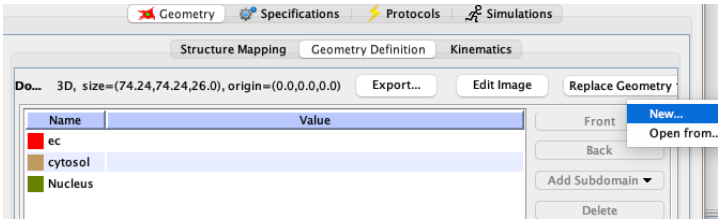
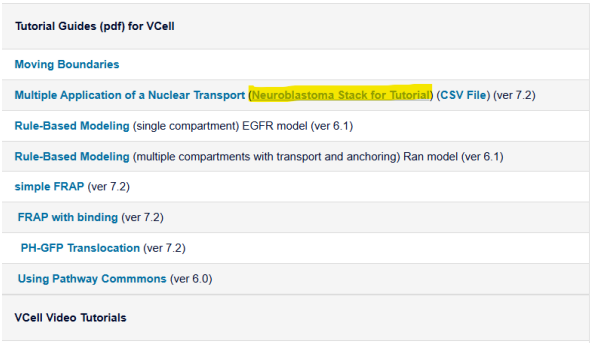
Virtual Cell Image-Based Geometry (VCell 7.7, July 2025)

Table of Contents:

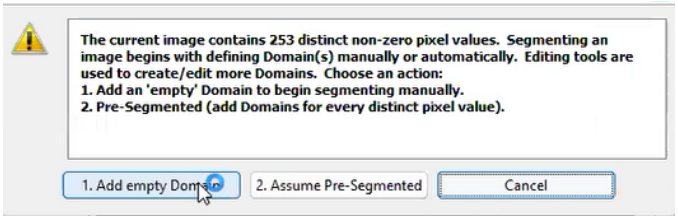
1. Initializing the Geometry:
Open VCell and open an application. Navigate Geometry → Geometry Definition to create a new geometry by clicking New → Image Based. You will then be prompted to select a file from your computer.



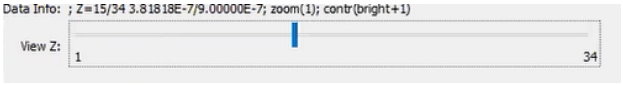
2. Importing the Image Stack:
Use your own images or download them from https://vcell.org/support.
The image can be scaled up or down in the next screen.



3. Creating a New Domain:
Each pixel in the gray-scale image has an intensity from 0 (black) to 255 (white). VCell informs you that there are 253 intensities, so it may define 253 domains based on the intensity. Choose option **2. Assume Pre-Segmented** if this is what you prefer. If you want to define domains yourself, choose **1. Add Empty Domain**, and name it (e.g. "Nuc" for nucleus).



4. Cropping the Image:
- Navigate through the image slices using the **Z slider** and adjust the zoom for visibility.
- Crop unnecessary parts of the image using the **cropping tool**. 



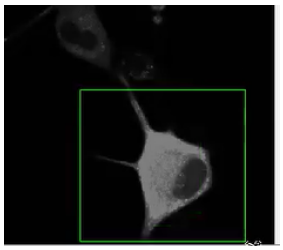
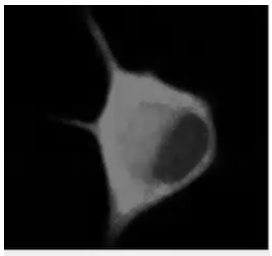


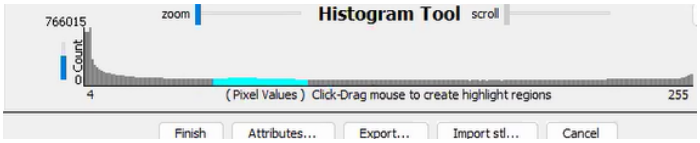
Table of Contents

5. Smoothing the Image:

Apply the averaging filter to smooth the image. The intensities of the pixels in each 9x9 box are averaged together to replace the original pixel values of the center pixel.



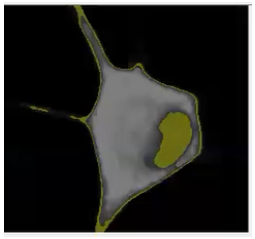
6. Domain Selection:



- The **histogram** at the bottom shows the pixels in the 3D image ordered by intensities.
- Using the histogram tool, select pixels with intensities most closely resembling the nucleus.

Note that it cannot be perfect, as many pixels have the same intensities elsewhere in the image. You can edit the selection later.

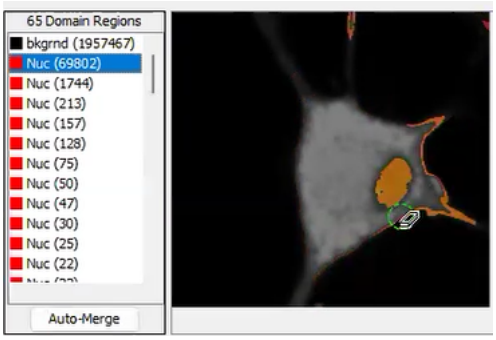
- View selections across different slices using the Z slider.



7. Updating Domain:

Click **Apply** and then **Update Domain** to finalize the initial selections.

8. Manual Editing (Erasing):

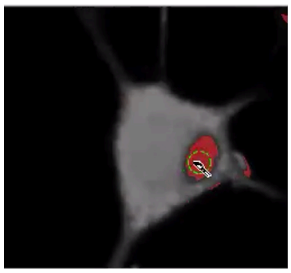


- Your selection usually generates a disjoint set of regions (65 in this case). The regions are ordered by size, from largest to smallest. The number in parentheses is the number of pixels in this region.
- Click on the largest region of interest to retain (highlighted as the largest Nuc domain). It will become orange.
- Using the **eraser tool,**  erase irrelevant orange pixels across ALL slices, carefully distinguishing and removing regions not belonging to the nucleus. You can change the size of the eraser by right-clicking the icon.
- Ensure accuracy by frequently zooming out and navigating the Z slider. Make sure to keep selecting the largest Nuc domain region as you erase.

Table of Contents

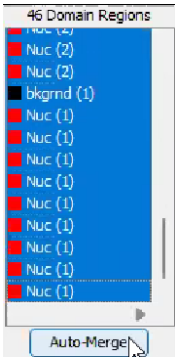
9. Filling in Nucleus Domain Gaps:

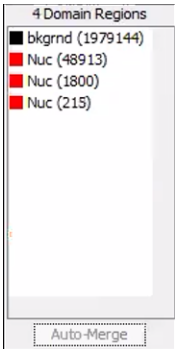
- Use the brush/paint tool  to fill in gaps within the nucleus.
- Adjust tool size by right-clicking for more precise editing.



10. Merging Regions:

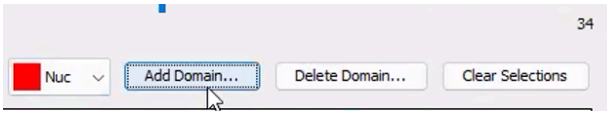
- Select smaller regions (everything besides the largest Nuc domain) and click **Automerge**. Automerging joins smaller regions to the largest adjacent regions.
- It is advised to automerge in sections, selecting regions starting from the smallest and ending with the largest, ensuring that the regions join the proper domain.
- Check accuracy often by revisiting the slices again with the Z slider.

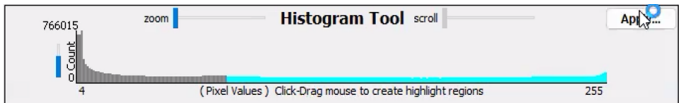


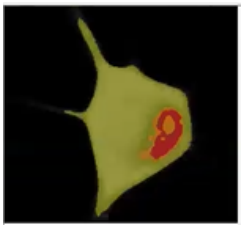


11. Adding the Cytoplasm Domain:

After the nucleus is defined, the rest of the cell will be set as the cytosol. This step is similar to adding the nucleus domain.







- Click **Add Domain** and name it "Cyt".
- Use histogram selection to identify pixels that comprise the cytoplasm, confirm by clicking **Apply**, and click **Update Domain.**
- Choose the option **Keep existing domain regions when overlapping** to maintain the integrity of the nucleus domain.

12. Finalizing Cytoplasm Domain:

- Auto-merge smaller regions, preserving the cytoplasmic region with the most pixels.
- Verify accuracy through slice-by-slice examination.

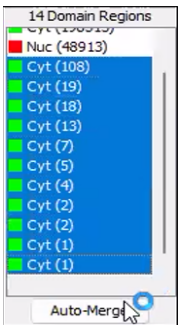


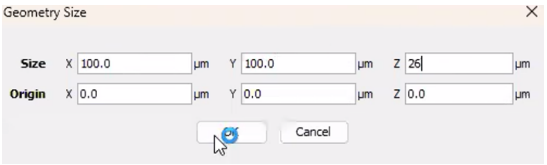
Table of Contents

13. Completing Geometry Setup:

- Click **Finish**, then select **Assign as default background**.
- Select **Add empty border** to guarantee that cytoplasm and nucleus do not touch the borders of the simulation volume.

14. Defining the Size of the Image:

The Z-stack may not have the information about the height of each image plane. The x and y coordinates may need to be scaled as well. Click Edit Domain and adjust the size. Set X and Y to 100.0 um and Z to 26.0 um.



Acknowledgements

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Table of Contents