solver	Running Status	Results
Simulation0	1.0	every 0.05 s	Fully-Implicit	not saved	no

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

Annotation:

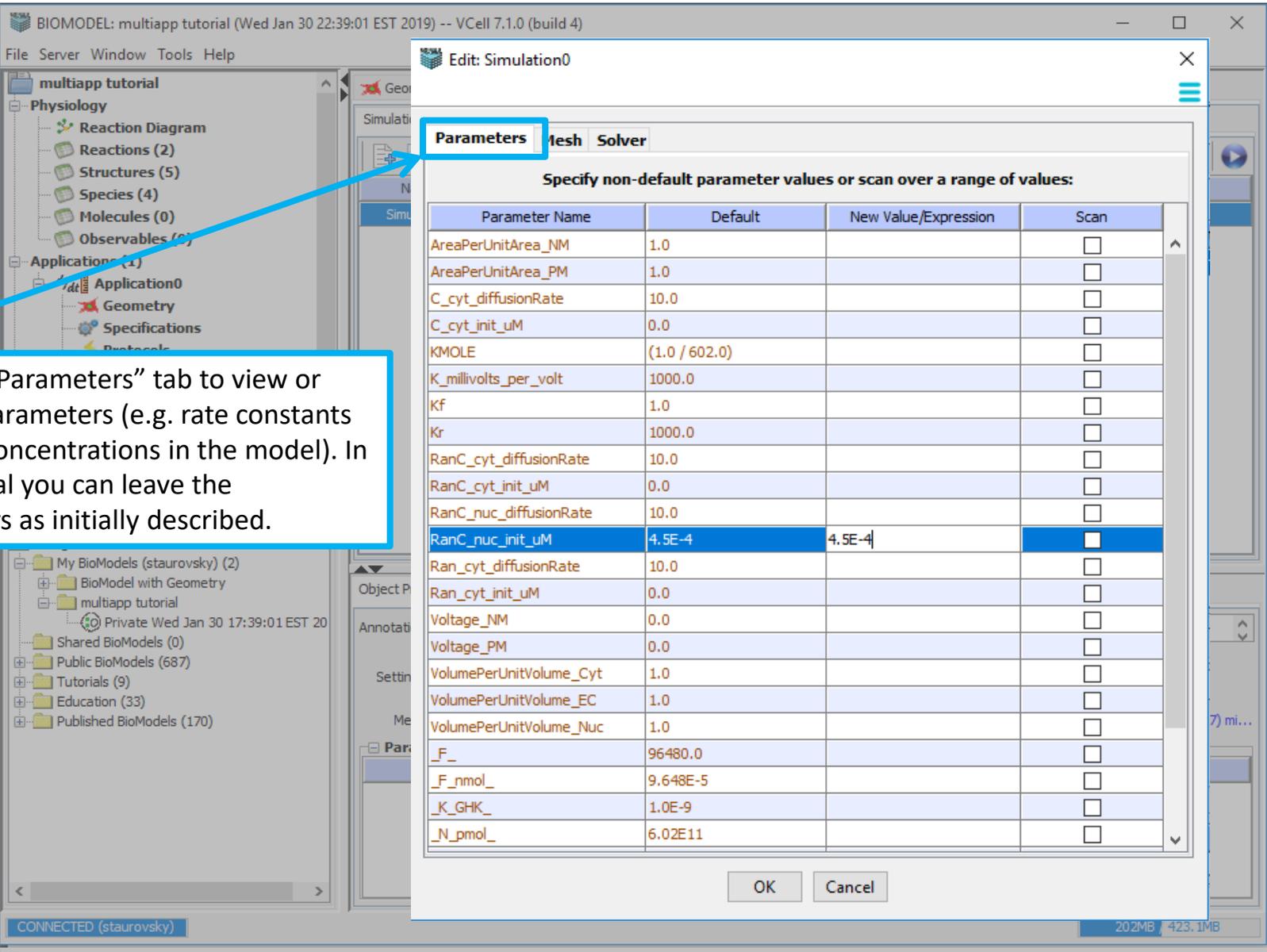
Settings:	Max timestep	Output	Rel tol	Abs tol
	0.1s	every 0.05 sec	1.0E-7	1.0E-9

Mesh: 168x210x5 = 176400 elements Geometry size: (3.01927734375E-5, 3.780234375E-5, 9.0E-7) microns

Parameters with values changed from defaults

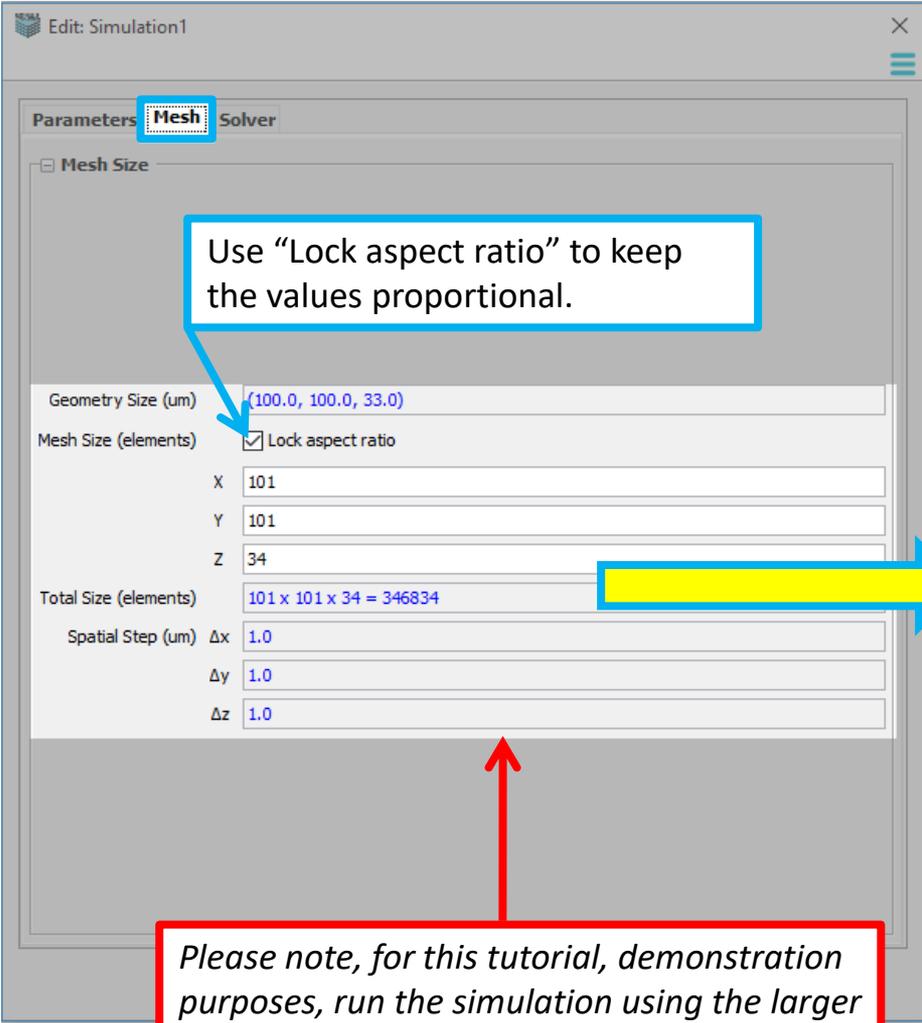
Parameter Name	Default	New Value/Expression	Scan
----------------	---------	----------------------	------

CONNECTED (staurovsky) 91.3MB / 374.9MB

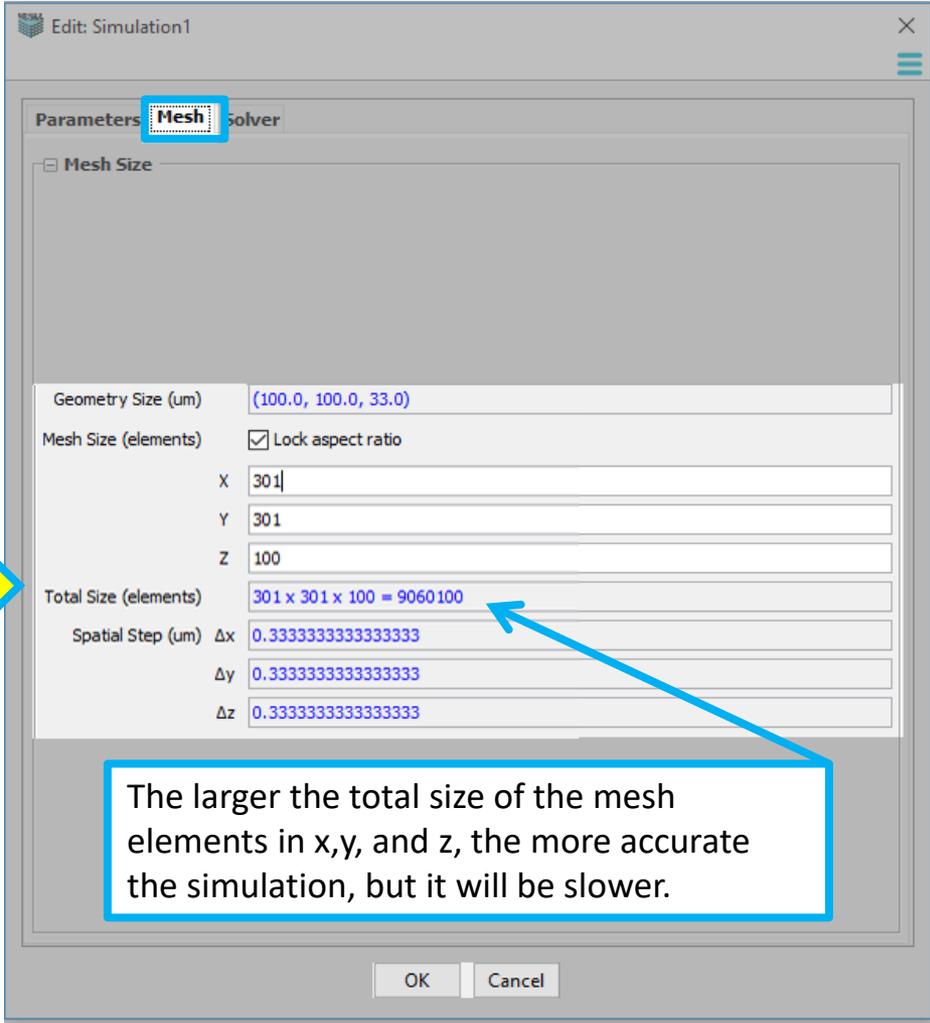


Click the "Parameters" tab to view or edit the parameters (e.g. rate constants or initial concentrations in the model). In this tutorial you can leave the parameters as initially described.

Select the "Mesh" tab to edit the mesh resolution for the simulation in the X, Y, and Z planes. Select "OK" to accept your changes.

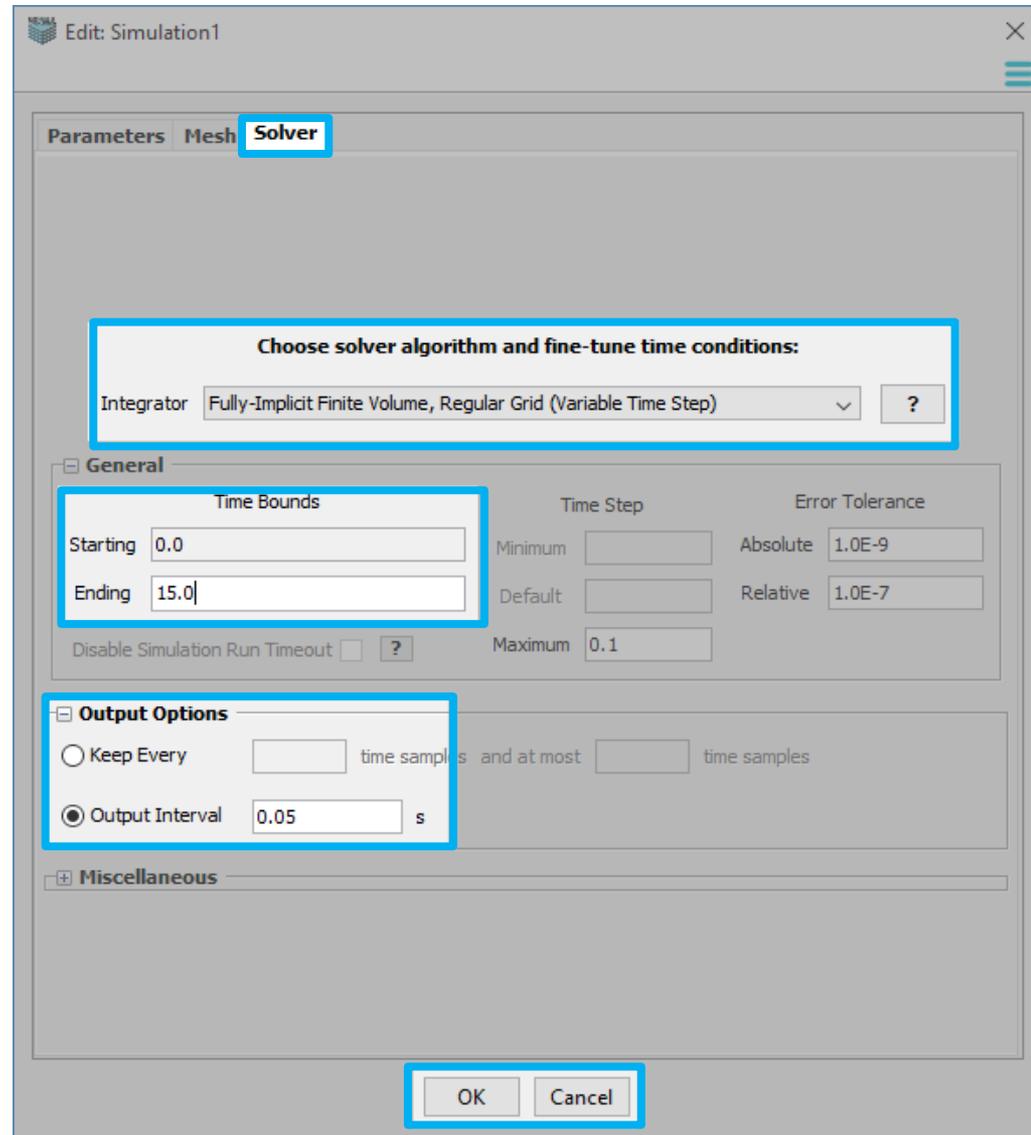


Use "Lock aspect ratio" to keep the values proportional.



The larger the total size of the mesh elements in x,y, and z, the more accurate the simulation, but it will be slower.

Please note, for this tutorial, demonstration purposes, run the simulation using the larger mesh elements to save on your simulation time.



Select the “Solver” tab to edit the solver run configuration as shown. Be sure to press “OK” to accept your changes.

You will receive a warning regarding the size of your simulation. You should select "OK" and run the simulation.

The screenshot shows a software interface with a warning dialog box in the center. The dialog box contains the following text:

Warnings from Simulation: 'Simulation0'!
The simulation has large result dataset (17323MB), 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

The background interface includes a left sidebar with a tree view of simulation components (Reactions, Structures, Species, Molecules, Observables, Applications, Parameters, Functions and UI, Pathway), a top menu bar (File, Server, Window, Tools, Help), a central workspace with a table of simulation results, and a bottom panel with 'Object Properties' and 'Database File Info' tabs. The 'Object Properties' panel shows settings for 'Max timestep' (0.1s), 'Output' (every 0.05 sec), 'Rel tol' (1.0E-7), and 'Abs tol' (1.0E-9). It also displays 'Mesh: 101x101x27 = 275427 elements' and 'Geometry size: (100.0,100.0,26.0) microns'.

The screenshot shows the VCell software interface. The 'Simulations' tab is active, displaying a table of simulation settings. A blue box highlights the 'Simulations' tab and the table. A green play button is visible in the top right of the highlighted area. A callout box points to the 'Simulation0' row and the play button.

Name	End Time	Output Option	Solver	Running Status	Results
Simulation0	10.0	every 0.05 s	Fully-Implicit	not saved	no

Be sure to select the correct simulation, if you have multiple simulations, and press the green arrow button to run and save a simulation to the VCell database.

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

Annotation:

Settings:	Max timestep	Output	Rel tol	Abs tol
	0.1s	every 0.5 sec	1.0E-7	1.0E-9

Mesh: 101x101x27 = 275427 elements Geometry size: (100.0,100.0,26.0) microns

The screenshot displays the Simulations panel in a software interface. The panel includes a toolbar with icons for running, stopping, and viewing results, and a table listing simulation parameters. The table has the following data:

Name	End Time	Output Option	Solver	Running Status	Results
Simulation0	10.0	every 0.5 s	Fully-Implicit	40%	yes

To view the status of the simulation, look under the "Running Status" column.

To view the results upon completion of the simulation, click on the Results icon.

The second screenshot shows the same Simulations panel after the simulation has completed. The 'Running Status' column now shows 'completed' and the 'Results' icon in the toolbar is highlighted, indicating that the results are available for viewing.

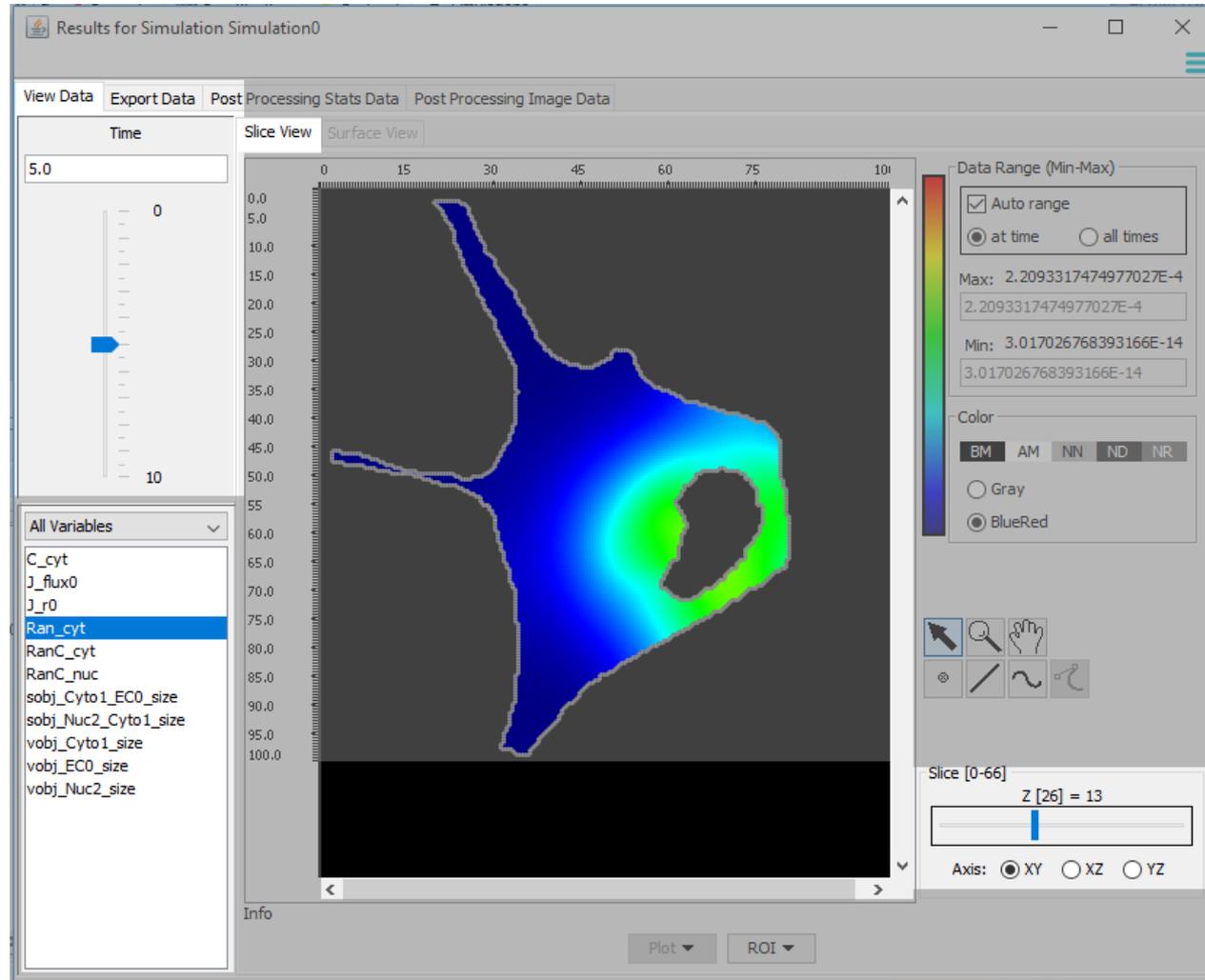
Name	End Time	Output Option	Solver	Running Status	Results
Simulation0	10.0	every 0.5 s	Fully-Implicit	completed	yes

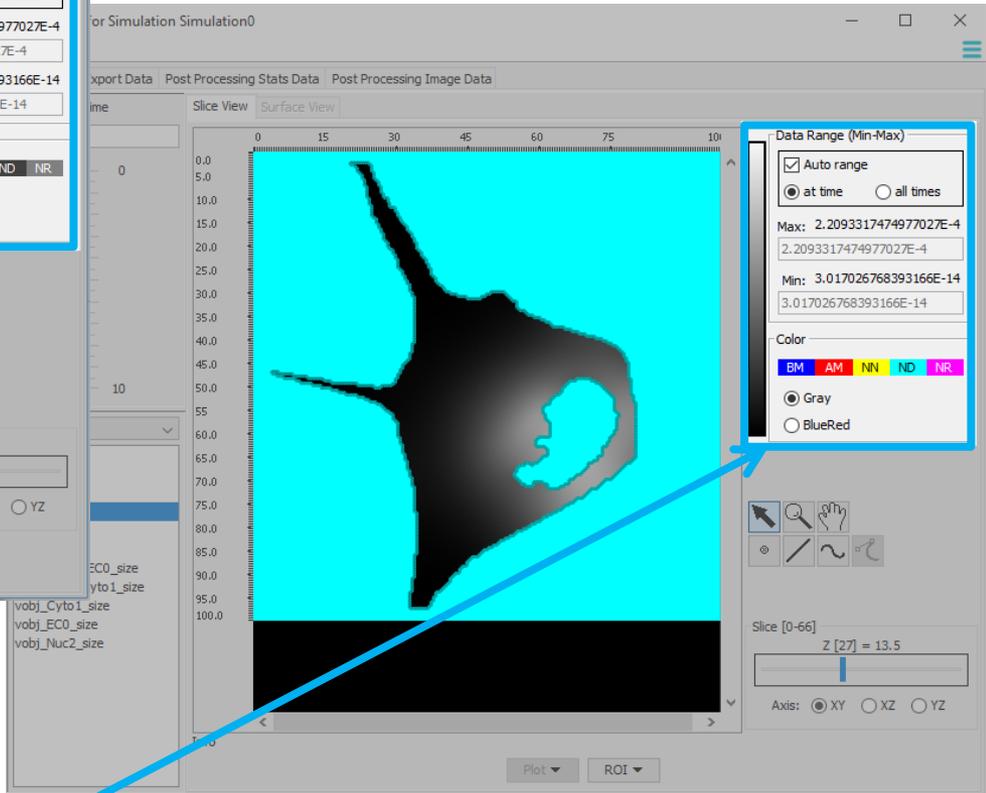
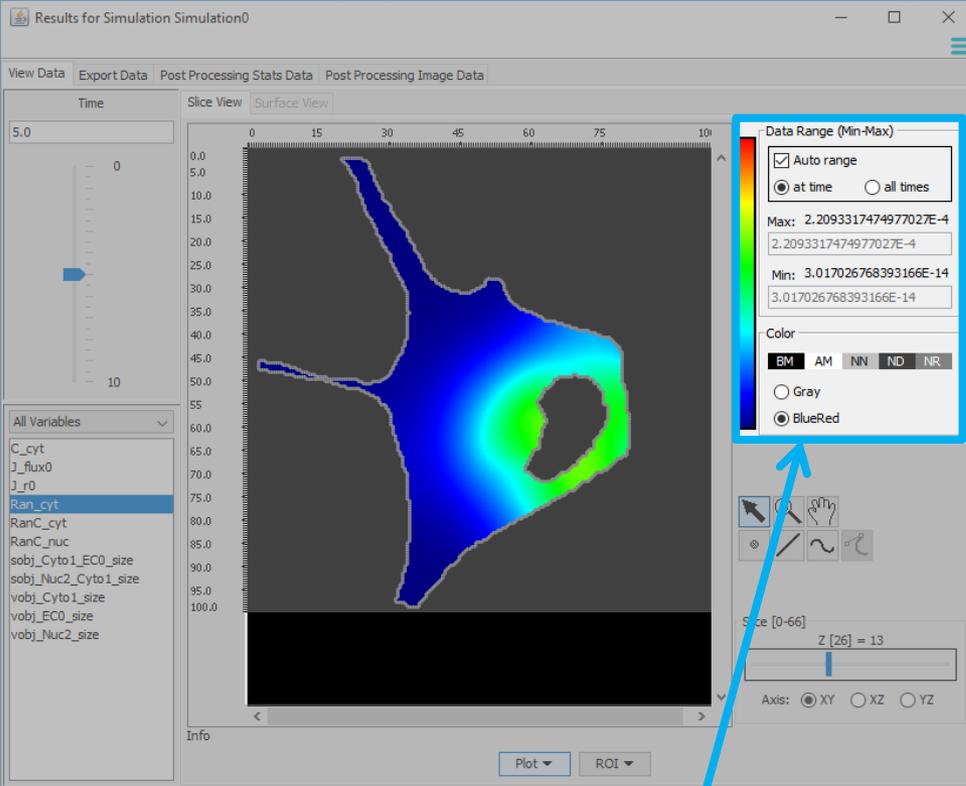
In order to view your results, be sure to adjust the following three parameters:

1. Time Point

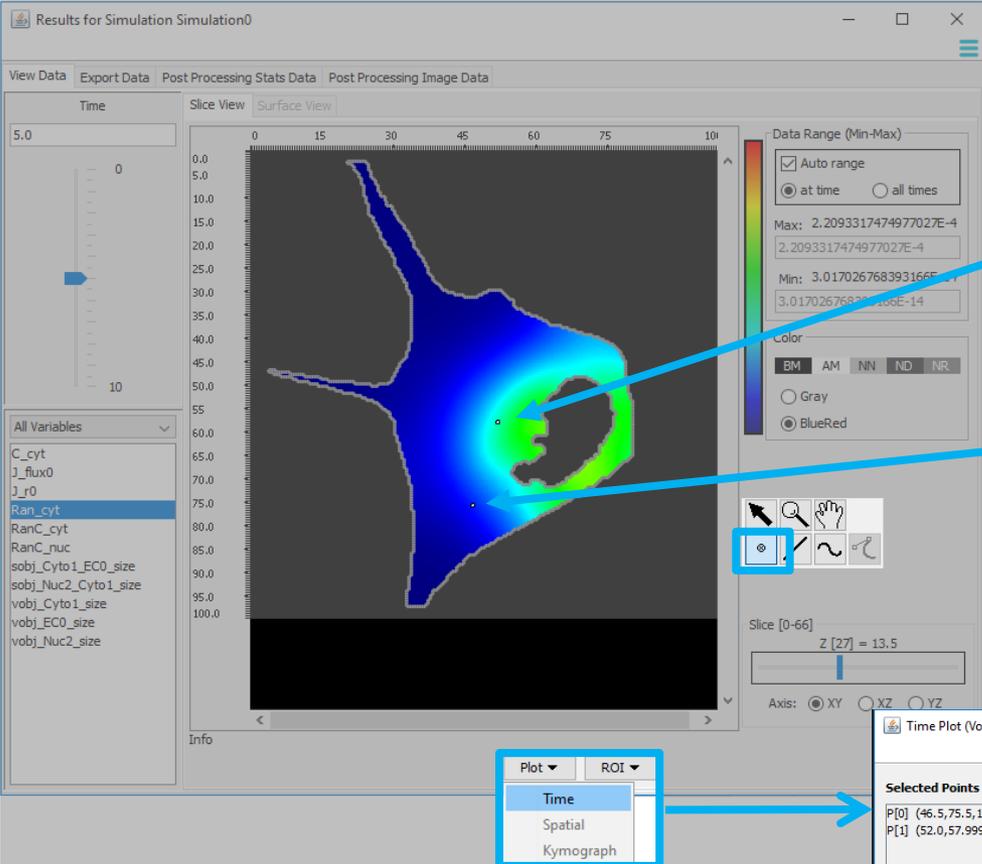
2. Variable

3. Z-Slice



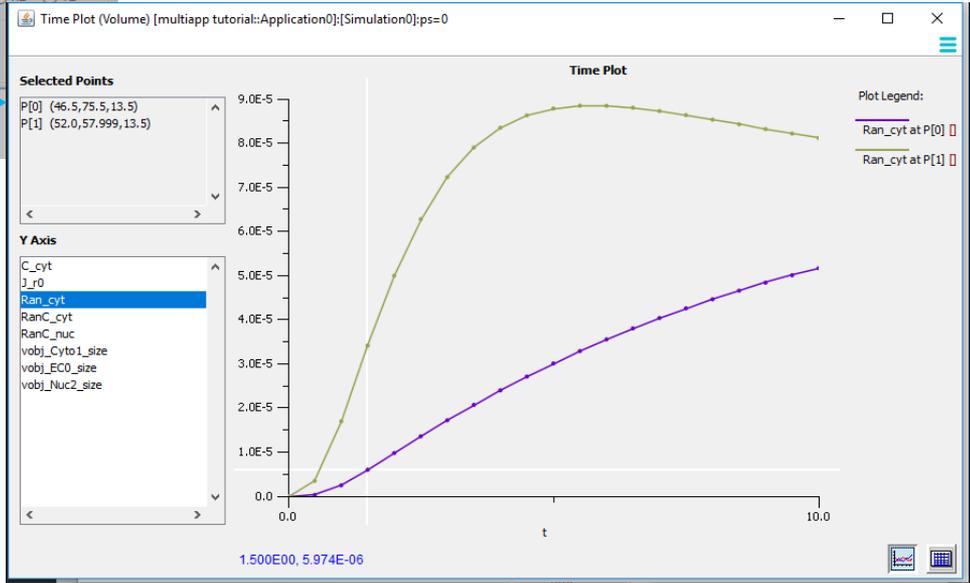


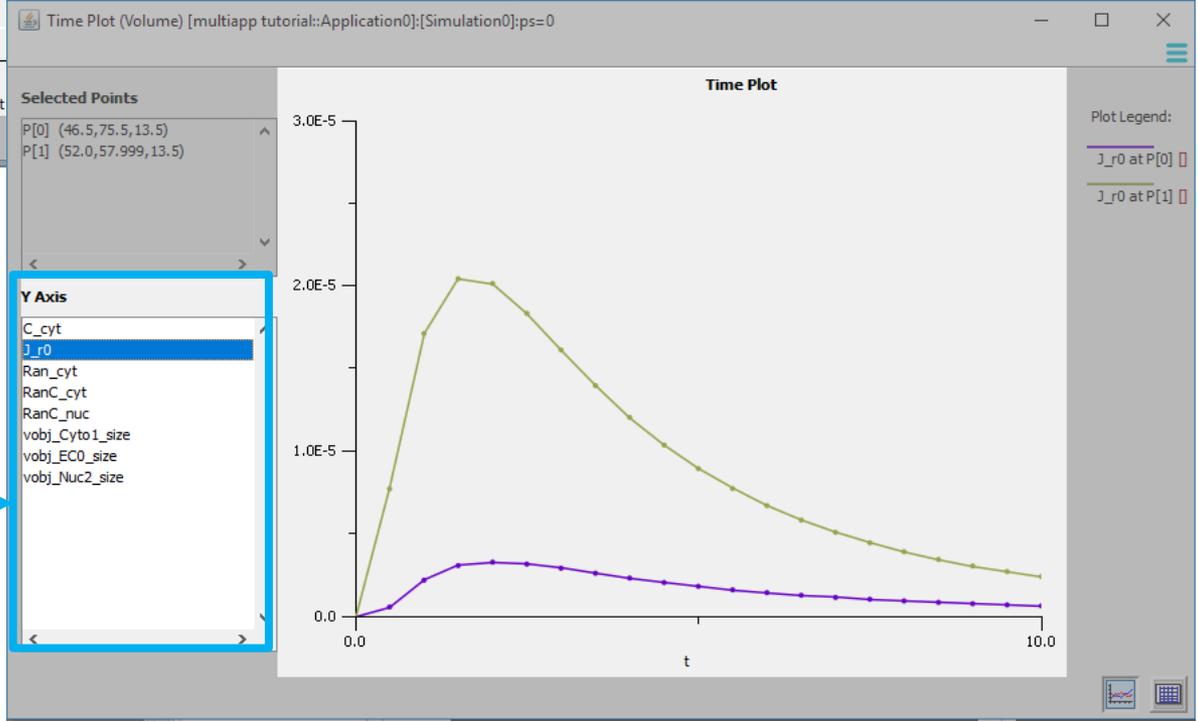
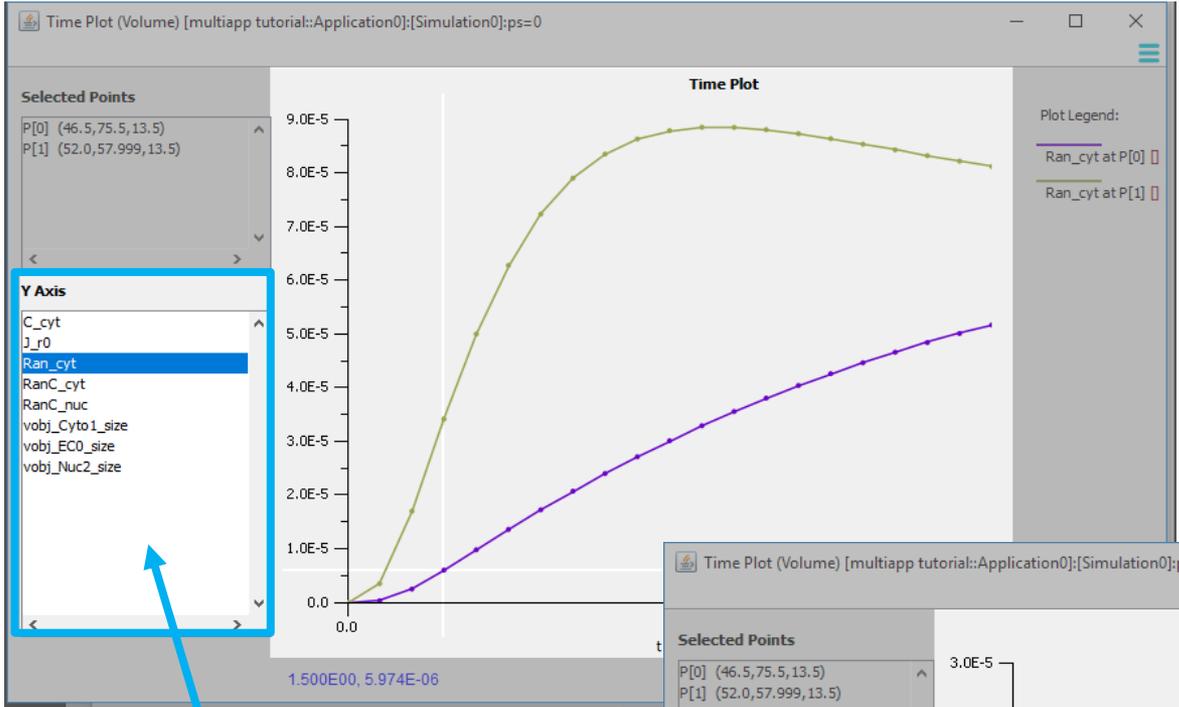
The Data Range shows the minimum and maximum concentrations displayed in the blue-red or greyscale/black-white, color map.



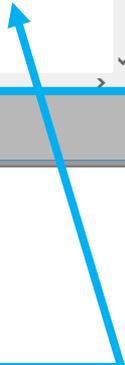
To create a time plot, select the time point tool and click within the geometry to create the desired point. You can define multiple time points within the geometry.

To view the time plot, click "Plot" > "Time".

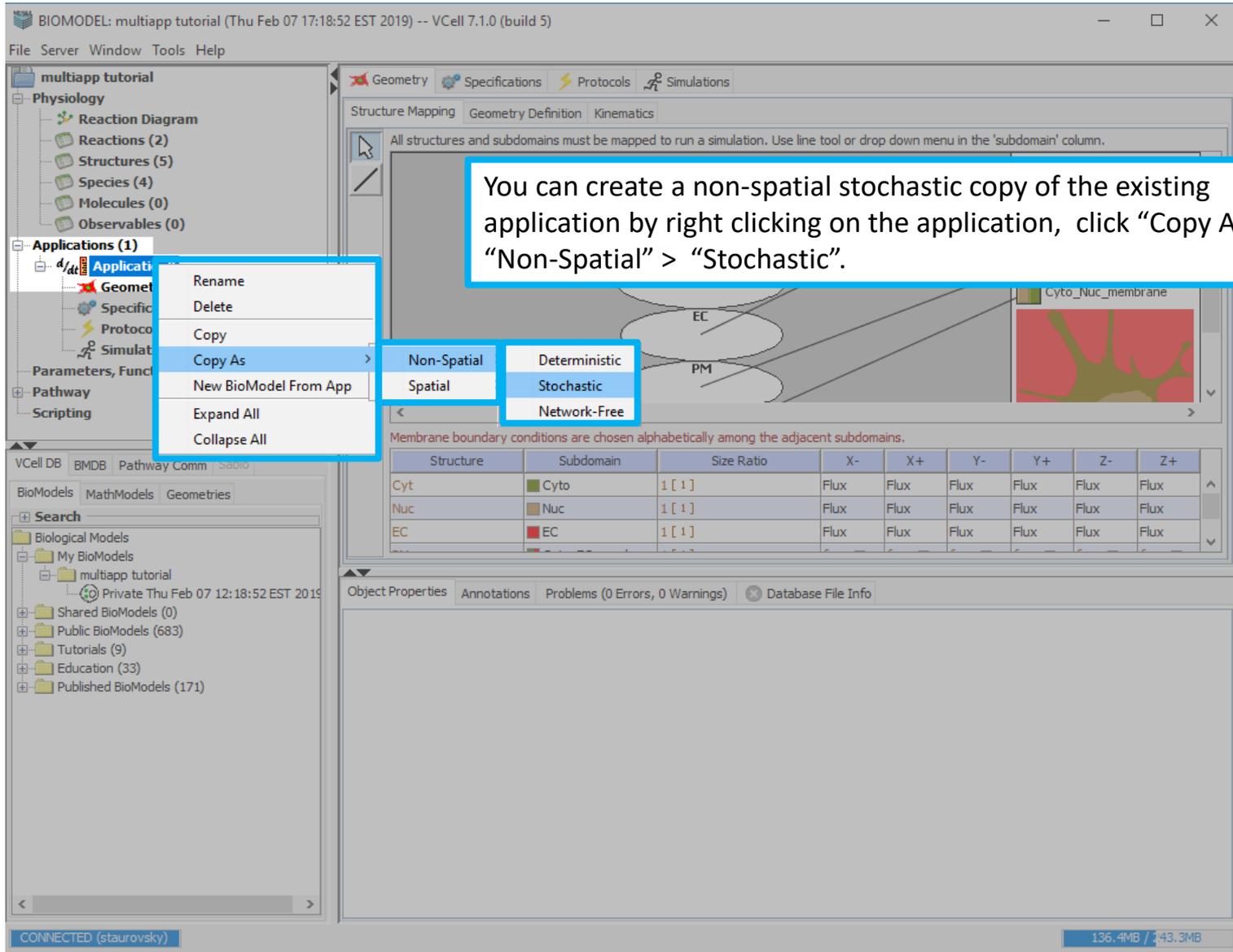




To change what species concentrations are being viewed, click on different species under "Y Axis".



Creating a New Application from an Existing Application



You can create a non-spatial stochastic copy of the existing application by right clicking on the application, click “Copy As” > “Non-Spatial” > “Stochastic”.

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

Warning

Simulations are not copied because new application is of different type.

OK

Select "OK".

BIOMODEL: multiapp tutorial (Thu Feb 07 17:18:52 EST 2019) -- VCell 7.1.0 (build 5)

File Server Window Tools Help

multiapp tutorial

- Physiology
 - Reaction Diagram
 - Reactions (2)
 - Structures (5)
 - Species (4)
 - Molecules (0)
 - Observables (0)
 - Applications (2)
 - Application0
 - Copy of Application0
 - Parameters, Functions and Units
 - Pathway
 - Scripting

Geometry Specifications Protocols Simulations

Structure Mapping Geometry Definition Kinematics

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

Physiology (structures)

- Cyt
- Nuc
- EC

Geometry (subdomains)

- EC
- Nuc
- Cyto
- Cyto_EC_membrane
- Cyto_Nuc_membrane

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
 - My BioModels
 - multiapp tutorial
 - Private Thu Feb 07 12:18:52 EST 2019
 - Shared BioModels (0)
 - Public BioModels (683)
 - Tutorials (9)
 - Education (33)
 - Published BioModels (171)

	Y-	Y+	Z-	Z+
Flux	Flux	Flux	Flux	Flux
Flux	Flux	Flux	Flux	Flux
Flux	Flux	Flux	Flux	Flux

CONNECTED (staurovsky) 192.5MB / 243.3MB

BIOMODEL: multiapp tutorial (Thu Feb 07 17:18:52 EST 2019) -- VCell 7.1.0 (build 5)

File Server Window Tools Help

multiapp tutorial

- Physiology
 - Reaction Diagram
 - Reactions (2)
 - Structures (5)
 - Species (4)
 - Molecules (0)
 - Observables (0)
- Applications (2)
 - Copy of Spatial Deterministic
 - Spatial Deterministic
- Parameters, Functions and Units
- Pathway
- Scripting

Structure Mapping Geometry Definition Kinematics

Physiology (structures)

- Cyt
- Nuc
- EC
- PM
- NM

Geometry (subd...)

- Compartment

Volume/Surface Calculator

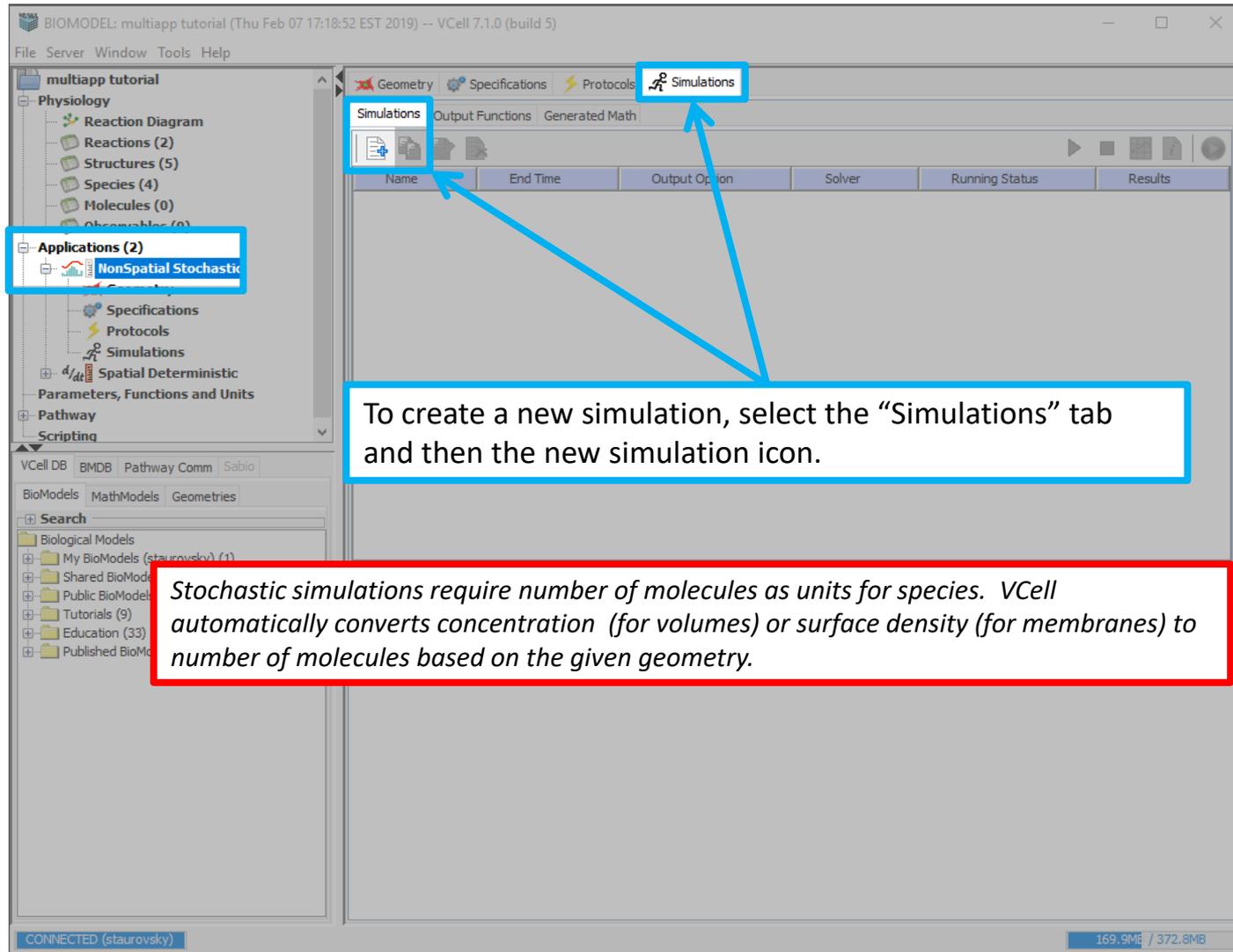
Structure Size

Cyt
Nuc
EC
PM

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

CONNECTED (staurovsky) 200.3MB / 360.2MB

To rename an application, right click on the application, click "Rename", type in a name, and press "Enter" on your keyboard.



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

- multiapp tutorial
 - Physiology
 - Reaction Diagram
 - Reactions (2)
 - Structures (5)
 - Species (4)
 - Molecules (0)
 - Observables (0)
 - Applications (2)**
 - NonSpatial Stochastic**
 - Specifications
 - Protocols
 - Simulations
 - Spatial Deterministic
 - Parameters, Functions and Units
 - Pathway
 - Scripting

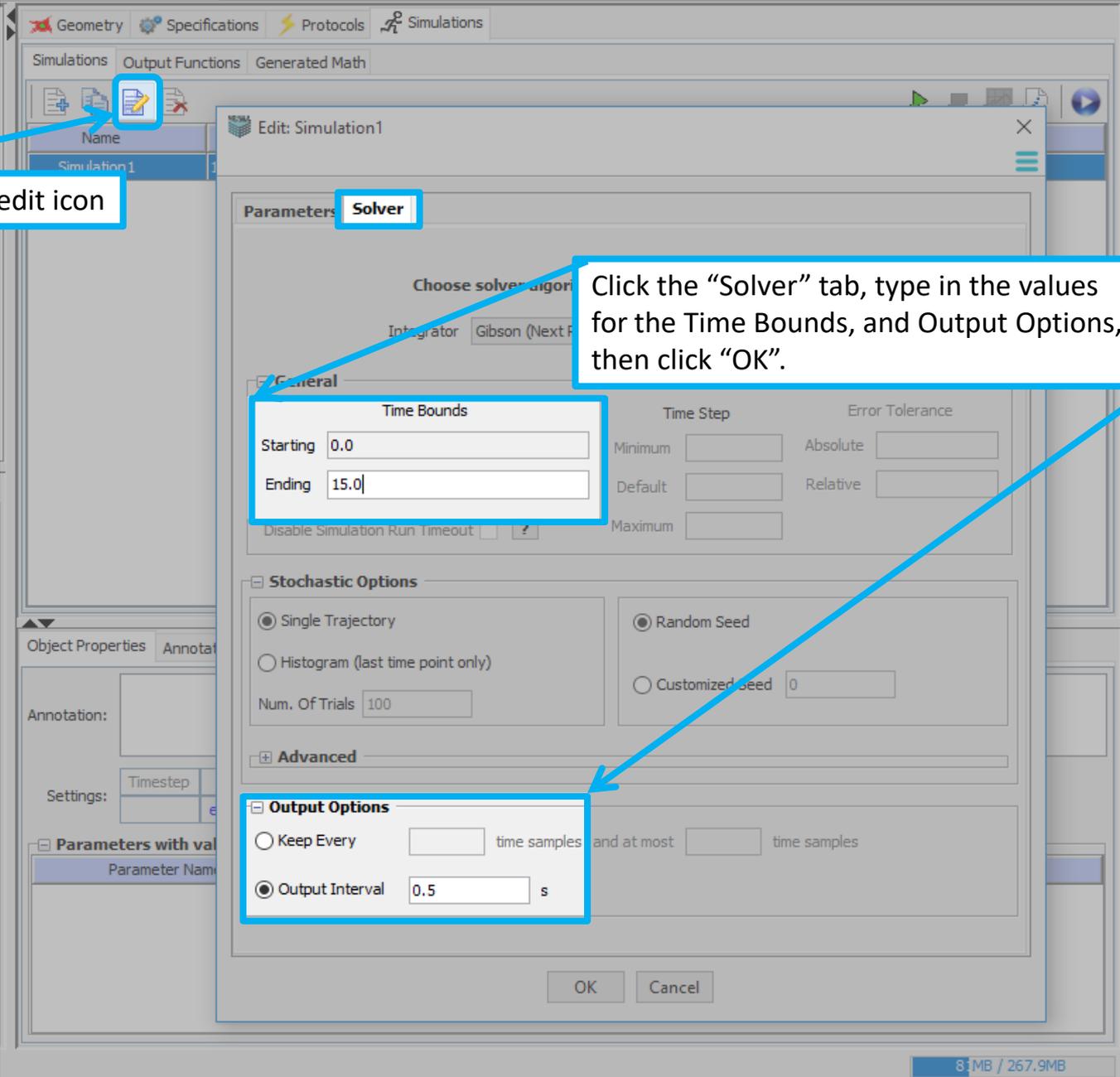
The main window has a menu bar with 'File', 'Server', 'Window', 'Tools', and 'Help'. Below the menu bar are tabs for 'Geometry', 'Specifications', 'Protocols', and 'Simulations'. The 'Simulations' tab is active, showing a sub-menu with 'Simulations', 'Output Functions', and 'Generated Math'. Below the sub-menu is a toolbar with icons for creating, saving, and running simulations. A table with columns 'Name', 'End Time', 'Output Option', 'Solver', 'Running Status', and 'Results' is visible below the toolbar.

Blue boxes highlight the 'Simulations' tab in the main window, the 'NonSpatial Stochastic' application in the sidebar, and the 'Simulations' sub-menu item. Blue arrows point from the 'Simulations' sub-menu item to the 'Simulations' tab and from the 'NonSpatial Stochastic' application to the 'Simulations' sub-menu item.

To create a new simulation, select the "Simulations" tab and then the new simulation icon.

Stochastic simulations require number of molecules as units for species. VCell automatically converts concentration (for volumes) or surface density (for membranes) to number of molecules based on the given geometry.

CONNECTED (staurovsky) 169.9MB / 372.8MB



Select the edit icon

Click the "Solver" tab, type in the values for the Time Bounds, and Output Options, then click "OK".

Time Bounds
Starting 0.0
Ending 15.0

Output Options
 Keep Every [] time samples and at most [] time samples
 Output Interval 0.5 s

OK Cancel

BIOMODEL: multiapp tutorial (Wed Mar 20 21:46:55 EDT 2019) -- VCell 7.1.0 (build 5)

File Server Window Tools Help

multiapp tutorial

- Physiology
 - Reaction Diagram
 - Reactions (2)
 - Structures (5)
 - Species (4)
 - Molecules (0)
 - Observables (0)
- Applications (2)
 - NonSpatial Stochastic**
 - Geometry
 - Specifications
 - Protocols
 - Simulations
 - Spatial Deterministic
- Parameters, Functions and Units
- Pathway
- Scripting

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
 - My BioModels
 - multiapp tutorial
 - Private Wed Mar 20 17:46:55 EDT 2019
 - Shared BioModels (0)
 - Public BioModels (683)
 - Tutorials (9)
 - Education (33)
 - Published BioModels (171)

Geometry Specifications Protocols Simulations

Simulations Output Functions Generated Math

Name	End Time	Output Option	Solver	Running Status	Results
Simulation 1	15.0	every 0.5 s	Gibson	not saved	no

Click the green play icon to run the simulation.

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

Annotation:

Settings: Timestep Output
every 0.5 sec

Parameters with values changed from defaults

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

CONNECTED 137.4MB 267.9MB

The screenshot shows the VCell software interface with the 'Simulations' tab selected. A table lists simulation details, and a callout box points to a results icon.

Name	End Time	Output Option	Solver	Running Status
Simulation1	15.0	every 0.5 s	Gibson	completed

To view simulation results, select the simulation and click the results icon.

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

Annotation:

Settings:

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

129.5MB / 268.4MB

BIOMODEL: multiapp tutorial (Thu Apr 25 19:56:06 EDT 2019) -- VCell 7.1.0 (build 5)

File Server Window Tools Help

multiapp tutorial

- Physiology
 - Reaction Diagram
 - Reactions (2)
 - Structures (5)
 - Species (4)
 - Molecules (0)
- Parameters, Functions and Units
- Pathway
 - Scripting

VCell DB BMDDB Pathway Comm Sabio

BioModels MathModels Geometries

Search

- Biological Models
 - My BioModels
 - multiapp tutorial
 - Private Thu Apr 25 19:56:06 EDT 2019
 - Shared BioModels (0)
 - Public BioModels (683)
 - Tutorials (9)
 - Education (33)
 - Published BioModels (171)

Geometry Specifications Protocols Simulations

Simulations Output Functions Generated Math

Name	End Time	Output Option	Solver	Running Status	Results
Simulation1	15.0	every 0.5 s	Gibson	completed	yes

Results for Simulation Simulation1

View Data Output Species

X Axis: t

Y Axis:

Display Options:

- Other
- Reactions
- Species

C_cyt

C_cyt_Count

Ran_cyt

Ran_cyt_Count

RanC_cyt

RanC_cyt_Count

RanC_nuc

RanC_nuc_Count

Plot Legend: C_cyt_Count [molecules]

2000.0

1000.0

0.0

0.0 10.0 20.0

t

Step View

To view a spreadsheet of the simulation results, click the spreadsheet icon.

CONNECTED

129.5MB / 268.4MB

The screenshot shows the BIOMODEL software interface. The main window displays simulation results for 'Simulation1'. A 'Results for Simulation Simulation1' dialog box is open, showing a table of species data over time. The 'RanC_cyt' species is highlighted in blue, and a context menu is open over it with 'Copy All' selected. The background interface includes a left sidebar with a project tree, a top menu bar, and a bottom status bar.

Simulation Results Table:

t	RanC_cyt
0	0
0.5	1.5904912E-5
1	2.1702762E-5
1.5	2.2016159E-5
2	1.9861553E-5
2.5	1.8413005E-5
3	
3.5	
4	
4.5	
5	
5.5	8.1091546E-6
6	7.4040108E-6
6.5	7.0122642E-6
7	6.032897E-6
7.5	6.033914E-6
8	6.0721E-6
8.5	5.523627E-6
9	5.9937230E-6

Context Menu:

- Copy Cells
- Copy Rows
- Copy All

For this tutorial, select the "RanC_cyt" species data to display. To copy the spreadsheet, right click on a cell and click "Copy All".

The screenshot shows a Microsoft Excel spreadsheet with the following data:

t	(Var=RanC_Cyt_Conc)	RanC_Cyt_Conc
0	0	0
0.5	1.71E-05	
1	1.07E-05	
1.5	6.47E-06	
2	4.79E-06	
2.5	2.52E-06	
3	2.26E-06	
3.5	1.49E-06	
4	1.36E-06	
4.5	1.16E-06	
5	8.41E-07	
5.5	7.76E-07	
6	5.82E-07	
6.5	8.41E-07	
7	9.05E-07	
7.5	1.29E-06	
8	7.76E-07	
8.5	7.76E-07	
9	8.41E-07	
9.5	7.11E-07	
10	6.47E-07	
10.5	8.41E-07	
11	7.11E-07	
11.5	8.41E-07	
12	8.41E-07	
12.5	7.11E-07	
13	7.76E-07	
13.5	9.05E-07	
14	9.05E-07	
14.5	5.82E-07	
15	9.05E-07	

A text box with a blue border is overlaid on the spreadsheet, containing the following text:

Open your favorite spreadsheet software, click on an empty cell, and paste the simulation results for RanC in the cytosol. You will use this data later to demonstrate parameter estimation tools.

Save As

Save in: Downloads

Name	Date	Type	Size	Tags
Experimental Data				

File name: Experimental Data

Save as type: CSV (Comma delimited)

Save

Cancel

Save the spreadsheet as a comma delimited format.

t	(Var=RanC_Cyt_Conc)	RanC_Cyt_Conc
0	0	
0.5	1.71E-05	
1	1.07E-05	
1.5	6.47E-06	
2	4.79E-06	
2.5	2.52E-06	
3	2.26E-06	
3.5	1.49E-06	
4	1.36E-06	
4.5	1.16E-06	
5	8.41E-07	
5.5	7.76E-07	
6	5.82E-07	
6.5	8.41E-07	
7	9.05E-07	
7.5	1.29E-06	
8	7.76E-07	
8.5	7.76E-07	
9	8.41E-07	
9.5	7.11E-07	
10	6.47E-07	
10.5	8.41E-07	
11	7.11E-07	
11.5	8.41E-07	
12	8.41E-07	
12.5	7.11E-07	
13	7.76E-07	
13.5	9.05E-07	
14	9.05E-07	
14.5	5.82E-07	
15	9.05E-07	

The screenshot shows a Microsoft Excel spreadsheet with a data table. The table has columns labeled A through M and rows numbered 1 through 36. The data in the table is as follows:

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	t	(Var=RanC	Cyt_Conc)	RanC	Cyt_Conc								
2		0	0										
3		0.5	1.71E-05										
4		1	1.07E-05										
5		1.5	6.47E-06										
6		2	4.79E-06										
7		2.5	2.52E-06										
8		3	2.26E-06										
9		3.5	1.49E-06										
10		4	1.36E-06										
11		4.5	1.16E-06										
12		5	8.41E-07										
13		5.5	7.76E-07										
14		6	5.82E-07										
15		6.5	8.41E-07										
16		7	9.05E-07										
17		7.5	1.29E-06										
18		8	7.76E-07										
19		8.5	7.76E-07										
20		9	8.41E-07										
21		9.5	7.11E-07										
22		10	6.47E-07										
23		10.5	8.41E-07										
24		11	7.11E-07										
25		11.5	8.41E-07										
26		12	8.41E-07										
27		12.5	7.11E-07										
28		13	7.76E-07										
29		13.5	9.05E-07										
30		14	9.05E-07										
31		14.5	5.82E-07										
32		15	9.05E-07										
33													
34													
35													
36													

A warning dialog box titled "Microsoft Excel" is overlaid on the spreadsheet. The dialog contains the following text:

The selected file type does not support workbooks that contain multiple sheets.

- To save only the active sheet, click OK.
- To save all sheets, save them individually using a different file name for each, or choose a file type that supports multiple sheets.

The "OK" button is highlighted with a blue box, and a blue arrow points from a text box labeled "Click 'OK'" to the "OK" button.

Microsoft Excel

Experimental Data.csv may contain features that are not compatible with CSV (Comma delimited). Do you want to keep the workbook in this format?

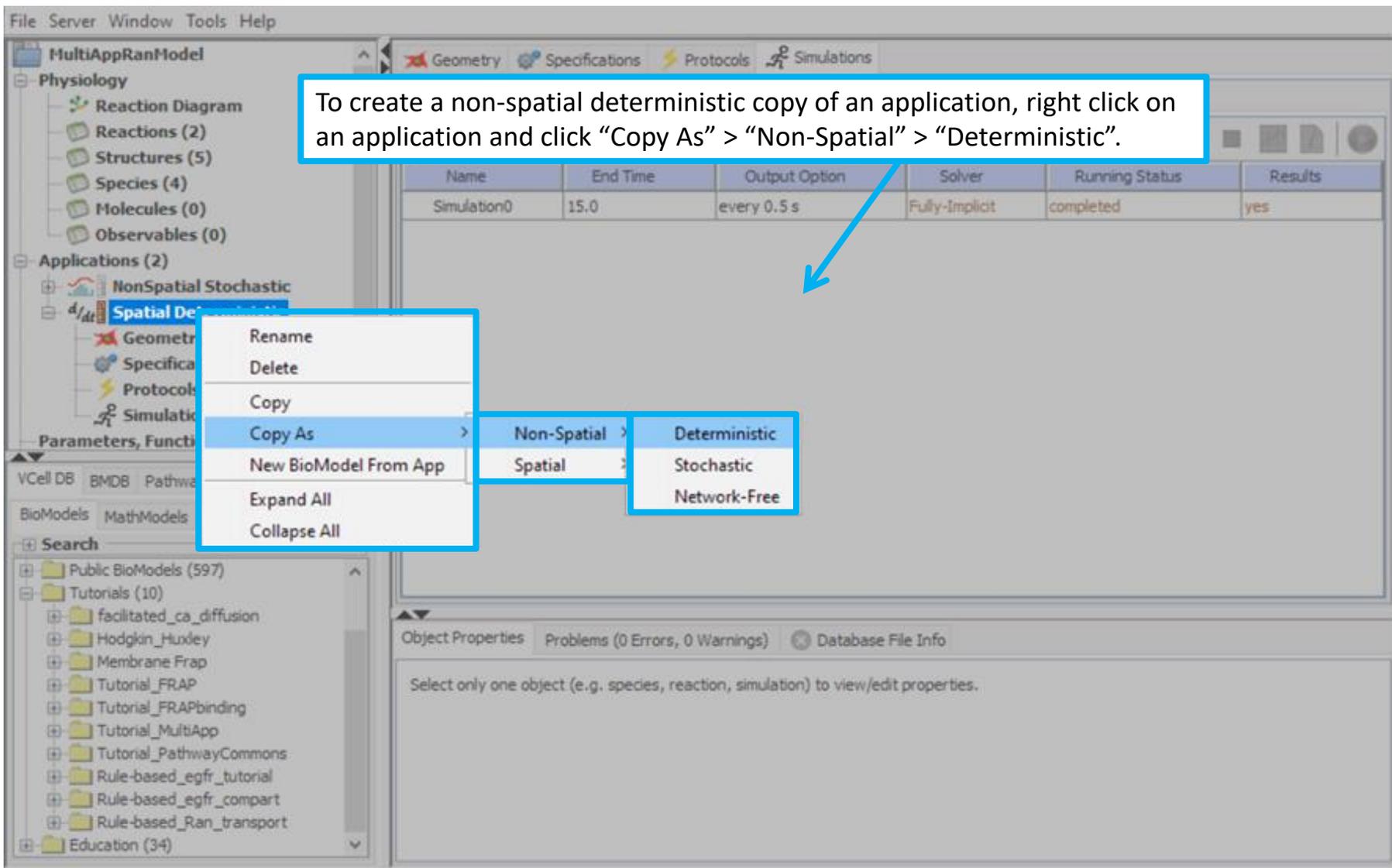
- To keep this format, which leaves out any incompatible features, click Yes.
- To preserve the features, click No. Then save a copy in the latest Excel format.
- To see what might be lost, click Help.

Yes No Help

Click "Yes".

The NonSpatial Stochastic application is now complete.

t	(Var=RanC_Cyt_Conc)	RanC_Cyt_Conc
0	0	
0.5	1.71E-05	
1	1.07E-05	
1.5	6.47E-06	
2	4.79E-06	
2.5	2.52E-06	
3	2.26E-06	
3.5	1.49E-06	
4	1.36E-06	
4.5	1.16E-06	
5	8.41E-07	
5.5	7.76E-07	
6	5.82E-07	
6.5	8.41E-07	
7	9.05E-07	
7.5	1.29E-07	
8	7.76E-07	
8.5	7.76E-07	
9	8.41E-07	
9.5	7.11E-07	
10	6.47E-07	
10.5	8.41E-07	
11	7.11E-07	
11.5	8.41E-07	
12	8.41E-07	
12.5	7.11E-07	
13	7.76E-07	
13.5	9.05E-07	
14	9.05E-07	
14.5	5.82E-07	
15	9.05E-07	



BIOMODEL: multiapp tutorial (Thu Apr 25 19:56:06 EDT 2019) -- VCell 7.1.0 (build 5)

File Server Window Tools Help

multiapp tutorial

- Physiology
 - Reaction Diagram
 - Reactions (2)
 - Structures (5)
 - Species (4)
 - Molecules (0)
 - Observables (0)
- Applications (3)
 - Copy of Spatial Deterministic
 - NonSpatial Stochastic
 - Spatial Deterministic
- Parameters, Functions and Units
- Pathway
- Scripting

Geometry Specifications Protocols Simulations

Structure Mapping Geometry Definition Kinematics

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

Physiology (structures)

Geometry (subdomains)

- EC
- Nuc
- Cyto
- Cyto_EC_membrane
- Cyto_Nuc_membrane

Warning

Simulations are not copied because new application is of different type.

OK

Select OK to proceed.

Y-	Y+	Z-	Z+
Flux	Flux	Flux	Flux
Flux	Flux	Flux	Flux
Flux	Flux	Flux	Flux

BIOMODEL: multiapp tutorial (Thu Apr 25 19:56:06 EDT 2019) -- VCell 7.1.0 (build 5)

File Server Window Tools Help

multiapp tutorial

- Physiology
 - Reaction Diagram
 - Reactions (2)
 - Structures (5)
 - Species (4)
 - Molecules (0)
 - Observables (0)
- Applications (3)
 - Copy of Spatial Deterministic
 - NonSpatial Stochastic
 - Spatial Deterministic
- Parameters, Functions and Units
- Pathway
- Scripting

Geometry Specifications Protocols Simulations Parameter Estimation

Structure Mapping Geometry Definition Kinematics

Physiology (structures)

Geometry (subd)

Cyt

Nuc

EC

PM

NM

Compartment

Volume/Surface Calculator

Structure	Size
	42403.165 [μm^2]
Nuc	7771.2418 [μm^2]
EC	279825.59 [μm^2]

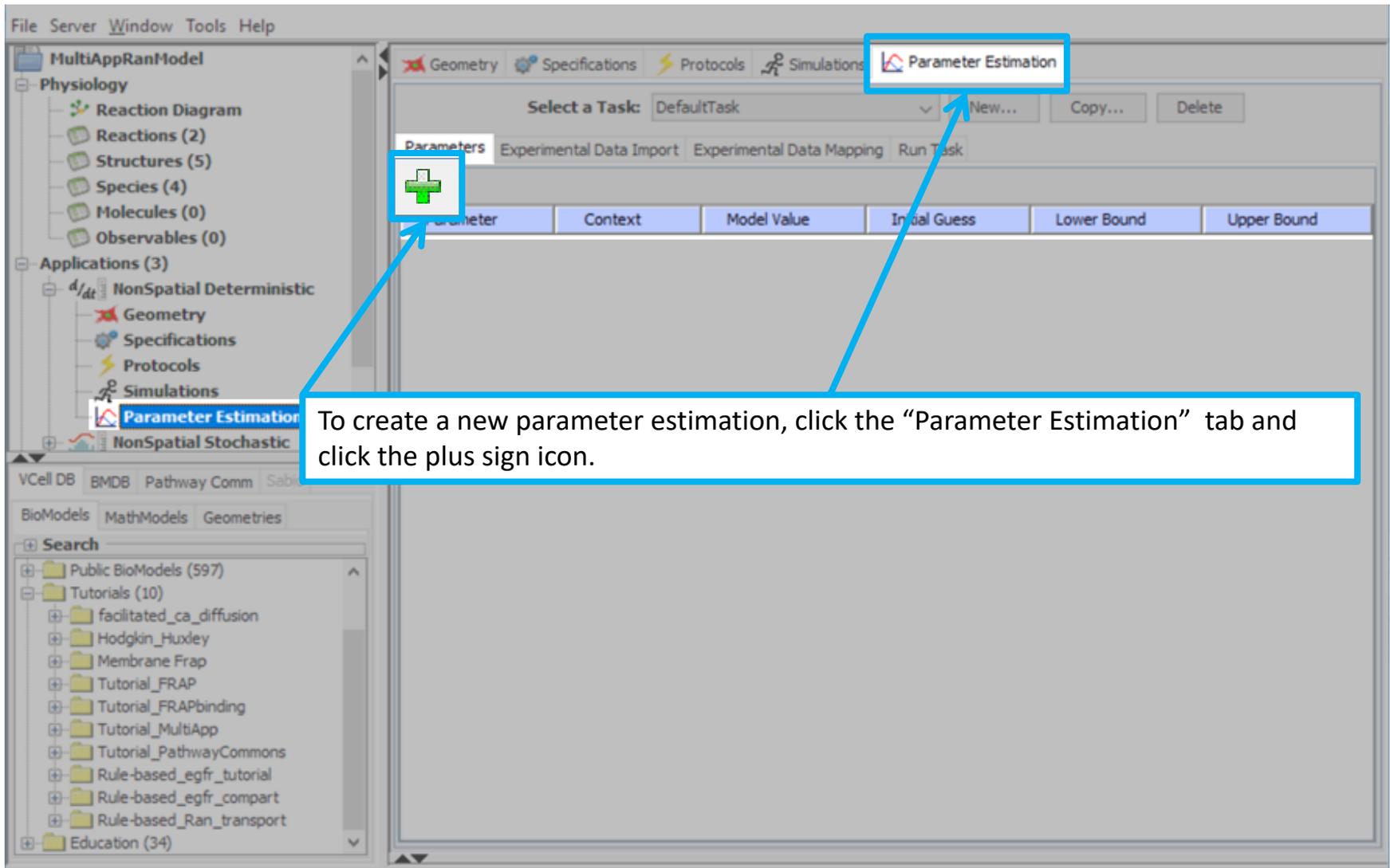
Object Properties Annotations Problems (0 Errors, 0 Warnings) Database File Info

To rename the new application, right click on an application and click "Rename". Type in a name and press "Enter" on your keyboard.

When you copy a spatial application to a non-spatial application, VCell automatically uses sizes for the compartments based on the image-based geometry used in the spatial application

Structure	Size
EC	229042.61 [μm^2]
cyt	27220.285 [μm^2]
nuc	3737.1007 [μm^2]
pm	7226.8656 [μm^2]
nm	1377.3093 [μm^2]

The NonSpatial Deterministic Application therefore is all ready to run simulations. In this tutorial, you will first use data to fit one of the parameters for the model



The screenshot displays the MultiAppRanModel software interface. The left sidebar shows a tree view with categories like Physiology and Applications. The main window has a toolbar with tabs for Geometry, Specifications, Protocols, Simulations, and Parameter Estimation. The Parameter Estimation tab is active, showing a 'Select a Task' dropdown menu and buttons for 'New...', 'Copy...', and 'Delete'. Below the toolbar, there is a table with columns: Parameter, Context, Model Value, Initial Guess, Lower Bound, and Upper Bound. A green plus sign icon is visible in the top-left corner of the main window area. A blue box highlights the plus sign icon, and another blue box highlights the 'Parameter Estimation' tab. A blue arrow points from the plus sign icon to the 'Parameter Estimation' tab. A text box at the bottom of the image contains the following text:

To create a new parameter estimation, click the "Parameter Estimation" tab and click the plus sign icon.

File Server Window Tools Help

MultiAppRanModel

- Physiology
 - Reaction Diagram
 - Reactions (2)
 - Structures (5)
 - Species (4)
 - Molecules (0)
 - Observables (0)
- Applications (3)
 - NonSpatial Deterministic
 - Geometry
 - Specifications
 - Protocols
 - Simulations
 - Parameter Estimation**
 - NonSpatial Stochastic

Geometry Specifications Protocols Simulations Parameter Estimation

Select a Task: DefaultTask New... Copy... Delete

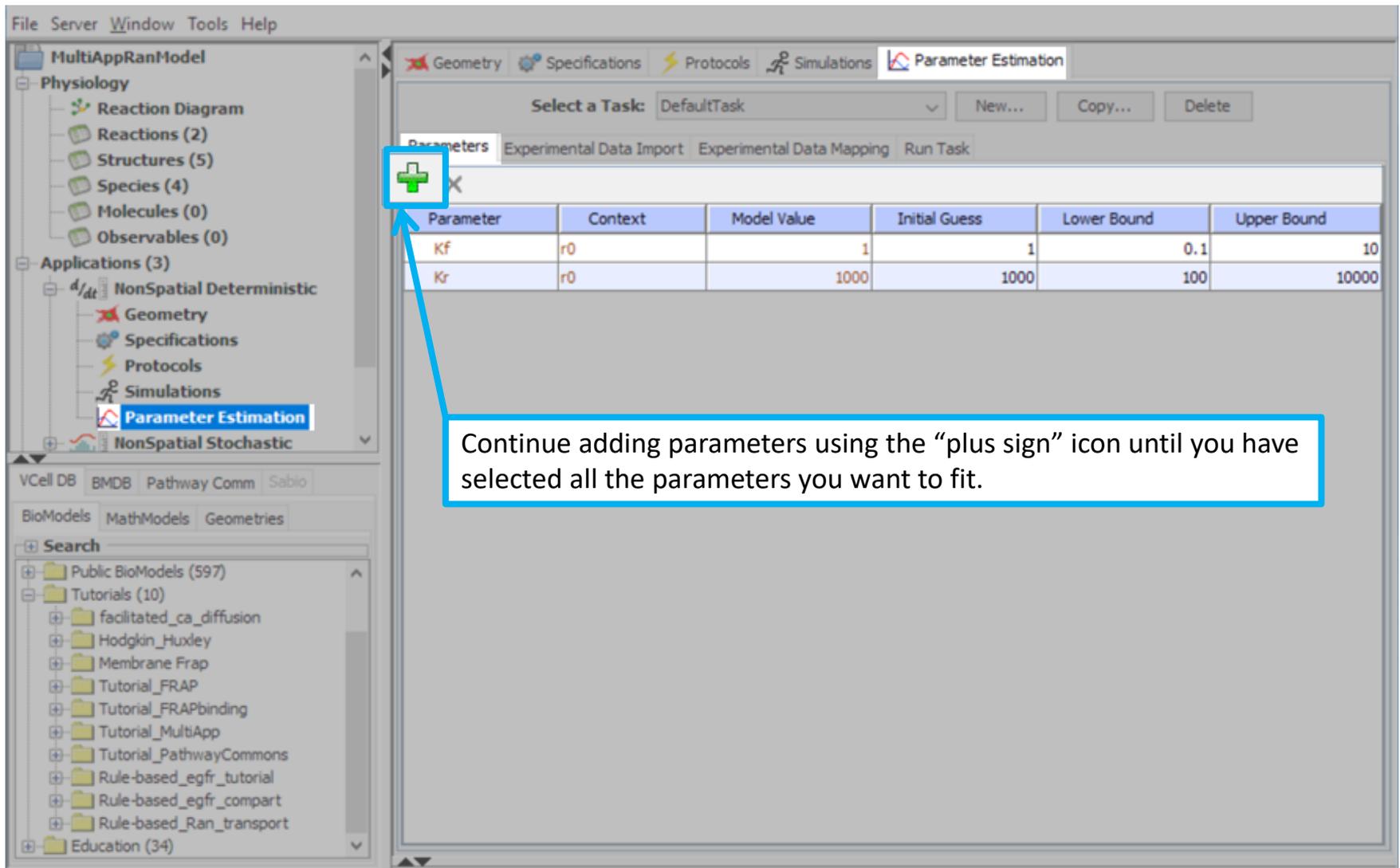
Select Parameters

Parameter	Context
Kf	r0
Kr	r0
netValence	flux0
kfi	flux0
initConc	Ran_cyt_scs
initConc	C_cyt_scs
initConc	RanC_cyt_scs
	RanC_nuc_scs
	pm_mapping
	nm_mapping

Lower Bound Upper Bound

OK Cancel

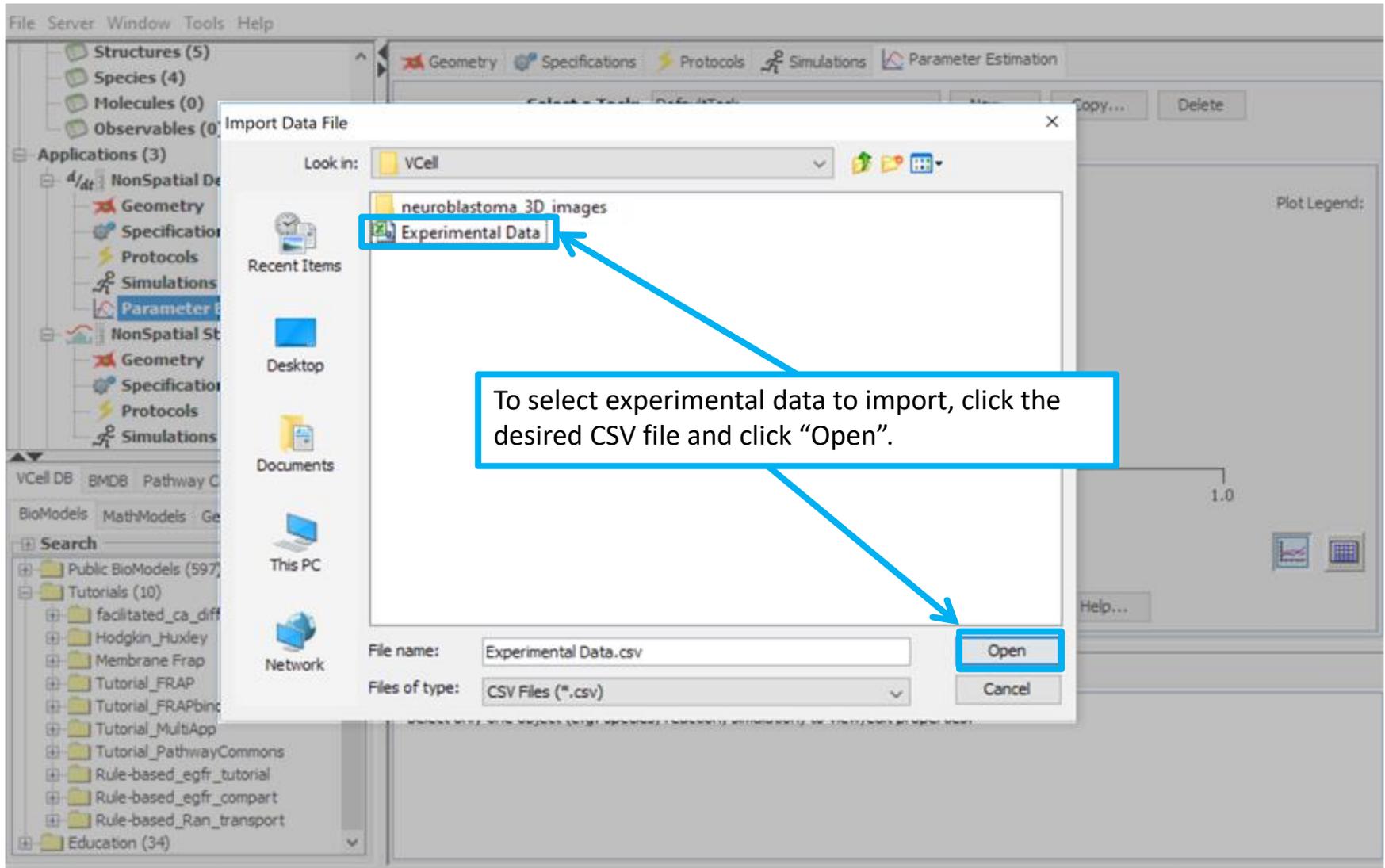
To select a parameter to fit, click on the specific parameter , in this case Kf, and click "OK".



The screenshot displays the MultiAppRanModel software interface. The left sidebar shows a tree view of the model structure, including Physiology (Reaction Diagram, Reactions (2), Structures (5), Species (4), Molecules (0), Observables (0)) and Applications (3). The main window is titled "Parameter Estimation" and shows a table of parameters to be fitted. A blue callout box points to a plus sign icon in the top-left corner of the parameter table, with the text: "Continue adding parameters using the 'plus sign' icon until you have selected all the parameters you want to fit."

Parameter	Context	Model Value	Initial Guess	Lower Bound	Upper Bound
Kf	r0	1	1	0.1	10
Kr	r0	1000	1000	100	10000

The screenshot displays the MultiApp software interface. On the left, a tree view shows the project structure under 'MultiAppRanModel', including 'Physiology' (Reaction Diagram, Reactions (2), Structures (5), Species (4), Molecules (0), Observables (0)) and 'Applications (3)' (NonSpatial Deterministic, Geometry, Specifications, Protocols, Simulations, Parameter Estimation, NonSpatial Stochastic). The 'Parameter Estimation' application is highlighted with a blue box. Below the tree view, there are tabs for 'VCell DB', 'BMDB', 'Pathway Comm', and 'Sabio', and a 'Search' section with a list of models including 'Public BioModels (597)', 'Tutorials (10)', and 'Education (34)'. The main window shows the 'Parameter Estimation' task selected, with a 'Select a Task' dropdown set to 'DefaultTask'. The 'Experimental Data Import' tab is active, showing a plot with a y-axis from -1.0 to 1.0 and an x-axis labeled 't' from -1.0 to 1.0. The 'Import from CSV file...' button is highlighted with a blue box. A blue arrow points from the 'Import from CSV file...' button to a text box containing the instruction: 'To import experimental data, use the "Experimental Data Import" tab, then "Import from CSV file..."'. Another blue arrow points from the 'Experimental Data Import' tab to a text box containing the instruction: 'You can use the CSV file of the simulation results for RanC_cyt, which was saved from the nonspatial stochastic application run earlier in this tutorial. Alternatively, you can download this file from [vcell.org /support](http://vcell.org/support)'.



The screenshot displays the software interface for parameter estimation. The left sidebar shows a tree view of applications, with 'Parameter Estimation' highlighted. The main window shows the 'Parameter Estimation' task selected, with the 'Experimental Data Mapping' dialog open. The dialog has a table with two columns: 'Experimental Data' and 'Model Association'. A row is highlighted with the text '(Var=RanC_cyt_Count) RanC_cyt_Count' under 'Experimental Data' and 'unmapped' under 'Model Association'. A button labeled 'Map Experimental Data...' is visible at the bottom of the dialog. A text box with arrows pointing to the highlighted row and the button contains the following text:

To map a concentration, click “Experimental Data Mapping”, select an unmapped concentration, and press “Map Experimental Data...”

File Server Window Tools Help

Geometry Specifications Protocols Simulations Parameter Estimation

Select a Task: DefaultTask New... Copy... Delete

Parameters Experimental Data Import Experimental Data Mapping Run Task

Experimental Data	Model Association
t	t
(Var=RanC_cyt_Count) RanC_cyt_Count	unmapped

Map Experimental Data

[C_cyt]
[RanC_cyt]
[RanC_nuc]
[Ran_cyt]
t

OK Cancel

Select the concentration to map, and press "OK".

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

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

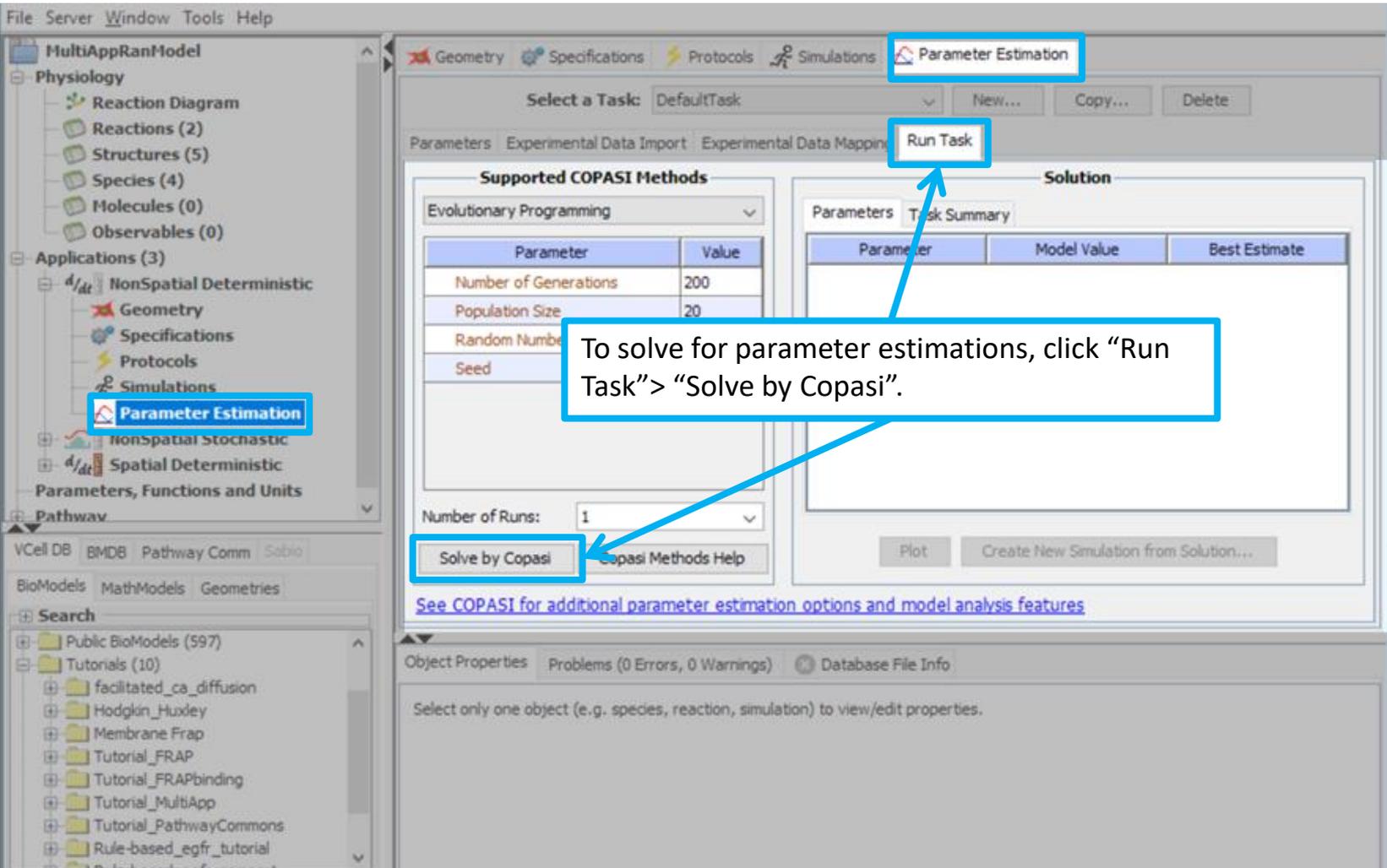
Applications (3)

- NonSpatial Deterministic
 - Geometry
 - Specifications
 - Protocols
 - Simulations
 - Parameter Estimation
- NonSpatial Stochastic
 - Geometry
 - Specifications
 - Protocols
 - Simulations

VCell DB BMDB Pathway Comm Sabio

BioModels MathModels Compartment

- facilitated_ca_diffusion
- Hodgkin_Huxley
- Membrane Frap
- Tutorial_FRAP
- Tutorial_FRAPbinding
- Tutorial_MultiApp
- Tutorial_PathwayCommons
- Rule-based_egfr_tutorial
- Rule-based_egfr_compart
- Rule-based_Ran_transport
- Education (34)



The screenshot displays the COPASI software interface with the 'Parameter Estimation' task selected. The left sidebar shows a project tree for 'MultiAppRanModel' with sub-items like 'Physiology', 'Applications', and 'NonSpatialDeterministic'. The main window shows the 'Parameter Estimation' task configuration, including a table of supported methods and a 'Solution' table. A callout box points to the 'Best Estimate' column in the 'Solution' table, highlighting the accuracy of the estimates. Another callout box points to the 'Plot' button, indicating how to visualize the results.

Notice how accurate the estimate is in relation to the model value

Parameter	Model Value	Best Estimate
Kf	1	1.00604
Kr	1000	952.967

To plot estimation values versus model values, click "Plot".

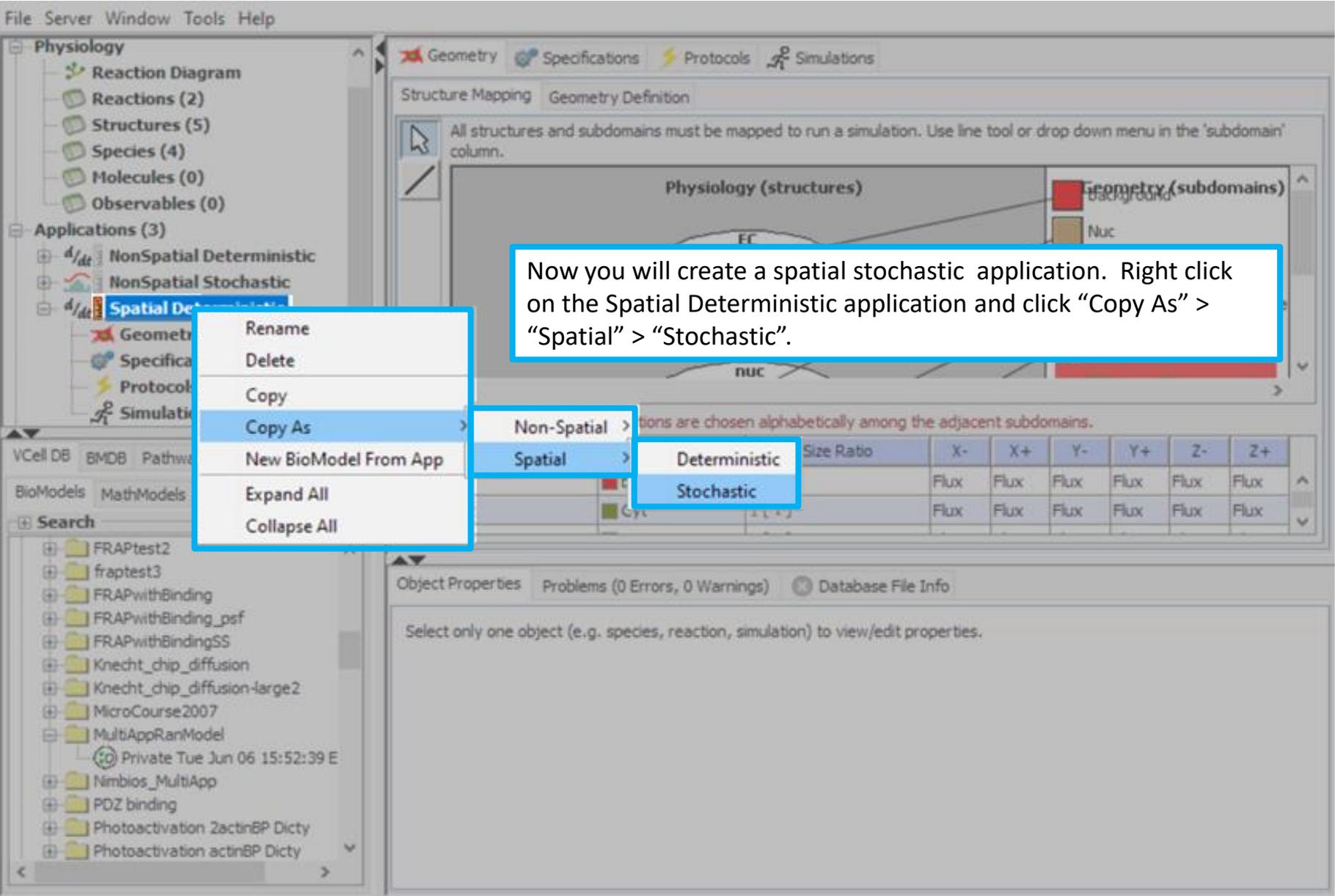
The screenshot shows the MultiApp software interface. The main window has a menu bar (File, Server, Window, Tools, Help) and a toolbar with icons for Geometry, Specifications, Protocols, Simulations, and Parameter Estimation. A tree view on the left shows the project structure under 'MultiAppRanModel', including 'Physiology' (Reaction Diagram, Reactions (2), Structures (5), Species (4), Molecules (0), Observables (0)) and 'Applications (3)' (NonSpatial Deterministic, Geometry, Specifications, Protocols, Simulations, Parameter Estimation). A search bar at the bottom left contains a list of models, with 'MultiAppRanModel' selected. A 'Parameter Estimation' dialog box is open in the center, featuring a list of parameters on the left and a plot on the right. The list includes 'EXPT: (Var=RanC_cyt) RanC_cyt' (selected), 'EST: RanC_cyt', 'EST: C_cyt', 'EST: J_flux0', 'EST: J_r0', 'EST: KFlux_nm_cyt', 'EST: KFlux_nm_nuc', 'EST: Ran_cyt', 'EST: RanC_nuc', 'EST: Size_cyt', 'EST: Size_EC', 'EST: Size_nm', 'EST: Size_nuc', and 'EST: Size_pm'. The plot shows a yellow line representing the fit for 'EST: RanC_cyt' and purple dots representing experimental data for 'EXPT: (Var=RanC_cyt) RanC_cyt'. The y-axis ranges from 0.0 to 2.0E-5, and the x-axis (t) ranges from 0.0 to 20.0. A legend on the right identifies the lines. A 'Close' button is at the bottom of the dialog.

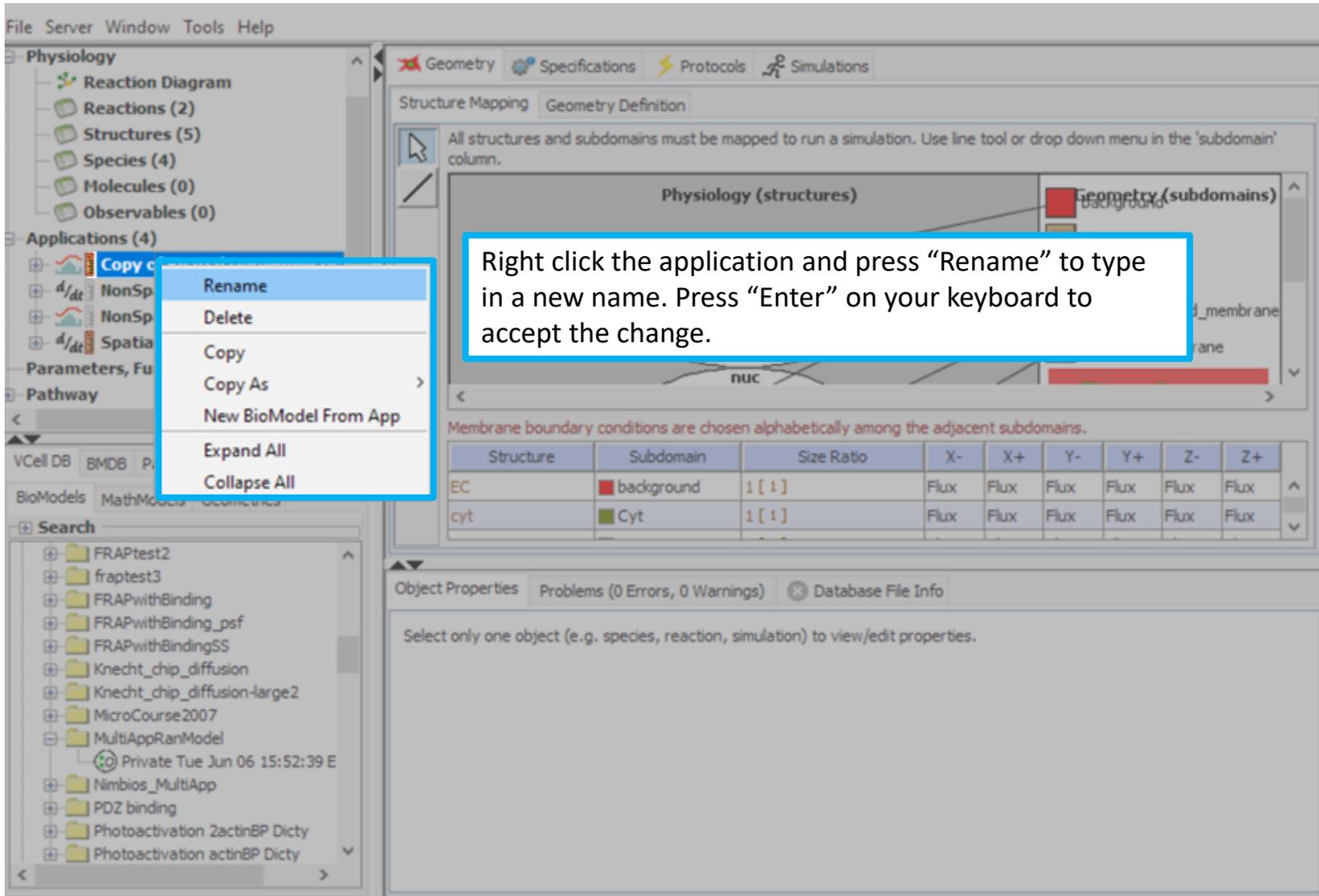
Select the estimation and experimental parameters you wish to compare based on the fit of their lines. Press "Close" when finished.

EXPT: (Var=RanC_cyt) RanC_cyt
EST: RanC_cyt
EST: C_cyt
EST: J_flux0
EST: J_r0
EST: KFlux_nm_cyt
EST: KFlux_nm_nuc
EST: Ran_cyt
EST: RanC_nuc
EST: Size_cyt
EST: Size_EC
EST: Size_nm
EST: Size_nuc
EST: Size_pm

Plot Legend:
EXPT: (Var=RanC_cyt) RanC_cyt
EST: RanC_cyt

Close





The screenshot shows the Multi-App software interface. On the left, a tree view displays a hierarchy of models, including 'Physiology' and 'Applications (4)'. A context menu is open over the 'Copy' application, listing options: 'Rename', 'Delete', 'Copy', 'Copy As', 'New BioModel From App', 'Expand All', and 'Collapse All'. The 'Rename' option is highlighted. The main workspace shows a 'Structure Mapping' view with a table of subdomains and a table of membrane boundary conditions.

Right click the application and press “Rename” to type in a new name. Press “Enter” on your keyboard to accept the change.

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

Membrane boundary conditions are chosen alphabetically among the adjacent subdomains.

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

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

The screenshot shows the software interface with the 'Specifications' tab selected. A yellow arrow points from the top table to the bottom table, indicating the change in initial conditions.

Initial Condition: Concentration Number of Particles

Species	Structure	Depiction	Clamped	Initial Condition	Well Mixed	Diffusion Constant	Force Continuous
RanC_cyt	Cyt		<input type="checkbox"/>	0.0 [μM]	<input type="checkbox"/>	10.0 [$\mu\text{m}^2.\text{s}^{-1}$]	<input type="checkbox"/>
C_cyt	Cyt		<input type="checkbox"/>	0.0 [μM]	<input type="checkbox"/>	10.0 [$\mu\text{m}^2.\text{s}^{-1}$]	<input type="checkbox"/>
Ran_cyt	Cyt		<input type="checkbox"/>	0.0 [μM]	<input type="checkbox"/>	10.0 [$\mu\text{m}^2.\text{s}^{-1}$]	<input type="checkbox"/>
RanC_nuc	Nuc		<input type="checkbox"/>	4.499509624492510	<input type="checkbox"/>	10.0 [$\mu\text{m}^2.\text{s}^{-1}$]	<input type="checkbox"/>

Initial Condition: Concentration Number of Particles

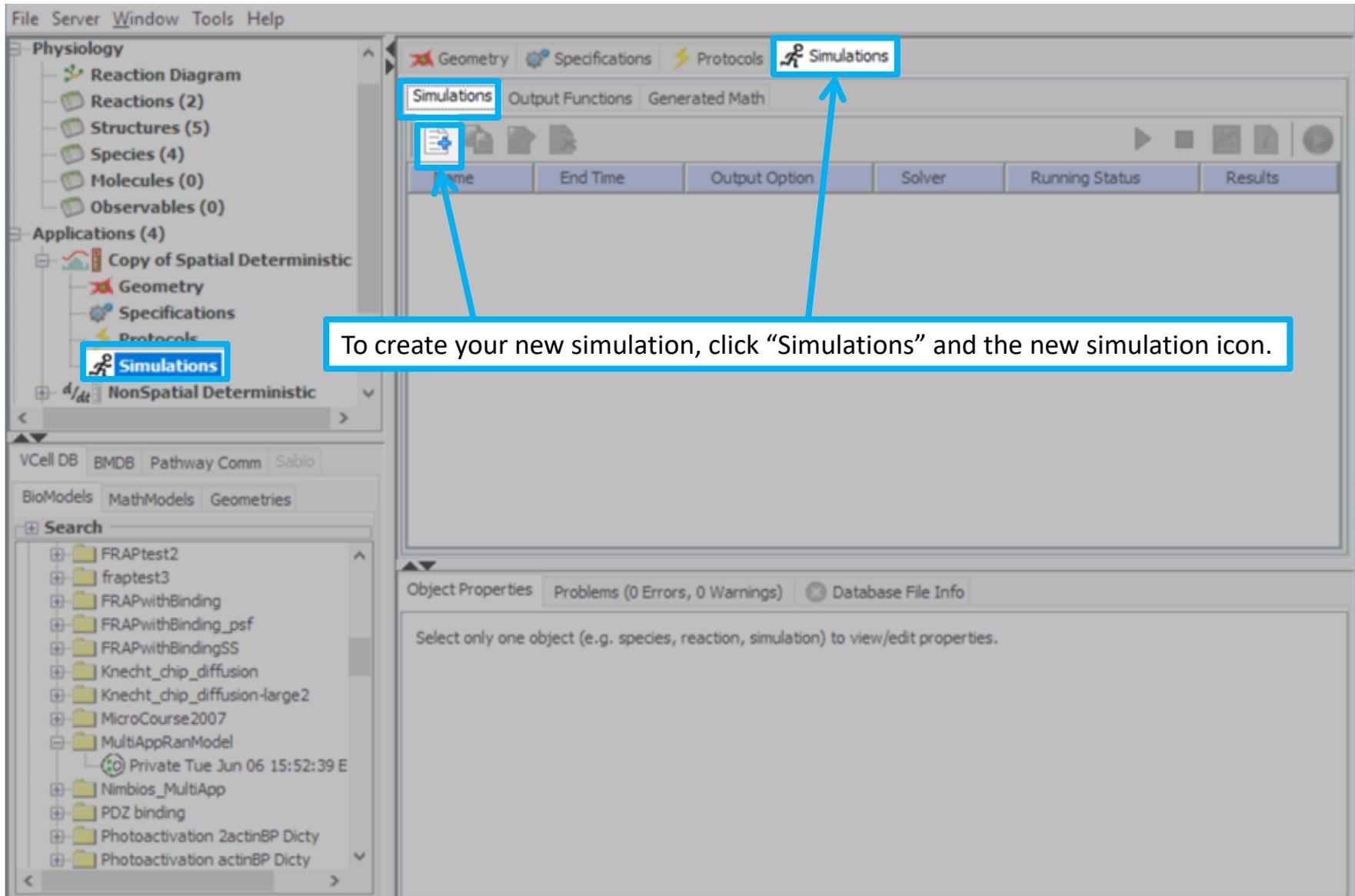
Species	Structure	Depiction	Clamped	Initial Condition	Well Mixed	Diffusion Constant	Force Continuous
RanC_cyt	Cyt		<input type="checkbox"/>	0.0 [molecules]	<input type="checkbox"/>	10.0 [$\mu\text{m}^2.\text{s}^{-1}$]	<input type="checkbox"/>
C_cyt	Cyt		<input type="checkbox"/>	0.0 [molecules]	<input type="checkbox"/>	10.0 [$\mu\text{m}^2.\text{s}^{-1}$]	<input type="checkbox"/>
Ran_cyt	Cyt		<input type="checkbox"/>	0.0 [molecules]	<input type="checkbox"/>	10.0 [$\mu\text{m}^2.\text{s}^{-1}$]	<input type="checkbox"/>
RanC_nuc	Nuc		<input type="checkbox"/>	2105.0 [molecules]	<input type="checkbox"/>	10.0 [$\mu\text{m}^2.\text{s}^{-1}$]	<input type="checkbox"/>

To work with number of particles instead of concentration (for stochastic models only), double click your new application to expand the options, and select "Specifications". On the species tab, select "Number of Particles".

The screenshot shows the VCell software interface. The left sidebar contains a tree view with 'Physiology' and 'Applications (4)'. Under 'Applications', 'Copy of Spatial Deterministic' is expanded to show 'Geometry', 'Specifications', 'Protocols', and 'Simulations'. The 'Specifications' tab is selected. The main window displays a table with columns: Species, Structure, Depiction, Clamped, Initial Condition, Well Mixed, Diffusion Constant, and Force Cont. The 'Initial Condition' column is highlighted with a blue box. A blue arrow points from a callout box to the 'Initial Condition' cell for the species 'RanC... nuc', which contains the value '1000'. The callout box contains the text: 'To change the number of particles of a species, type in a value under the "Initial Condition" column.'

Species	Structure	Depiction	Clamped	Initial Condition	Well Mixed	Diffusion Constant	Force Cont
Ran_...	cyt	●	<input type="checkbox"/>	0.0 [molecules]	<input type="checkbox"/>	10.0 [$\mu\text{m}^2 \cdot \text{s}^{-1}$]	<input type="checkbox"/>
C_cyt	cyt	●	<input type="checkbox"/>	0.0 [molecules]	<input type="checkbox"/>	10.0 [$\mu\text{m}^2 \cdot \text{s}^{-1}$]	<input type="checkbox"/>
RanC...	cyt	●	<input type="checkbox"/>	0.0 [molecules]	<input type="checkbox"/>	10.0 [$\mu\text{m}^2 \cdot \text{s}^{-1}$]	<input type="checkbox"/>
RanC...	nuc	●	<input type="checkbox"/>	1000	<input type="checkbox"/>	10.0 [$\mu\text{m}^2 \cdot \text{s}^{-1}$]	<input type="checkbox"/>

Description	Parameter	Expression	Units
initial count for RanC_nuc for RanC_nuc	initCount	1012.0	molecules
diffusion constant for RanC_nuc for RanC_nuc	diff	10.0	$\mu\text{m}^2 \cdot \text{s}^{-1}$
Boundary Condition X- for RanC_nuc for RanC_nuc	BC_Xm	<zero flux>	$\mu\text{M} \cdot \mu\text{m} \cdot \text{s}^{-1}$
Boundary Condition X+ for RanC_nuc for RanC_nuc	BC_Xp	<zero flux>	$\mu\text{M} \cdot \mu\text{m} \cdot \text{s}^{-1}$
Boundary Condition Y- for RanC_nuc for RanC_nuc	BC_Ym	<zero flux>	$\mu\text{M} \cdot \mu\text{m} \cdot \text{s}^{-1}$
Boundary Condition Y+ for RanC_nuc for RanC_nuc	BC_Yp	<zero flux>	$\mu\text{M} \cdot \mu\text{m} \cdot \text{s}^{-1}$
Boundary Condition Z- for RanC_nuc for RanC_nuc	BC_Zm	<zero flux>	$\mu\text{M} \cdot \mu\text{m} \cdot \text{s}^{-1}$
Boundary Condition Z+ for RanC_nuc for RanC_nuc	BC_Zp	<zero flux>	$\mu\text{M} \cdot \mu\text{m} \cdot \text{s}^{-1}$



The screenshot displays the software interface with the following components:

- Left Panel:** A tree view under 'Physiology' and 'Applications (4)'. The 'Simulations' folder under 'Applications' is highlighted with a blue box.
- Top Panel:** A tabbed interface with 'Geometry', 'Specifications', 'Protocols', and 'Simulations'. The 'Simulations' tab is active and highlighted with a blue box.
- Sub-panels:** Below the 'Simulations' tab are sub-panels for 'Simulations', 'Output Functions', and 'Generated Math'. The 'Simulations' sub-panel contains a 'New Simulation' icon (a document with a plus sign) and a table with columns: 'Name', 'End Time', 'Output Option', 'Solver', 'Running Status', and 'Results'. The 'New Simulation' icon is highlighted with a blue box.
- Bottom Panel:** A search bar and a list of models. The 'MultiAppRanModel' folder is expanded, showing a sub-entry 'Private Tue Jun 06 15:52:39 E'.
- Bottom Right Panel:** 'Object Properties' and 'Problems (0 Errors, 0 Warnings)' tabs. A message reads: 'Select only one object (e.g. species, reaction, simulation) to view/edit properties.'

To create your new simulation, click "Simulations" and the new simulation icon.

The screenshot shows a software interface with a sidebar on the left and a main workspace on the right. The sidebar contains a tree view with categories like 'Physiology' and 'Applications'. The 'Simulations' icon in the 'Applications' section is highlighted with a blue box. The main workspace has a top menu with 'Geometry', 'Specifications', 'Protocols', and 'Simulations'. Below this is a toolbar with icons for simulation management. A table below the toolbar lists simulation details:

Name	End Time	Output Option	Solver	Running Status	Results
Simulation2	1.0	every 0.05 s	Smoldyn	not saved	no

A blue arrow points from a callout box to the 'Simulation2' row in the table. The callout box contains the text: 'To edit your simulation, click the simulation and click on the edit simulation icon.'

At the bottom of the interface, there is an 'Object Properties' panel with tabs for 'Problems (0 Errors, 0 Warnings)' and 'Database File Info'. It includes an 'Annotation' field, 'Settings' for 'Timestep' (1.0E-4s) and 'Output' (every 0.05 sec), and a 'Parameters with values changed from defaults' table.

Parameter Name	Default	New Value/Expression	Scan
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File Server Window Tools Help

Physiology

- Reaction Diagram
- Reactions (2)
- Structures (5)
- Species (4)
- Molecules (0)
- Observables (0)

Applications (4)

- Copy of Spatial Deterministic
- Geometry
- Specifications
- Protocols
- Simulations
- NonSpatial Deterministic

VCell DB BMBD Pathway Comm Sabio

BioModels MathModels Geometries

Search

- FRAPtest2
- fraptest3
- FRAPwithBinding
- FRAPwithBinding_psf
- FRAPwithBindingSS
- Knecht_chip_diffusion
- Knecht_chip_diffusion-large2
- MicroCourse2007
- MultiAppRanModel
- Private Tue Jun 06 15:52
- Nimbios_MultiApp
- PDZ binding
- Photoactivation 2actinBP Dicty
- Photoactivation actinBP Dicty

Edit: Simulation2

Parameters **Mesh**

Mesh Size

Geometry Size (um) (100.0, 100.0, 25.0)

Mesh Size (elements) Lock aspect ratio

X	101
Y	101
Z	27

Total Size (elements) 101 x 101 x 27 = 275427

Spatial Step (um)

Δx	1.0
Δy	1.0
Δz	1.0

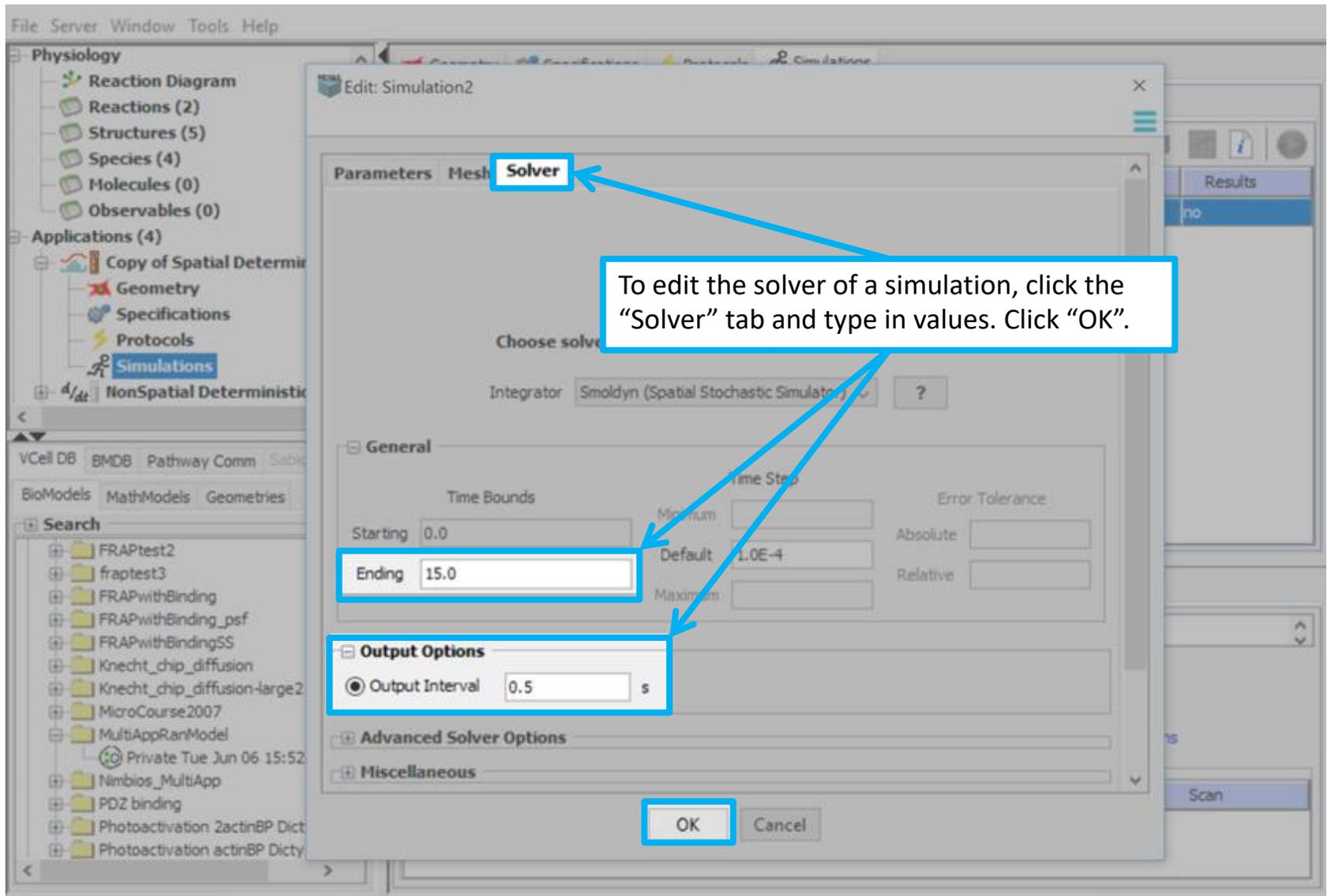
OK Cancel

Results

no

Scan

To edit the mesh of a simulation, click the "Mesh" tab and type in the desired values.



You can now run your simulation, and view your results as previously described in this tutorial.

Name	End Time	Output Option	Solver	Running Status	Results
Simulation2	15.0	every 0.5 s	Smoldyn	not saved	no

Name	End Time	Output Option	Solver	Running Status	Results
1000 particles	10.0	every 0.5 s	Smoldyn	completed	yes
100 particles	10.0	every 0.1 s	Smoldyn	completed	yes