

# Simmune and Its Support to SBML and SBML packages

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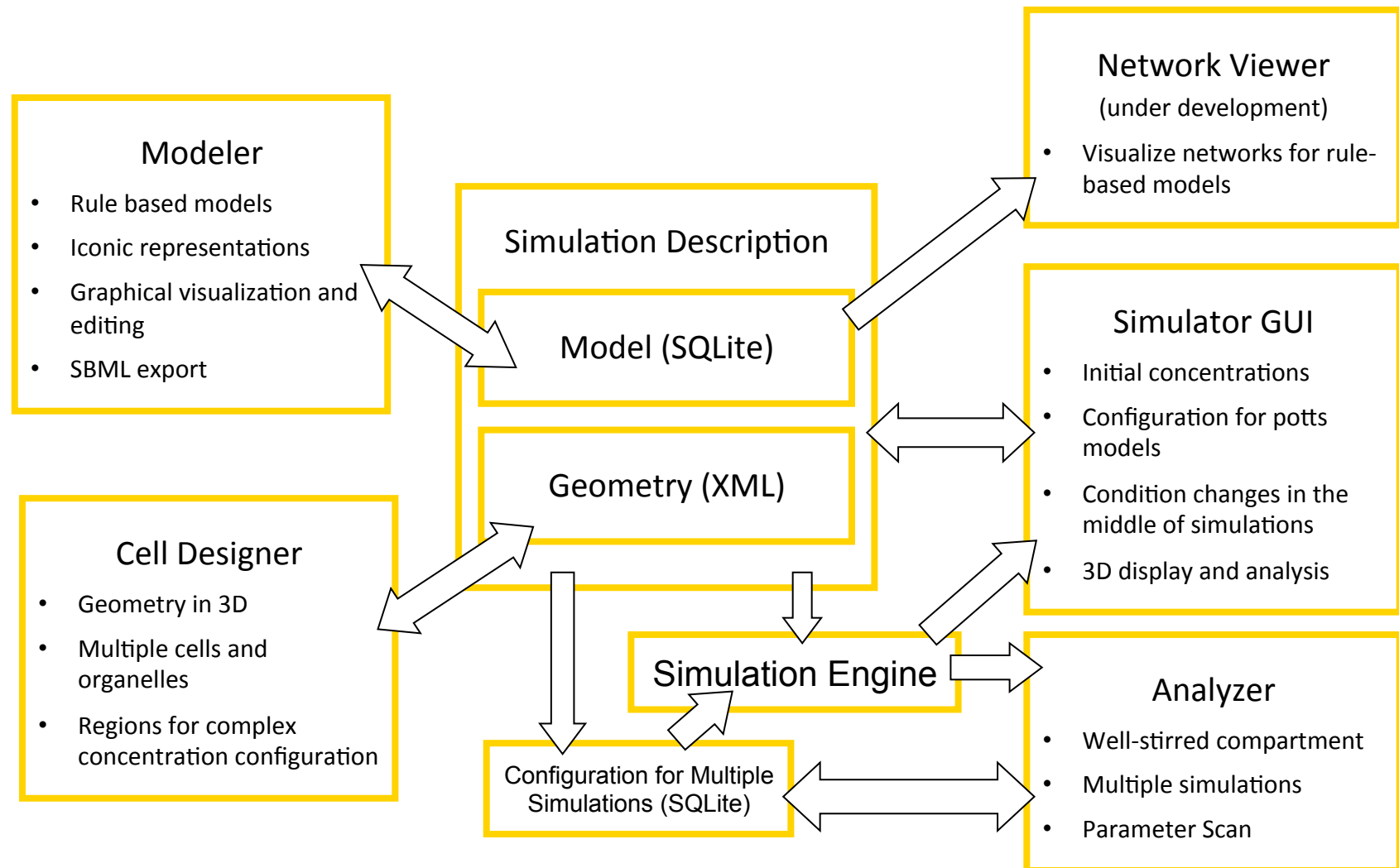
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# Outline

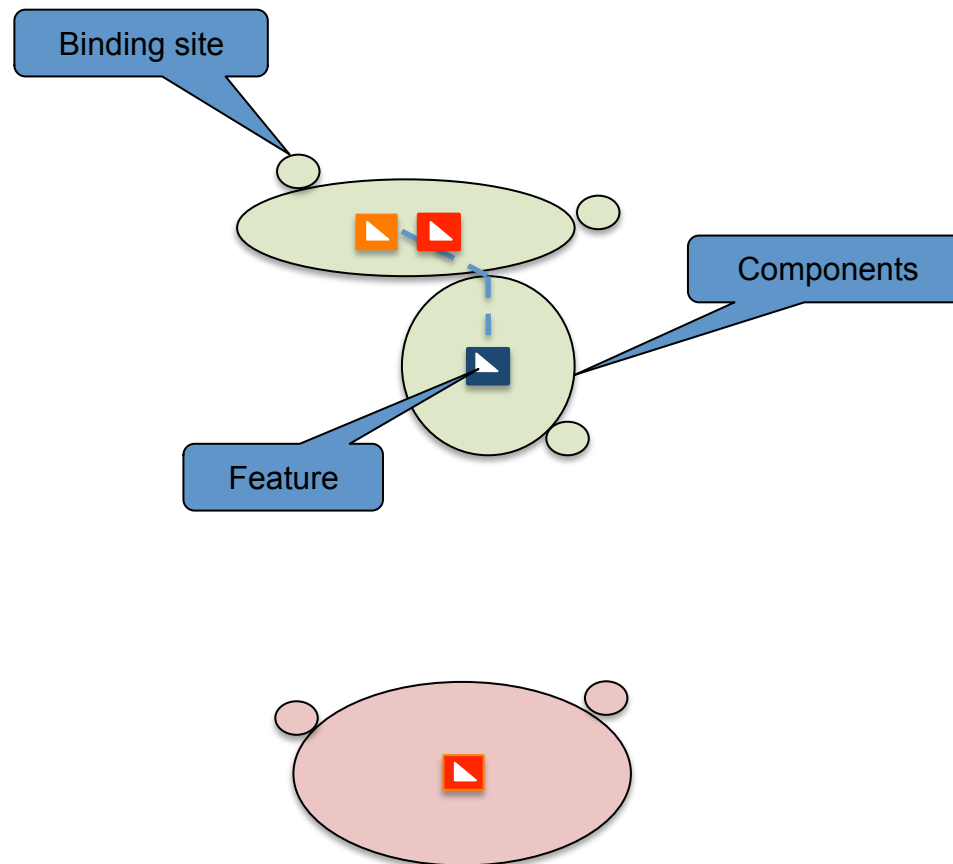
- Simmune infrastructure and work flow
- Simmune graphical representations
- Simmune: (Yeast Model)
  - Simmune Modeler
  - Simmune CellDesigner
  - Simmune Simulator
- SBML support

# Simmune Structure and Workflow



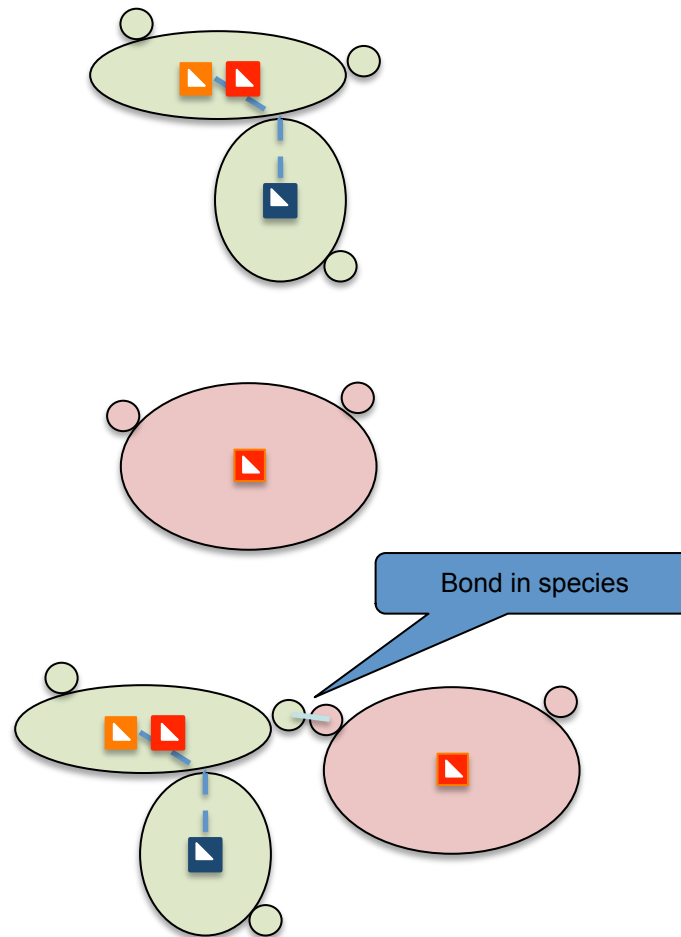
# Graphical Representation of Simmune Models

*Molecule: Component, binding sites, features*



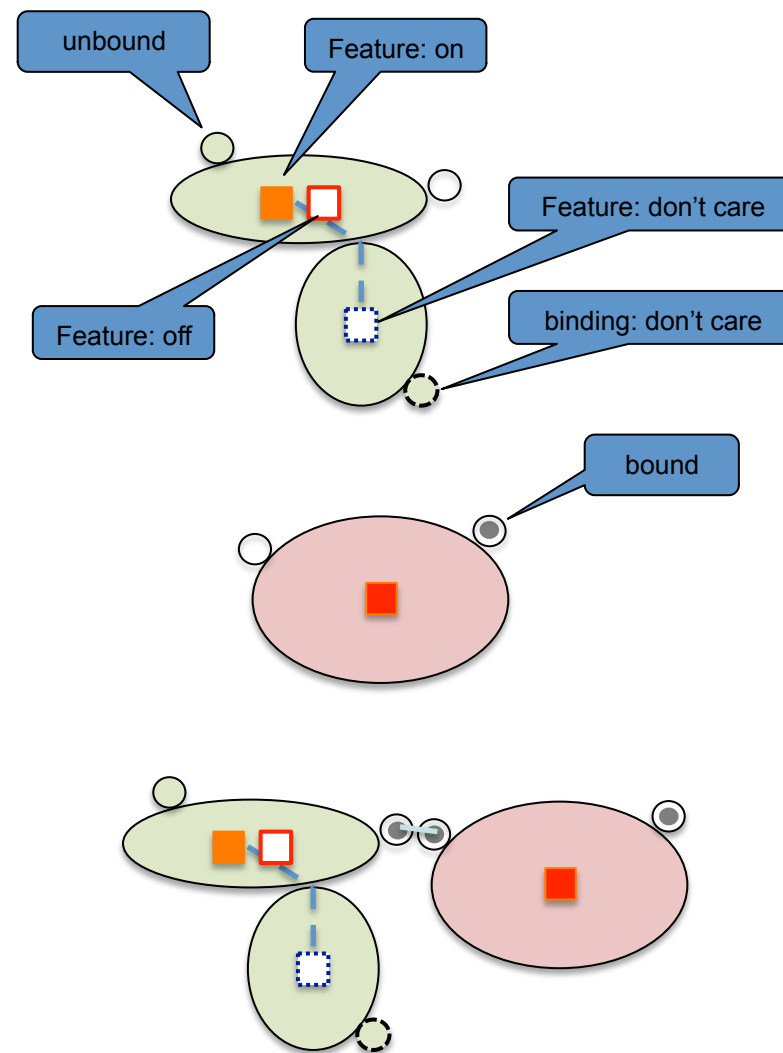
# Graphical Representation of Simmune Models

## *Complex Species*



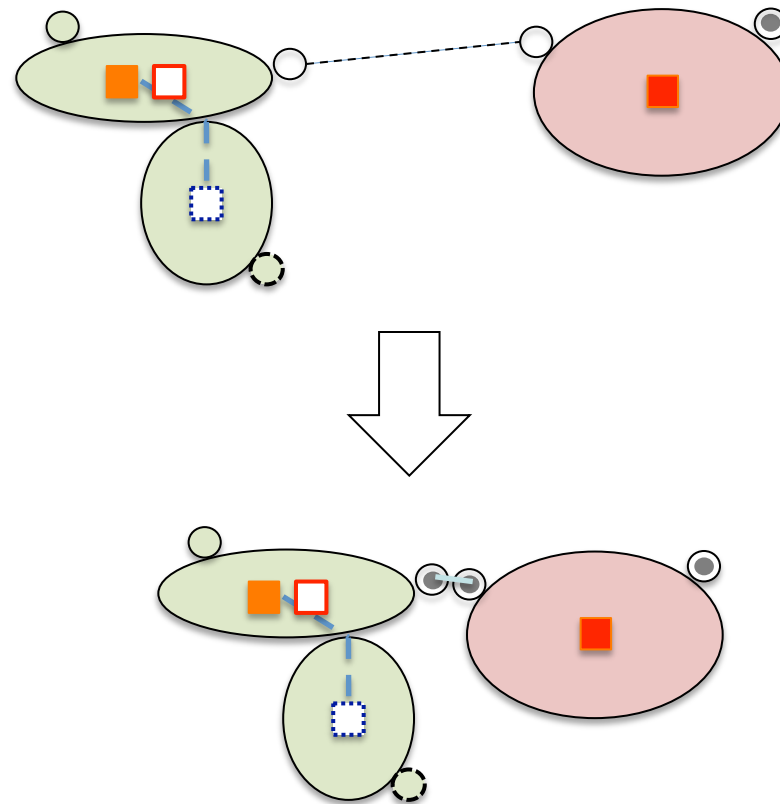
# Graphical Representation of Simmune Models

## *Complex*



# Graphical Representation of Simmune Models

## *Reaction*



# Simmune Modeler: Yeast Model: Molecules

The screenshot displays the Simmune Modeler 2.1.0 software interface. The title bar indicates the current model file is C:/Program Files (x86)/Simmune 2.1.1909/examples/data/models/YeastMAPK.dbf. The menu bar includes Model, View, Tools, and Help. The toolbar contains icons for file operations and model management.

The main window is divided into several panels:

- Molecules Panel (Left):** Lists available molecules with icons and names: Cdc14, Dig, Fus3, Fus3\_anchor, Gbg, MP2C, and Msg5. Each molecule has a small icon and a number indicating its status or count.
- Molecule Panel (Center):** Displays a visual representation of a molecule, labeled 'Molecule'. It shows a blue oval with a red square inside, labeled with '1' and '2'.
- Molecule Interactions Panel (Right):** Lists interactions with IDs: mli-000004, mli-000005, and mli-000013.
- Molecule Composition Panel (Bottom Left):** Shows the composition of a selected molecule, 'Molecule: Ste11'. It lists components and binding sites: 'Molecule component 1: mcp-000005', 'Binding site 1: activation site', and 'Binding site 2: Ste5 binding site'.
- Properties of Molecule Panel (Bottom Right):** Contains fields for molecule properties: Short Name (Ste11), Full Name (Ste11), Type (Protein), Diff\_Coeff (4 microns<sup>2</sup>/s), Category (Kinase), Accession, and Annotation. The annotation text describes Ste11 as a kinase (MAPKKK) activating Ste7 (MAPKK) in a Ste5-dependent manner during the pheromone response of yeast.

A yellow note at the bottom of the Molecule Composition panel states: "Note: Related items found, can NOT add/remove."



# Simmune Modeler: Yeast Model: **Complex Species**

The screenshot displays the Simmune Modeler 2.1.0 interface. The title bar indicates the current model file is 'C:/Program Files (x86)/Simmune 2.1.1909/examples/data/models/YeastMAPK.dbf'. The main window is divided into several panels:

- Complexes Panel (Left):** Lists available species: Gbg\_Ste5, MP2C, MP2C\_St..., Msg5, Msg5\_Fus3, and Spa2p. It includes 'New', 'View', and 'Delete' buttons.
- Complex Species Panel (Center):** Shows a visual representation of the 'MP2C\_Ste11' complex with two molecules (1 and 2) and their binding sites. It includes 'Edit Options' (Move, Change Layout, Rotate +90°, Rotate -90°, Flip) and action buttons (Enable Editing, Clear, Create A Copy, Delete).
- Composition Panel (Bottom Left):** Details the components of the 'Complex Species: MP2C\_Ste11':
  - Molecule 1: Ste11
    - Molecule component 1: mcp-000005 (Binding site 1: activation site)
    - Molecule component 2: Ste5 binding site
  - Molecule 2: MP2C
    - Molecule component 1: mcp-000009 (Binding site 1: bst-000016)
- Properties of Complex Species Panel (Bottom Right):** Fields for Short Name (MP2C\_Ste11), Full Name (MP2C\_Ste11), Accession, and Annotation.
- Relations Panel (Far Right):** Shows the 'Complex' section with 'MP2C\_Ste11\_1' and 'MP2C\_Ste11\_2'. The 'Transformation' section shows 'Ste11 dephosphorylation'. The 'Association' section shows 'As Source' and 'As Result'.

A yellow note at the bottom of the Composition panel states: 'Note: Related items found, can NOT add/remove.'

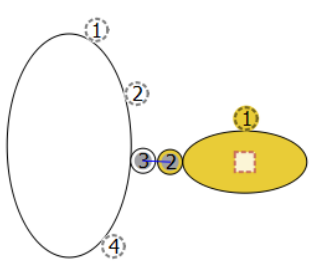
# Simmune Modeler: Yeast Model: **Complex**

Simmune Modeler 2.1.0 (current model file: C:/Program Files (x86)/Simmune 2.1.1909/examples/data/models/YeastMAPK.dbf)

Model View Tools Help

Model Molecule Complex

Complex



Complex Name: Ste5\_Ste7\_all  
Species Name: Ste5\_Ste7  
Annotation:  
☐ Display in Complex List

Save  
Back  
Delete

Relations

New View Delete

Transformation

As Source

As Result

Association

As Source

As Result

Ste5\_Ste7 assoc

Dissociation

As Source

Ste5\_Ste7 dissociation

Molecule Component Tag States and Binding Status

Component	State
Complex	
Molecule 1: Ste5	
Molecule Component 1: mcp-000004	
Binding Sites	
1: Gbg binding site	Don't Care
2: Ste11 binding site	Don't Care
3: Ste7 binding site	Bound
4: Fus3 binding site	Don't Care
Molecule 2: Ste7	
Molecule Component 1: mcp-000006	
Tag	
phosphorylated	Don't Care
Binding Sites	
1: activation site	Don't Care
2: Ste5 binding site	Bound

# Simmune Modeler: Yeast Model: Reaction

Simmune Modeler 2.1.0 (current model file: C:/Program Files (x86)/Simmune 2.1.1909/examples/data/models/YeastMAPK.dbf)

Model View Tools Help

Model Molecule Complex

Add Complex

Add

Species: Cdc14

Species: Cdc14\_Ste7

Species: Dig

Species: Fus3

Species: Fus3.Ste5.Ste7

Species: Fus3\_Dig

☐ Show Complexes and Species

☒ Show Complex Species Only

☐ Display Hidden Complexes

Complex Association

Source Complexes

Result Complex

Save

Back

Delete

☐ No orientation

☐ trans-binding

☐ cis-binding

☐ Display Molecule Mapping

Assoc Name: MP2C\_pSte11 assoc

Assoc Rate: 1e+06

Rate Unit: /mol\*s

☐ 2D ☒ 3D ☐ Intra Complex

Annotation:

Create Reverse Dissociation

Source Complex 1

Complex Name: pSte11\_unbound

Save Complex

Species Name: Ste11

Select Complex

☐ Display in Complex List

Component	State
Complex: pSte11_unbound	
Molecule 1: Ste11	
Molecule Component 1: mcp-000005	
Tag	
phosphorylated	On
Binding Sites	
1: activation site	Unbou
2: Ste5 binding site	Unbou

Source Complex 2

Complex Name: MP2C

Save Complex

Species Name: MP2C

Select Complex

☒ Display in Complex List

Component	State
Complex: MP2C	
Molecule 1: MP2C	
Molecule Component 1: mcp-000009	
Binding Site	
1: bst-000016	Unbound

Result Complex

Complex Name: MP2C\_Ste11\_1

Save Complex

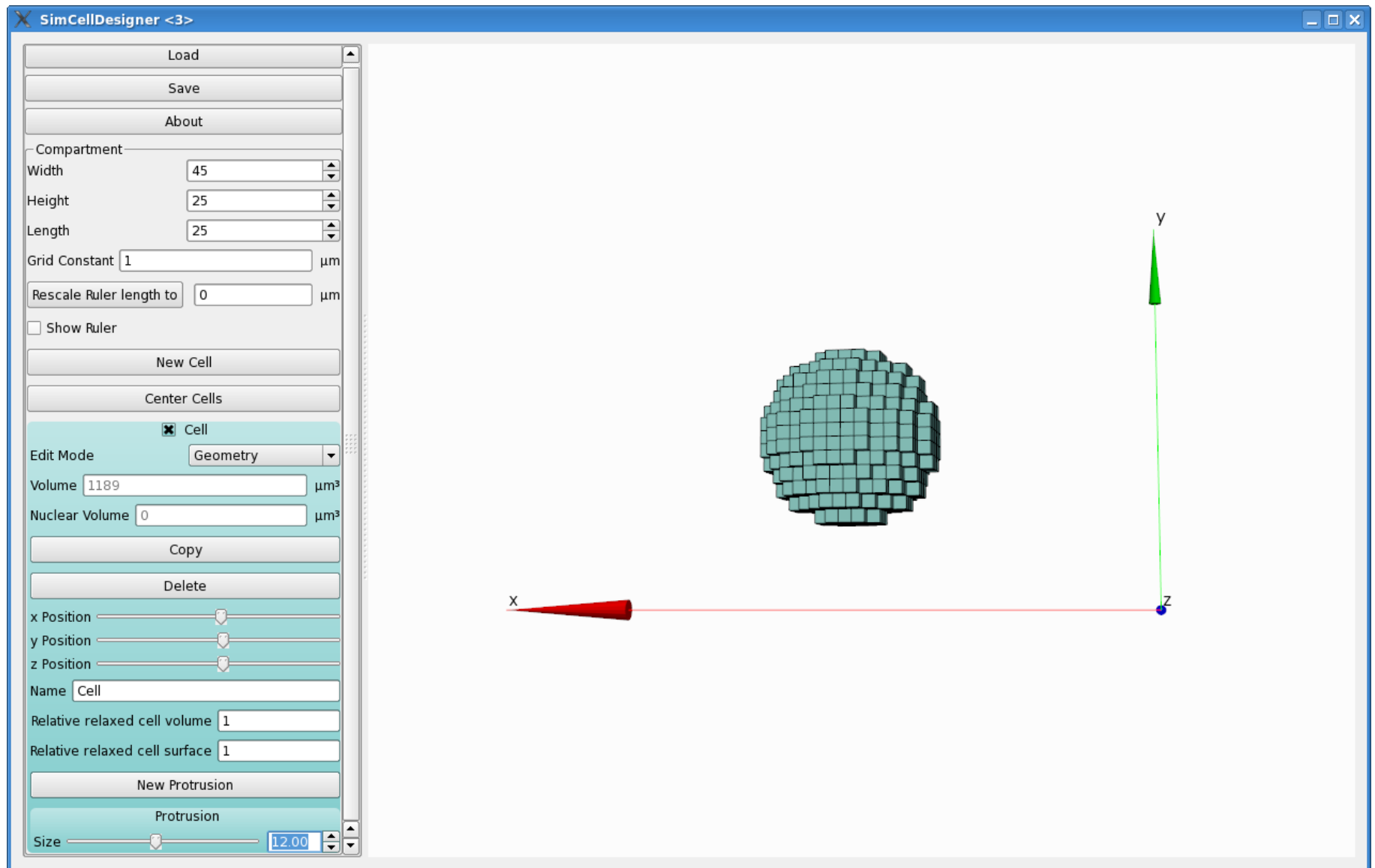
Species Name: MP2C\_Ste11

Select Complex

☐ Display in Complex List

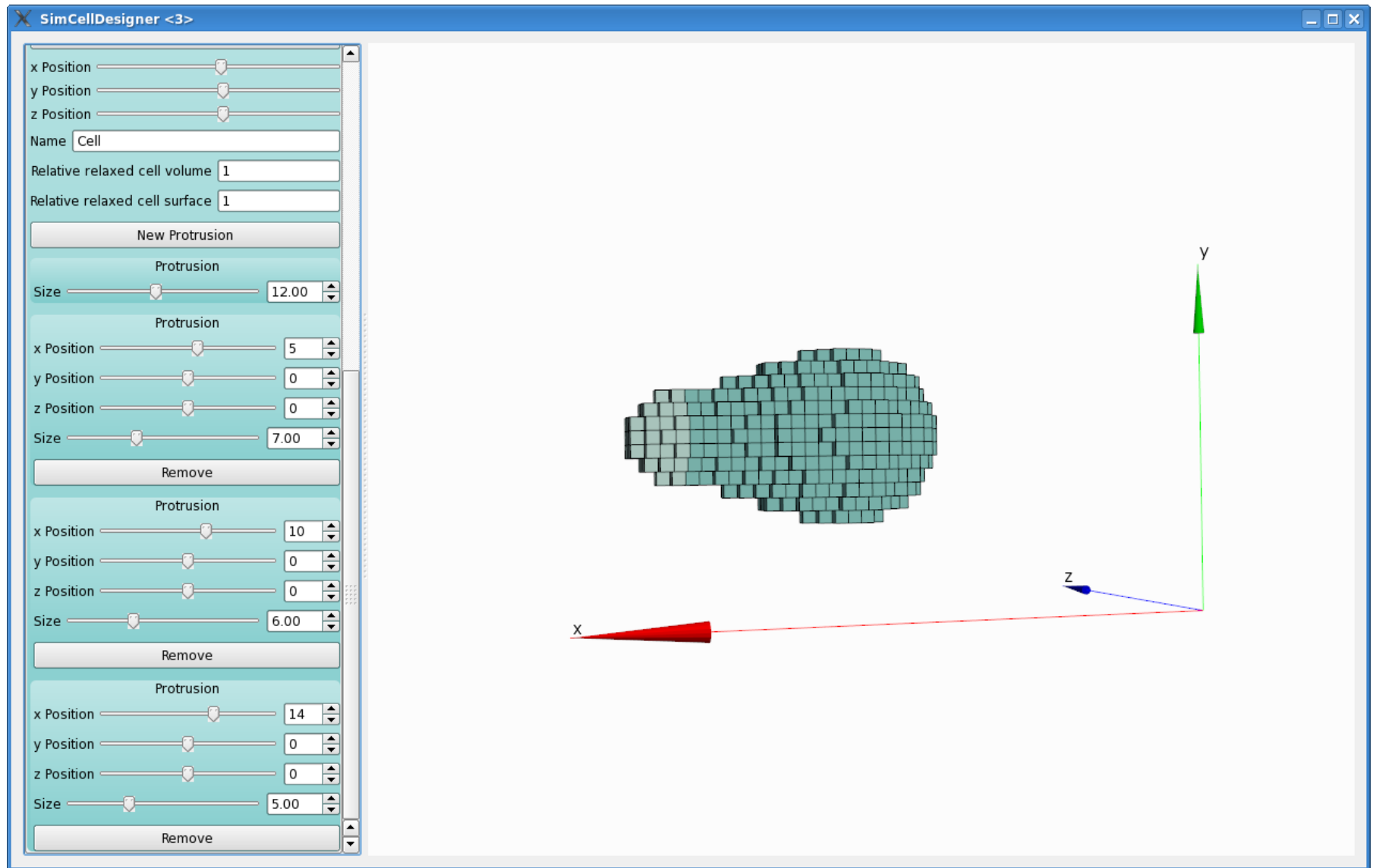
Component	State
Complex: MP2C_Ste11_1	
Molecule 1: Ste11	
Molecule Component 1: mcp-000005	
Tag	
phosphorylated	On
Molecule 2: MP2C	
Molecule Component 1: mcp-000009	

# SimCellDesigner: Yeast Geometry: Cell

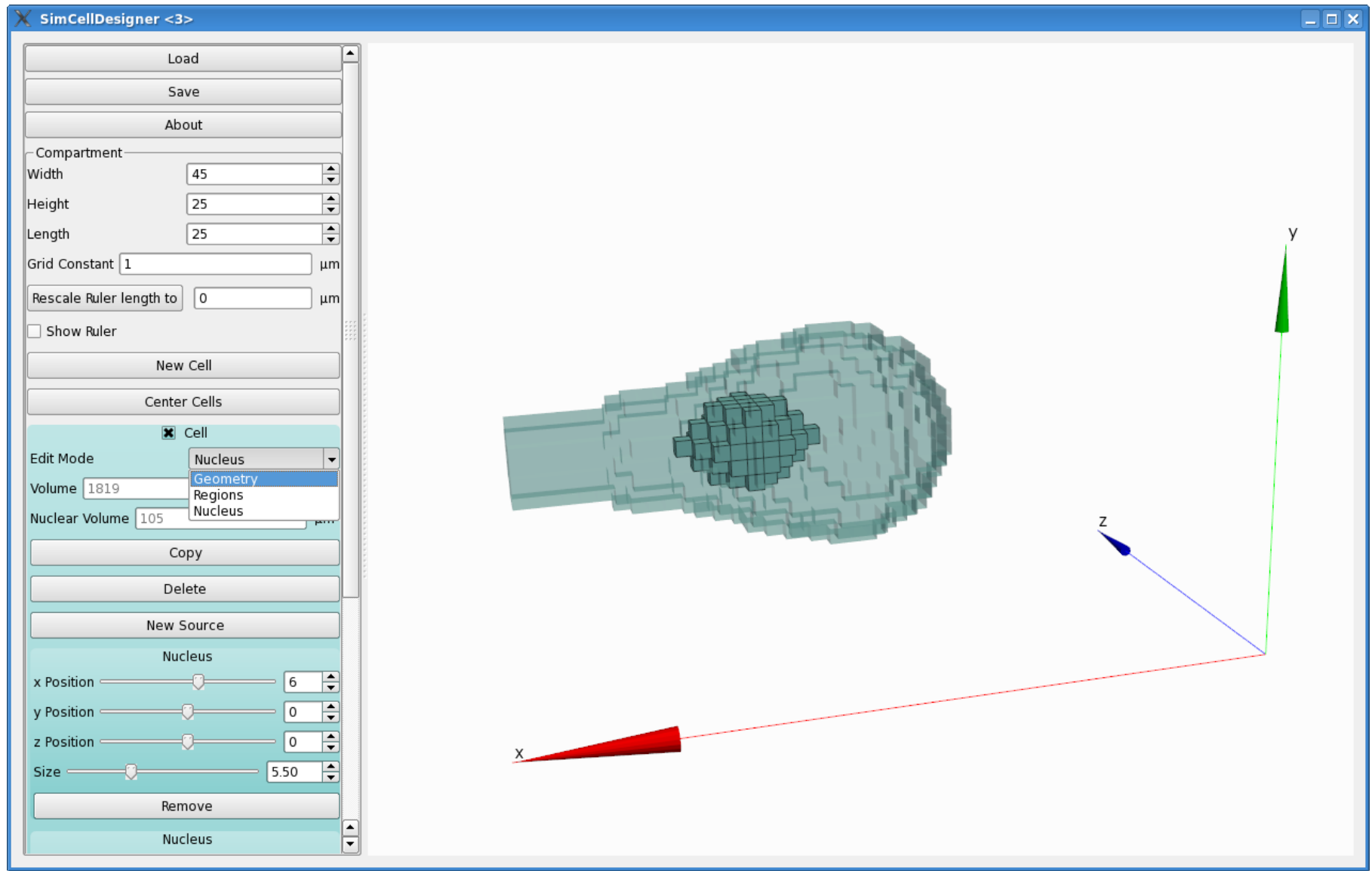


# Simmune CellDesigner: Yeast Geometry:

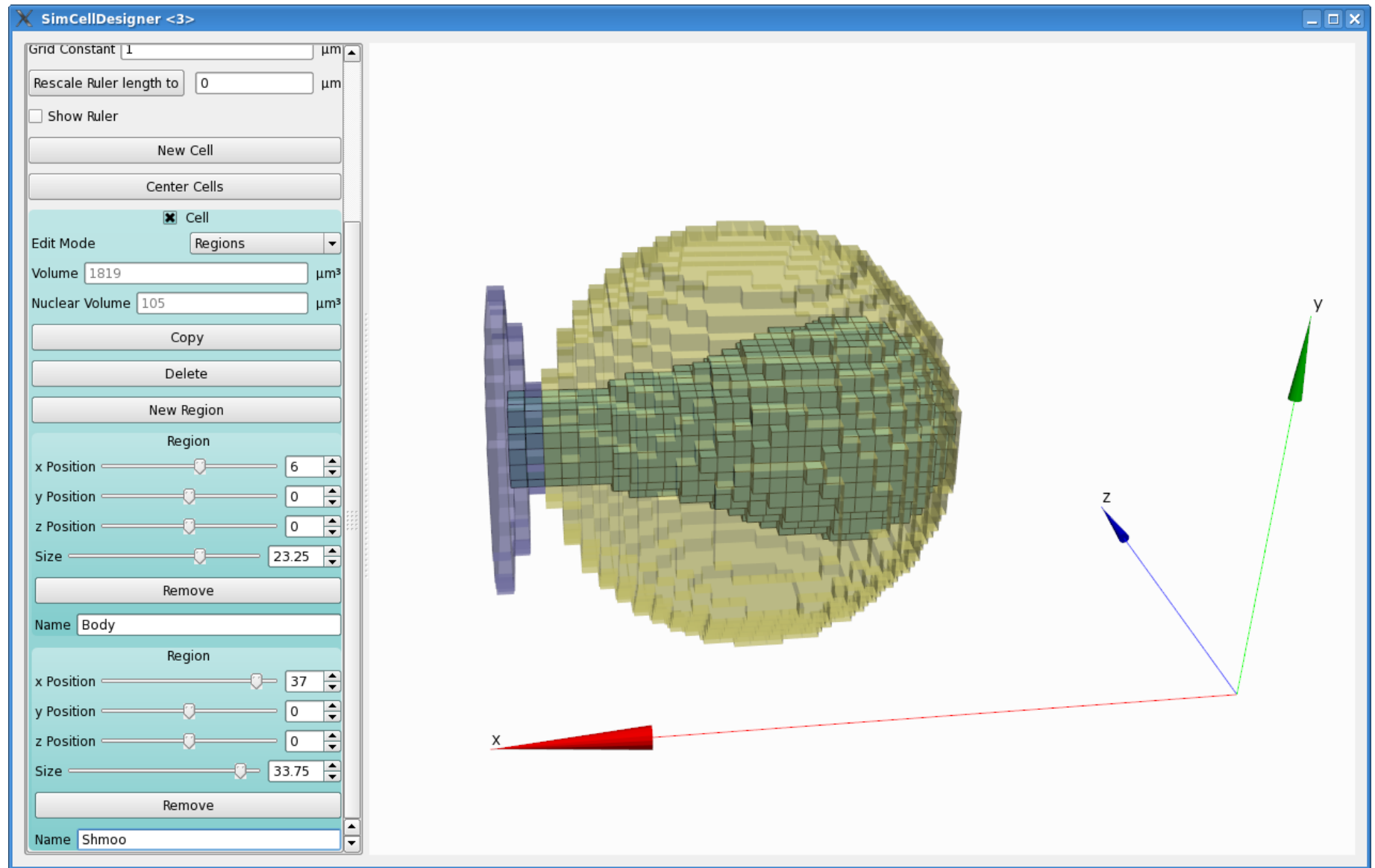
## Flexible Cell Shape Configuration



# Simmune CellDesigner: Yeast Geometry: **Oganelle**



# Simmune CellDesigner: Yeast Geometry: Regions



# Simmune Simulation : Yeast : Initial Condition

SimulatorGui

Select a cell to populate  
Cell

Select a region to populate  
Body

Select an organelle to populate  
Cytosol

Select a complex to populate the region with  
Cdc14

☐ Create membrane pore ☒ 3d concentration

Concentration  Set mol/l

Cell	Region	Organelle	Complex	Concentration
Cell	Body	Cytosol	Msg5	1.5e-07
Cell	Body	Nucleus (Exporting...	Fus3_basal	33
Cell	Body	Cytosol	Ste7_basal	9e-08
Cell	Body	Cytosol	Ste20_inactive	1e-07
Cell	Body	Nucleus (Importin...	pFus3_free	100
Cell	Shmoo	Cytosol (Membrane)	Fus3_anchor_basal	400
Cell	Body	Nucleus (Exporting...	Msg5	100
Cell	Shmoo	Cytosol (Membrane)	Spa2p	80
Cell	Body	Cytosol	MP2C	3e-08
Cell	Body	Nucleus (Importin...	Msg5	66
Cell	Body	Cytosol	Ste11_basal	3.3e-08
Cell	Body	Cytosol	Cdc14	6e-08
Cell	Body	Nucleus	Dig	8e-07

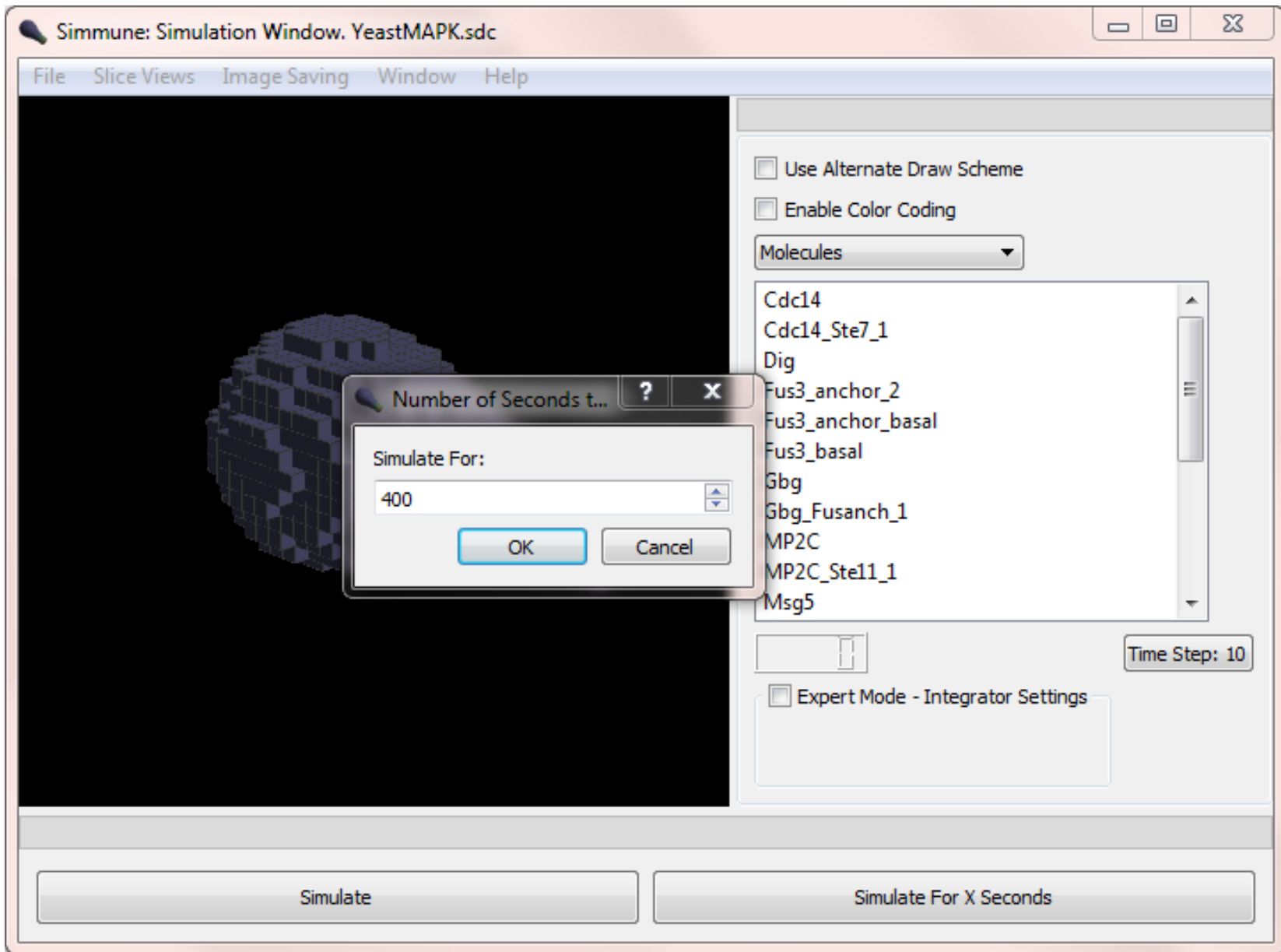
Delete

Maximum Complex Size 8

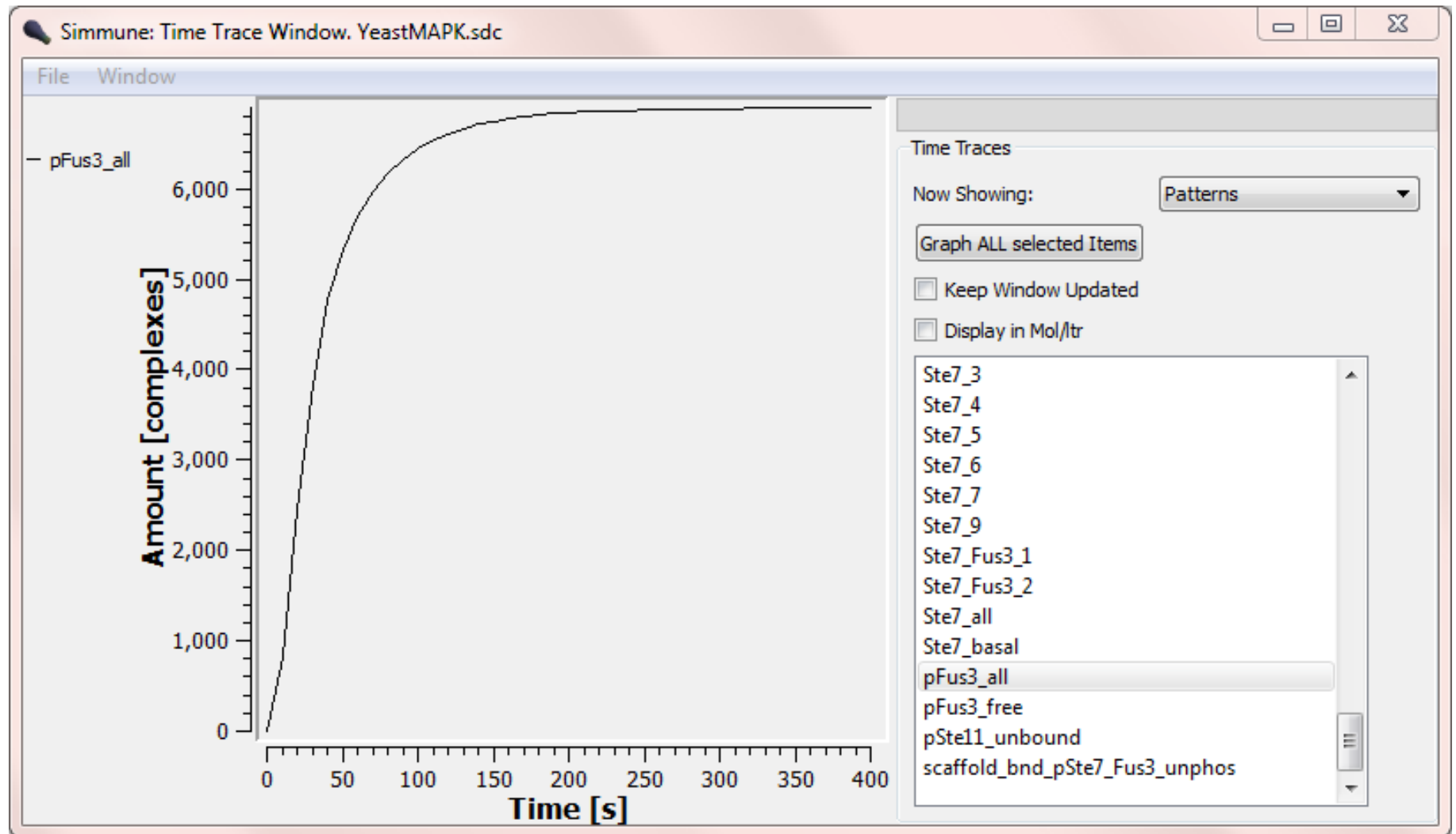
Ok



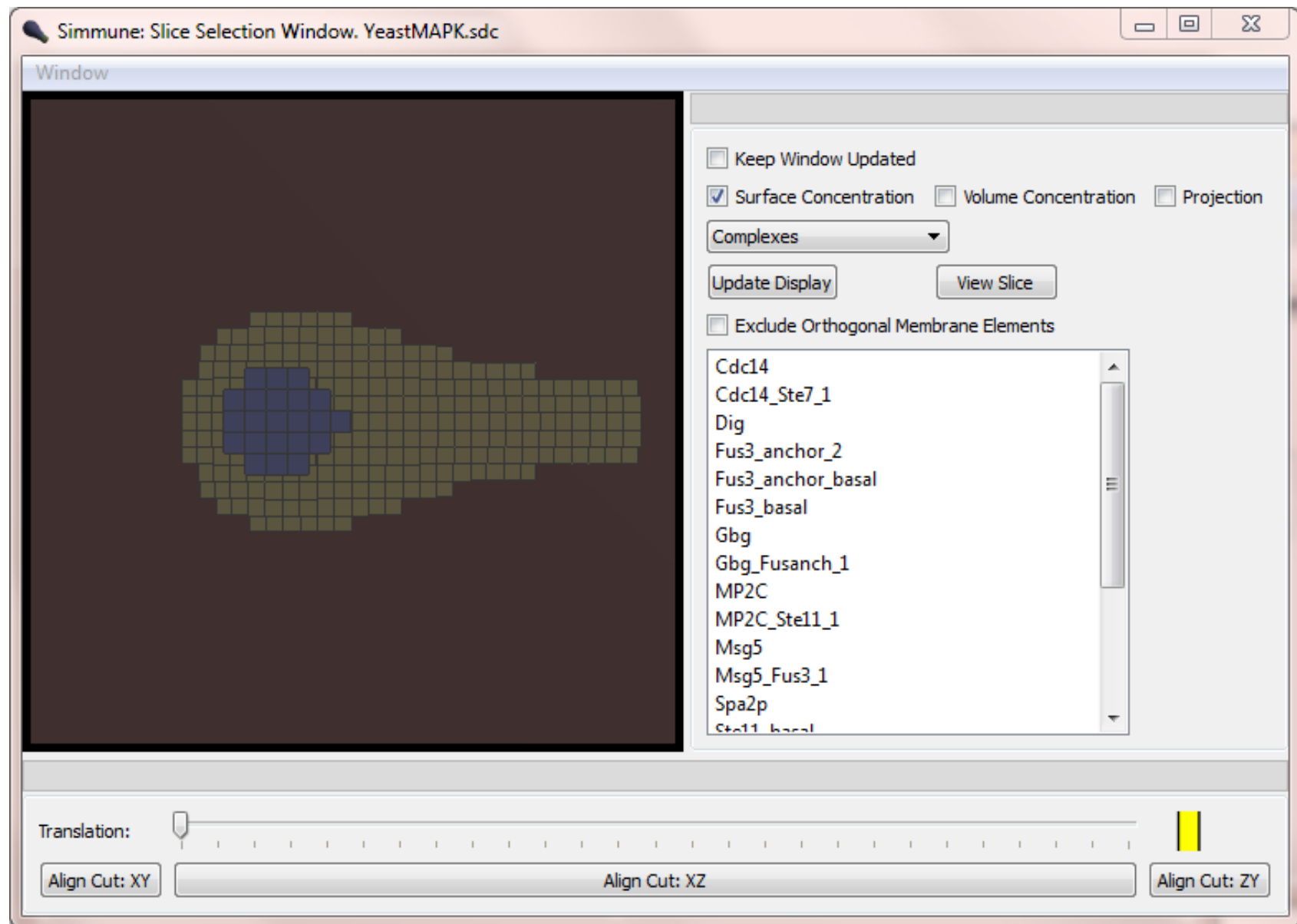
## Simmune Simulation : Yeast : **Simulation Setup**



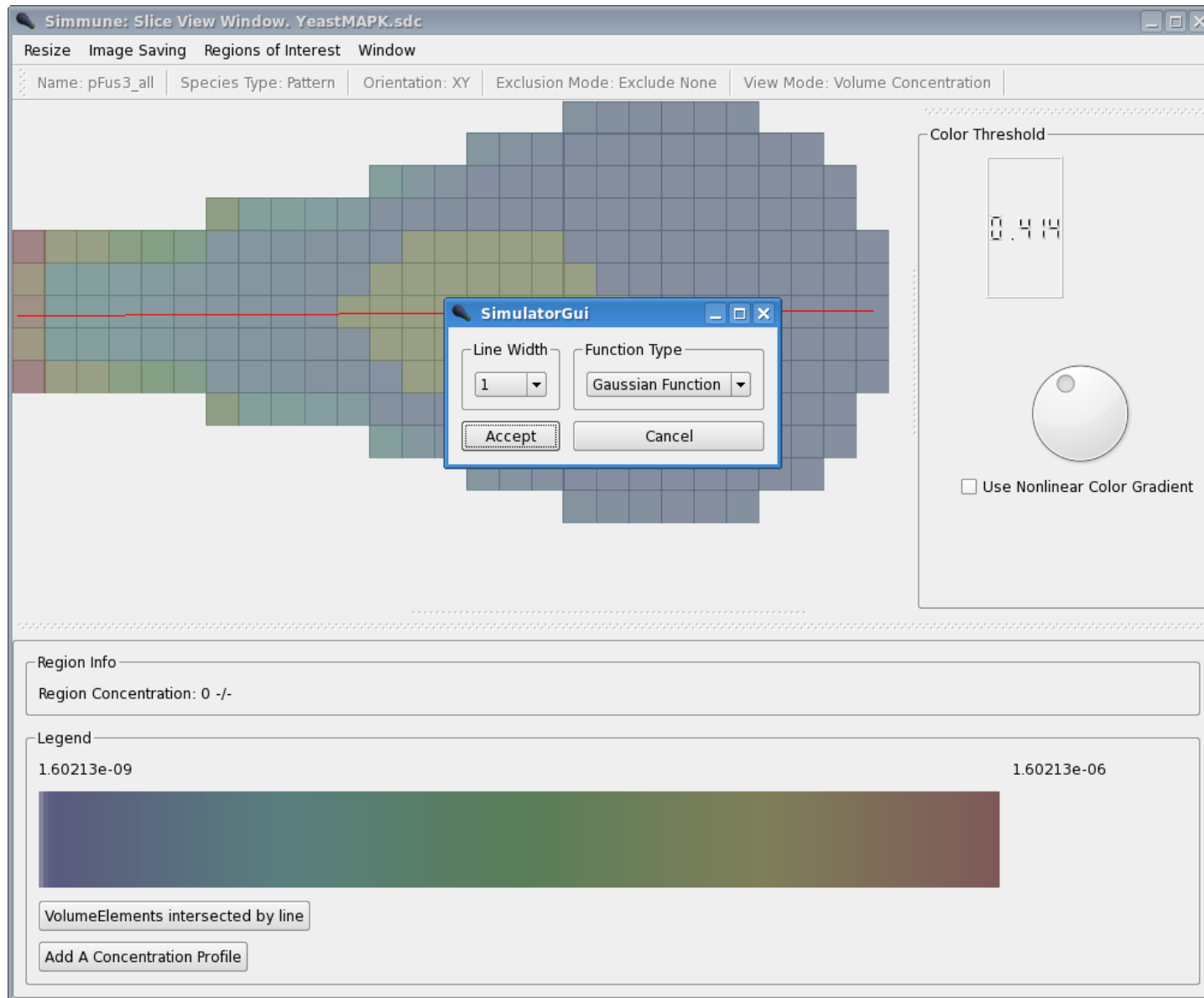
## Simmune Simulation : Yeast : Time Plot



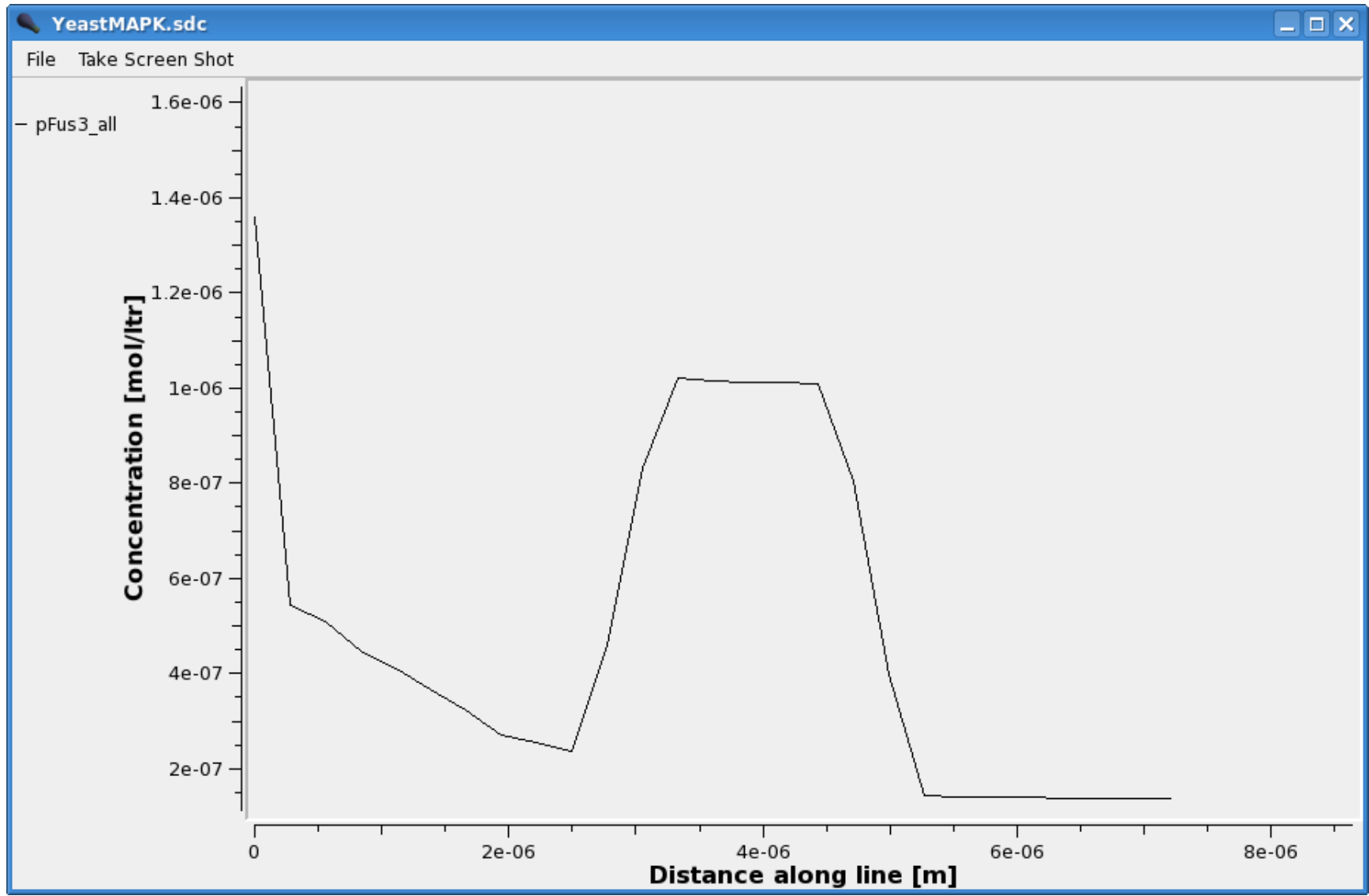
## Simmune Simulation : Yeast : Concentration Distribution



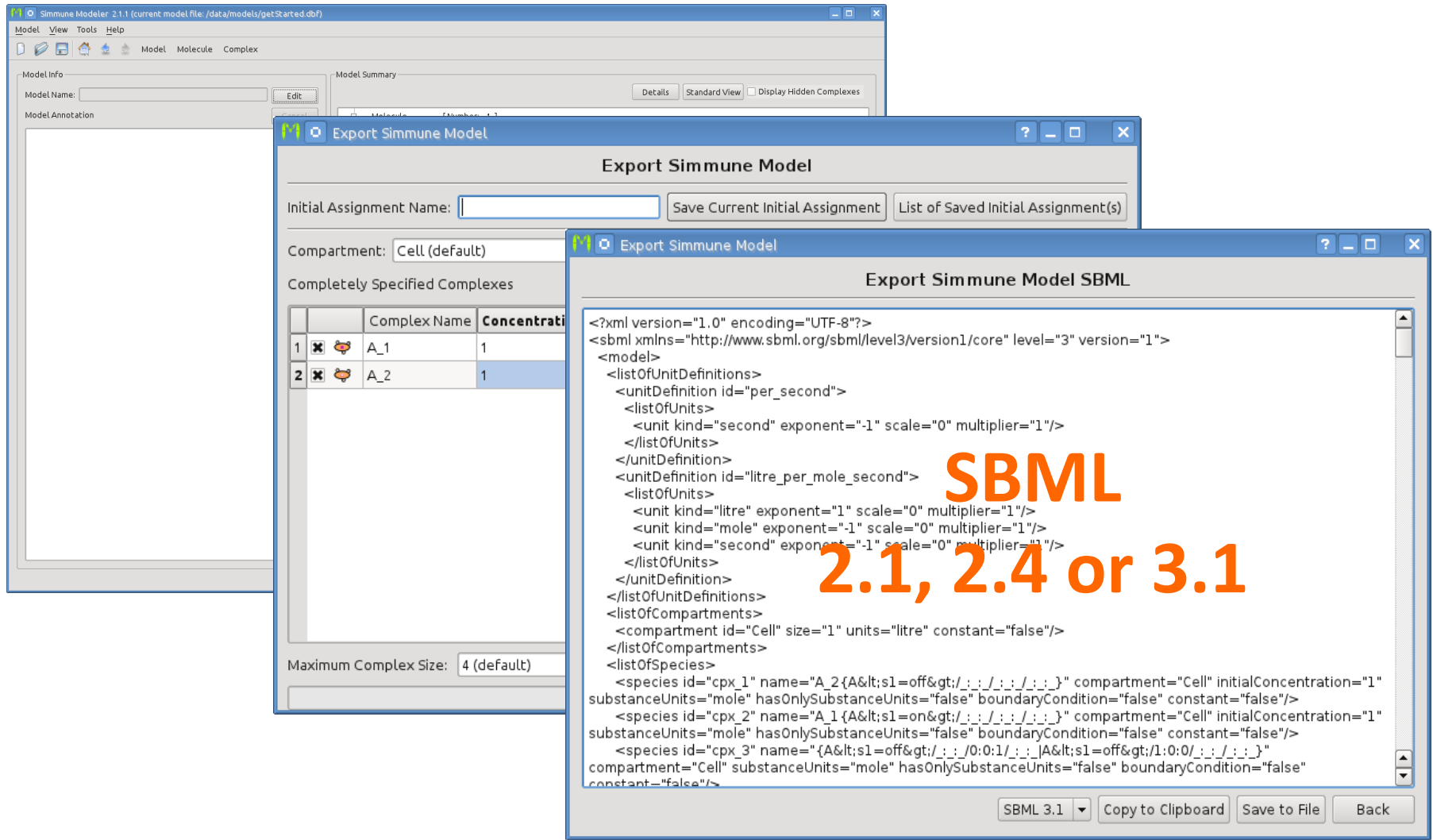
# Simmune Simulation : Yeast : Line Configuration



## Simmune Simulation : Yeast : Concentration Line Profile



# Simmune SBML Support



# Simmune SBML Support

## **Support SBML Packages:**

- SBML-Multi: Rule – based models  
(Under development)
- SBML-Spatial: Geometry  
(Able to be supported with multi?)

## **Other:**

- SED-ML (in consideration)

# Simmune

- Rule-based spatially resolved models of cellular signaling networks
- Implemented with Qt, boost, fortran, OpenGL, VTK, libSBML
- Can run on Linux, Mac and Windows
- Standard alone and distributed (in progress)
- Free for academic use and available for download at:  
[http://www.niaid.nih.gov/labsandresources/labs/aboutlabs/lb/  
Pages/simmuneproject.aspx](http://www.niaid.nih.gov/labsandresources/labs/aboutlabs/lb/Pages/simmuneproject.aspx)



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Institutes of Health.