VCell

The Virtual Cell

A modeling environment for the simulation of cellular events. Download at vcell.org
Version 7.7 July 2025

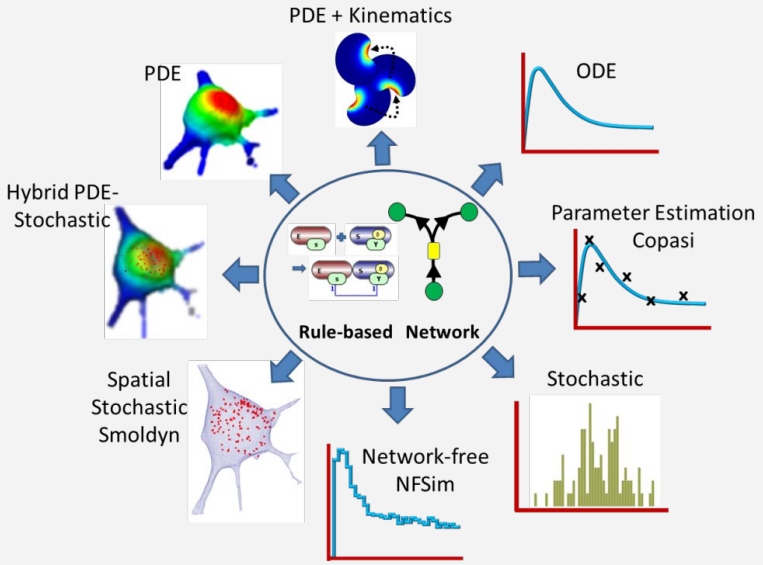


Image Based Geometry

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

NIH National Institute of General Medical Sciences
VCell is funded by the NIGMS

CCAM VCell is developed at CCAM
Center for Cell Analysis & Modeling

VCell Image-Based Geometry

Objective:

Create a single Biomodel of Ran nuclear transport using Virtual Cell modeling and analysis software.

Goals:

- ➔ Use the model created in Tutorial I to import fluorescence images into VCell and segment a 3D image to create a geometry.

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

Model building can be matched to the BioModel **Tutorial_MultiApp** in the Tutorial folder in the **VCell Database.**

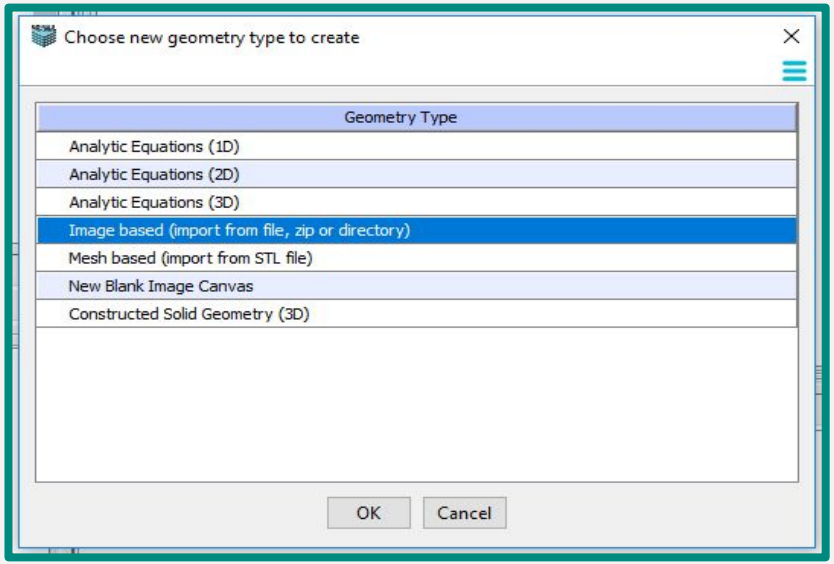
Table of Contents

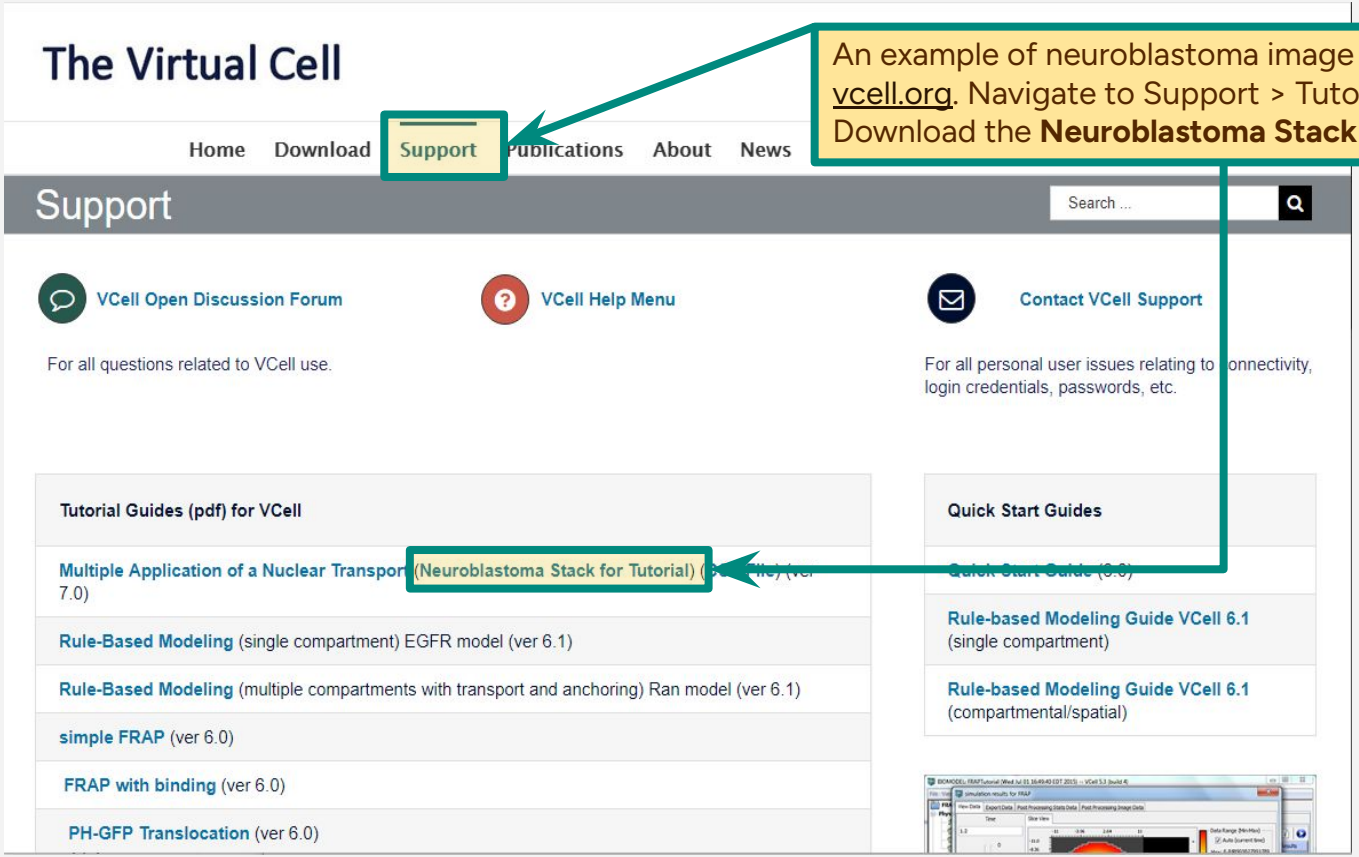
Click on a section title to go to that section.

01

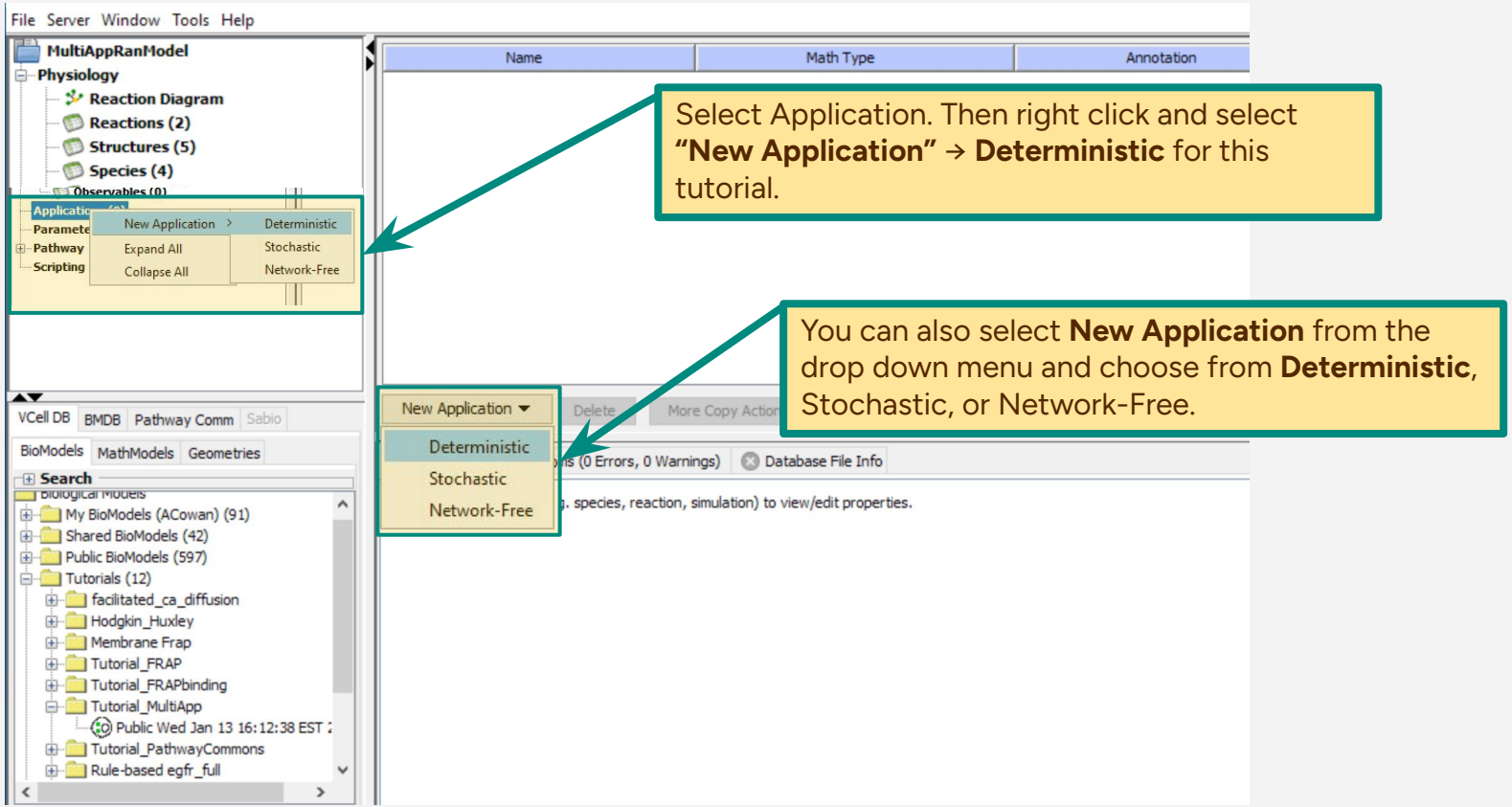
Starting Image-Based Geometry

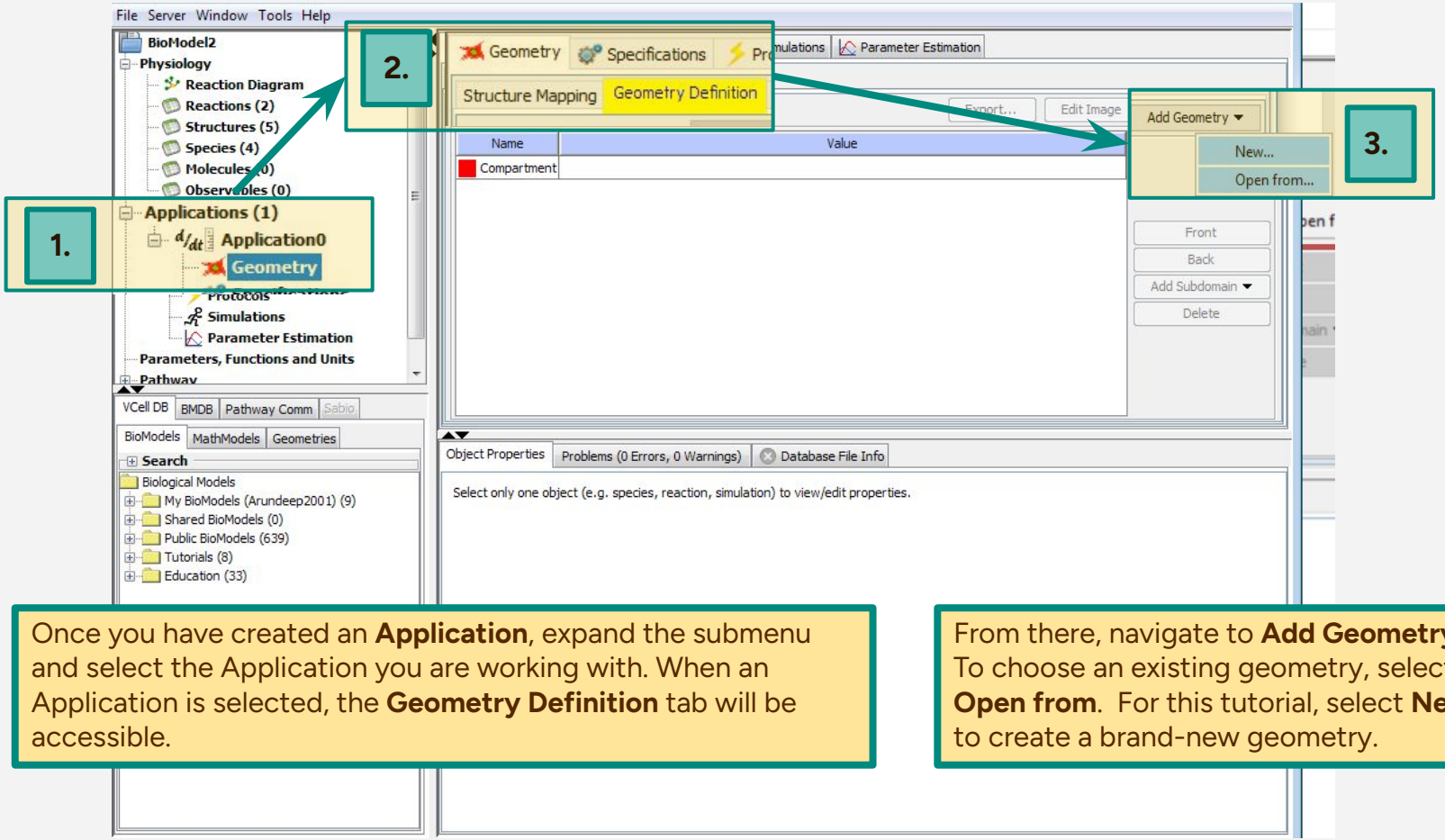
- Define an application to create a geometry
- Import a 3D microscopy image that consists of a z-stack of 34 2D images of a neuroblastoma cell.





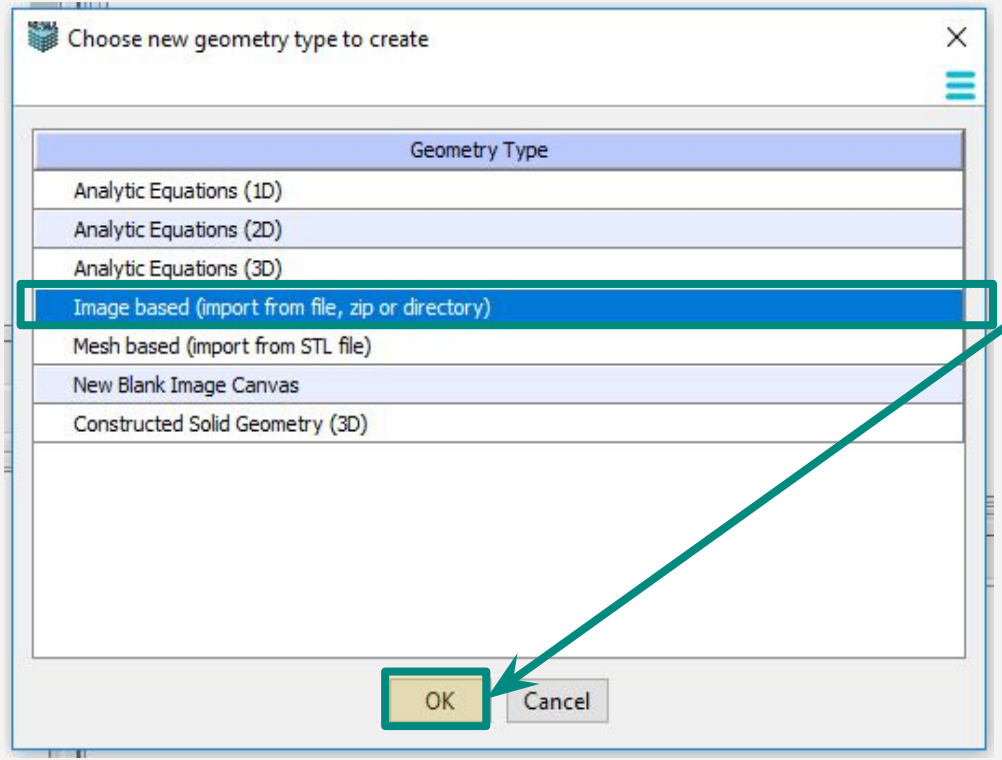
An example of neuroblastoma image is located on vcell.org. Navigate to Support > Tutorial Guides. Download the **Neuroblastoma Stack for Tutorial**.


File Server Window Tools Help
MultiAppRanModel
Physiology
Reaction Diagram
Reactions (2)
Structures (5)
Species (4)
New Application
Expand All
Collapse All
Deterministic
Stochastic
Network-Free
Name
Math Type
Annotation
Select Application. Then right click and select "New Application" → Deterministic for this tutorial.
You can also select New Application from the drop down menu and choose from Deterministic, Stochastic, or Network-Free.
New Application
Delete
Deterministic
Stochastic
Network-Free
Database File Info
species, reaction, simulation) to view/edit properties.
VCell DB
BMDB
Pathway Comm
BioModels
MathModels
Geometries
Search
My BioModels (ACowan) (91)
Shared BioModels (42)
Public BioModels (597)
Tutorials (12)
facilitated_ca_diffusion
Hodgkin_Huxley
Membrane Frap
Tutorial_FRAP
Tutorial_FRAPbinding
Tutorial_MultiApp
Tutorial_PathwayCommons
Rule-based egfr_full



Once you have created an **Application**, 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.** To choose an existing geometry, select **Open from**. For this tutorial, select **New** to create a brand-new geometry.

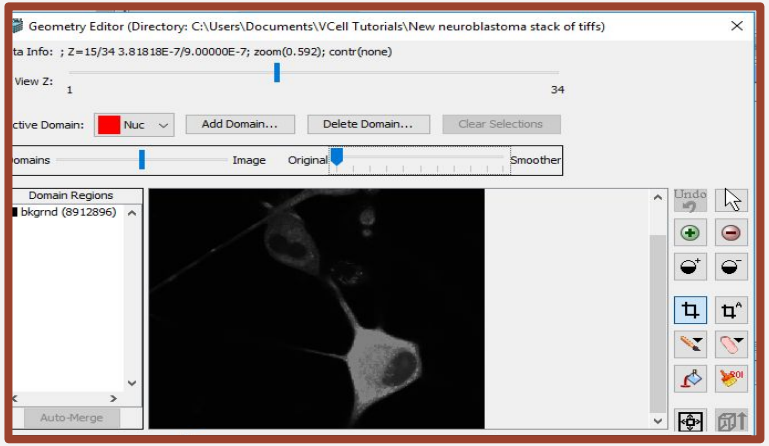


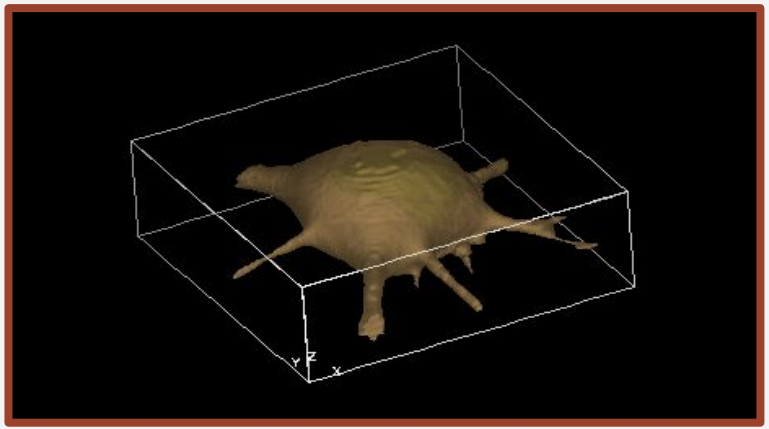
Select **Image based (import images from file, zip or directory)** and press **OK**.

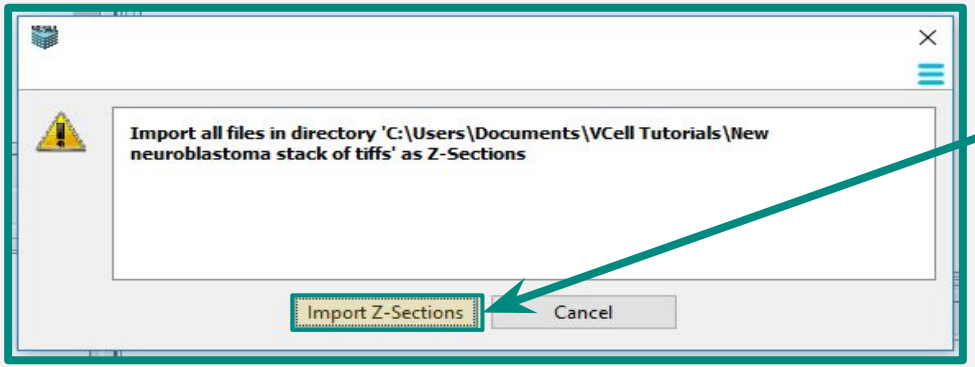
02

Creating and Editing Image-Based Geometry

- Create and an image-based geometry model using a 3D image of a neuroblastoma cell.

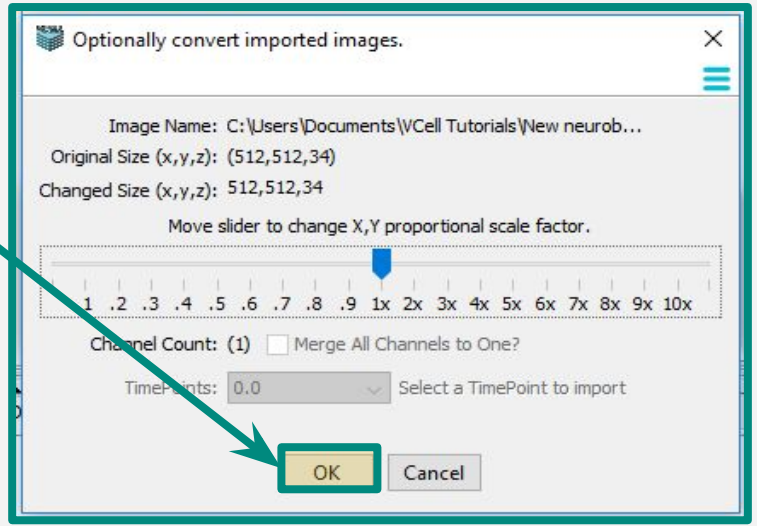




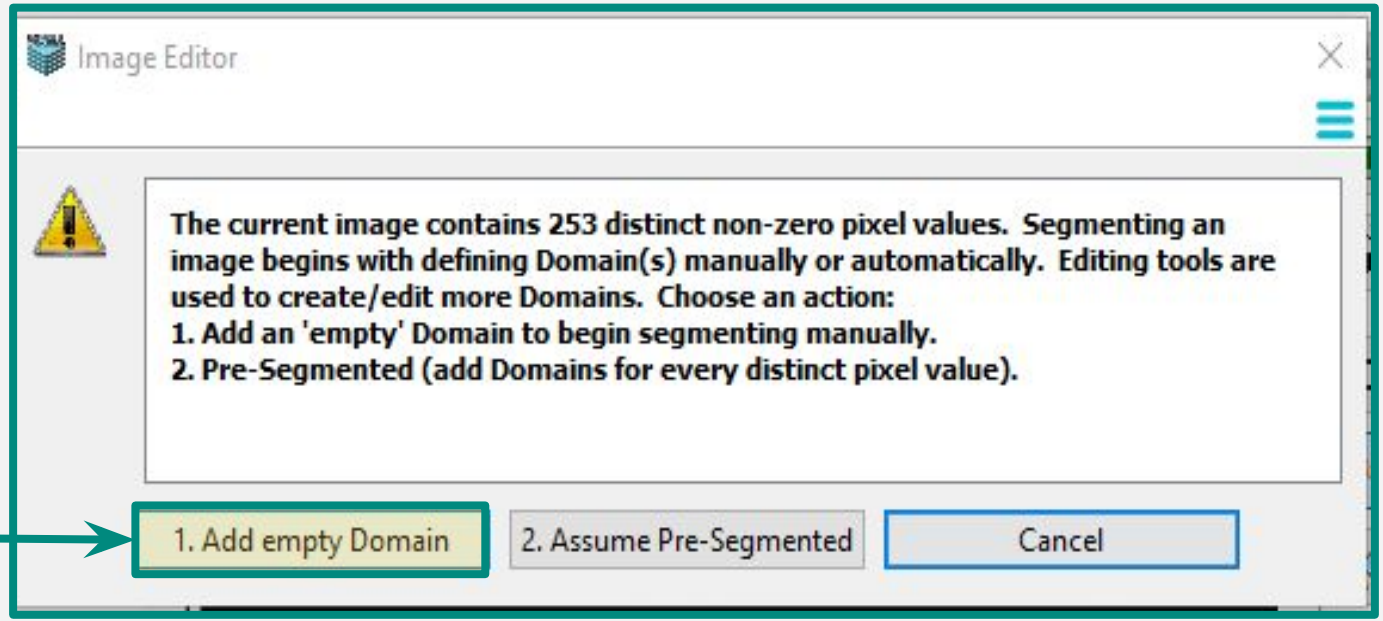


After you have selected the folder containing the series of images, confirm that you want to import the stack.

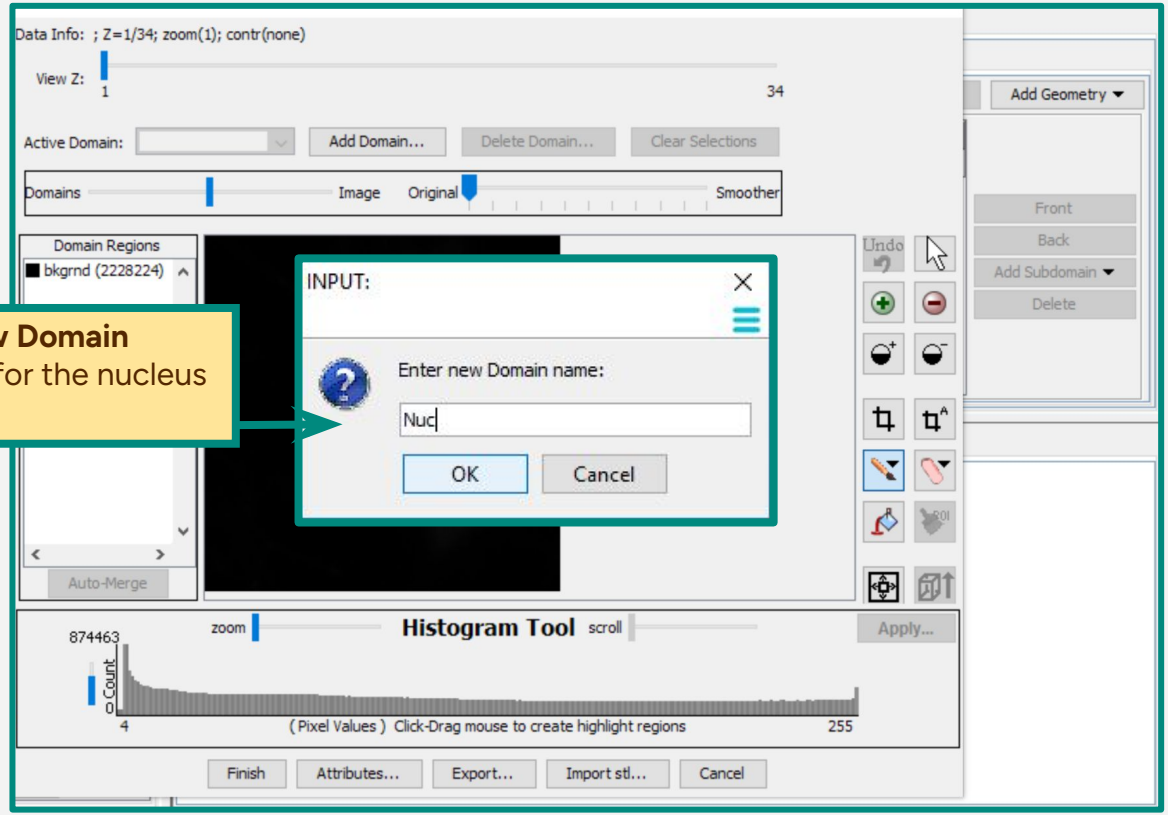
To adjust the resolution of your images, use your cursor to **adjust the slider** to the desired scale factor. Images can either be reduced or enlarged according to the original size.
For this tutorial, we keep the image the same.



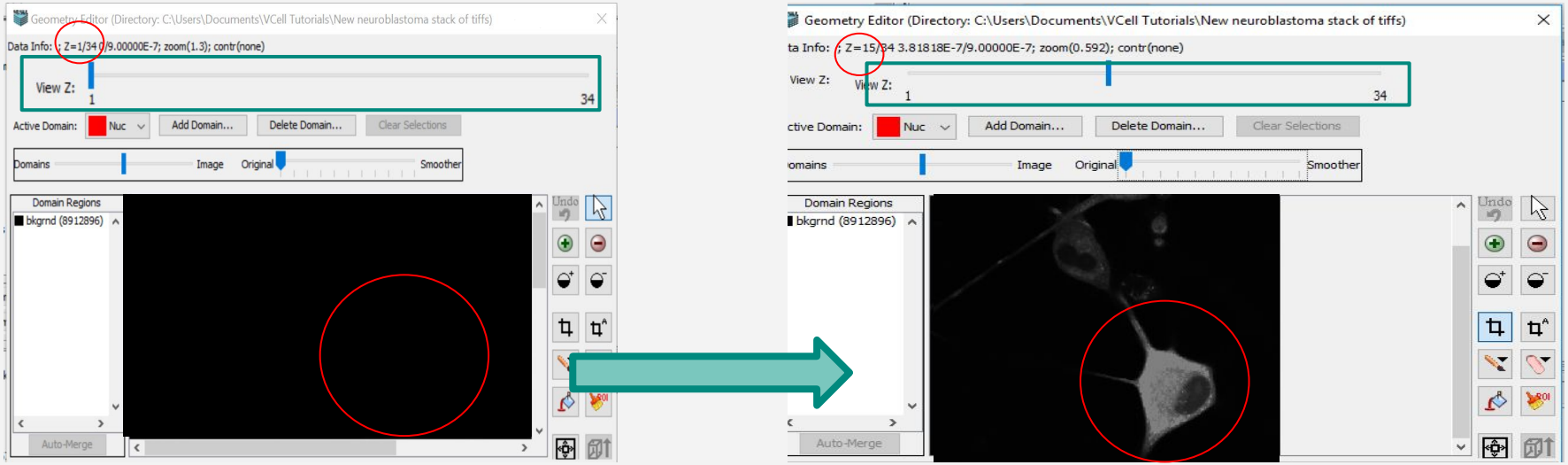
Manually segment the image by selecting **1. Add empty Domain**.



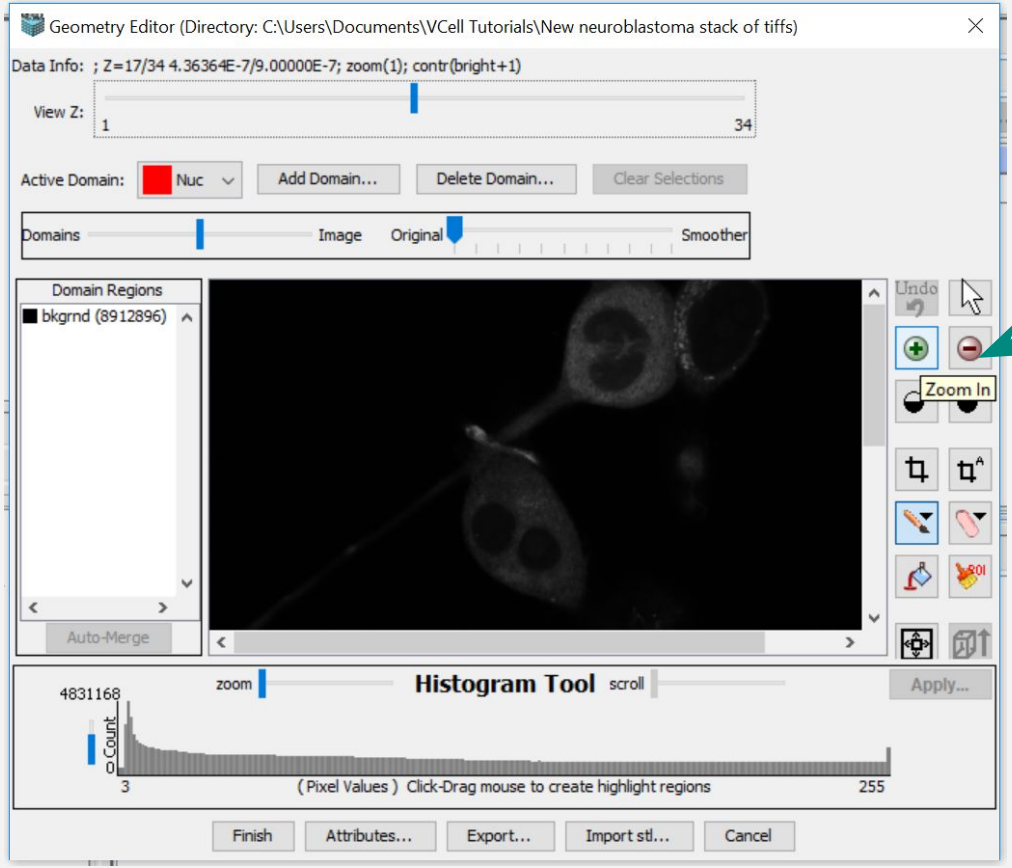
Define the **new Domain Name** as **Nuc** for the nucleus and press **OK**.

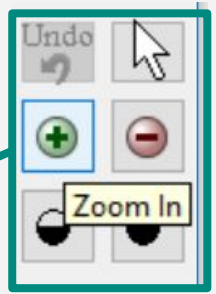


After importing the images, adjust the **z plane** so you can see your cells. The stack defaults to z=1, so you may not be able to see your cells until you focus up through the stack.

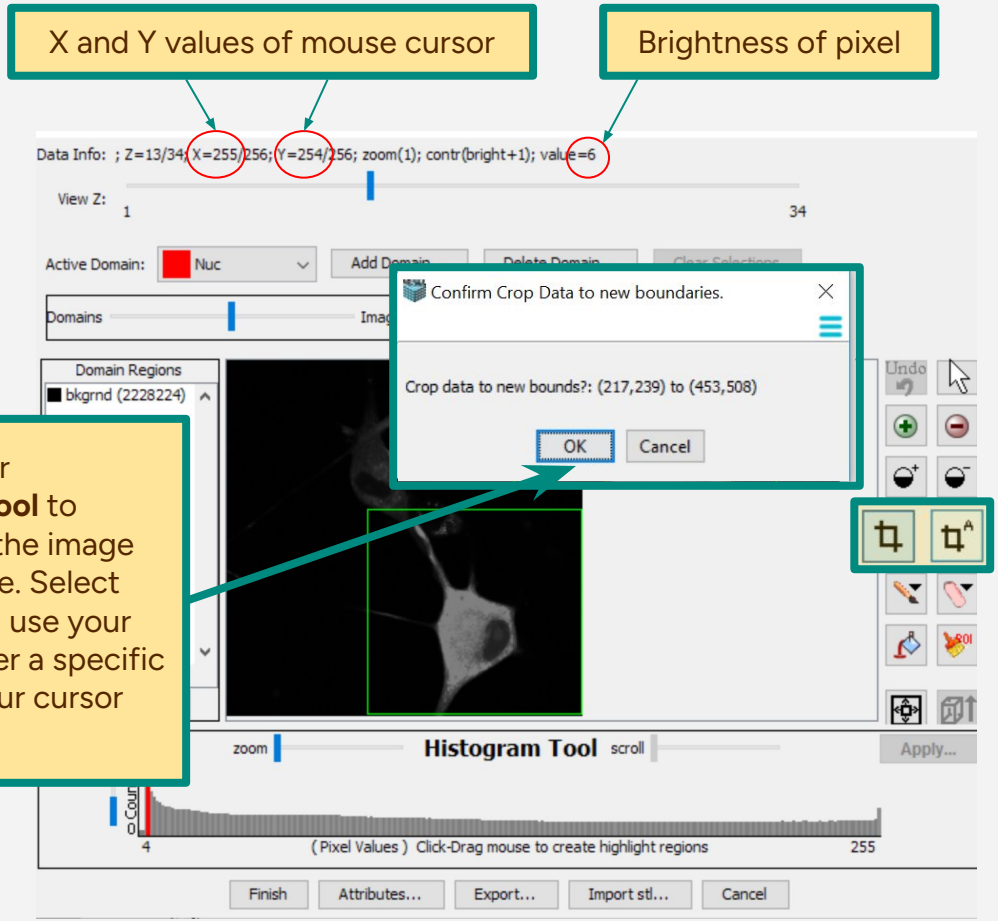


Note: The Z-Slider is used to view different slices of the cell





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

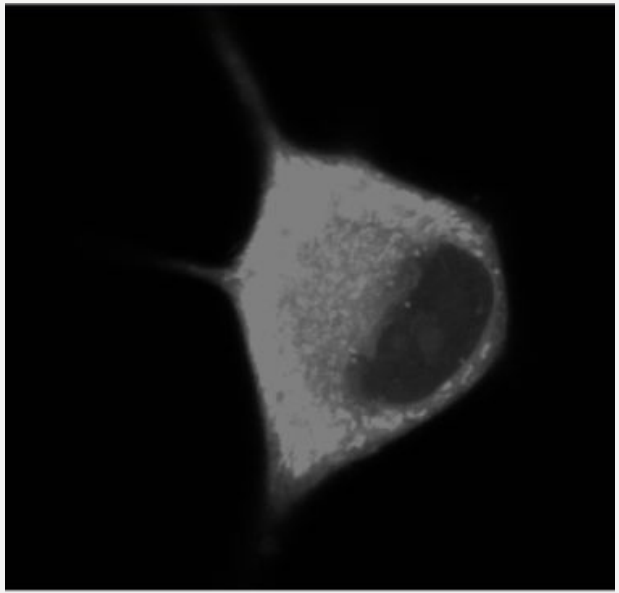


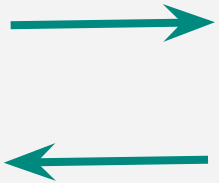
Use the **manual** or **automatic crop tool** to select an area of the image and reduce its size. Select the crop tool, and use your cursor to drag over a specific area. Let go of your cursor and click **OK.**

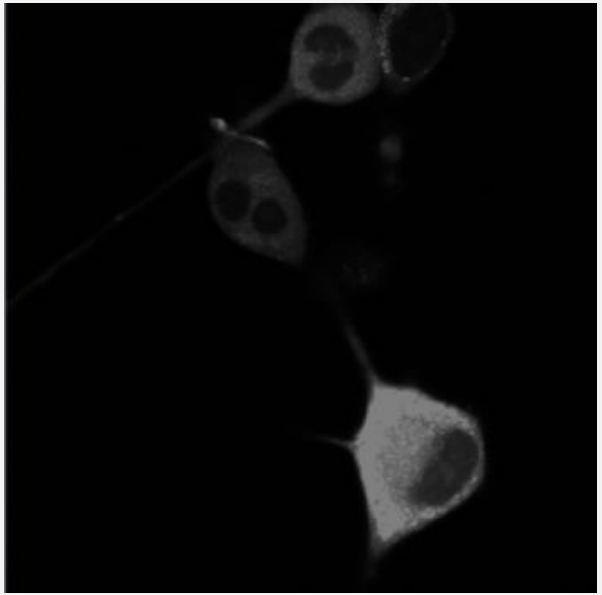
NOTE: Crop the image to the dimensions (217, 239) to (453, 508) by dragging the mouse. The number at the top will show the location and change as you move the cursor.

NOTE: You cannot uncrop the image after you hit "OK," and would have to restart.

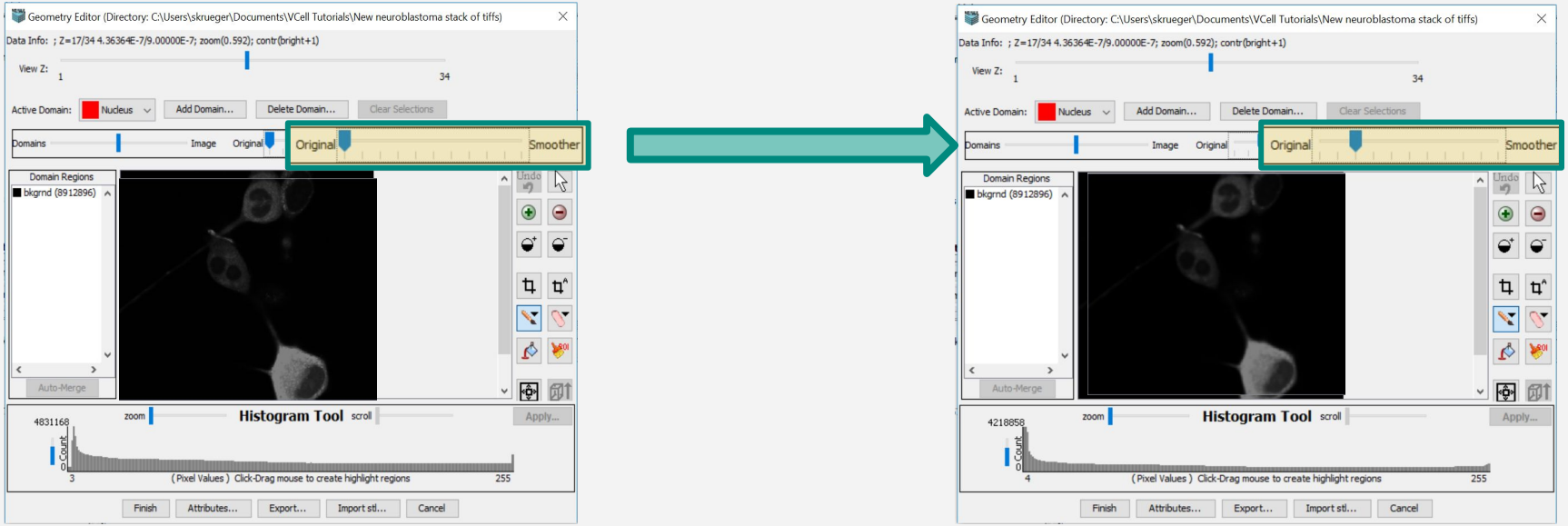
Use the **zoom tool** to increase, (zoom in) or decrease (zoom out) the image magnification.





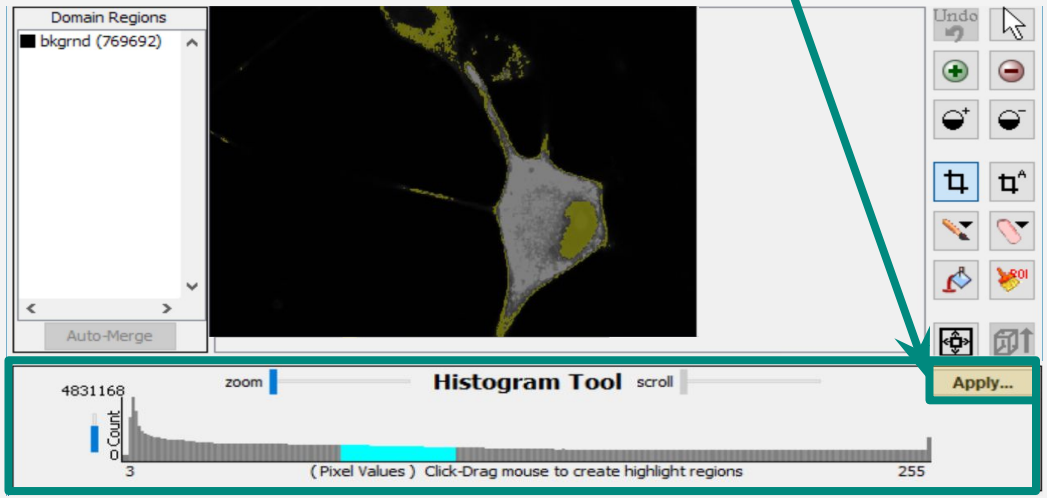


In order to reduce noise in the images, you can apply an **averaging filter** to the stack.

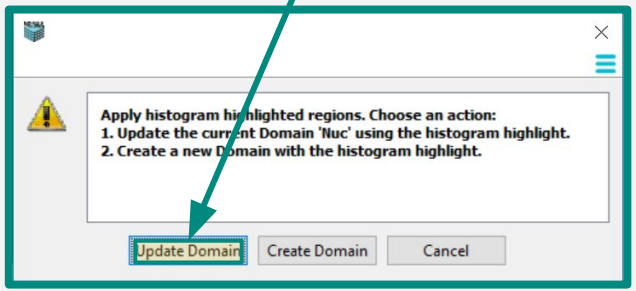


With the Averaging Filter, each pixel and it's immediate neighbor's intensity values are averaged. For example, in a 2-D image, each pixel has 8 surrounding neighbors. The 9 values are added together and divided by 9; that value replaces the center pixel's value.

1. Use the **Histogram Tool** to select pixel values in your image for thresholding specific regions. Hit **Apply** to accept the values. In the tutorial, the range 77-109 was used.



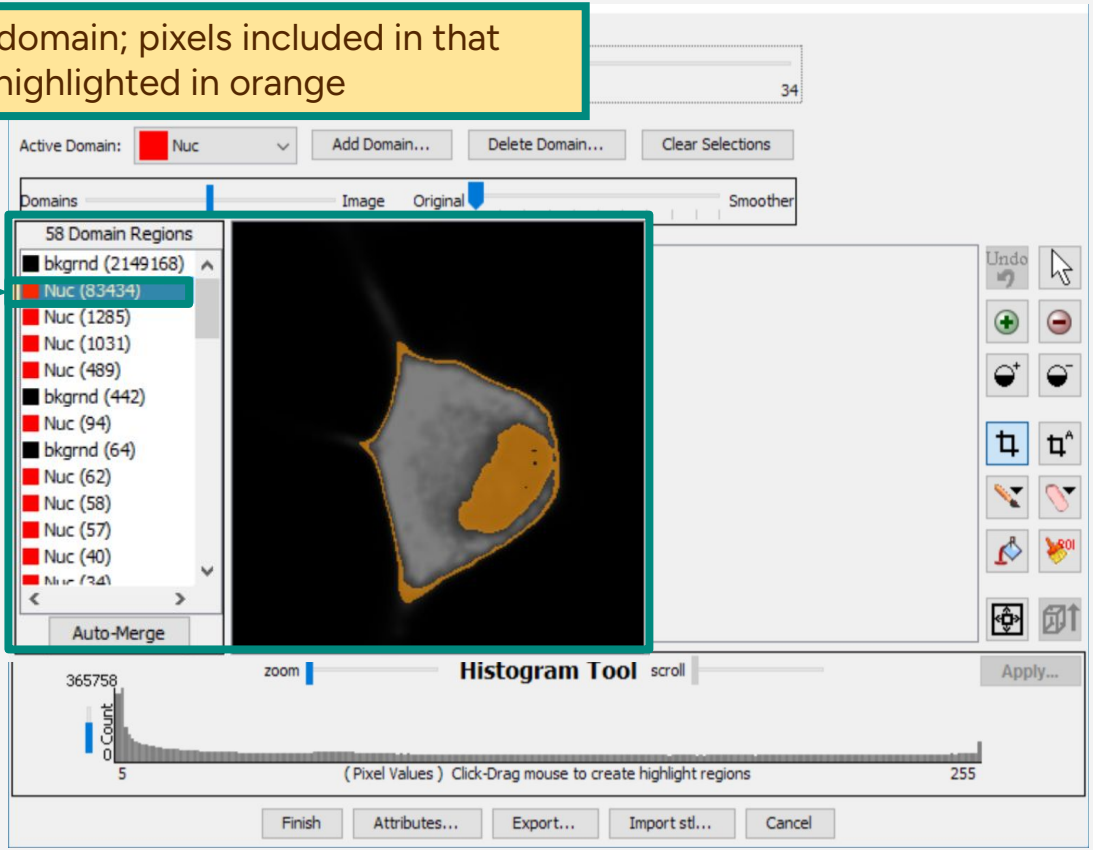
2. An **Update Domain** confirmation will appear. You can update the domain you initially defined, or you can create a new domain and apply the threshold values. For this tutorial, click **Update Domain.**

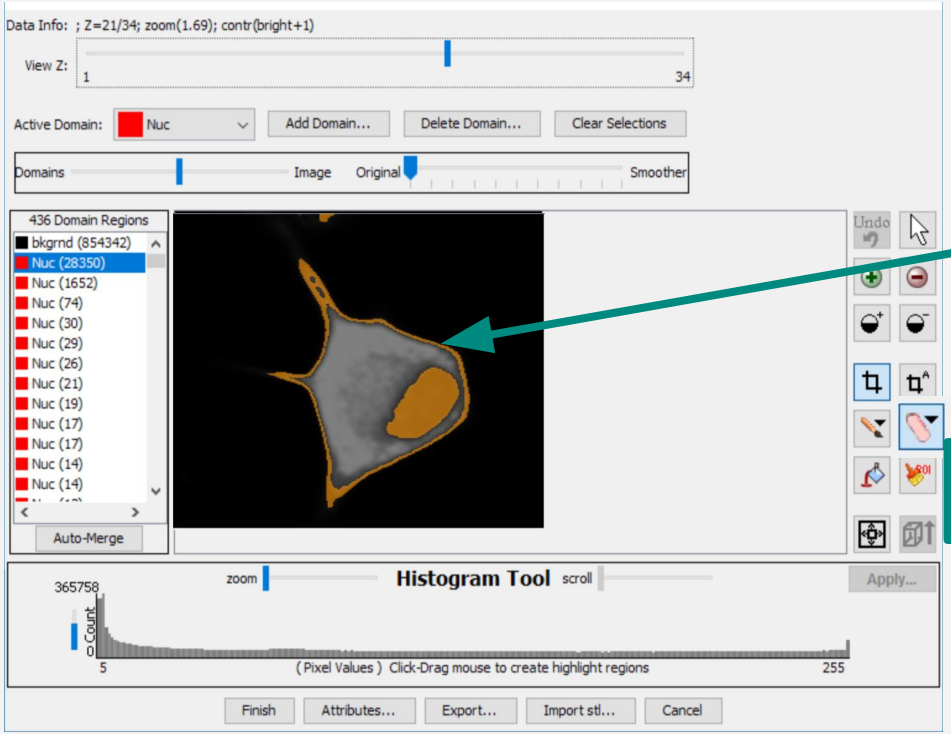


The Histogram Tool is used to visualize the distribution of pixels in your image.

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

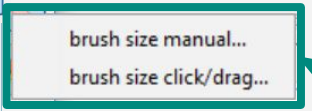
The largest Nuc domain contains the pixels of the nucleus, but may include pixels that are outside of it.





IMPORTANT: Start from z=1 and go through all the slices in order for these next few steps.

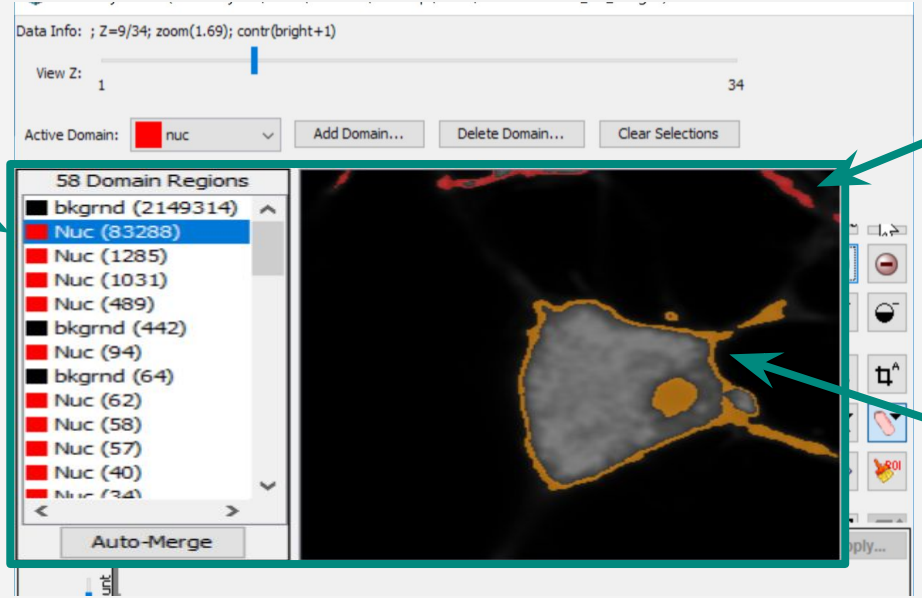
Select the largest **Nuc** domain. Use the **eraser tool** to erase **orange** highlighted pixels in the membrane that are **not part of the nucleus**. Pixels in **red** belong to other domain regions, so you don't need to erase them yet (see the next slide). **You will have to select the largest Nuc domain every time you erase, as it will deselect**.



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

Note: You must go through ALL 34 slices and ensure that only the nucleus is highlighted for this domain.

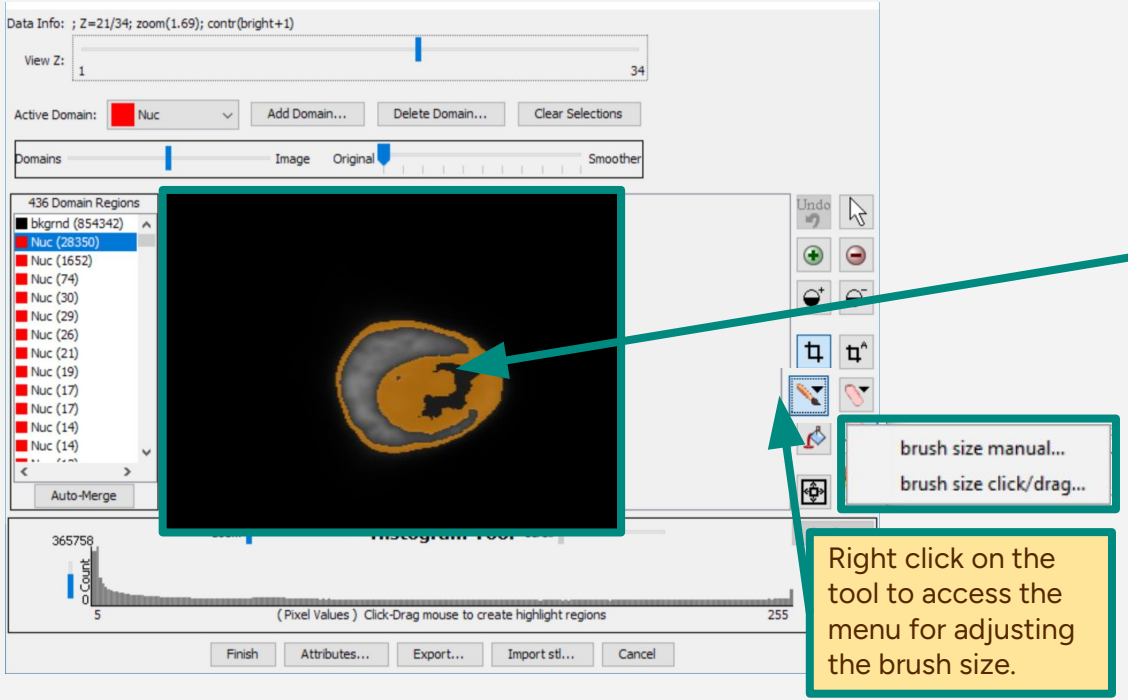
Largest Nuc domain



Red further away → KEEP

Orange near the nucleus → ERASE

Again, **start from z=1** and work your way through. Keep an eye out for any changes to your previous work and alter as needed.



The largest "Nuc" domain may also be missing some pixels that should be part of the nucleus.

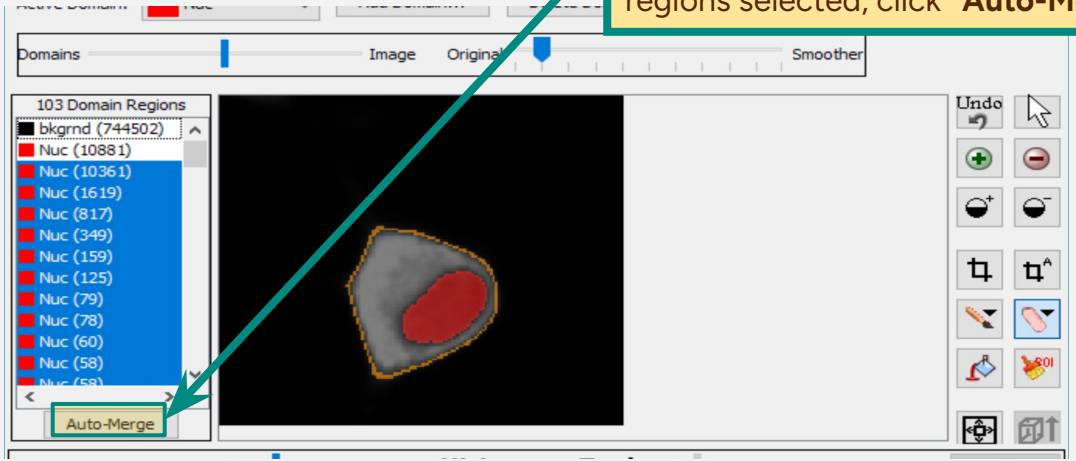
Use the **paint tool** to add highlighted pixels that should be within the nucleus.

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

TIP: Do not hit the undo button while manually editing because it will undo previous edits and/or the selection from the histogram

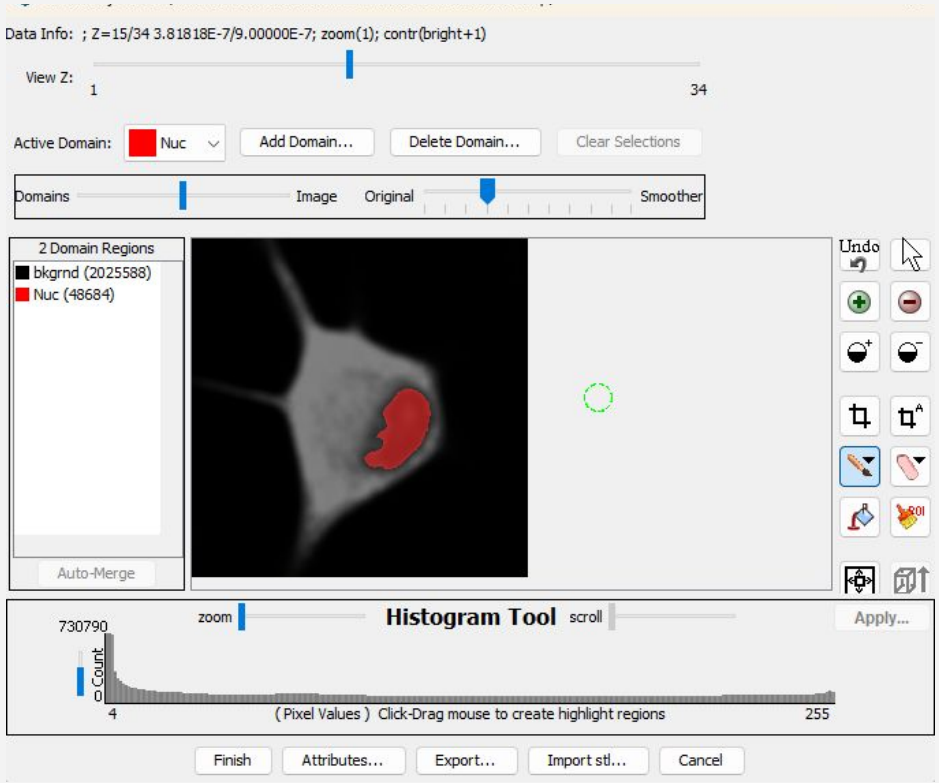
TIP #1:
To select multiple regions at a time, press Shift and the Down Arrow Button.

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

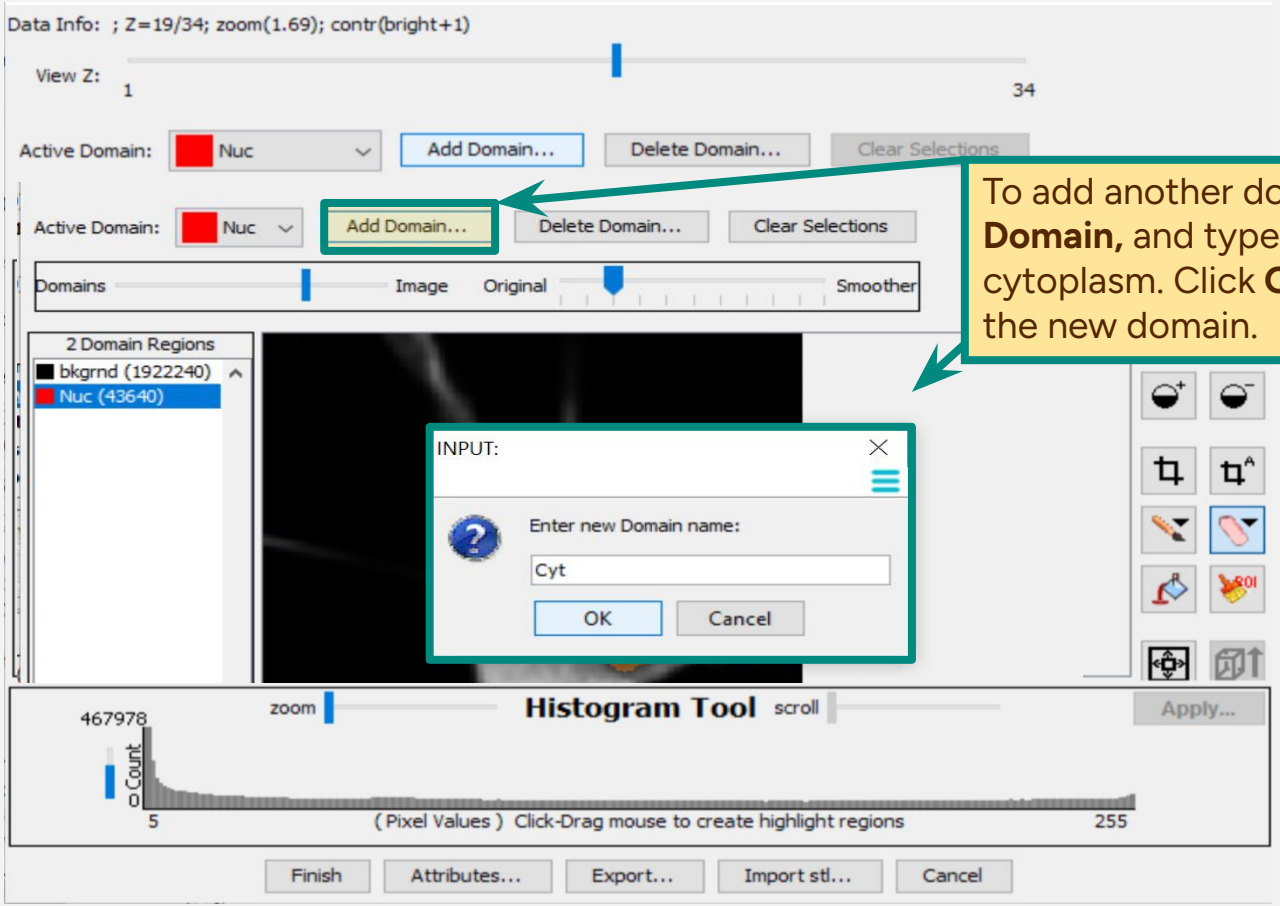


TIP #2:
Select and auto merge Nuc domains in sections starting from the smallest regions, especially if you have multiple domains with a large amount of pixels.

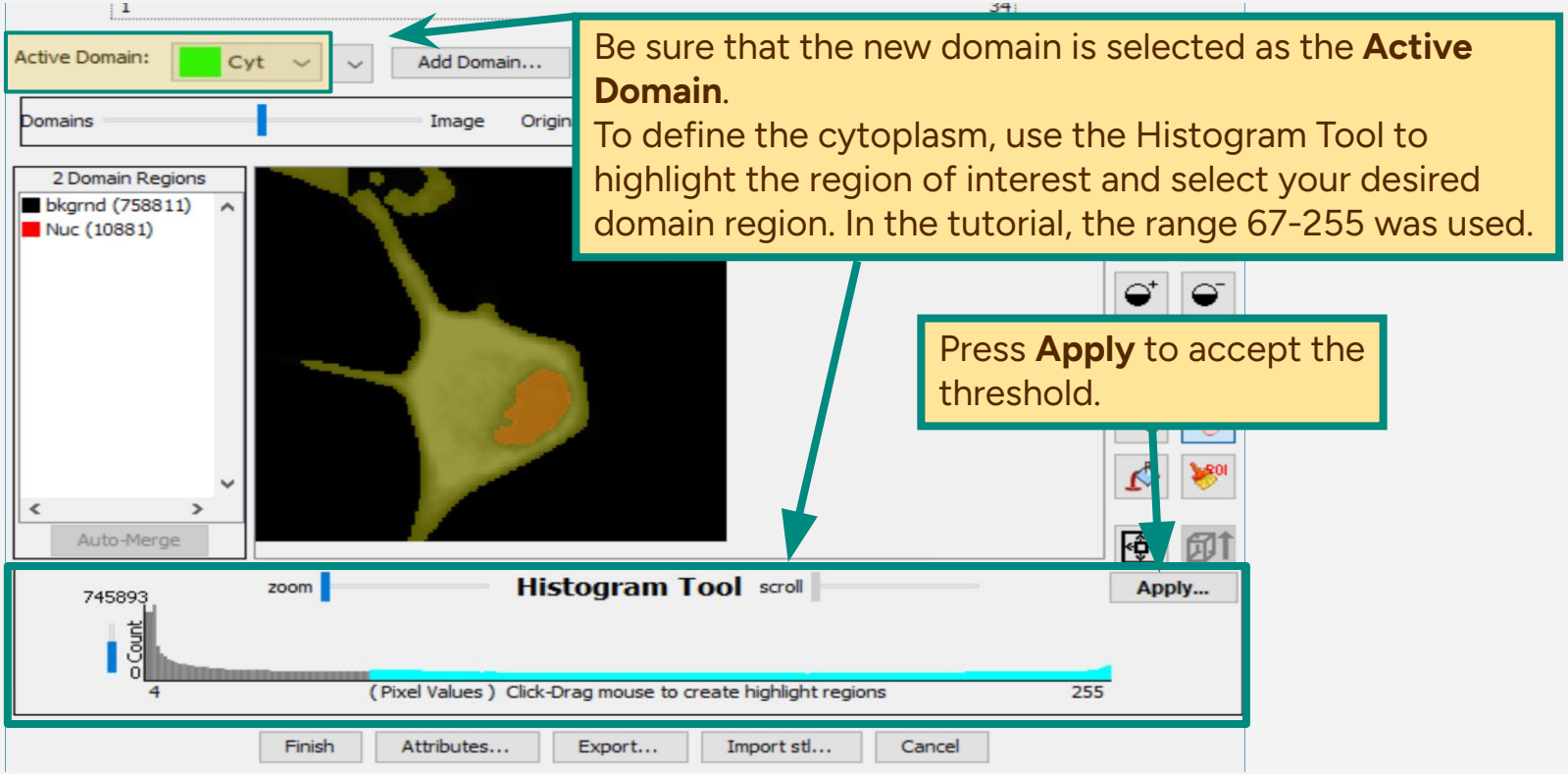
Be sure to scroll through all the sections once again to ensure that you have properly removed all non-nuclear regions. If you still have some areas, repeat the process.

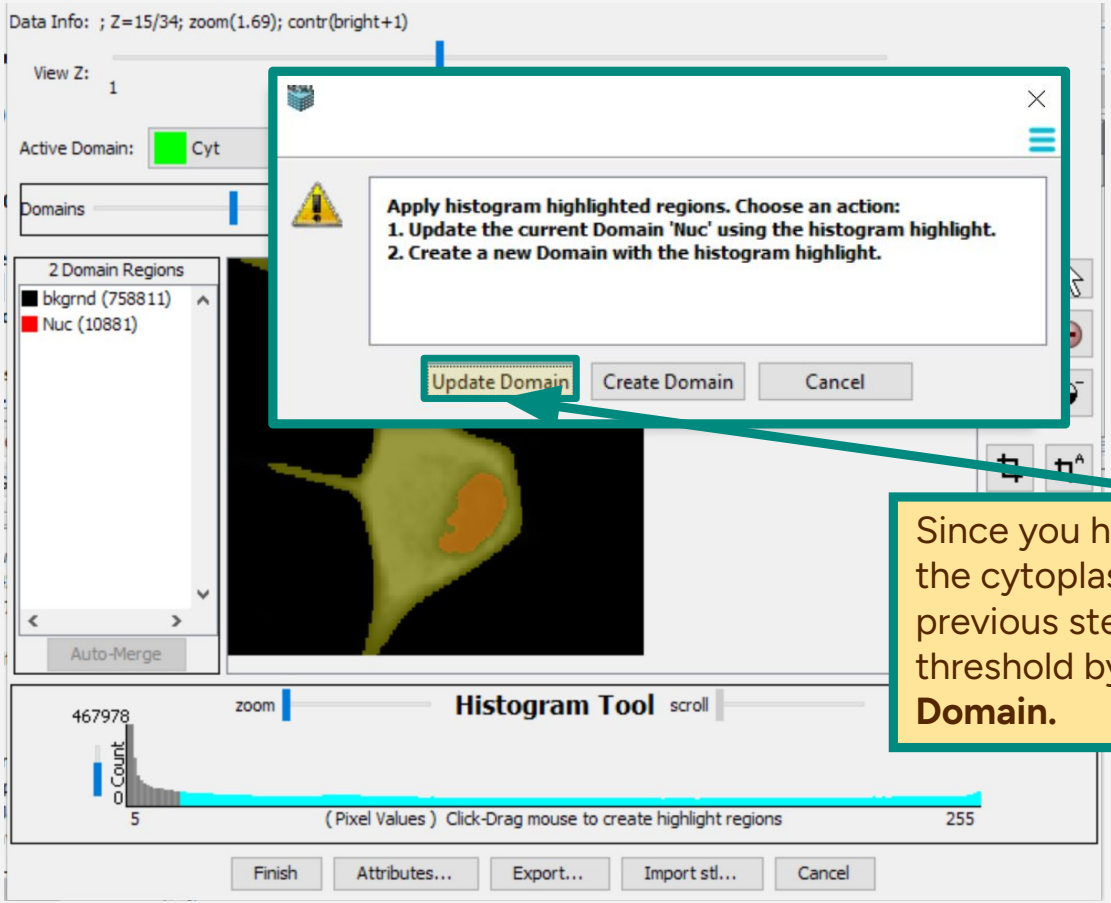


Now you have finished editing the Nuc domain. Next, we will move on to the cytoplasm.



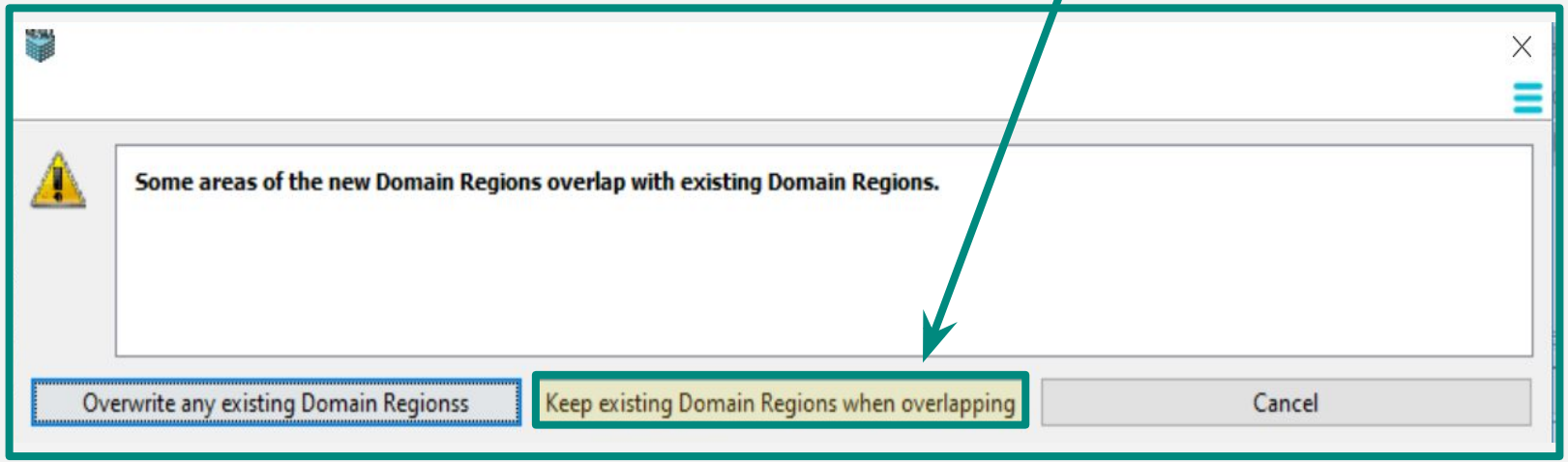
To add another domain, click **Add Domain,** and type in Cyt for cytoplasm. Click **OK** to accept the new domain.

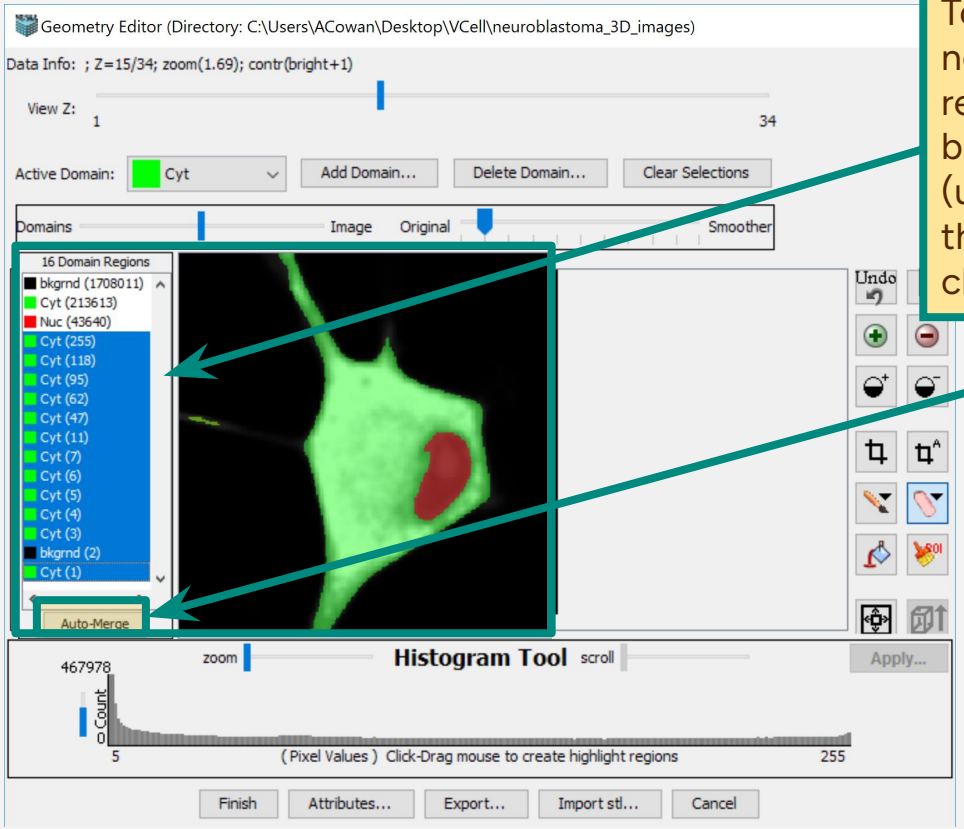

Active Domain:
Cyt
Add Domain...
Domains
Image
2 Domain Regions
bkgrnd (758811)
Nuc (10881)
Auto-Merge
Be sure that the new domain is selected as the **Active Domain**.
To define the cytoplasm, use the Histogram Tool to highlight the region of interest and select your desired domain region. In the tutorial, the range 67-255 was used.
Press **Apply** to accept the threshold.
zoom
Histogram Tool
scroll
Apply...
745893
Count
4
(Pixel Values) Click-Drag mouse to create highlight regions
255
Finish
Attributes...
Export...
Import stl...
Cancel



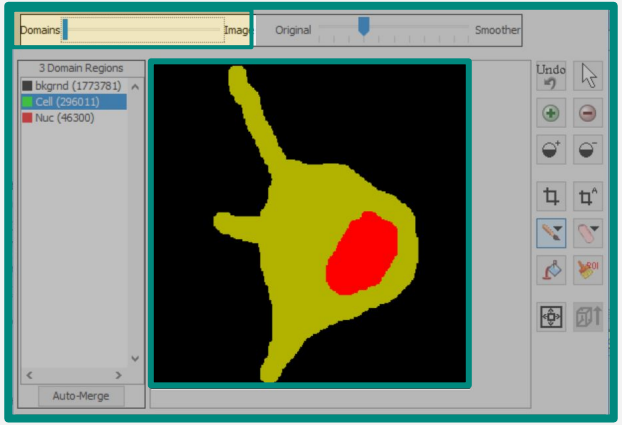
Since you have already created the cytoplasmic domain, in the previous steps, confirm the threshold by selecting **Update Domain.**

To prevent the new domain selection from over-writing the Nuc domain region, click **Keep existing Domain Regions when overlapping.**

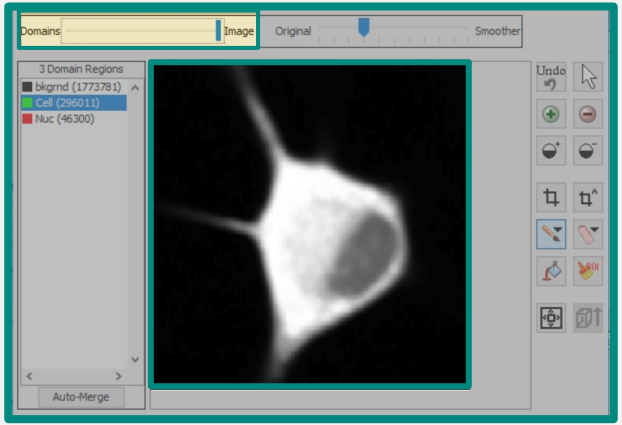


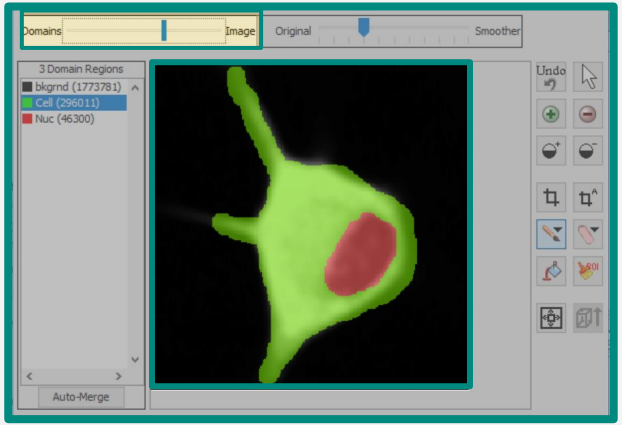


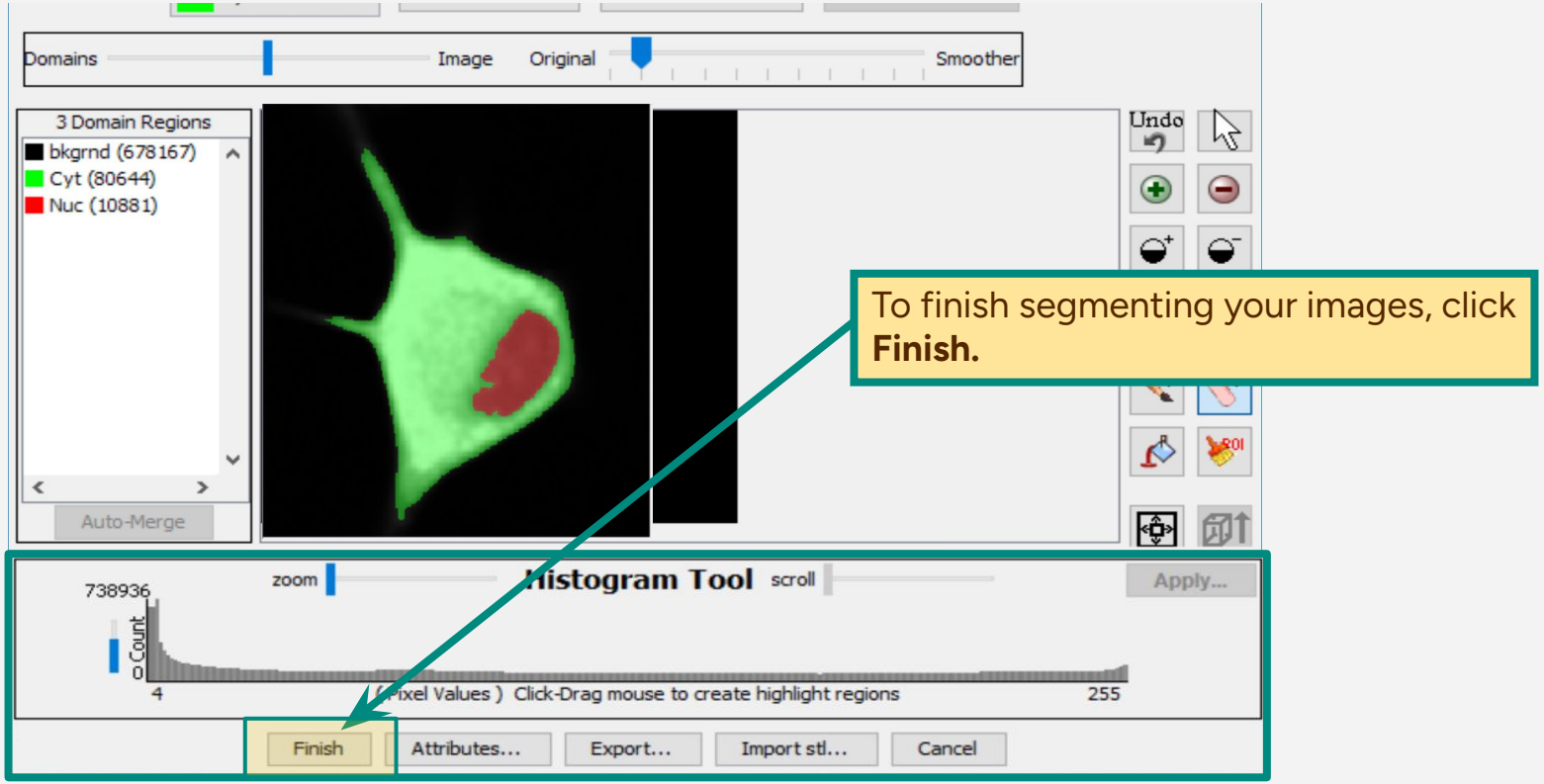
To remove all non-cytoplasmic and non-nuclear regions, select all the regions except the most numerous bkgrnd, Cyt, and Nuc regions, (usually the three top regions). With the remaining regions selected, click **Auto-Merge.**

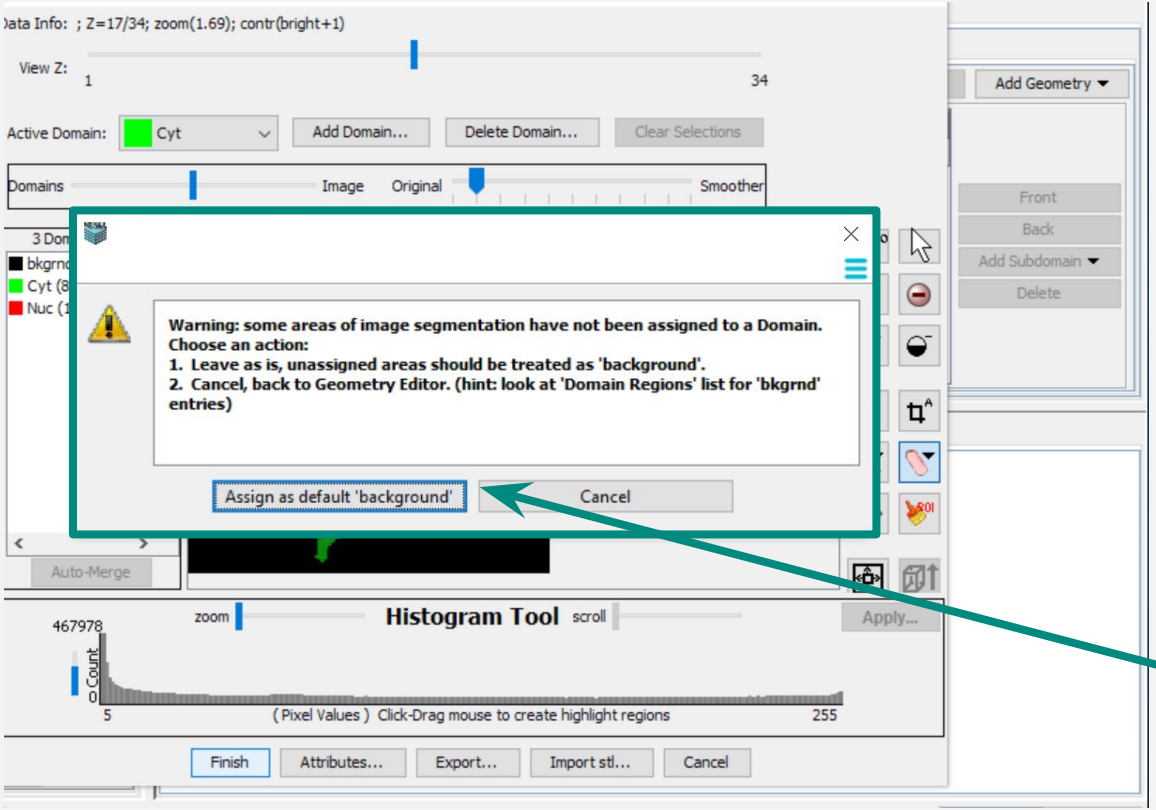


Use the **Domains to Image** display slider to adjust the way your image is displayed. This can show the image as segmented domains, the image only, or a overlay of the two.
This tool is helpful for visualizing your cell while defining the domains.

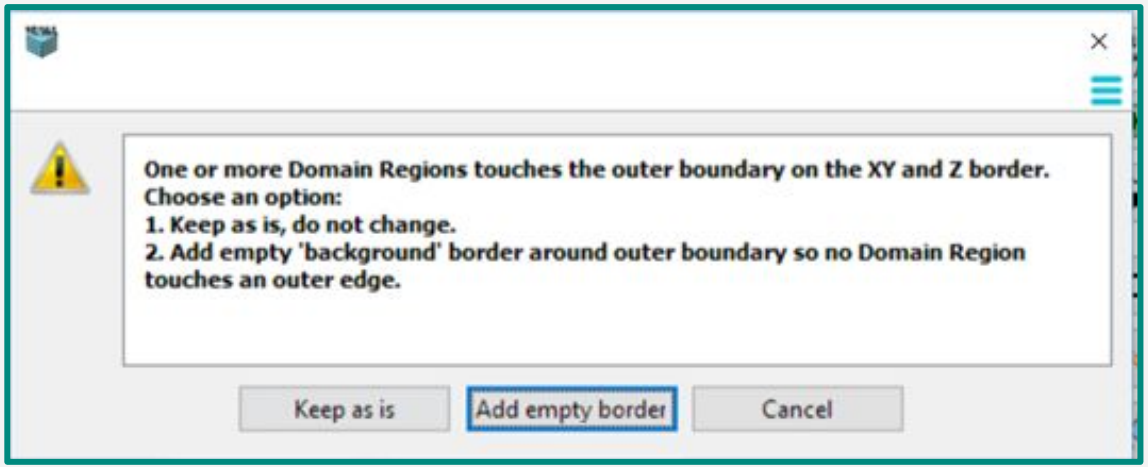





Domains
Image
Original
Smoother
3 Domain Regions
bkgrnd (678167)
Cyt (80644)
Nuc (10881)
Auto-Merge
Undo
ROI
zoom
Histogram Tool
scroll
Apply...
738936
Count
4
(Pixel Values) Click-Drag mouse to create highlight regions
255
Finish
Attributes...
Export...
Import stl...
Cancel
To finish segmenting your images, click **Finish.**



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

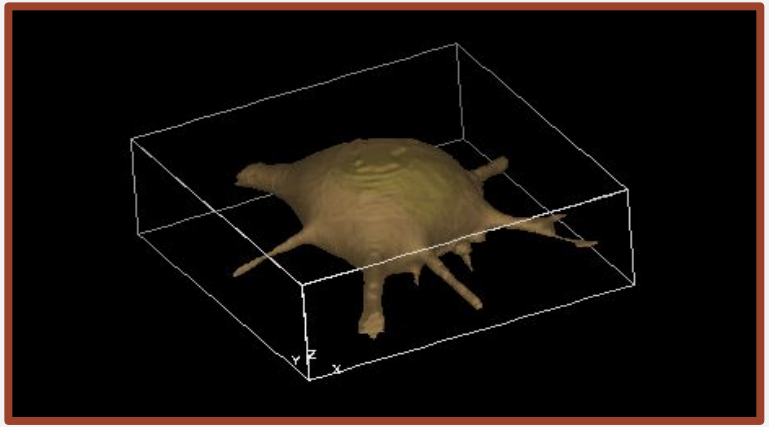


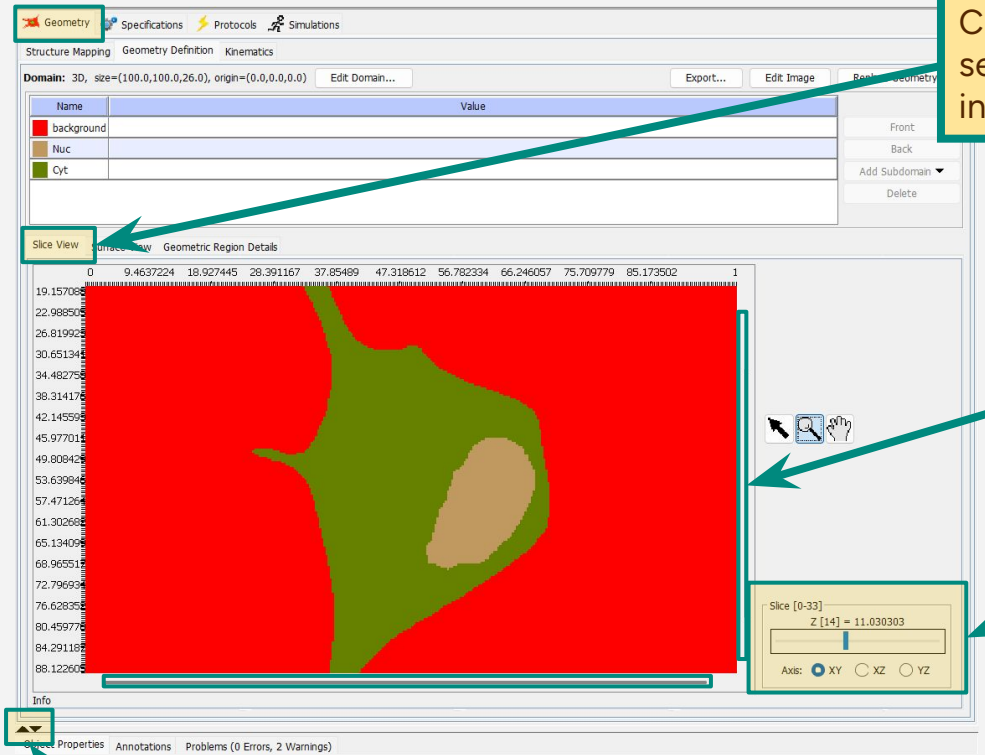
Click **Add empty border** to insert a blank (background) image on top of the 1st image and below the last image in the Z stack and to pad the x,y boundary with a row of background pixels.

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 of the simulation space.

03

Viewing and Defining Image-Based Geometry Size



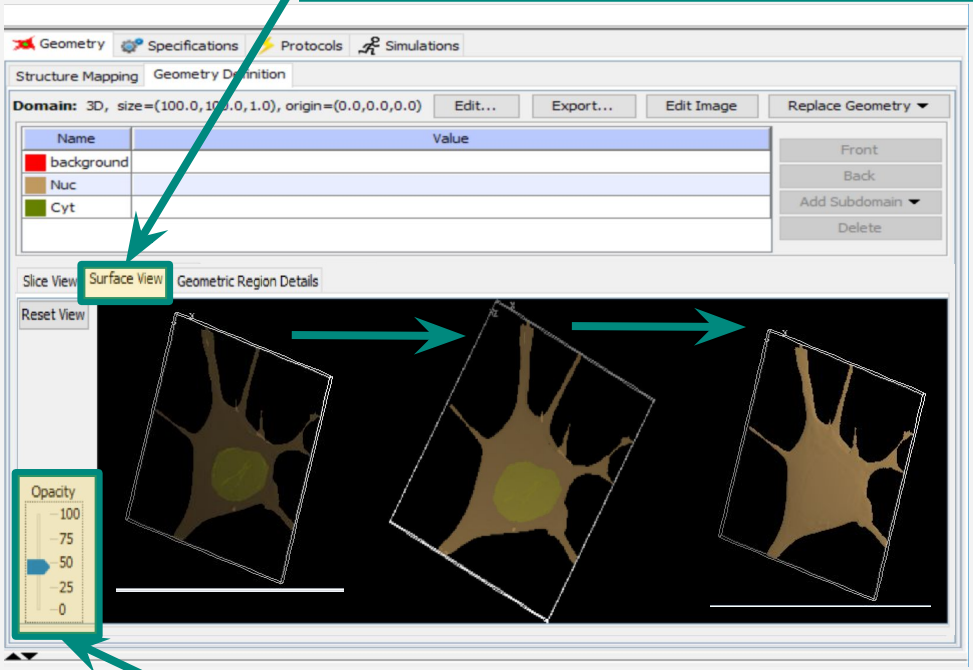


Click **Slice View** to view the segmented compartments by individual slices.

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

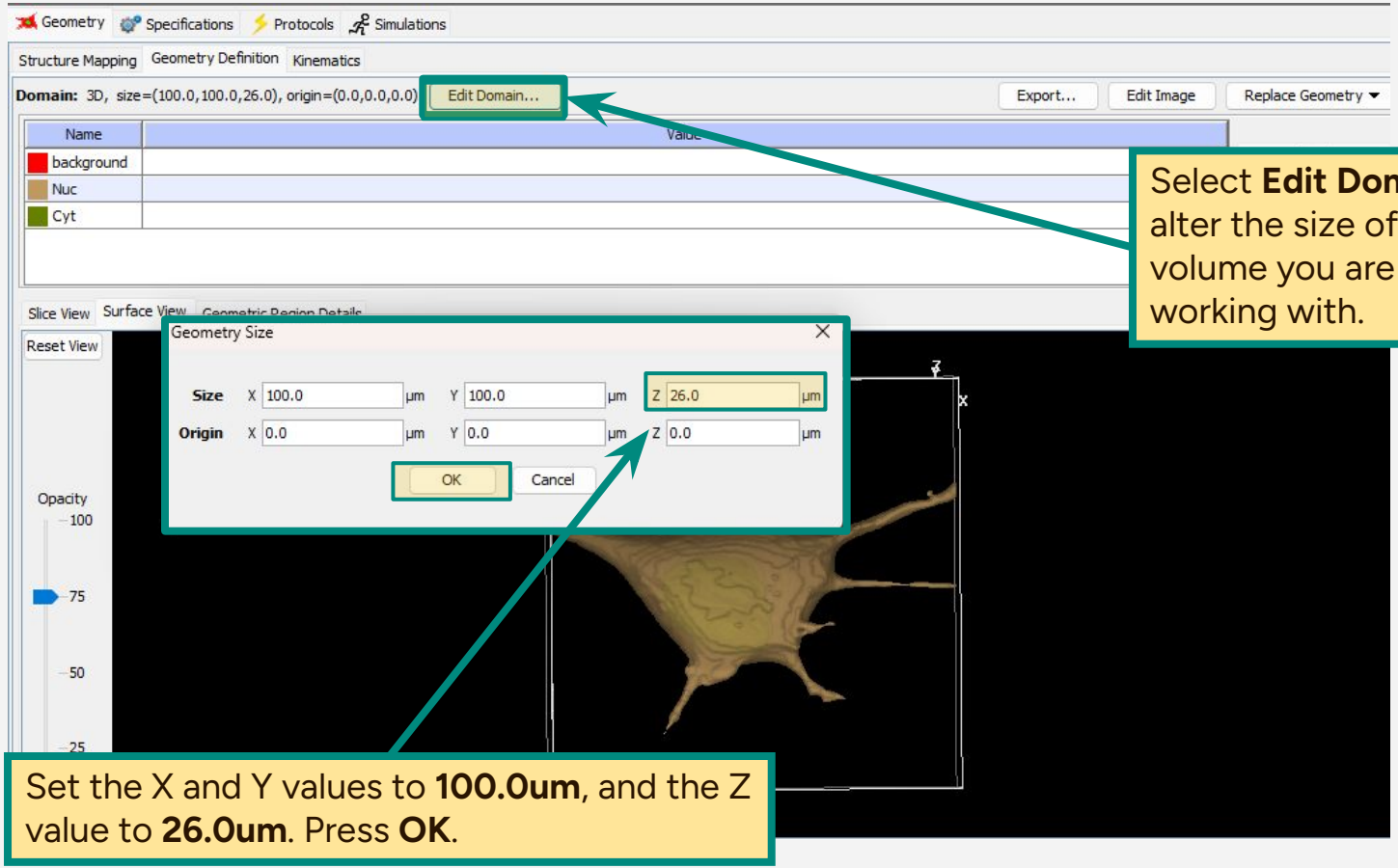
Press the up or down arrow to increase or decrease the window size to view more or less of the displayed image.

Click **Surface View** to view the volume in 3D.

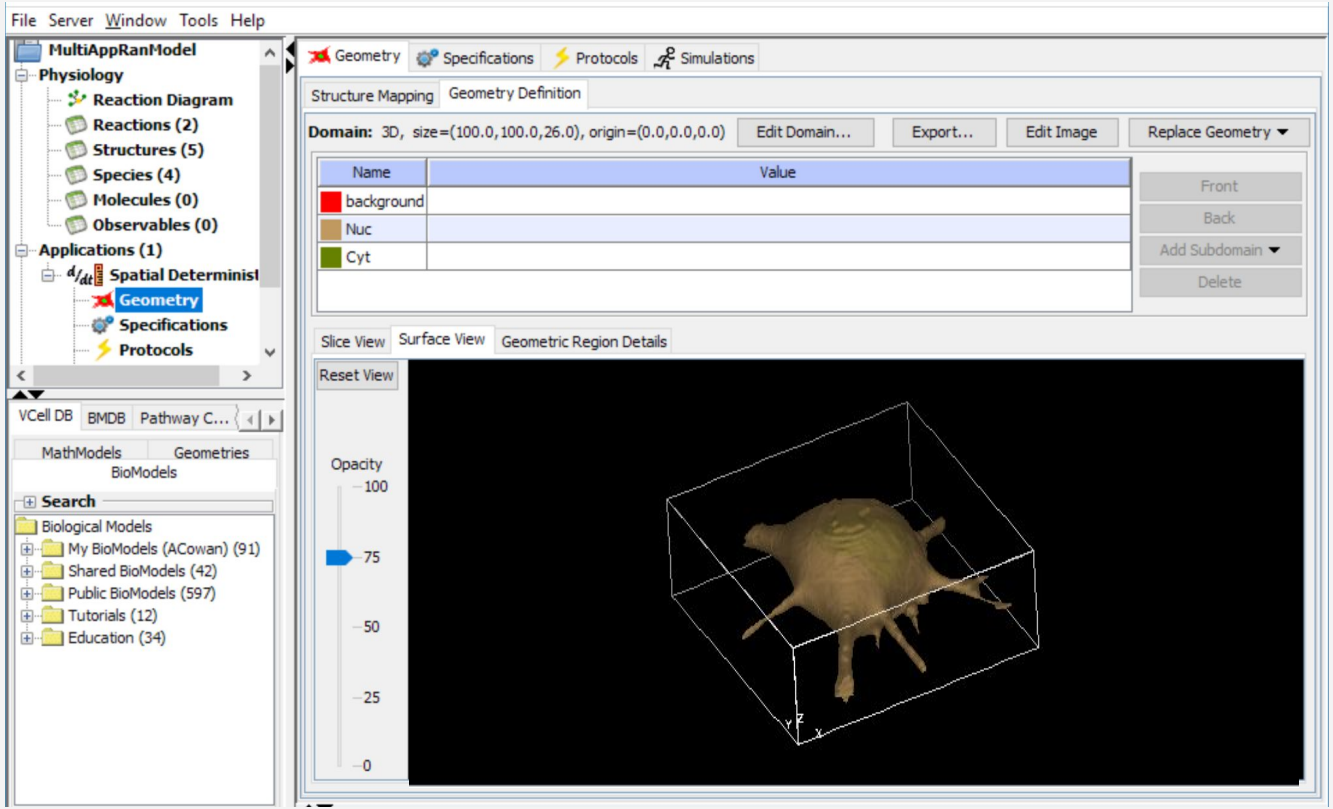


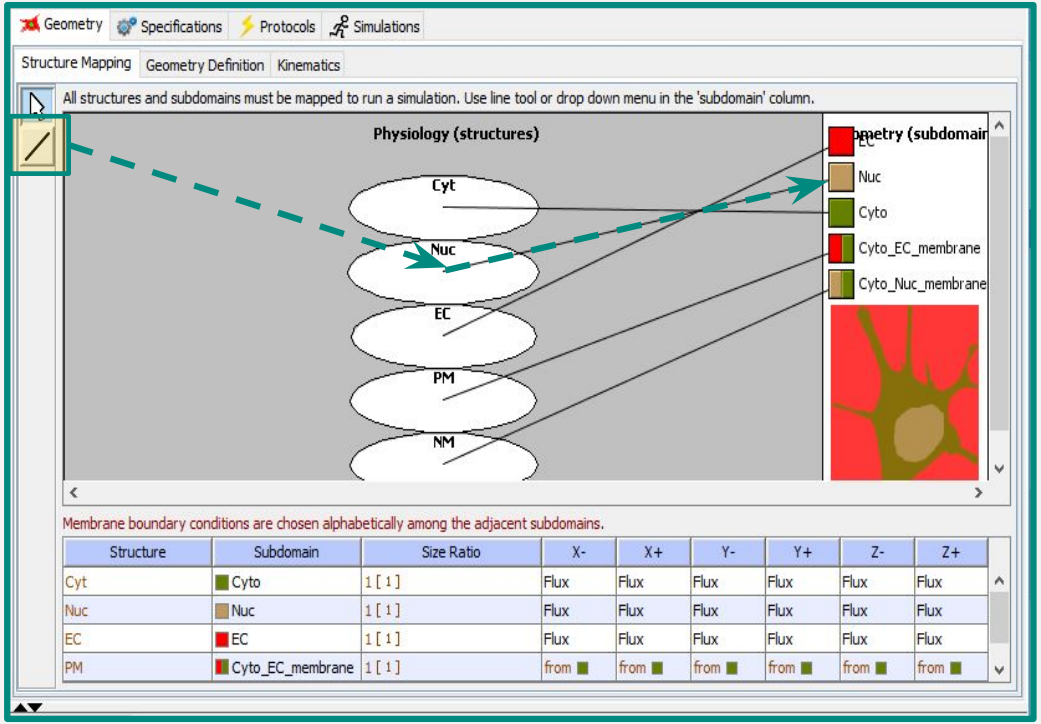
The cell here looks flat because there was no data on Z dimension in the images to define the domain size. This will be corrected in the next slide.

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


Geometry
Specifications
Protocols
Simulations
Structure Mapping
Geometry Definition
Kinematics
Domain: 3D, size=(100.0,100.0,26.0), origin=(0.0,0.0,0.0)
Edit Domain...
Export...
Edit Image
Replace Geometry
Name
background
Nuc
Cyt
Slice View
Surface View
Reset View
Opacity
100
75
50
25
Geometry Size
Size X 100.0 µm Y 100.0 µm Z 26.0 µm
Origin X 0.0 µm Y 0.0 µm Z 0.0 µm
OK
Cancel
Select Edit Domain to alter the size of the volume you are working with.
Set the X and Y values to 100.0um, and the Z value to 26.0um. Press OK.

The geometry of your model is now complete!





On the Geometry tab, click **Structure Mapping**. Then use the **line tool** to drag a line with a mouse from the physiology structure to the appropriate geometry subdomain.

Physiology	Geometry
Cyt	Cyto
Nuc	Nuc
EC	EC
PM	Cyto_EC_membrane
NM	Cyto_Nuc_membrane

Acknowledgments

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