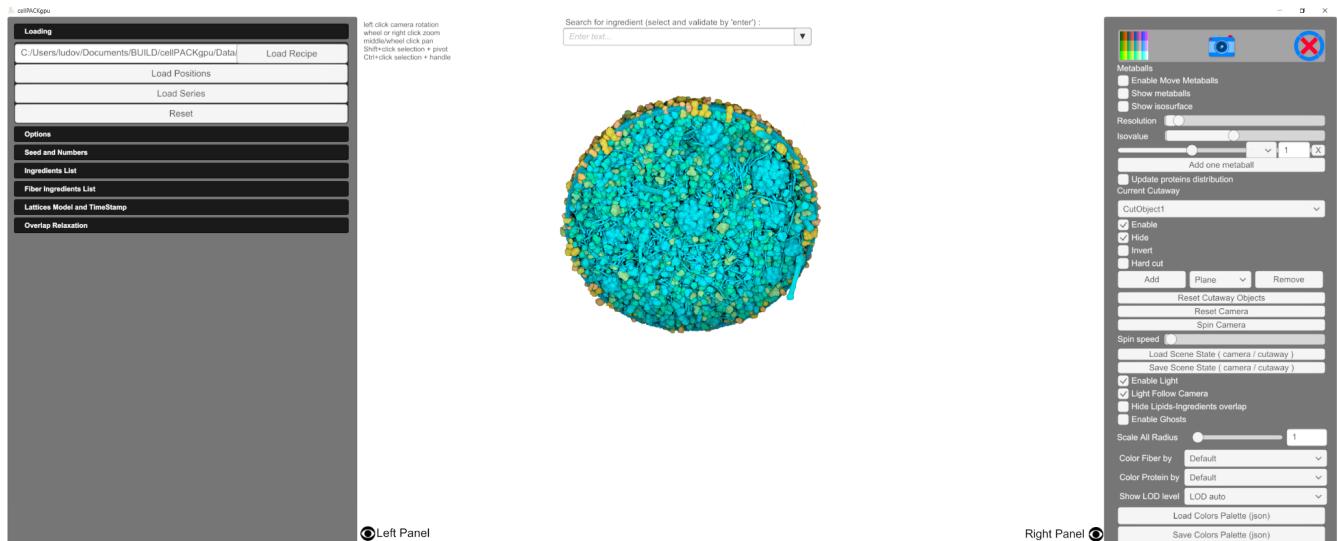


Modelling Mycoplasma Genitalium in cellPACKgpu

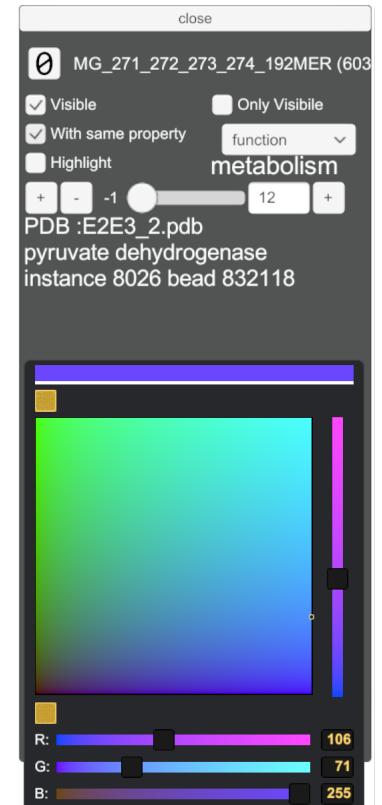
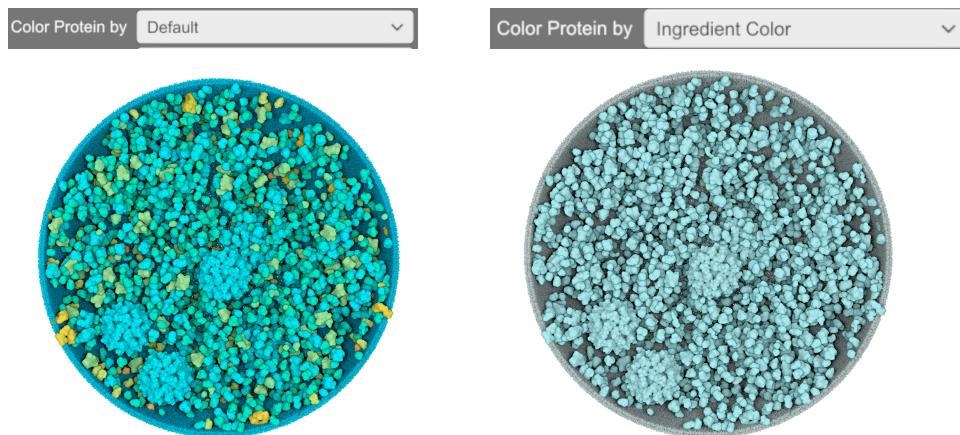
After starting cellPACKgpu.exe you should see by default the model built for the curated recipe and the frame 149 from the whole cell simulation. The scene is clipped with a plane placed at the center of the cell. The color is the default automatic coloring per compartment. The ingredient defined color is based on the function categories.



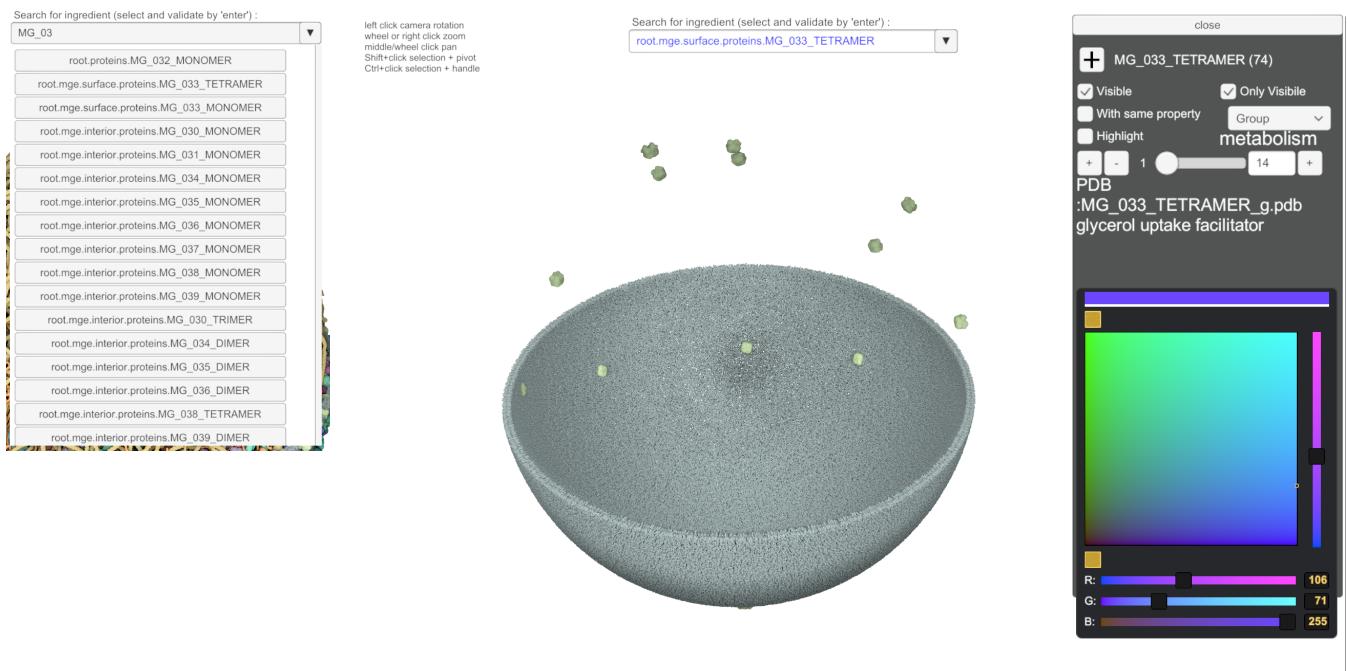
[Have a look at the User Interface quick description](#)

1- Exploring the model

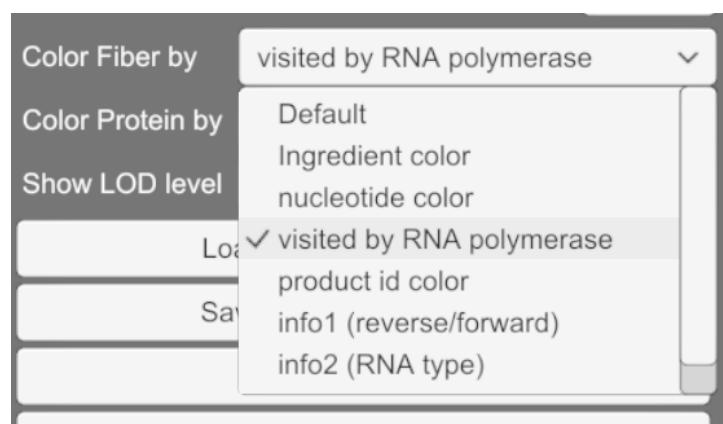
You can explore the model by looking at the individual protein by selecting them e.g. **ctrl+left-click** this will pop-up the Ingredient panel. It will tell you the name, the PDB file associated and a description of the selected molecule. This panel give you different options in terms of visibility. Next to the name there is a three state toggle that changes the clipping states (-1 completely invisible, 0 cut by the current cutaway object, +1 not cut by the current cutaway object). You can completely hide all instances of the molecule with the “visible” toggle. Or you can hide everything else using the “Only visible” toggle. The “With same property” will make only visible the current molecule and any molecule that share the same selected property. In the adjacent image, we choose to show only the molecules with the same function (here “metabolism”).



If you don't visually find a given molecule, you can use the search bar and provide a name. The search bar is case-sensitive and every molecule name in the whole cell simulation data is upper case and based on the gene name. Below is an example: after typing 'MG_03', the panel will show you all molecules with a name starting with MG_03. We then picked MG_033_TETRAMER, click in the field and type enter. This will select the molecule. Then clicking "Only visible" will show only all instance of that given molecule.



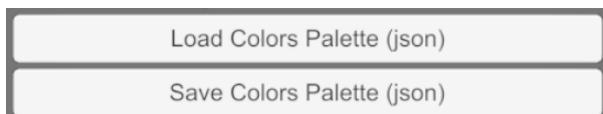
For this particular release we have added more coloring schemes for the nucleic acid (DNA and RNA).



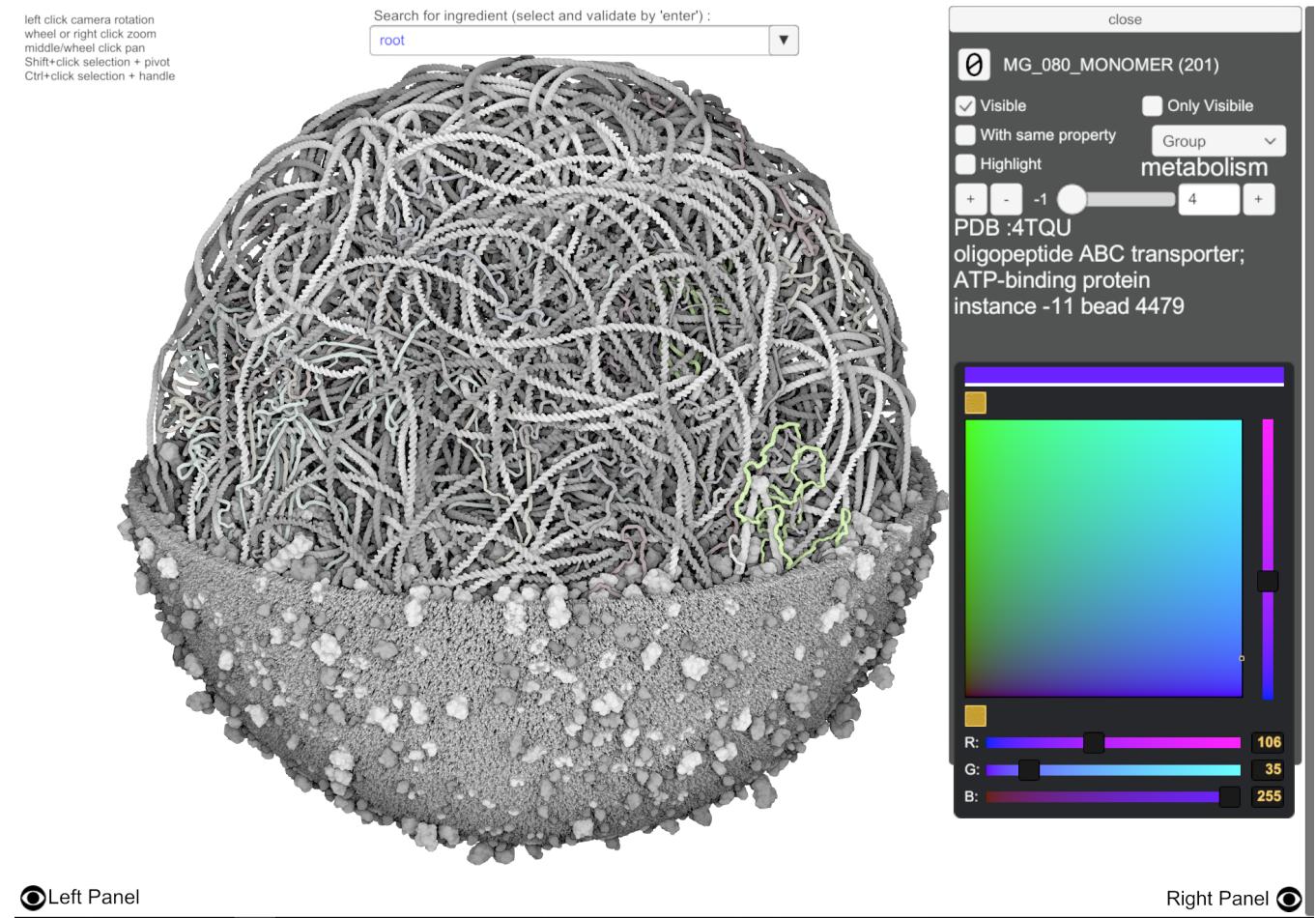
- Default use the automatic color assignation based on compartment
- Ingredient color use the color define in the recipe (here generated in mesoscope based on the ingredient function)
- Nucleotide color use a color per base pair
- Visited by RNA polymerase for the given frame, use two color : one for visited and another for unvisited
- Product id color: use the color of the protein that the gene is coding for.

- Color by the sens of the gene
- Color by the type of RNA this gene code for (mRNA, rRNA, etc...)

Note that any of this color can be changed using the color widget and then save/load.



When using the color fiber by product id color, the selection system changes for the fiber. If you ctrl+left click on the RNA or DNA it will who in the Ingredient panel the protein for which they code for. Below is an example with the mRNA encoding for MG_080_MONOMER highlighted.



2- Cutaway Objects

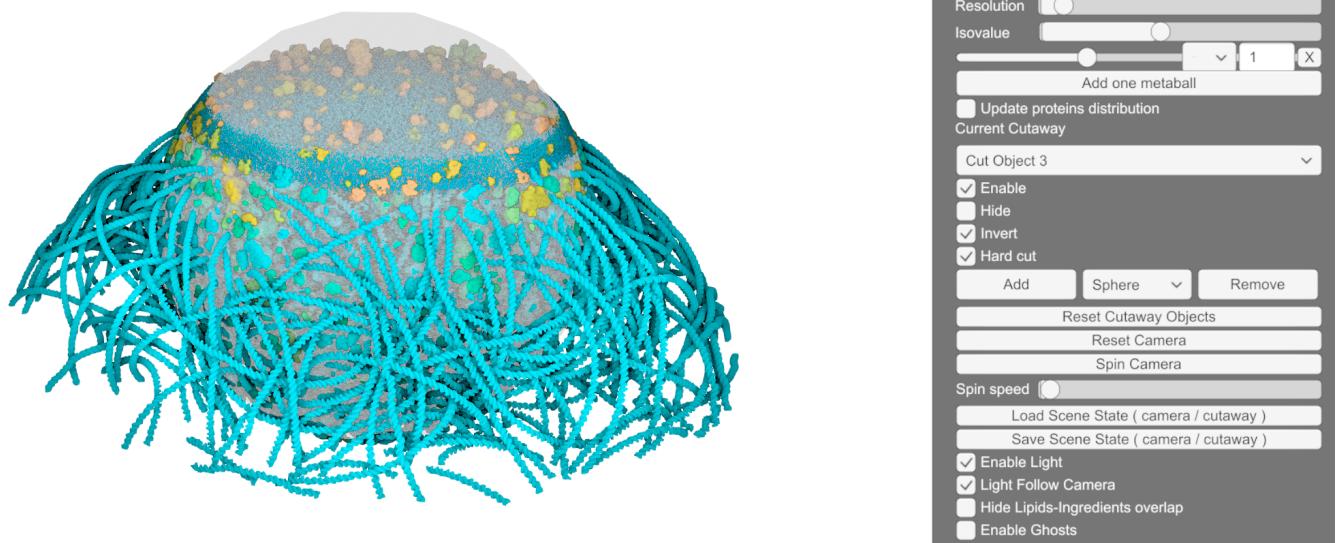


At start there is always a cutaway plane object. You can control all the clipping options from the right panel. All the toggle buttons will apply to the current selected cutaway object from the pull down menu.

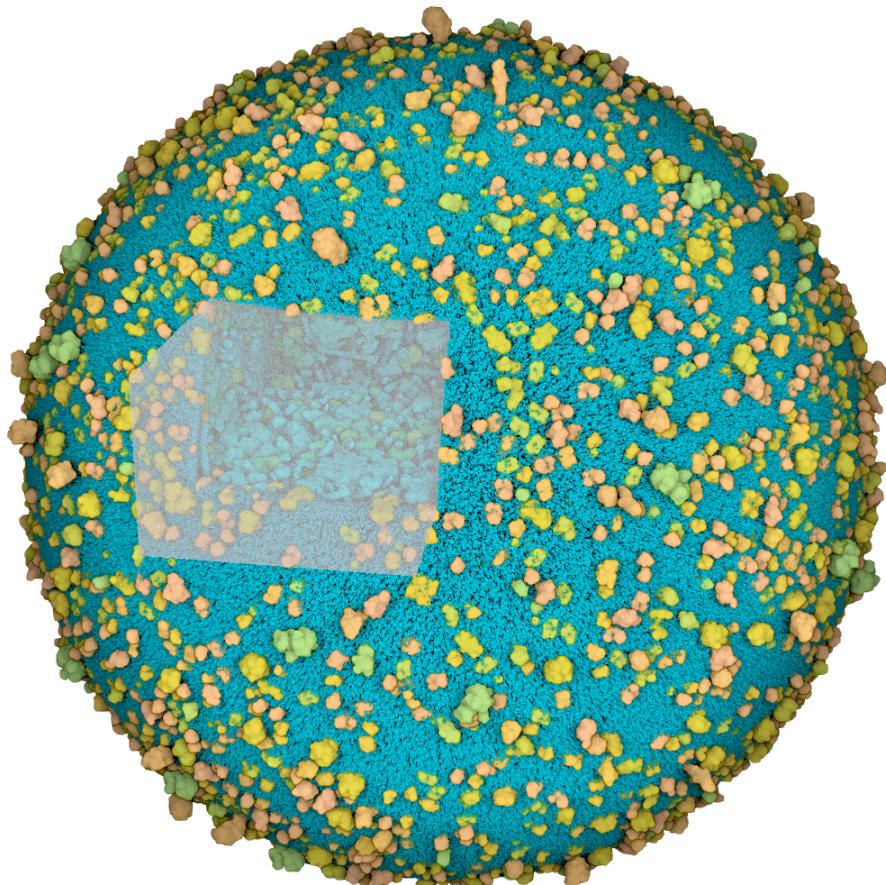
The hard-cut option will cut at the atom/bead level, while the default will cut at the molecule level. When enabled you can unhide it to make it visible and selectable. You can select the object with ctrl+left-click. The transform handle will appear to

let you interactively move it. To rotate it or scale it you can change the handle type using the keyboard keys : 1-translate, 2-rotate, 3-scale. Once selected you can also change the type.

Below as an example, we change the plane to a sphere and invert it to cut away outside the sphere. We excluded the DNA for being affected by it and we added a plane cutaway to affect everything.



Another example with a visible cube cutaway, with hardcut mode.



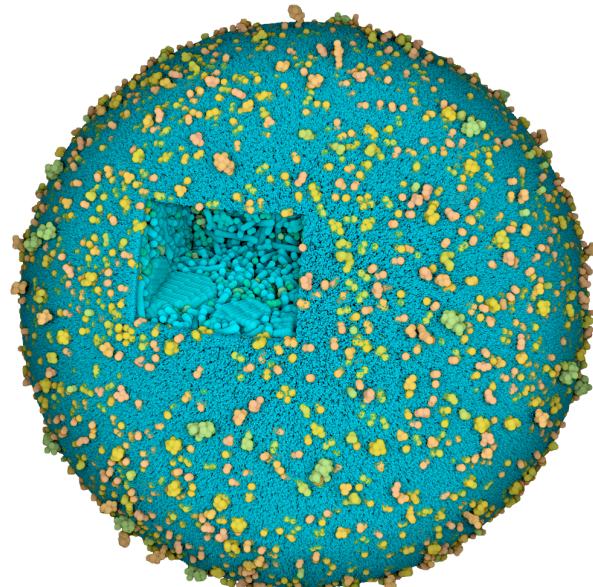
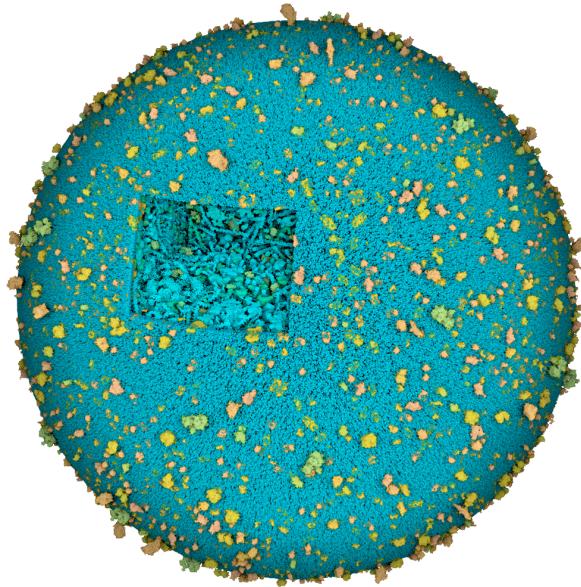
2- Level of Details

cellPACKgpu is built on top of cellVIEW which uses dynamic LOD with the camera distance. However we provide a pulldown menu which can enforce one given level. Levels go from 0 (all atom), 1-2-3 (automatically build beads), 4-5 (defined in the recipe).

Scale All Radius	<input type="range" value="1"/>
Color Fiber by	Default
Color Protein by	Default
Show LOD level	LOD auto

Show LOD level

Show LOD level



3- Changing recipe and frame

At the start all the left panel sections collapsed. Click on the title to open/close each section. Click on LAttices Model and TimeStamp to open the special section for mycoplasma genitalium. You can load each of the three timestamps selected for this project. And you can switch to the alternate automatic recipe which only uses automatically assigned structure for every ingredient.

When switching between recipes, be patient as the application will reload all the different protein structures.

149/150
✓ 149/150
1184/1189
6973/6960

Curated
✓ Curated
Automatic

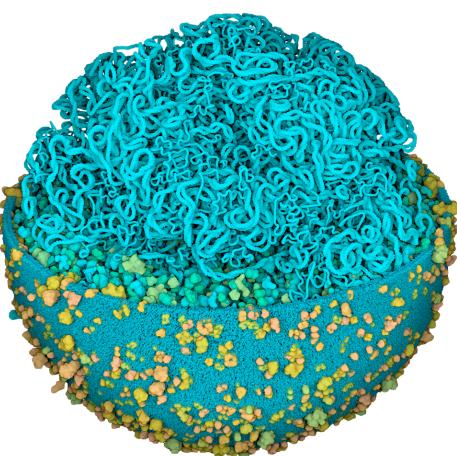
Loading	
C:/Users/ludov/Documents/BUILD/cellPACKgpu/Data/	Load Recipe
Load Positions	
Load Series	
Reset	
Options	
Seed and Numbers	
Ingredients List	
Fiber Ingredients List	
Lattices Model and TimeStamp	
Recipe	
Curated	
TimeStamp (MONOMER/COMPLEX)	
149/150	Calculate PL
Overlap Relaxation	

4-Creating a Model

In this section we will show you how to create your own model.

4.1 Change the distribution

By simply changing the random seed you will generate new models with a different spatial distribution for all the soluble and surface proteins. However, the nucleic acids as well as all the dna-binding proteins will stay identical and are coming from LatticeNucleoid. They are generated for each timestamp.

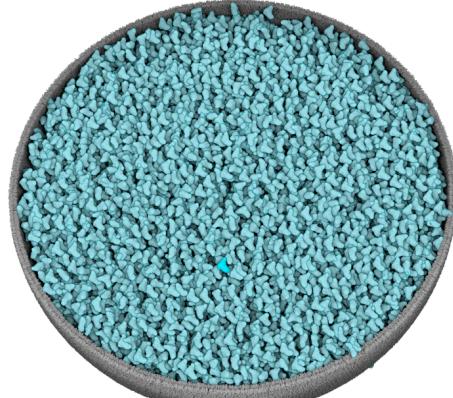


Ingredient Id	Compartment ID	Count
MG_032_MONOM		2
MG_074_MONOM		50
MG_096_MONOM		21
MG_129_MONOM		14
MG_146_MONOM		11
MG_220_MONOM		7
MG_286_MONOM		30
MG_310_MONOM		48

All the count / copy numbers are coming from the given timestamp from the whole cell simulation data. However, you are free to change any of the counts. This will automatically change the distribution. Its possible to stop preloading by unchecking the toggle named “Populate procedural ingredient” in the options section.

Below is an example of distributing only tRNA in the cell.

Ingredient Id	Compartment ID	Count
MGmNA23S (685)	-1	0
MGmA5S (686)	-1	0
tRNA (687)	-1	3981
tRNA-aminoacylat	-1	0
MG_0001 (689)	-1	0
MG_0002 (690)	-1	0
MG_0003 (691)	-1	0
MG_0004 (692)	-1	0



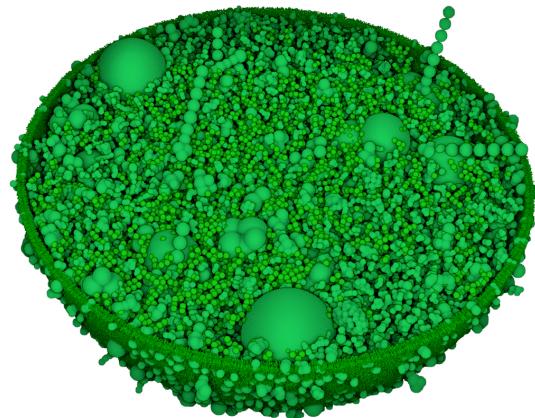
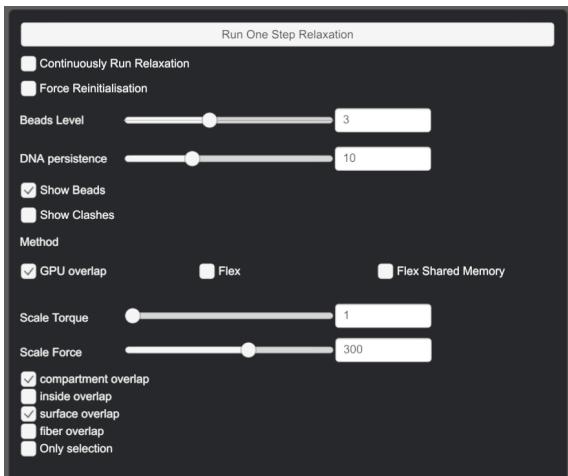
Ingredient Id	Compartment ID	Count
tRNA (687)		3981

4.2 Relax

Once you are satisfied with a distribution you will notice a lot of molecules are overlapping with each other. We can reduce most of this overlap in a two step protocol: coarse (GPU) and refined (Flex) displacement.

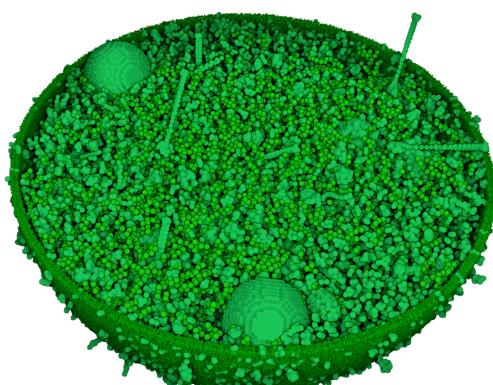
4.2.1 Gpu Relax

Before enabling the gpu relax method change the options as below. First, pick the beads level 3. This level corresponds to level 0 in the recipe and tries to lower the number of beads (low resolution). Toggle the show beads to visually ensure we selected the correct bead level. Then adapt the calculation to only enforce molecules to stay inside the compartments, and relax all the membrane protein overlap. Finally you can toggle on the “Continuously Run Relaxation” and see molecules going back inside the compartment, and surface protein going away from each other. Once all membrane proteins are free of overlap toggle off to stop the relaxation and switch to Flex.



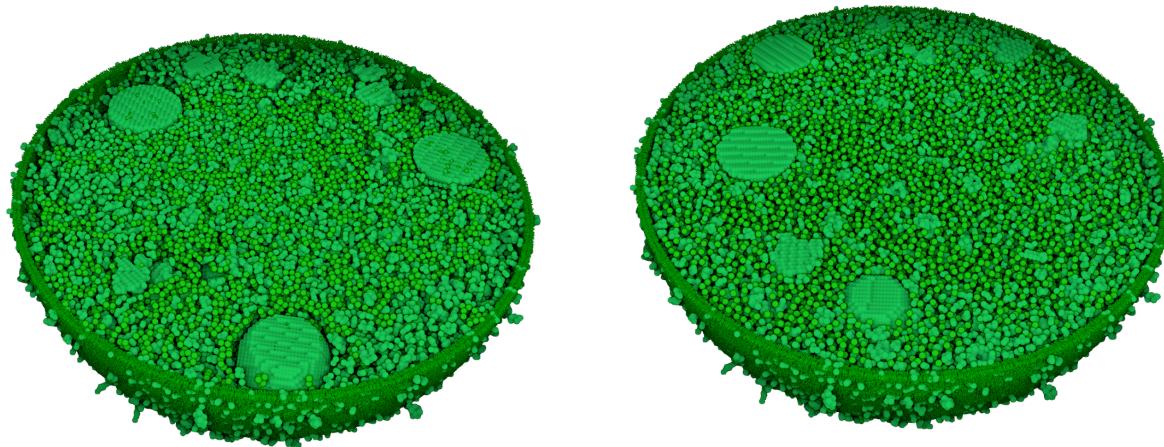
4.2.2 Flex Relax

Change the options as below. Pick the beads level “4” which was built specifically for flex, where all beads have the same radius (here 17.0Angstrom). Change the DNA persistence to 1.0. This controls the stiffness of the DNA.

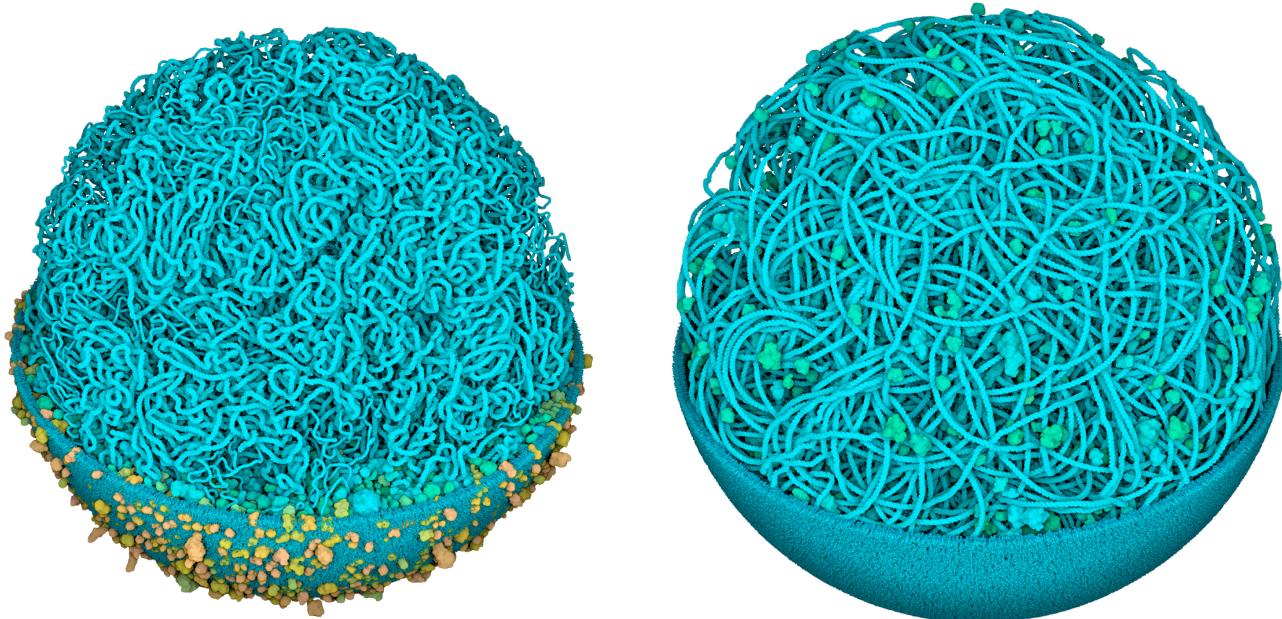


Before running continuously, click “Run Once Step Relaxation”, this will set up Flex and run one step. The app is going to be unresponsive for a couple of seconds. Once you get control back, toggle on the run continuously.

Using the hard cut mode, you should see that molecules are trapped inside the big PDH complex. To resolve this issue, we can force the beads radius to increase/decrease in cycle. Toggle on the “Expand radius loop” and look for the model and wait for 2-3cycle of increase. Toggle off.



The DNA topology should have stayed closed to the initial conformation generated by LatticeNucleoids. However, DNA has a high persistence length (~30-50 nm), we can relax the DNA putting some stiffness and constraint on it by changing the DNA persistence mode slider to 10 or 12. Since we changed one critical parameter of the relaxation we need to reinitialize it. Toggle the “Force reinitialisation” button and then click again the “run one step” button. This will reinitialize flex, and add spring constraint along the DNA at every control point. Once the system is reinitialized you can toggle the “run continuously”



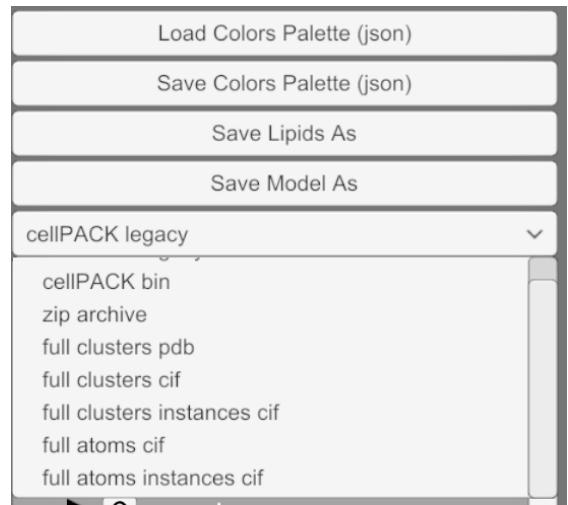
4.3 Save the model

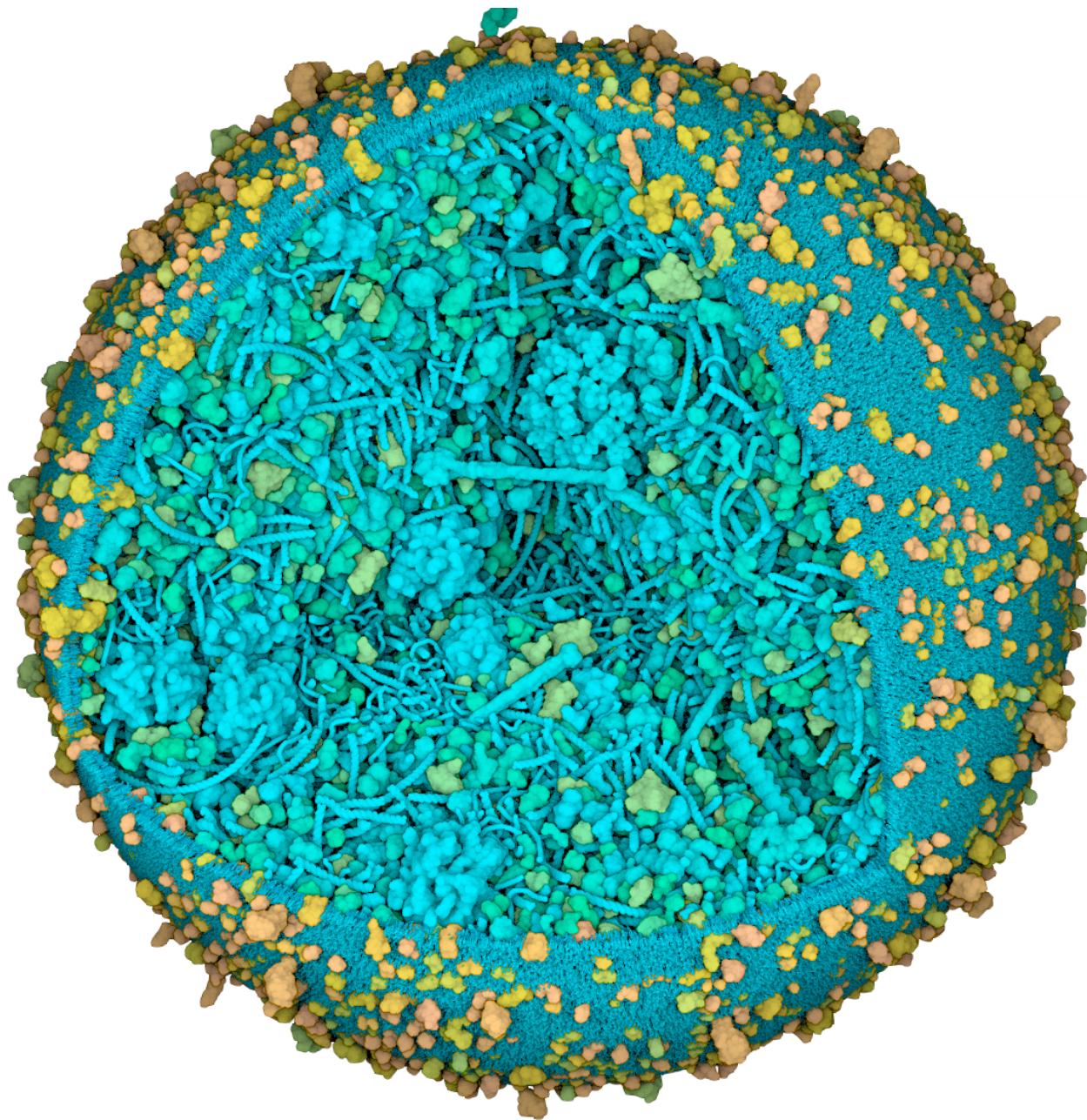
Once you are satisfied with a given model we provide different options to save them. You can save them as

- . cellPACK legacy, which will save a json file holding the position/rotation and control points of each molecule.
- . cellPACK bin, is the format supported by cellPACKgpu and that you can load using the load position button in the left panel.
- . full cluster pdb: using the PDB format, every individual bead is saved. This used the currently selected beads level in the Relaxation panel.
- . full cluster cif: same as above but using the cif format.
- . full cluster instance cif : using the cif format save the individual molecules at the given cluster level, and then save the transformation matrix for every instances.
- . full atom cif : Attention, this will take a long time to process and will create a 8Gb file as it will write down every individual atom in the model.
- . full atom instance cif: only write atoms for individual and center molecules, then write for each the transformation matrix.

In addition, you can export the lipids bilayer as a cif file. We only write down representative lipids and their transformation matrix (per triangle).

The cif files can be loaded in molstar embedded in mesoscope or directly in the molstar viewer.





In the above screenshot we toggle the “hide lipids” feature which will not render any lipids that overlap with one sphere defined in the currently selected bead level for every protein.

Beads Level



3



Hide Lipids-Ingredients overlap

TROUBLESHOOTING

- If the viewport becomes black restart the app.
- If the app becomes unresponsive, force quit it.

