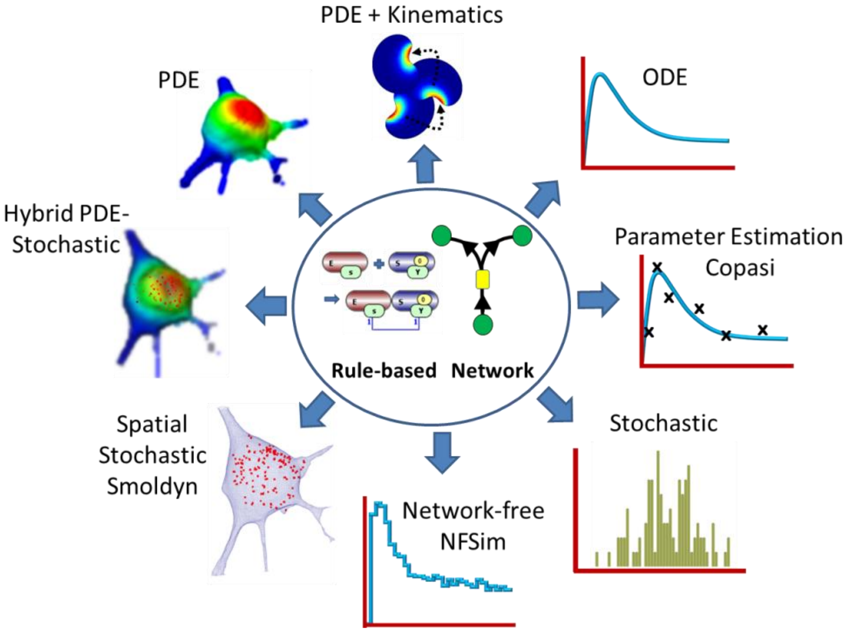
VCell

modeling environment for mathematical simulation of cellular events.

To run VCell go to:

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)

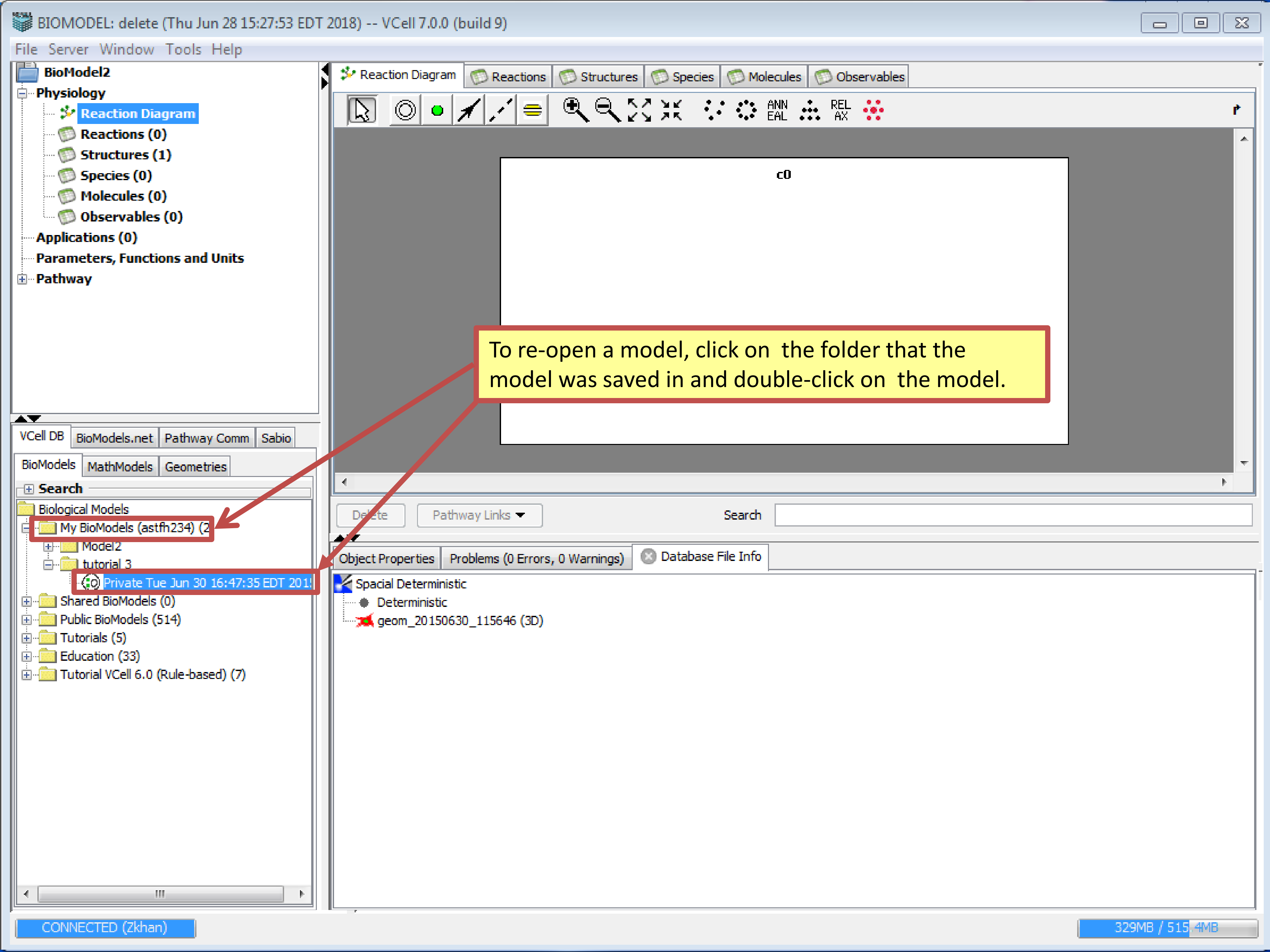
VCell Tutorial

FRAP with binding

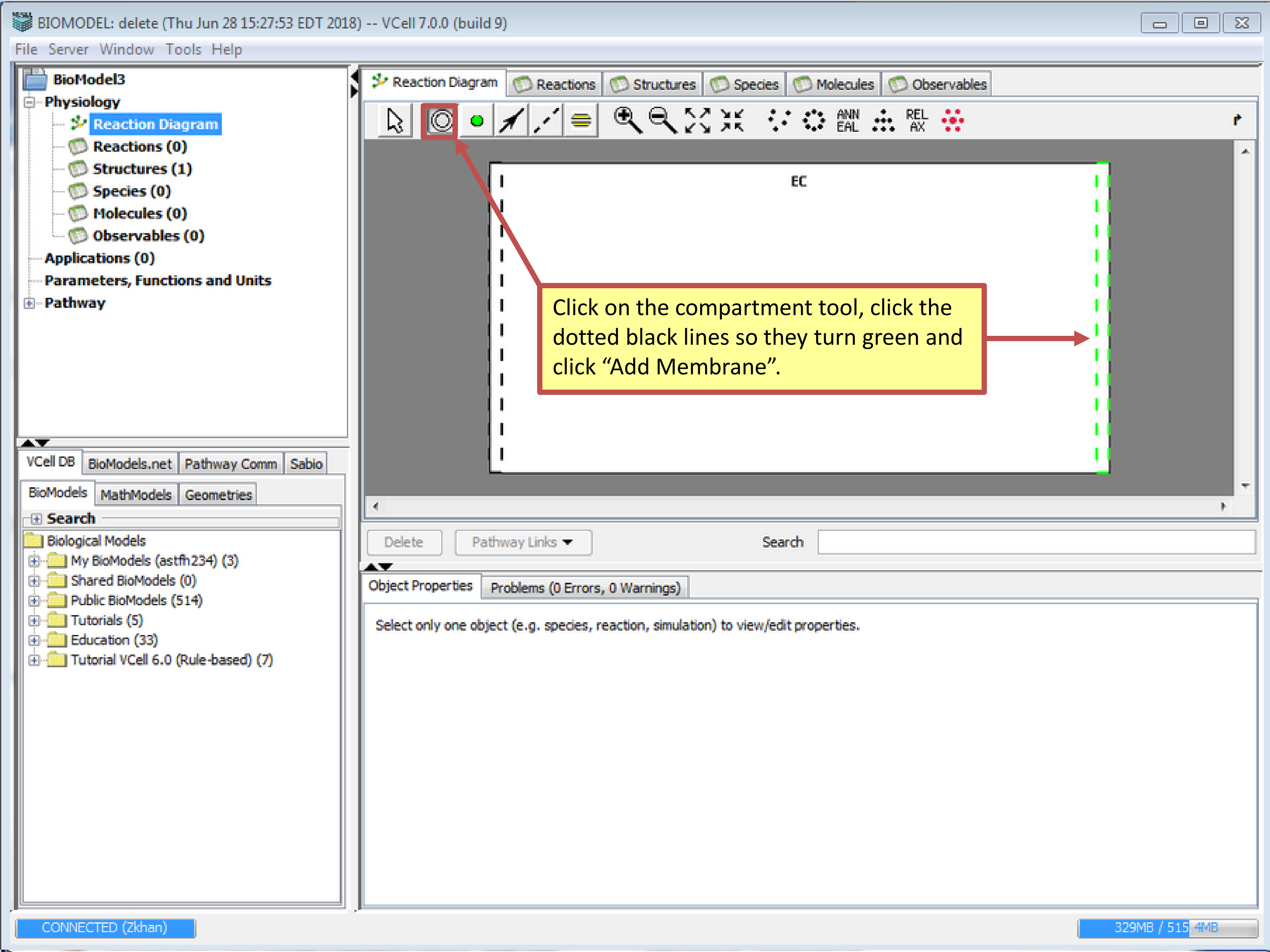
Create a simple biomodel and spatial (PDE) application to simulate a photobleaching experiment with both diffusion and binding.

In this tutorial…

- Gain a basic introduction to the Virtual Cell interface
- Create a simple biomodel with species and reactions
- Create a compartmental (ODE) application of the model to determine steady state binding conditions.
- Create a spatial deterministic (PDE) application using analytic equations to create a simple geometry
- Define initial concentrations that are non-uniform using Boolean expressions
- Created a timed event in a spatial simulation.
- View and analyze results of a spatial simulation.

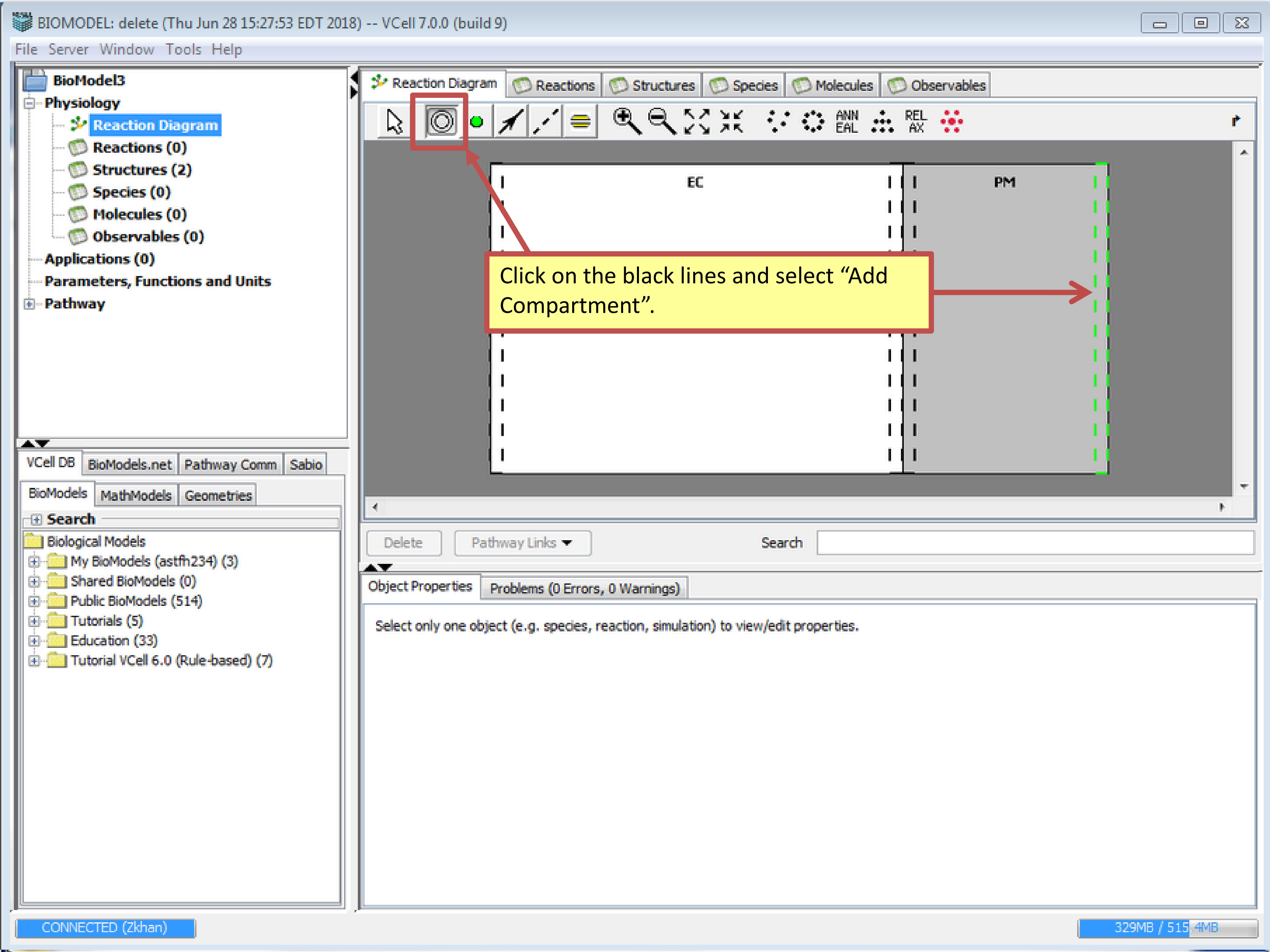


To re-open a model, click on the folder that the model was saved in and double-click on the model.



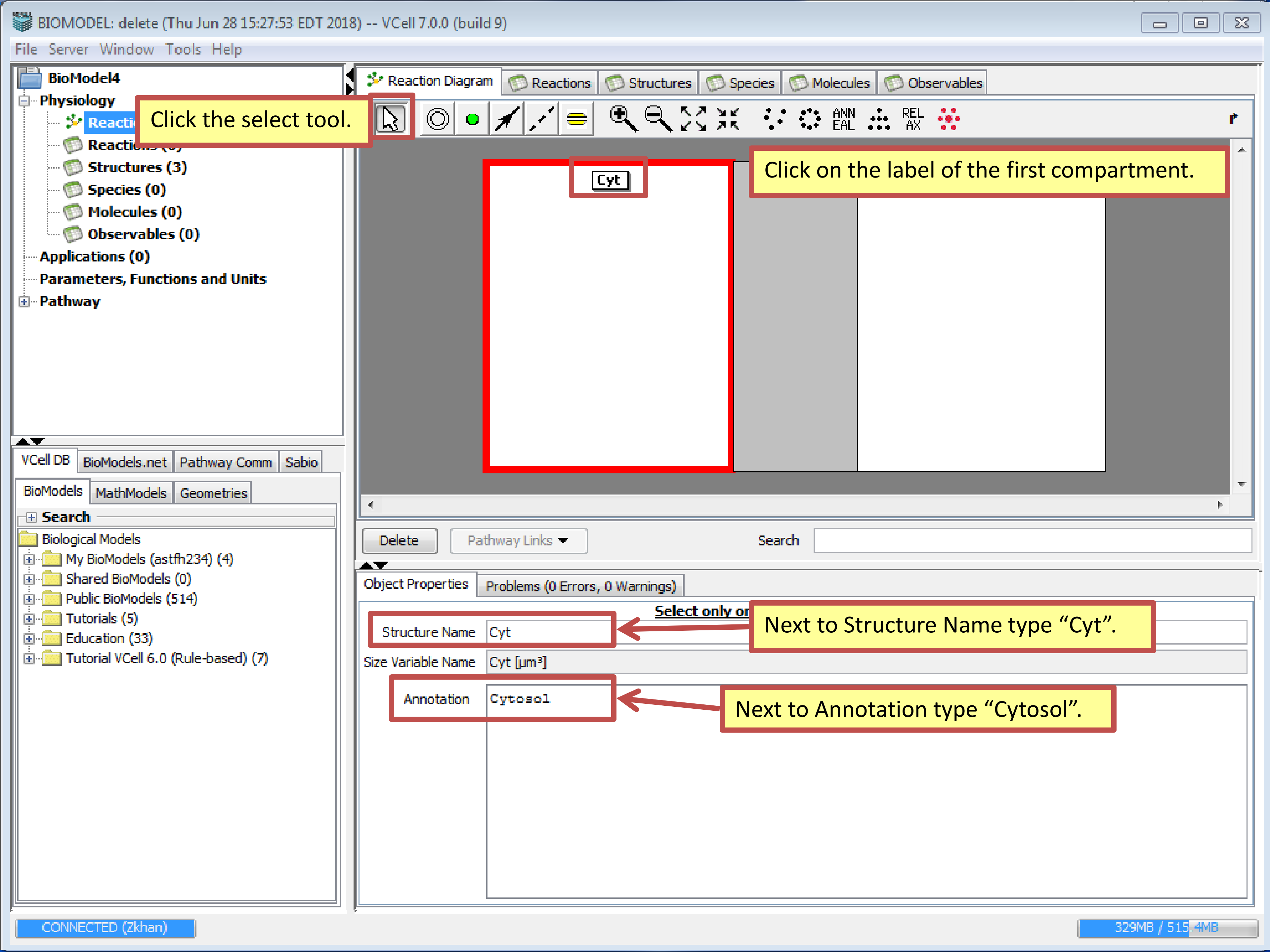
Select only one object (e.g. species, reaction, simulation) to view/edit properties.

Click on the compartment tool, click the dotted black lines so they turn green and click “Add Membrane”.



Click on the black lines and select “Add Compartment”.

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



Click the select tool.

Click on the label of the first compartment.

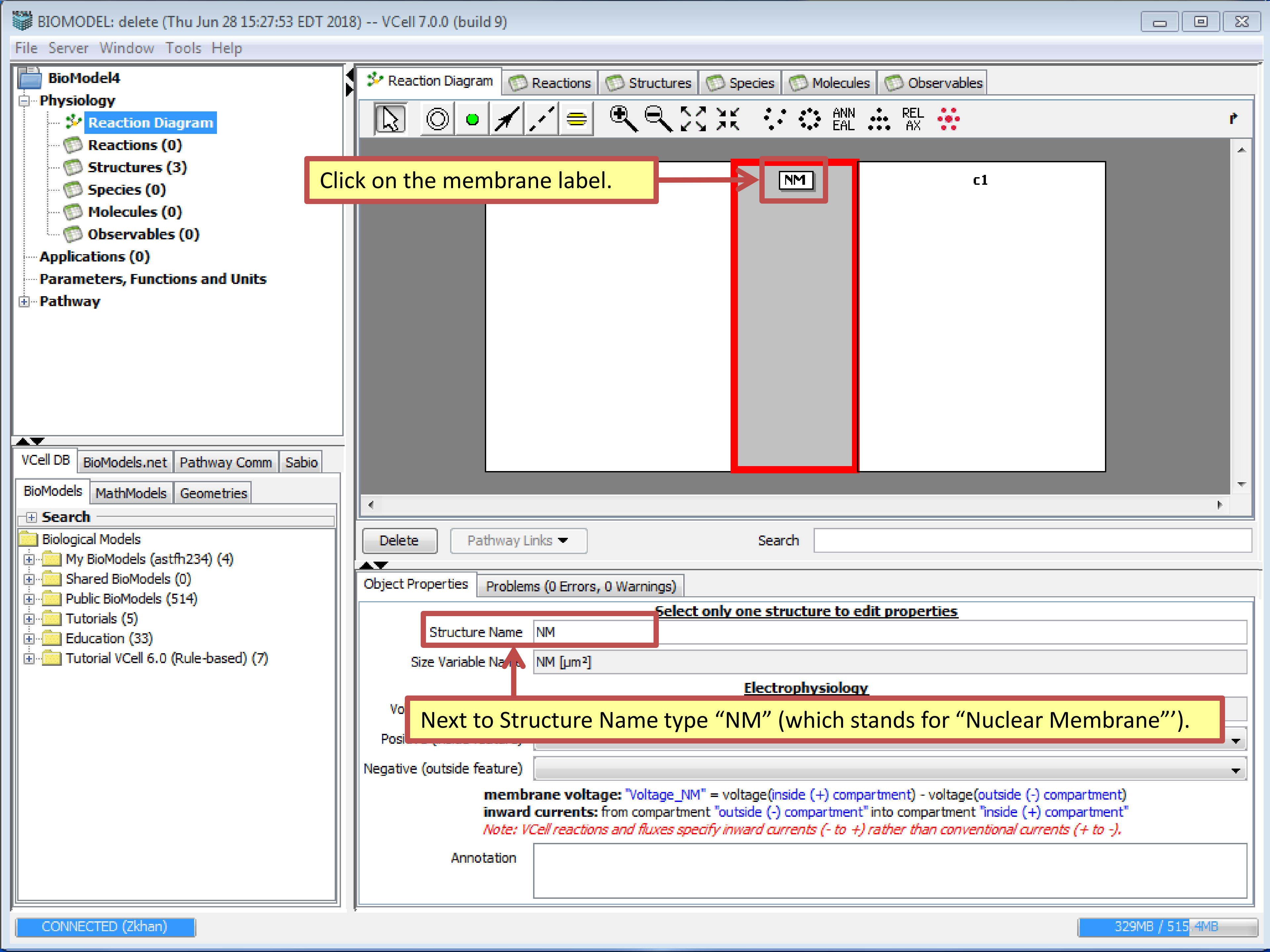
Structure Name: Cyt

Size Variable Name: Cyt [µm³]

Annotation: Cytosol

Next to Structure Name type “Cyt”.

Next to Annotation type “Cytosol”.



Click on the membrane label.

Select only one structure to edit properties

Structure Name NM

Size Variable Name NM [µm²]

Electrophysiology

Next to Structure Name type “NM” (which stands for “Nuclear Membrane”).

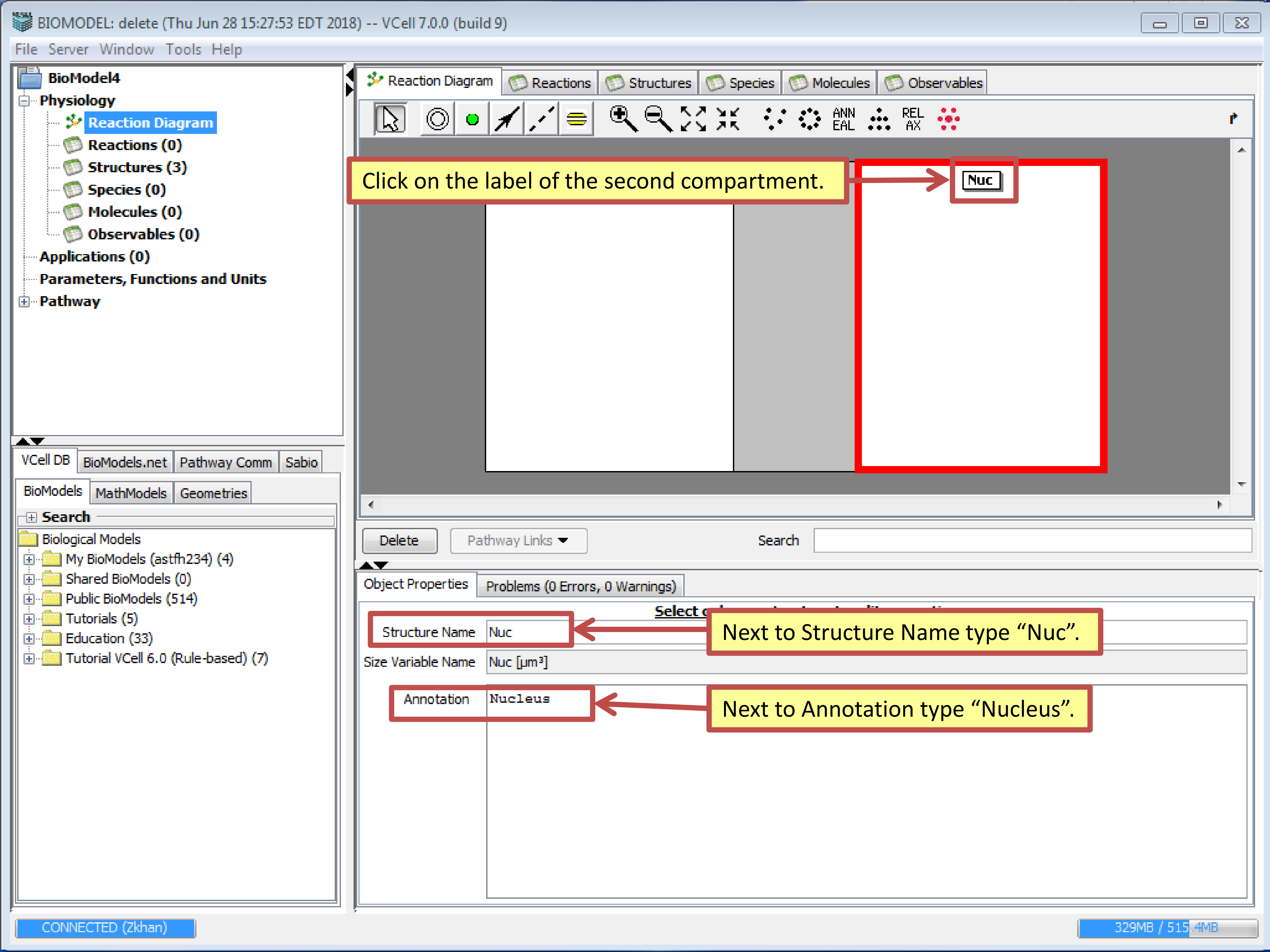
Negative (outside feature)

membrane voltage: "Voltage_NM" = voltage(inside (+) compartment) - voltage(outside (-) compartment)

inward currents: from compartment "outside (-) compartment" into compartment "inside (+) compartment"

Note: VCell reactions and fluxes specify inward currents (- to +) rather than conventional currents (+ to -).

Annotation



Click on the label of the second compartment.

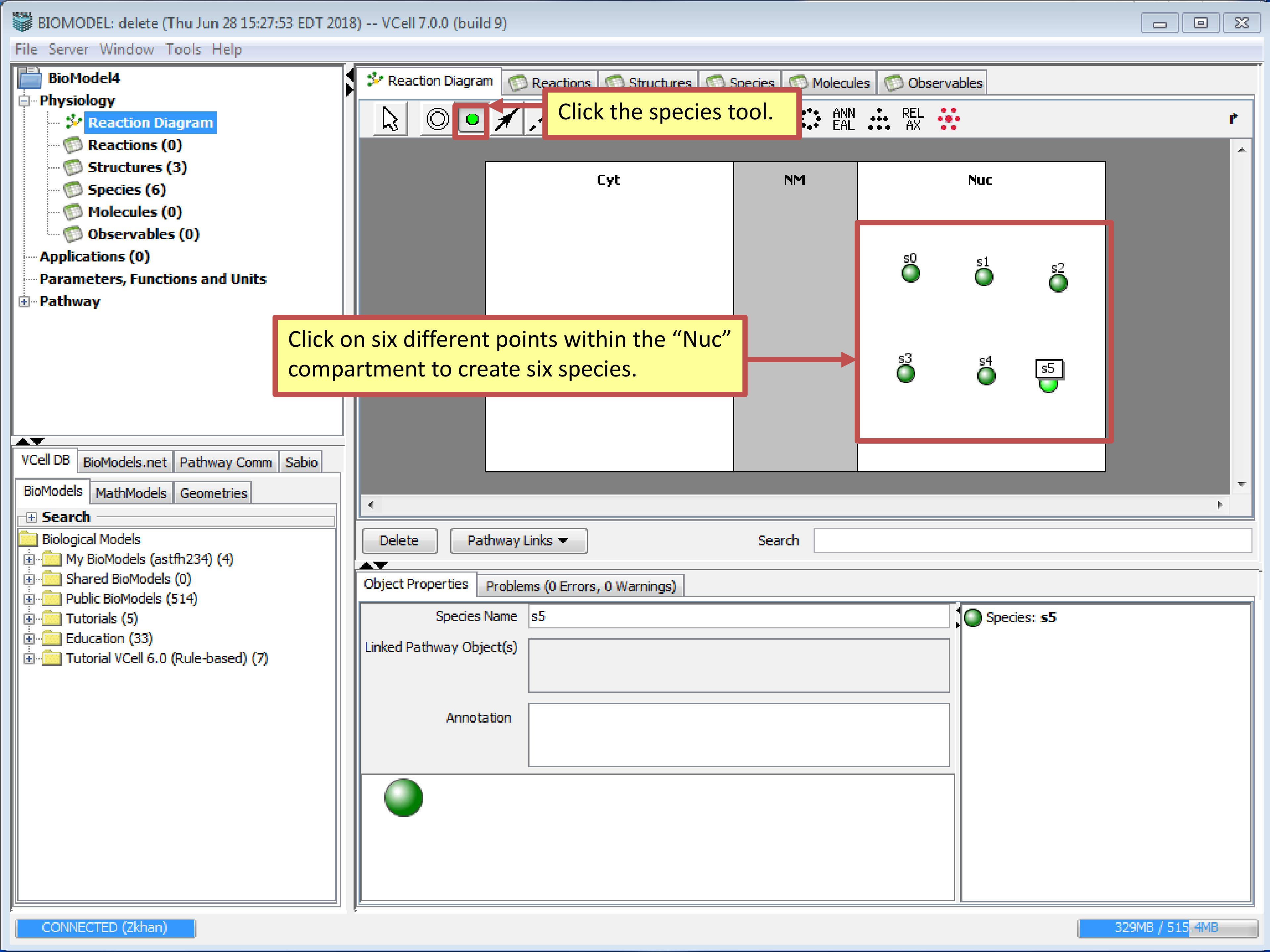
Structure Name: Nuc

Size Variable Name: Nuc [µm³]

Annotation: Nucleus

Next to Structure Name type “Nuc”.

Next to Annotation type “Nucleus”.



Click the species tool.

Click on six different points within the "Nuc" compartment to create six species.

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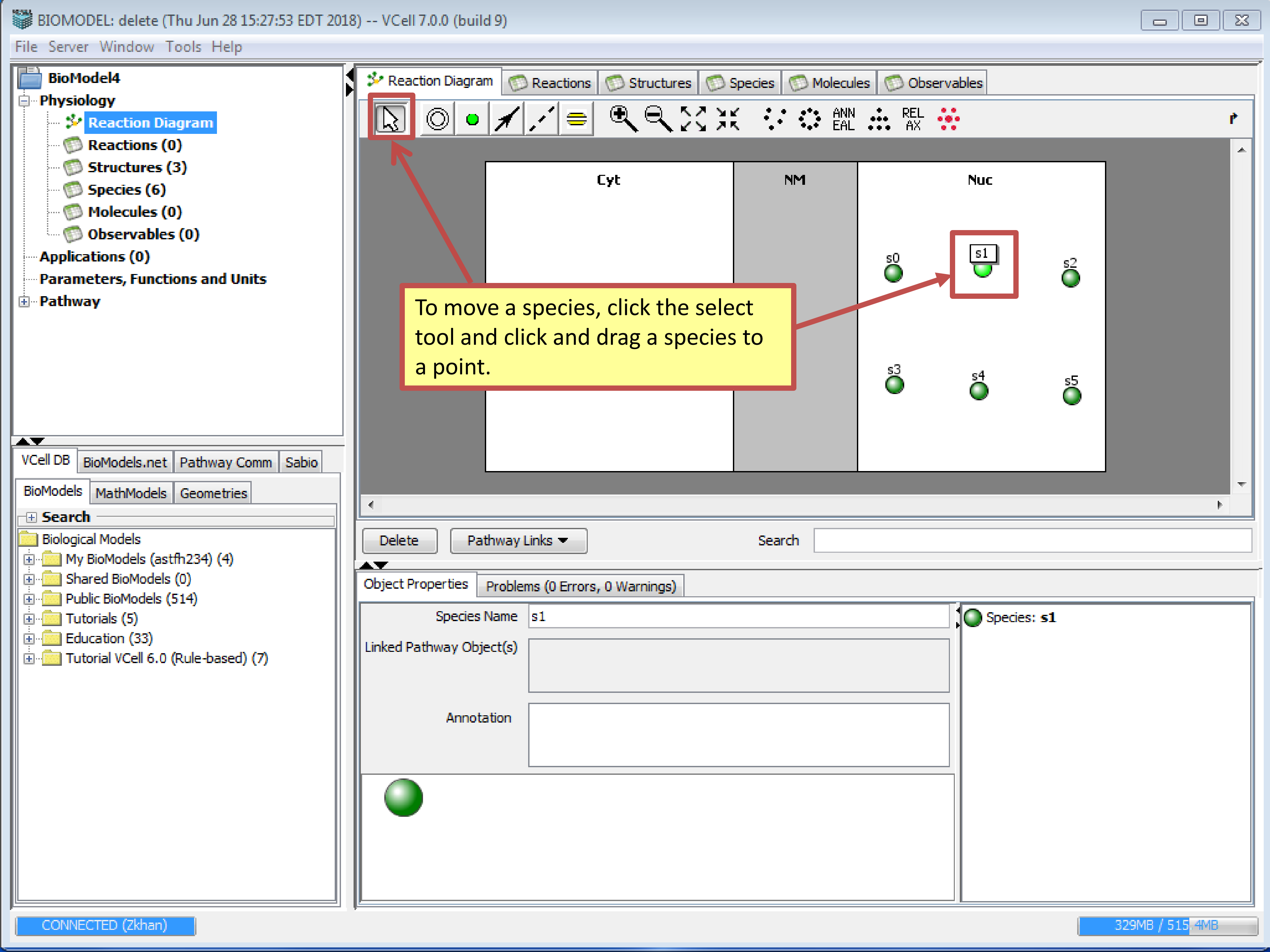
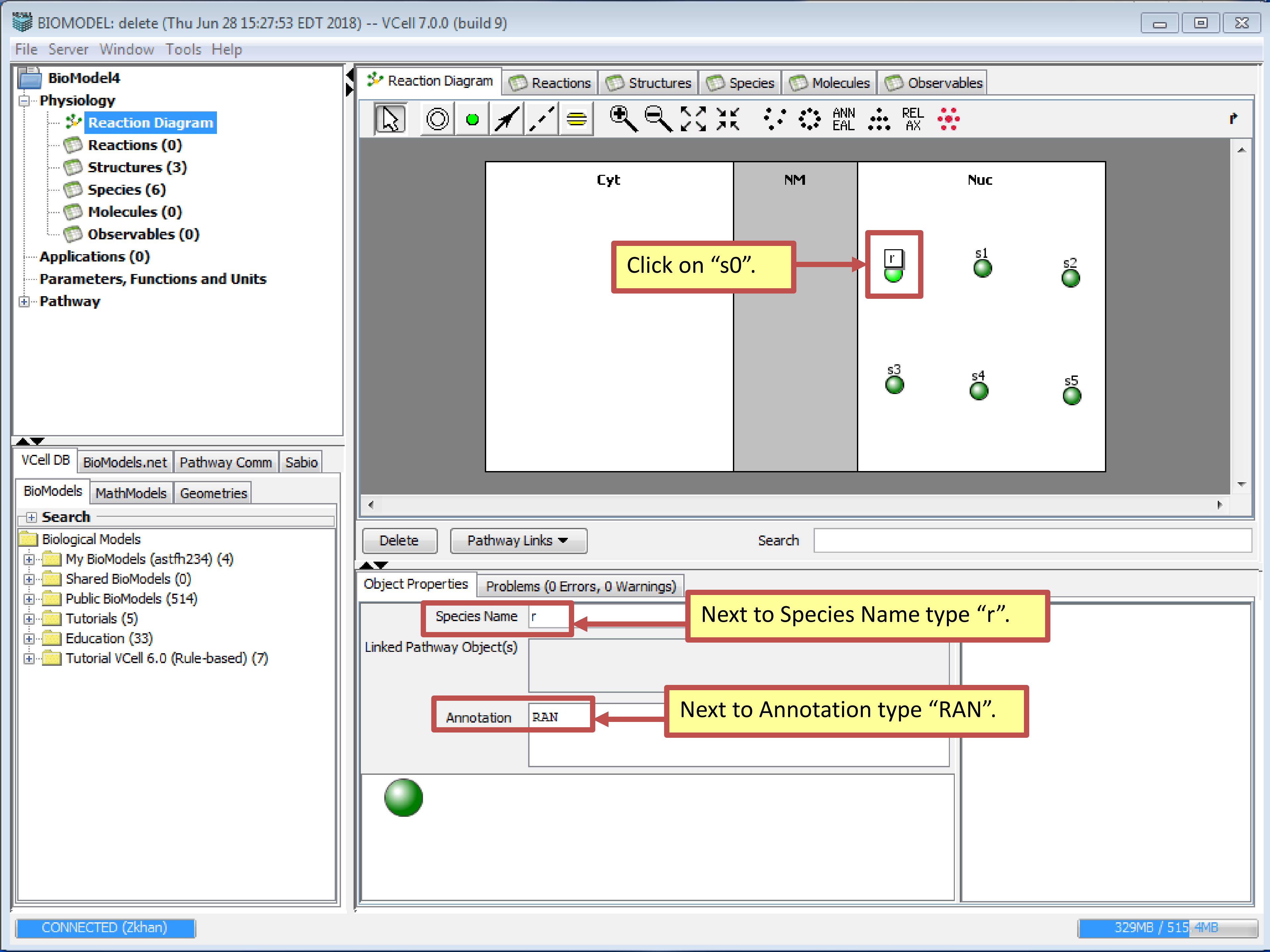
Species Name: s5

Species: **s5**



To move a species, click the select tool and click and drag a species to a point.

Species Name: s1



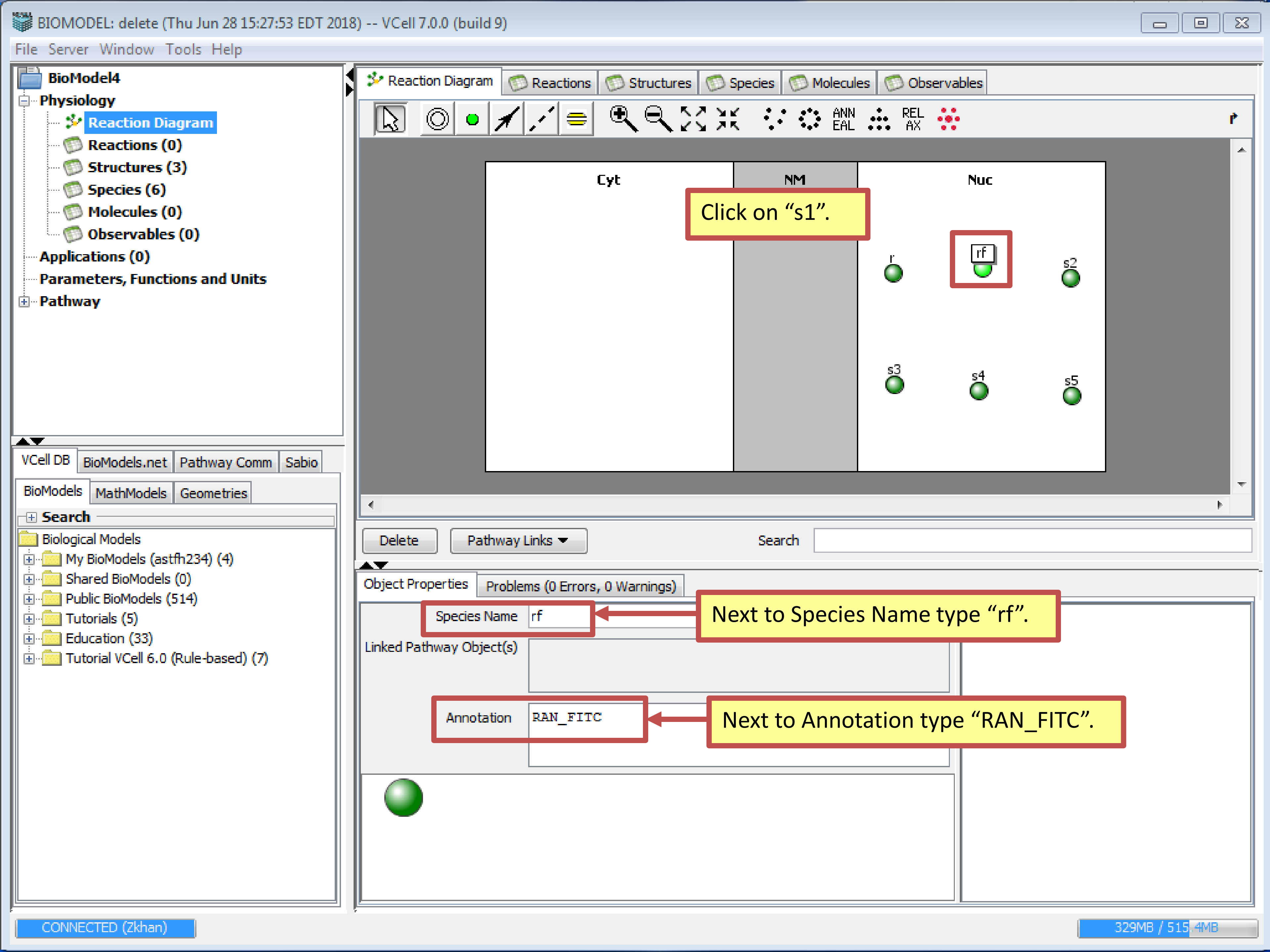
Click on “s0”.

Species Name r

Next to Species Name type “r”.

Annotation RAN

Next to Annotation type “RAN”.



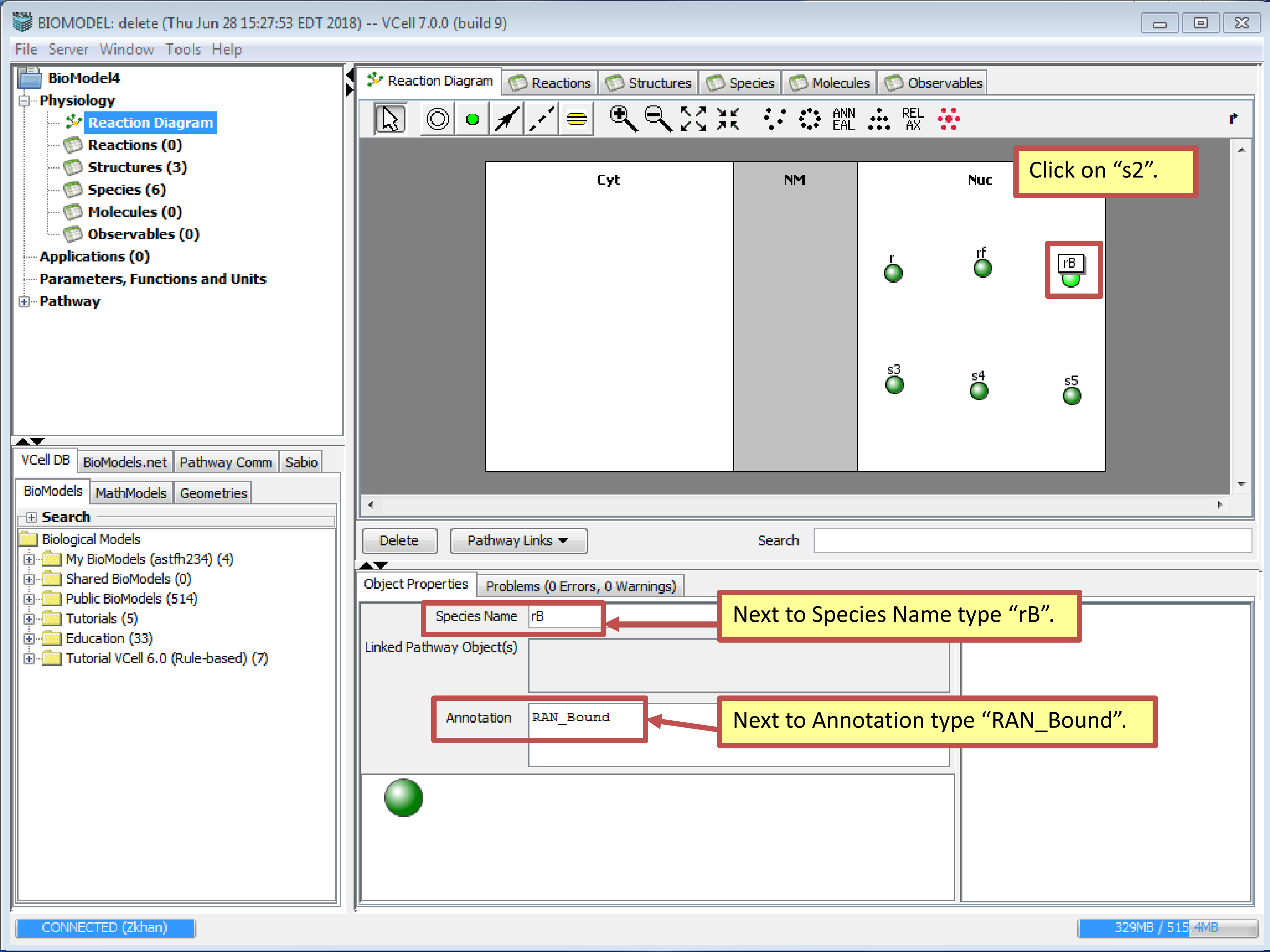
Click on “s1”.

Species Name: rf

Annotation: RAN_FITC

Next to Species Name type “rf”.

Next to Annotation type “RAN_FITC”.



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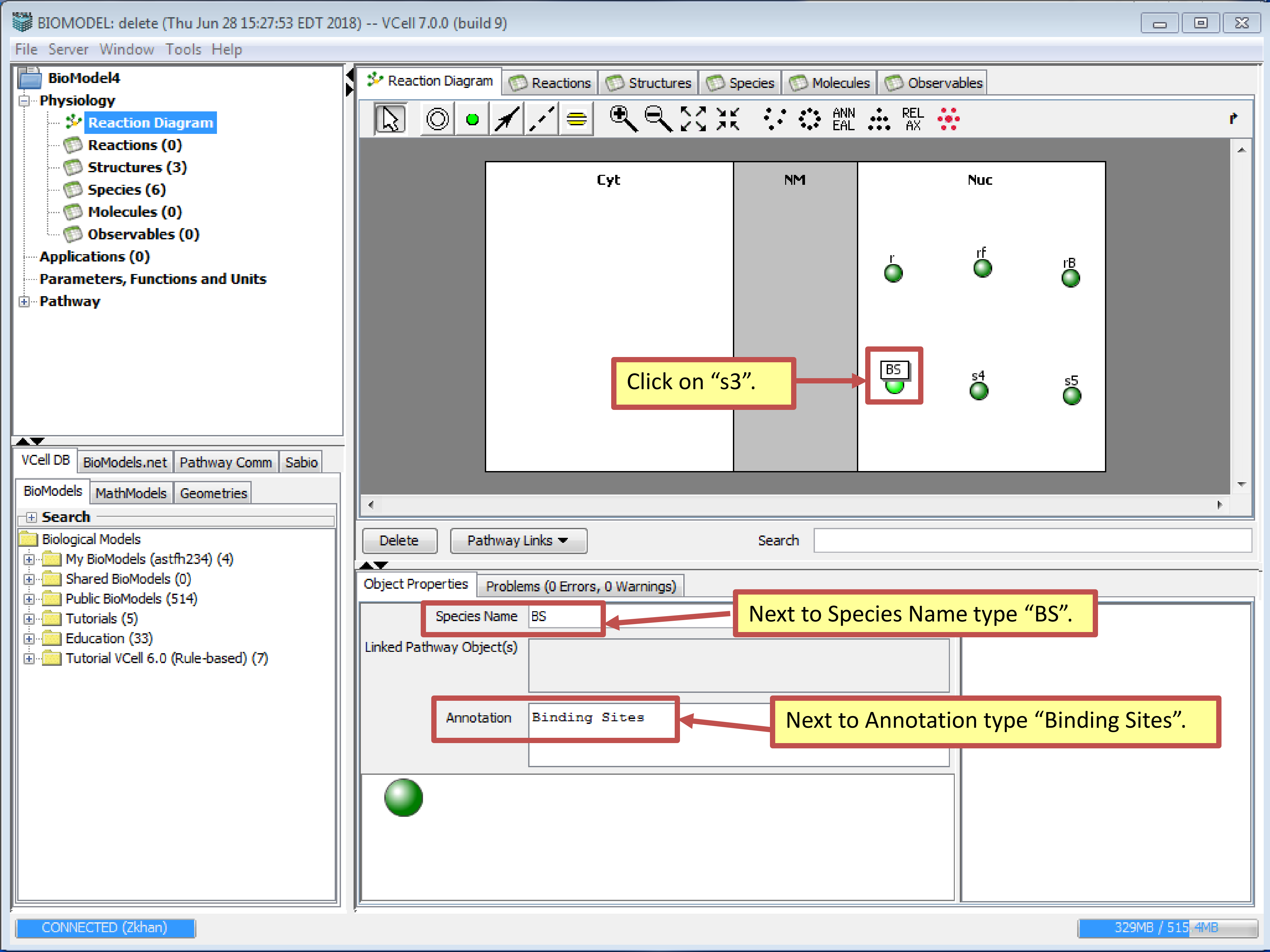
Click on “s2”.

Species Name rB

Annotation RAN_Bound

Next to Species Name type “rB”.

Next to Annotation type “RAN_Bound”.



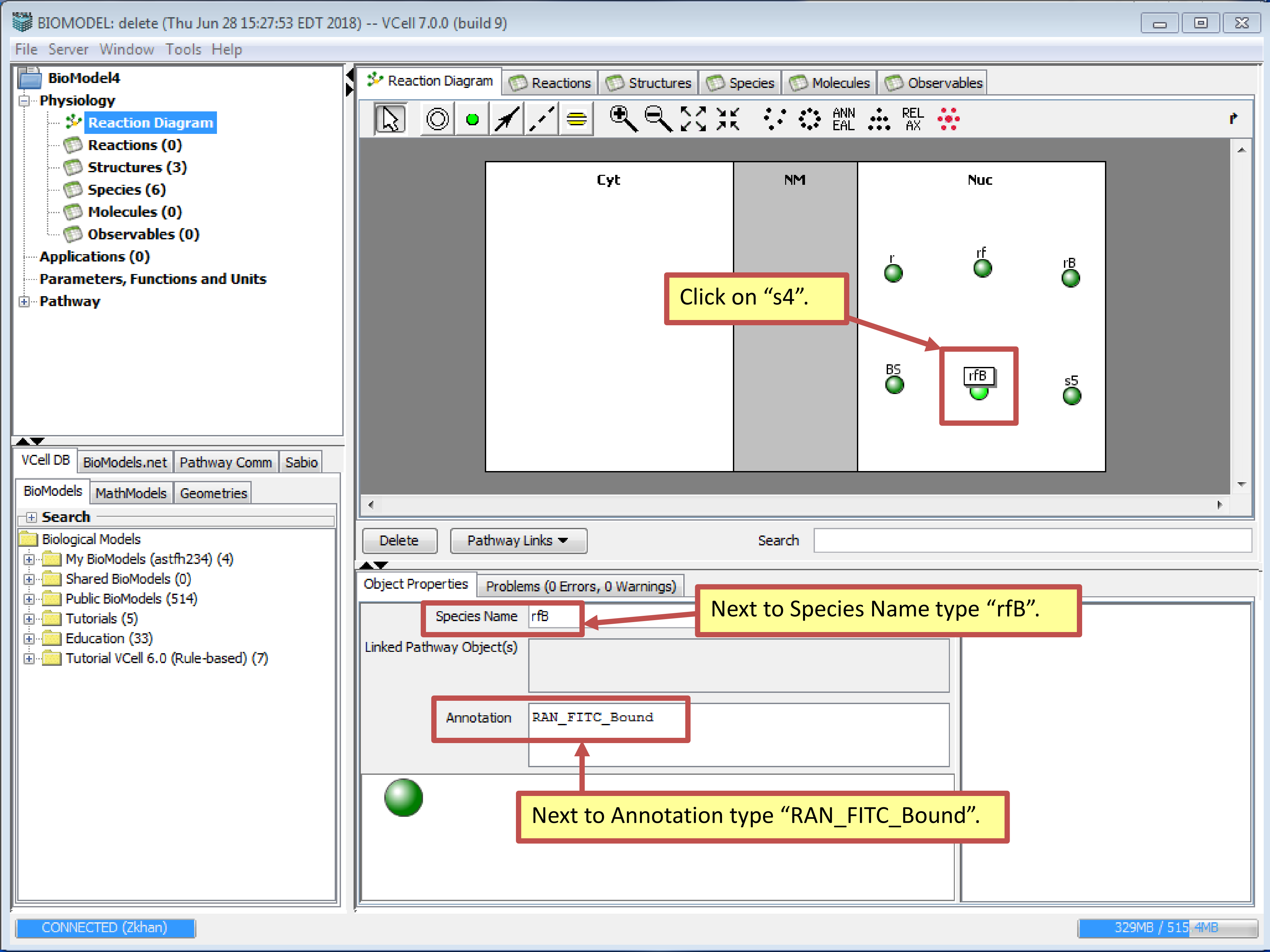
Click on “s3”.

Species Name: BS

Annotation: Binding Sites

Next to Species Name type “BS”.

Next to Annotation type “Binding Sites”.



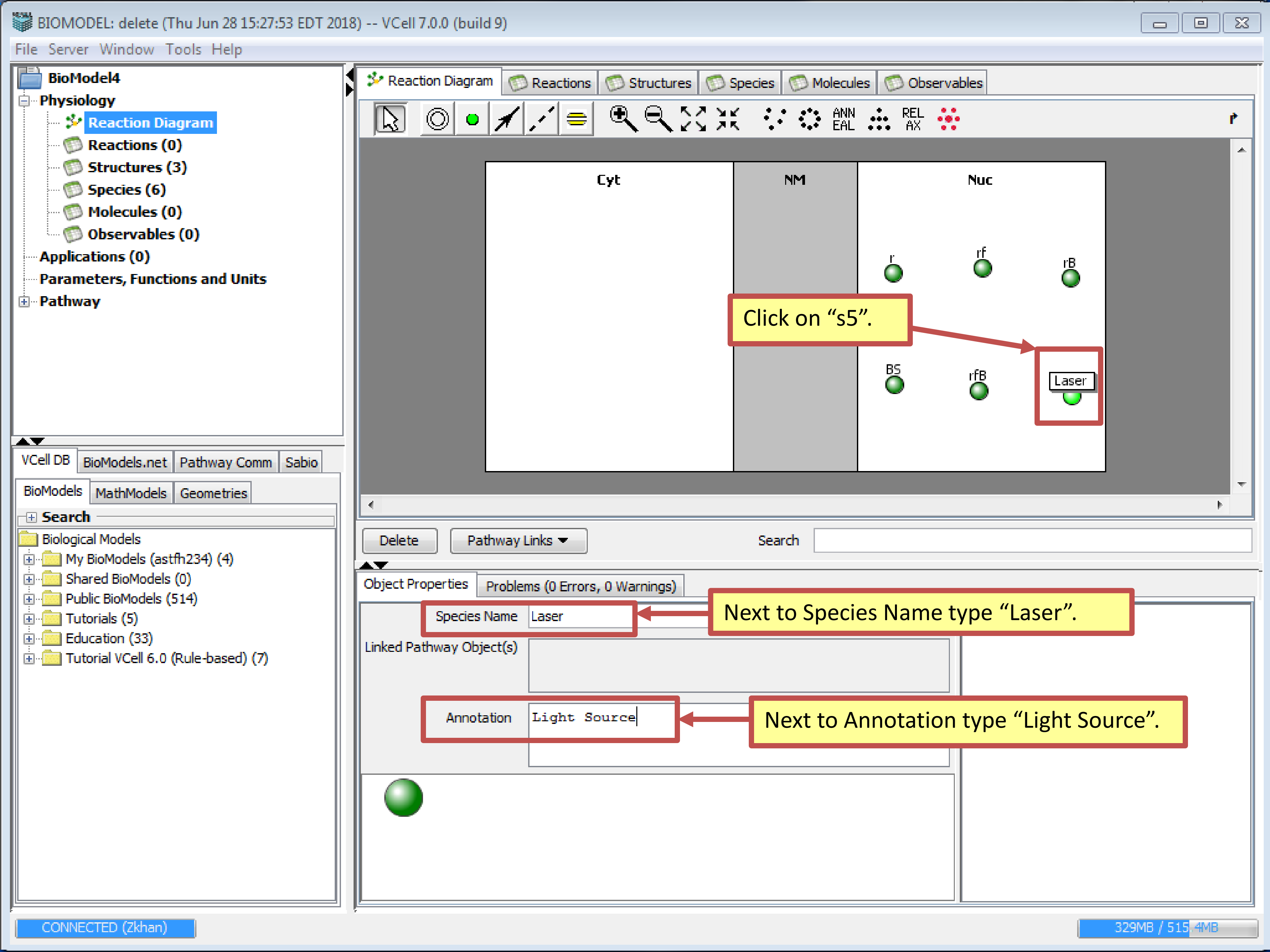
Click on "s4".

Species Name rfB

Next to Species Name type "rfB".

Annotation RAN_FITC_Bound

Next to Annotation type "RAN_FITC_Bound".



Click on “s5”.

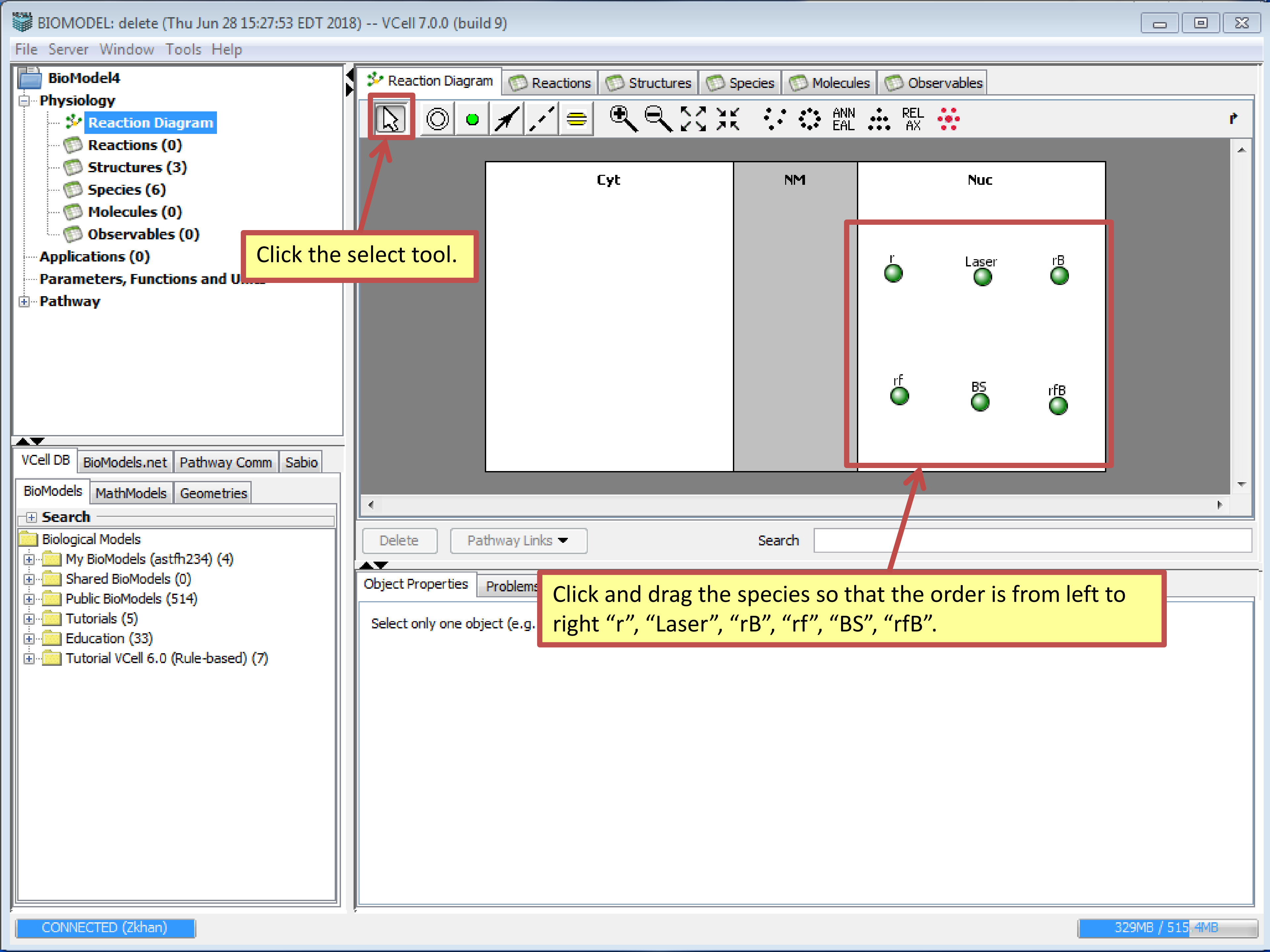
Species Name: Laser

Linked Pathway Object(s)

Annotation: Light Source

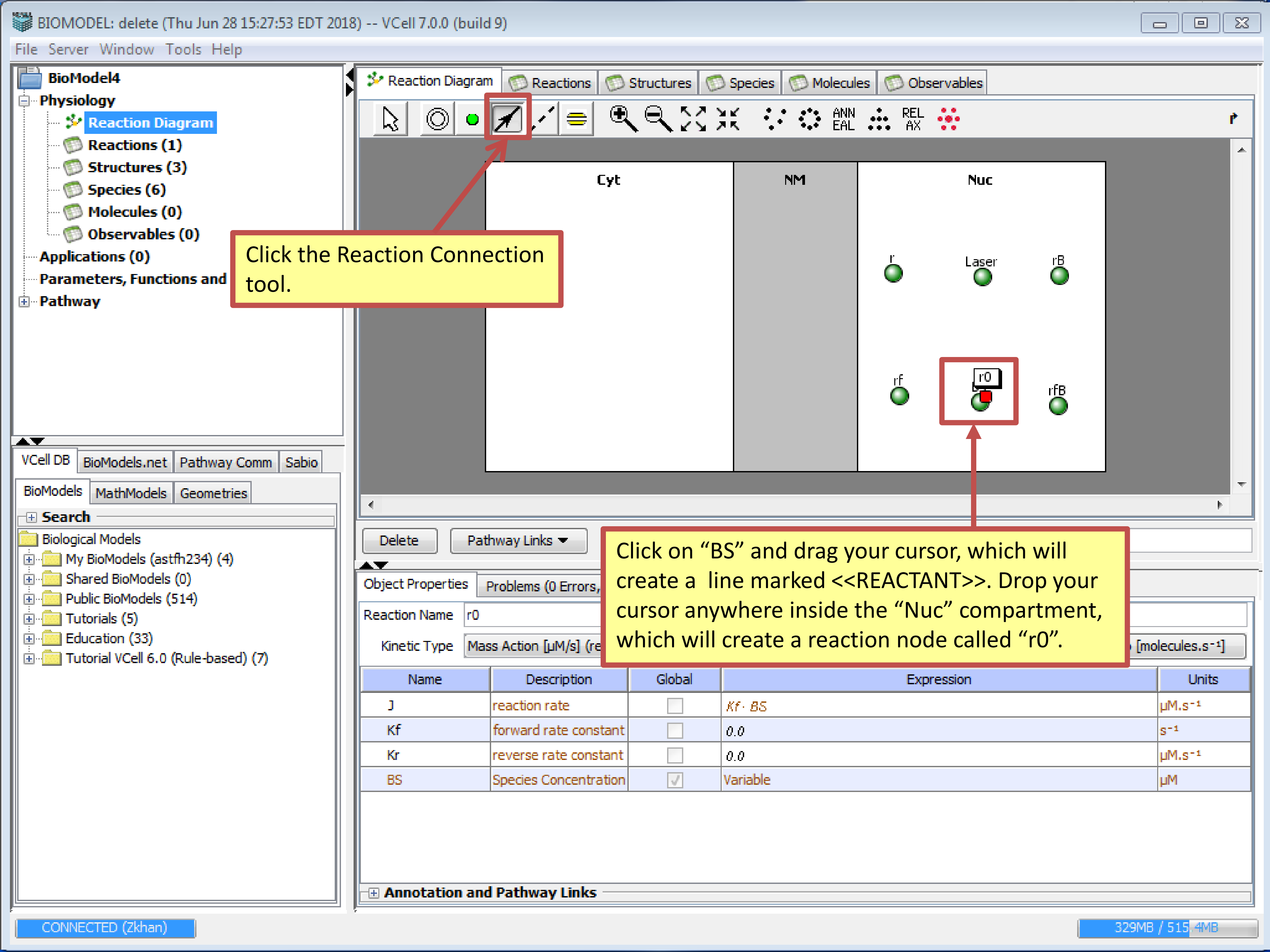
Next to Species Name type “Laser”.

Next to Annotation type “Light Source”.



Click the select tool.

Click and drag the species so that the order is from left to right “r”, “Laser”, “rB”, “rf”, “BS”, “rfB”.



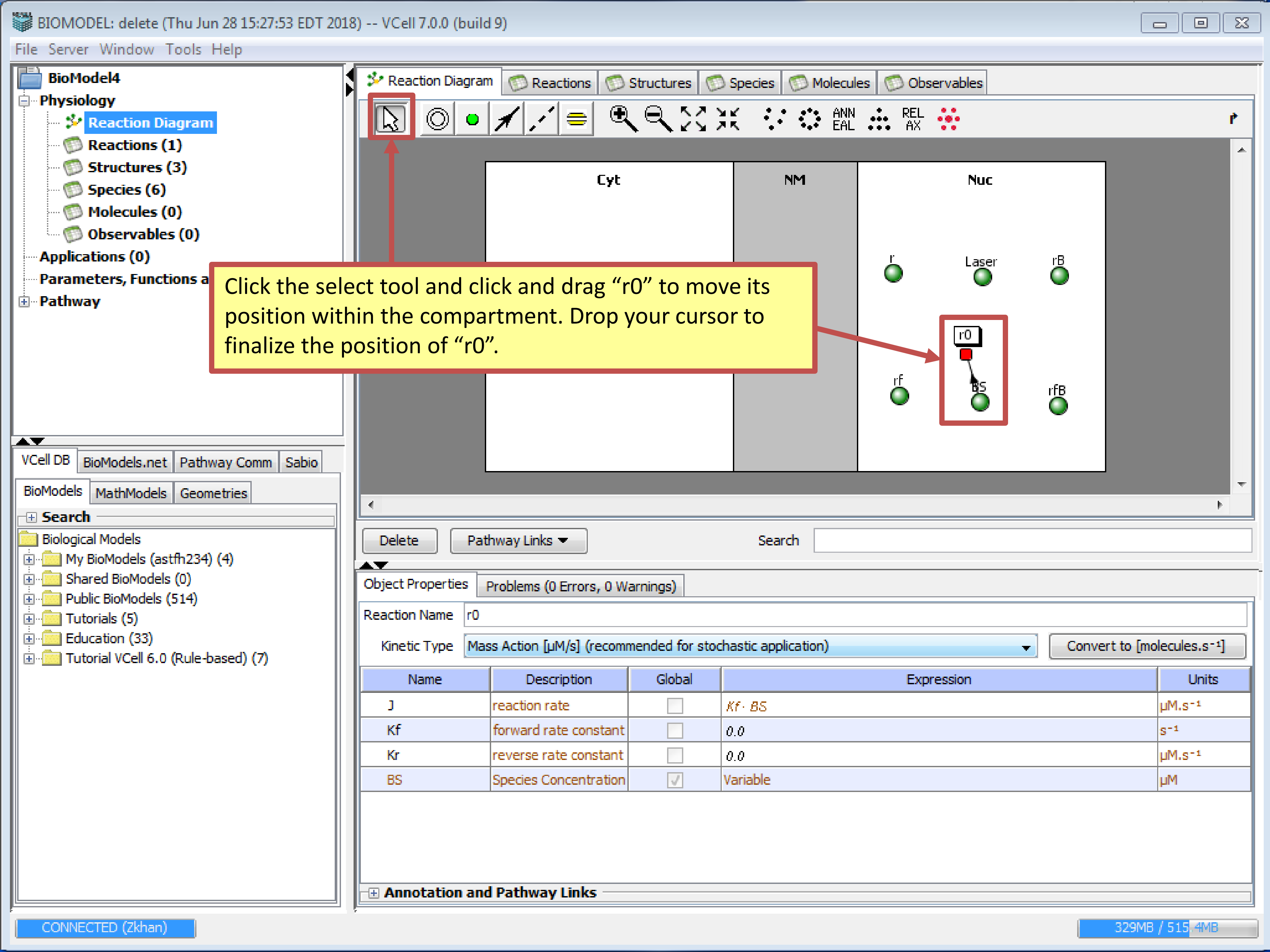
Click the Reaction Connection tool.

Click on “BS” and drag your cursor, which will create a line marked <<REACTANT>>. Drop your cursor anywhere inside the “Nuc” compartment, which will create a reaction node called “r0”.

Reaction Name: r0

Kinetic Type: Mass Action [μM/s] (re

Name	Description	Global	Expression	Units
J	reaction rate	☐	$Kf \cdot BS$	$\mu M.s^{-1}$
Kf	forward rate constant	☐	0.0	s^{-1}
Kr	reverse rate constant	☐	0.0	$\mu M.s^{-1}$
BS	Species Concentration	☑	Variable	μM

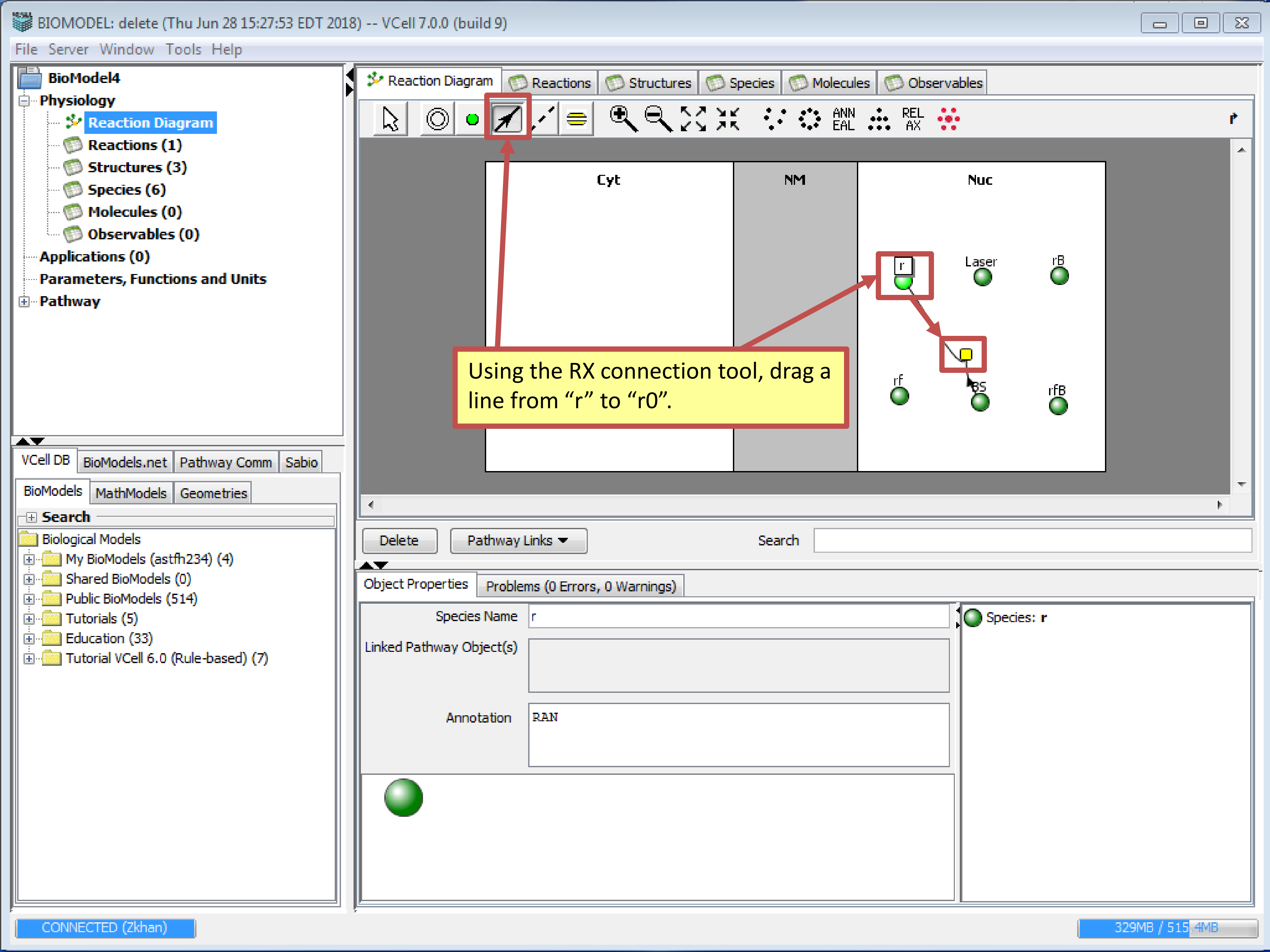


Click the select tool and click and drag “r0” to move its position within the compartment. Drop your cursor to finalize the position of “r0”.

Reaction Name: r0

Kinetic Type: Mass Action [µM/s] (recommended for stochastic application)

Name	Description	Global	Expression	Units
J	reaction rate	☐	Kf · BS	µM.s⁻¹
Kf	forward rate constant	☐	0.0	s⁻¹
Kr	reverse rate constant	☐	0.0	µM.s⁻¹
BS	Species Concentration	☑	Variable	µM



Using the RX connection tool, drag a line from “r” to “r0”.

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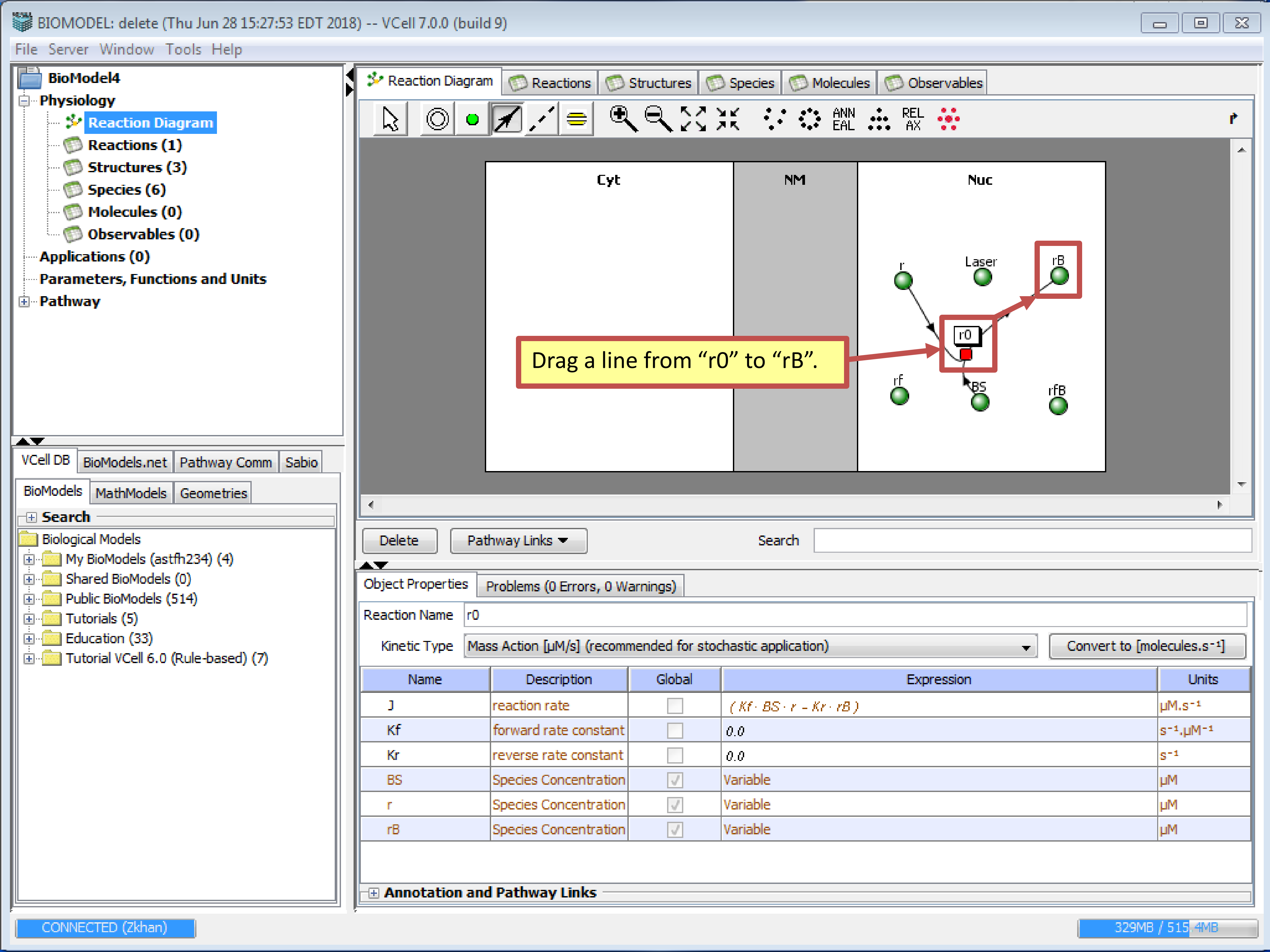
Species Name: r

Linked Pathway Object(s):

Annotation: RAN

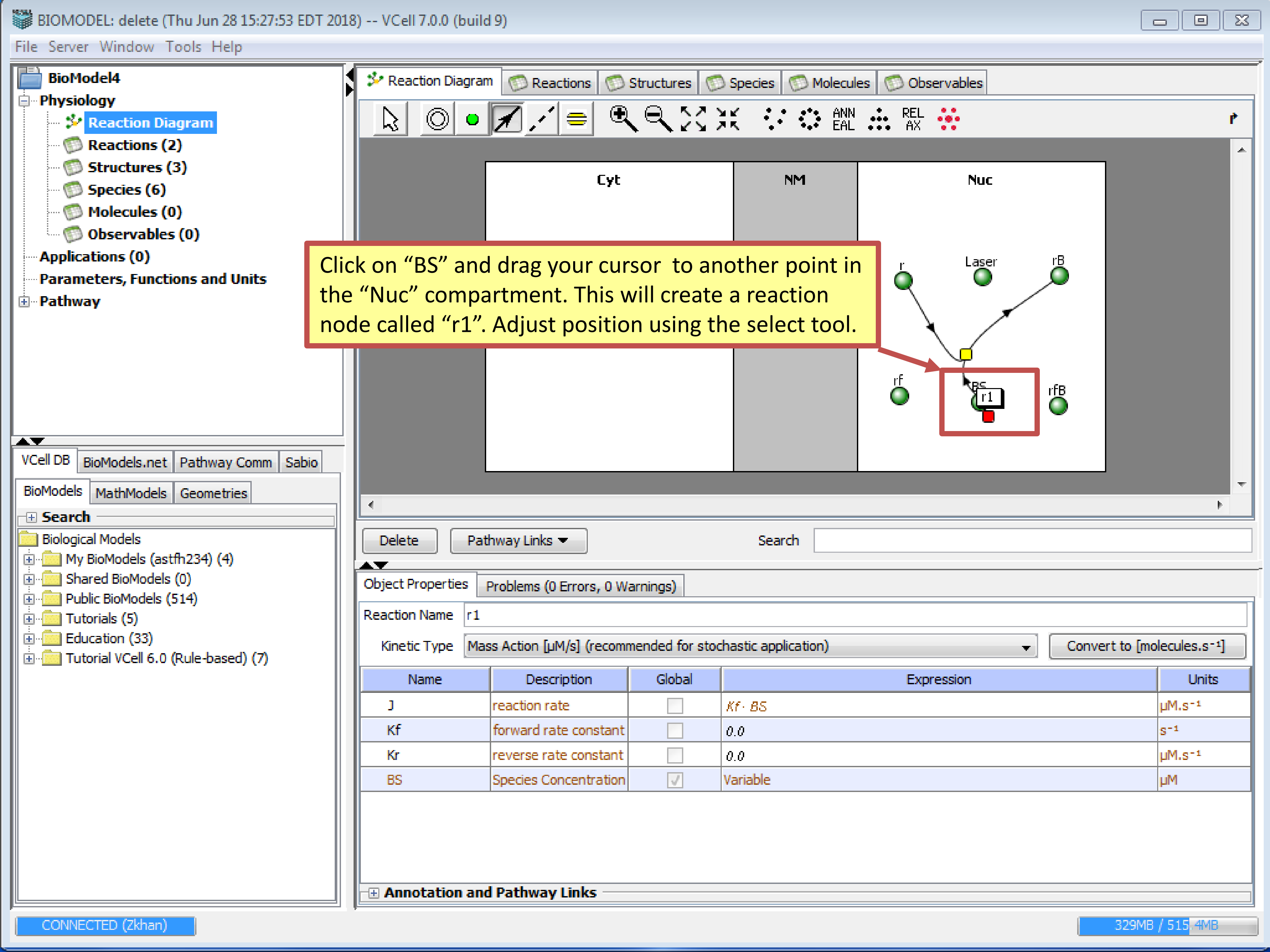


Drag a line from “r0” to “rB”.

Reaction Name: r0

Kinetic Type: Mass Action [μM/s] (recommended for stochastic application)

Name	Description	Global	Expression	Units
J	reaction rate	☐	$(Kf \cdot BS \cdot r - Kr \cdot rB)$	$\mu M.s^{-1}$
Kf	forward rate constant	☐	0.0	$s^{-1}.\mu M^{-1}$
Kr	reverse rate constant	☐	0.0	s^{-1}
BS	Species Concentration	☑	Variable	μM
r	Species Concentration	☑	Variable	μM
rB	Species Concentration	☑	Variable	μM

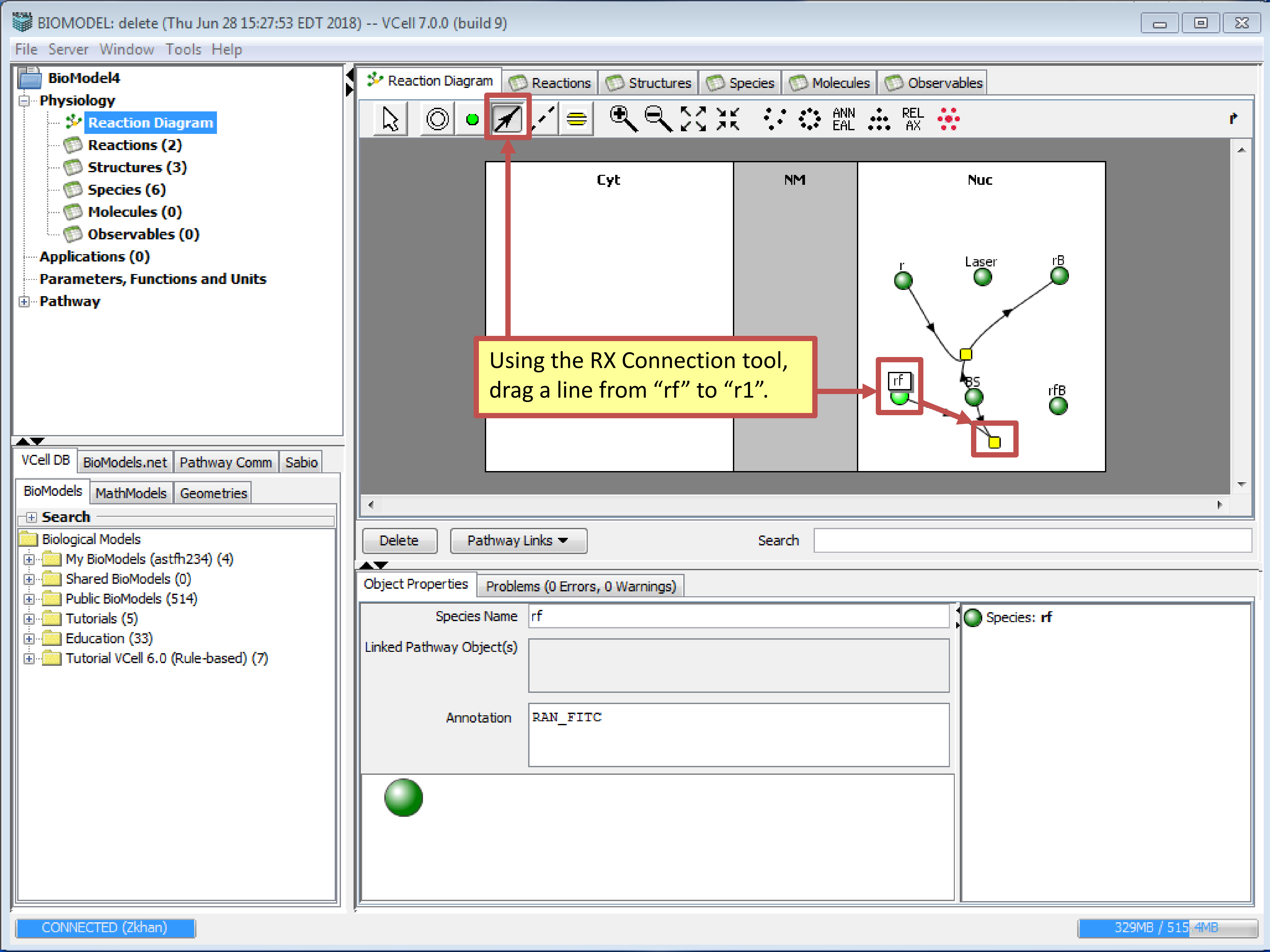


Click on “BS” and drag your cursor to another point in the “Nuc” compartment. This will create a reaction node called “r1”. Adjust position using the select tool.

Reaction Name: r1

Kinetic Type: Mass Action [μM/s] (recommended for stochastic application)

Name	Description	Global	Expression	Units
J	reaction rate	☐	$Kf \cdot BS$	$\mu M.s^{-1}$
Kf	forward rate constant	☐	0.0	s^{-1}
Kr	reverse rate constant	☐	0.0	$\mu M.s^{-1}$
BS	Species Concentration	☑	Variable	μM



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- BioModel4
  - Physiology
    - Reaction Diagram
    - Reactions (2)
    - Structures (3)
    - Species (6)
    - Molecules (0)
    - Observables (0)
  - Applications (0)
  - Parameters, Functions and Units
  - Pathway

- Biological Models
  - My BioModels (astfh234) (4)
  - Shared BioModels (0)
  - Public BioModels (514)
  - Tutorials (5)
  - Education (33)
  - Tutorial VCell 6.0 (Rule-based) (7)

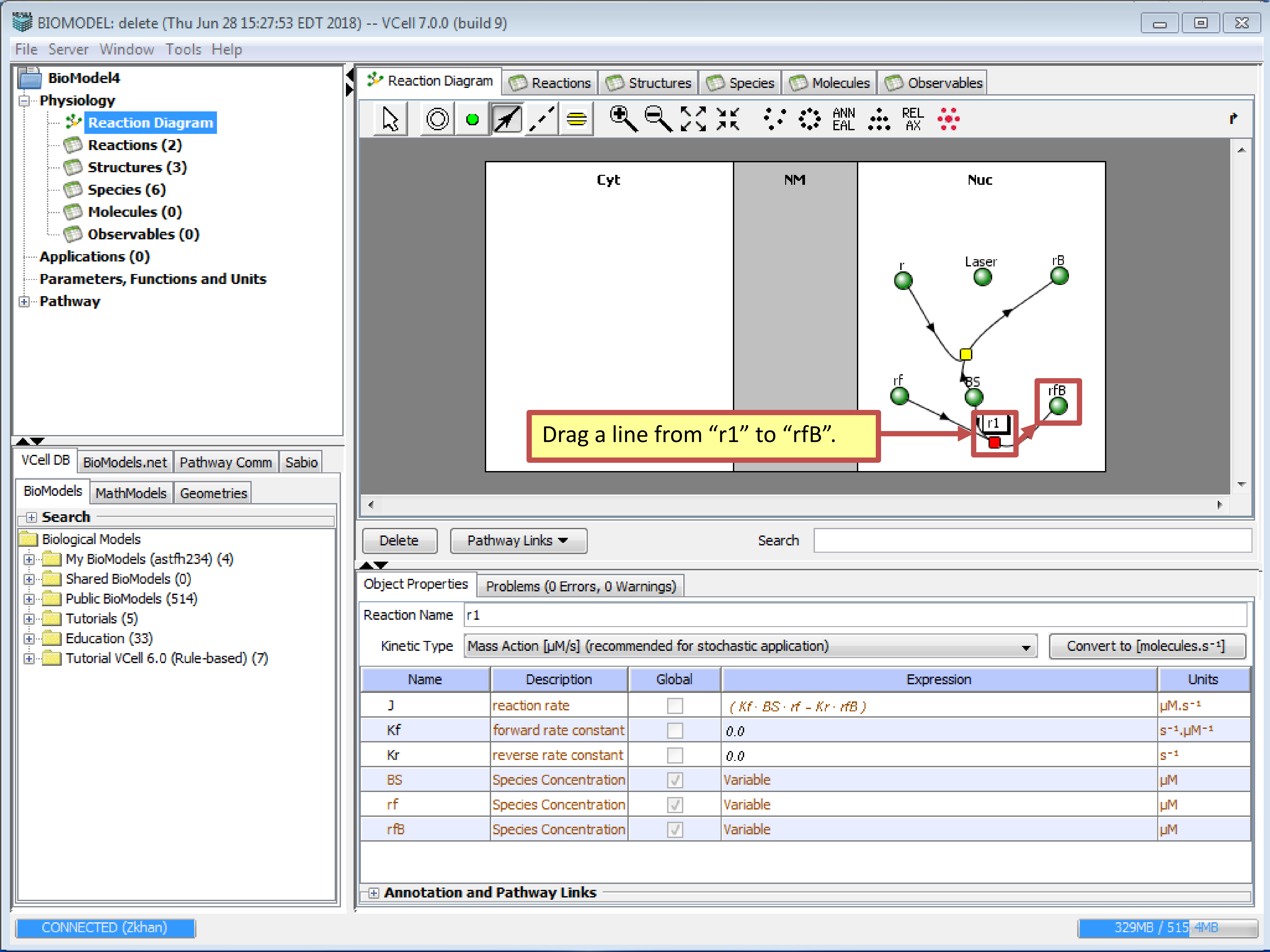
Using the RX Connection tool, drag a line from “rf” to “r1”.

Species Name: rf

Linked Pathway Object(s):

Annotation: RAN_FITC

Species: **rf**



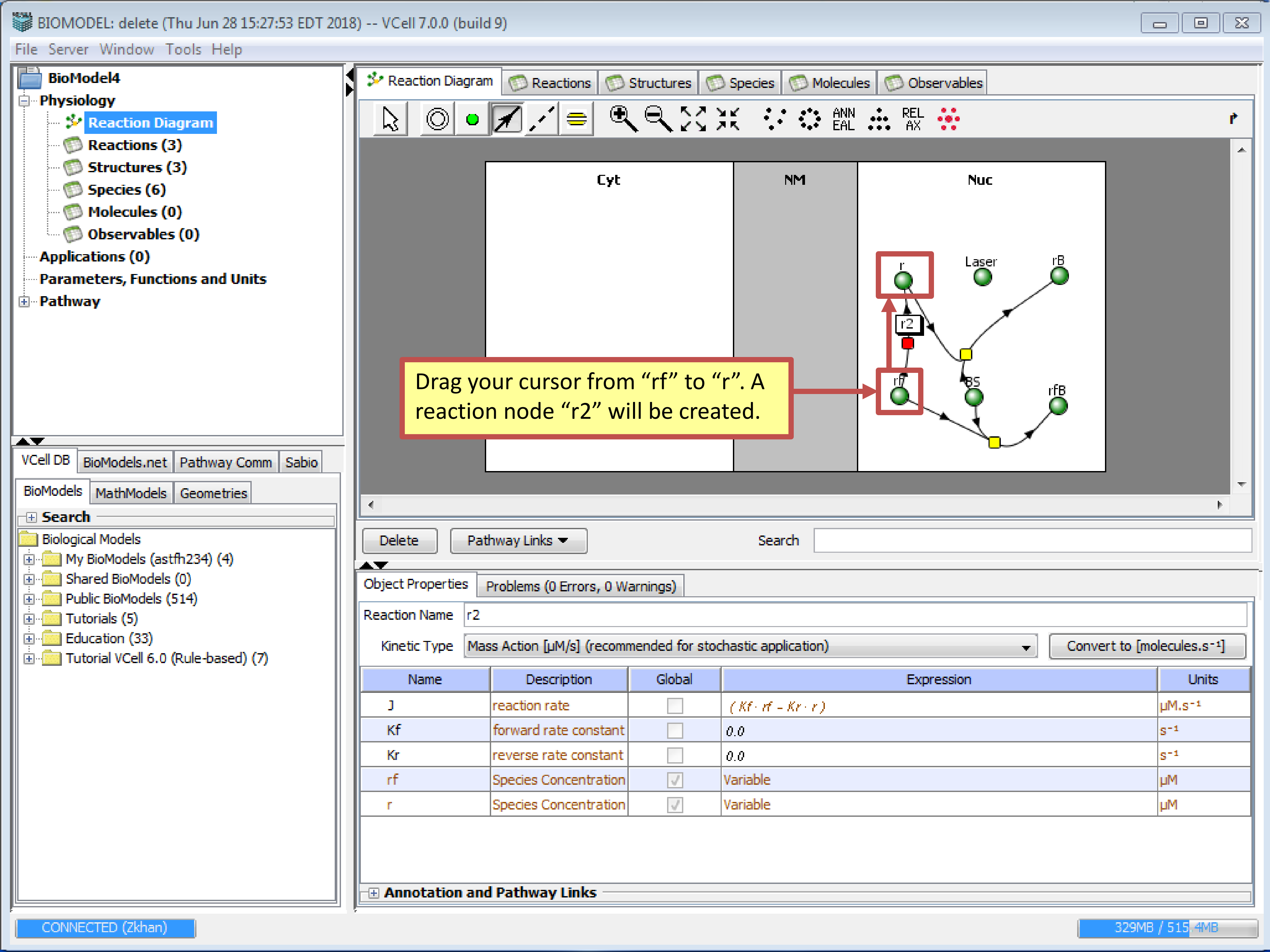
Drag a line from “r1” to “rfB”.

Reaction Name: r1

Kinetic Type: Mass Action [µM/s] (recommended for stochastic application)

Convert to [molecules.s⁻¹]

Name	Description	Global	Expression	Units
J	reaction rate	☐	(Kf · BS · rf - Kr · rfB)	µM.s⁻¹
Kf	forward rate constant	☐	0.0	s⁻¹.µM⁻¹
Kr	reverse rate constant	☐	0.0	s⁻¹
BS	Species Concentration	☑	Variable	µM
rf	Species Concentration	☑	Variable	µM
rfB	Species Concentration	☑	Variable	µM

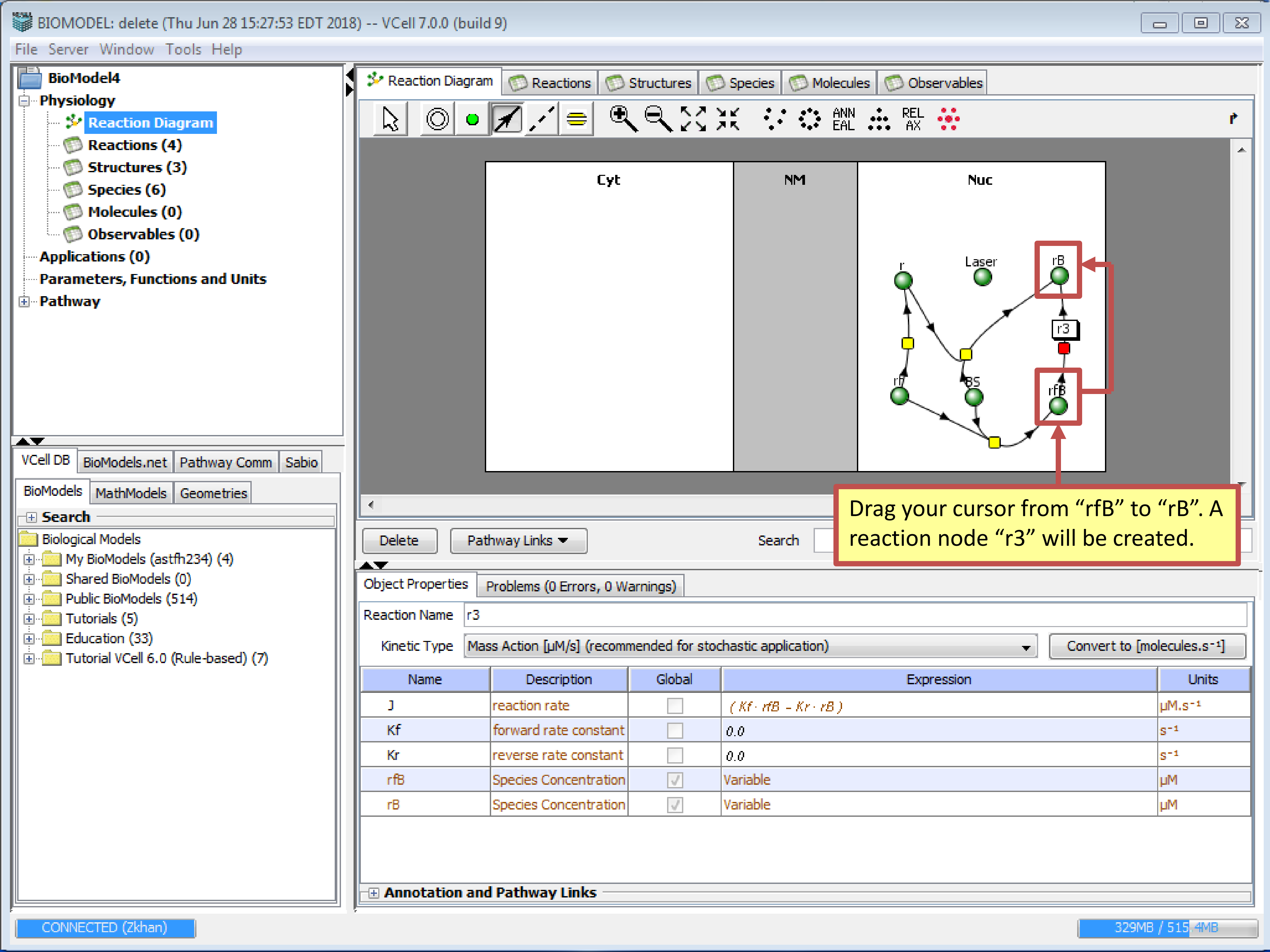


Drag your cursor from “rf” to “r”. A reaction node “r2” will be created.

Reaction Name: r2

Kinetic Type: Mass Action [µM/s] (recommended for stochastic application)

Name	Description	Global	Expression	Units
J	reaction rate	☐	$(Kf \cdot rf - Kr \cdot r)$	$\mu M.s^{-1}$
Kf	forward rate constant	☐	0.0	s^{-1}
Kr	reverse rate constant	☐	0.0	s^{-1}
rf	Species Concentration	☑	Variable	µM
r	Species Concentration	☑	Variable	µM

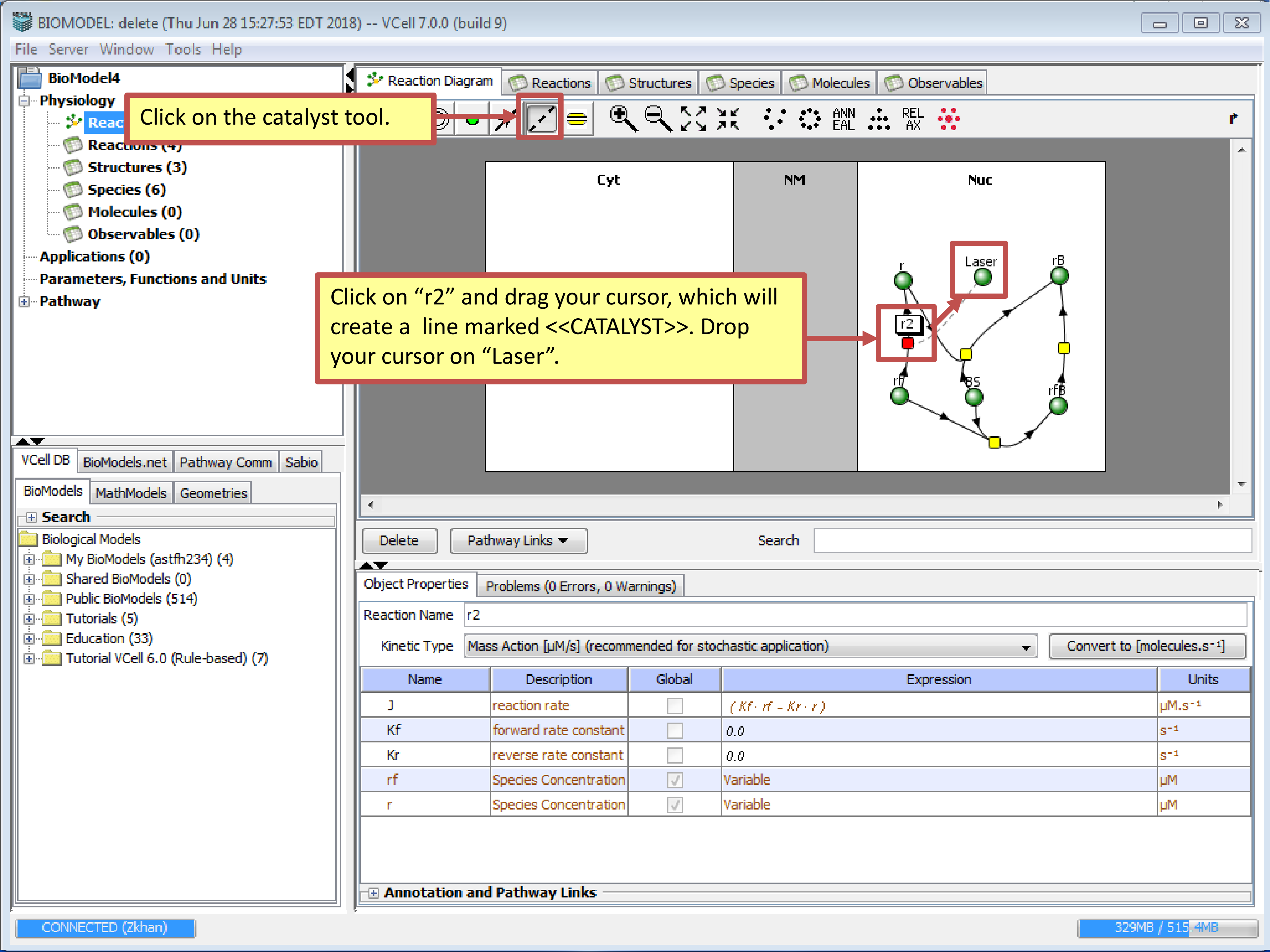


Drag your cursor from “rfB” to “rB”. A reaction node “r3” will be created.

Reaction Name: r3

Kinetic Type: Mass Action [µM/s] (recommended for stochastic application)

Name	Description	Global	Expression	Units
J	reaction rate	☐	(Kf · rfB - Kr · rB)	$\mu M.s^{-1}$
Kf	forward rate constant	☐	0.0	s^{-1}
Kr	reverse rate constant	☐	0.0	s^{-1}
rfB	Species Concentration	☑	Variable	µM
rB	Species Concentration	☑	Variable	µM



Click on the catalyst tool.

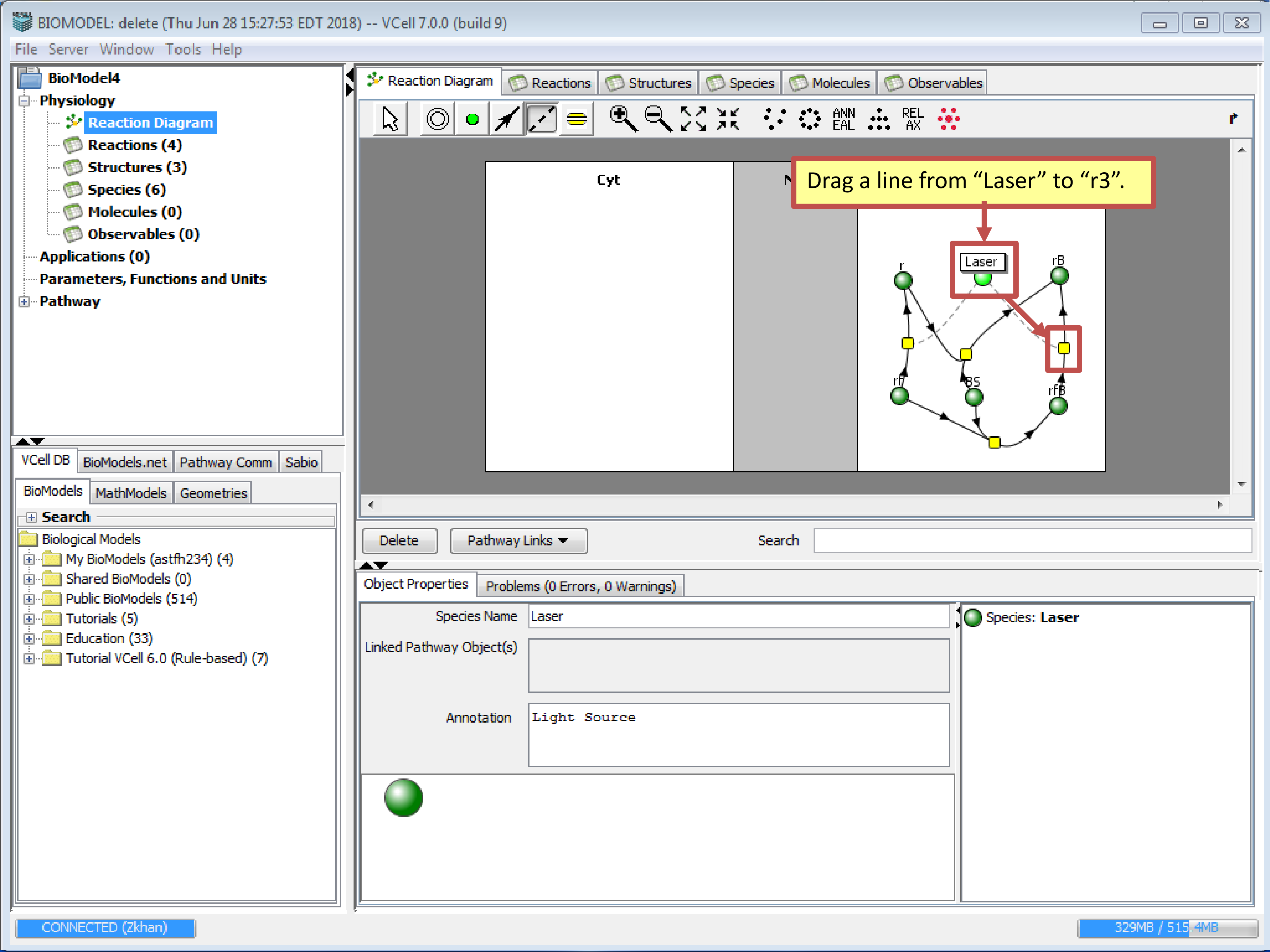
Click on “r2” and drag your cursor, which will create a line marked <<CATALYST>>. Drop your cursor on “Laser”.

Reaction Name: r2

Kinetic Type: Mass Action [μM/s] (recommended for stochastic application)

Convert to [molecules.s⁻¹]

Name	Description	Global	Expression	Units
J	reaction rate	☐	(Kf · rf - Kr · r)	$\mu M.s^{-1}$
Kf	forward rate constant	☐	0.0	s^{-1}
Kr	reverse rate constant	☐	0.0	s^{-1}
rf	Species Concentration	☑	Variable	μM
r	Species Concentration	☑	Variable	μM



Drag a line from “Laser” to “r3”.

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Species Name: Laser

Linked Pathway Object(s):

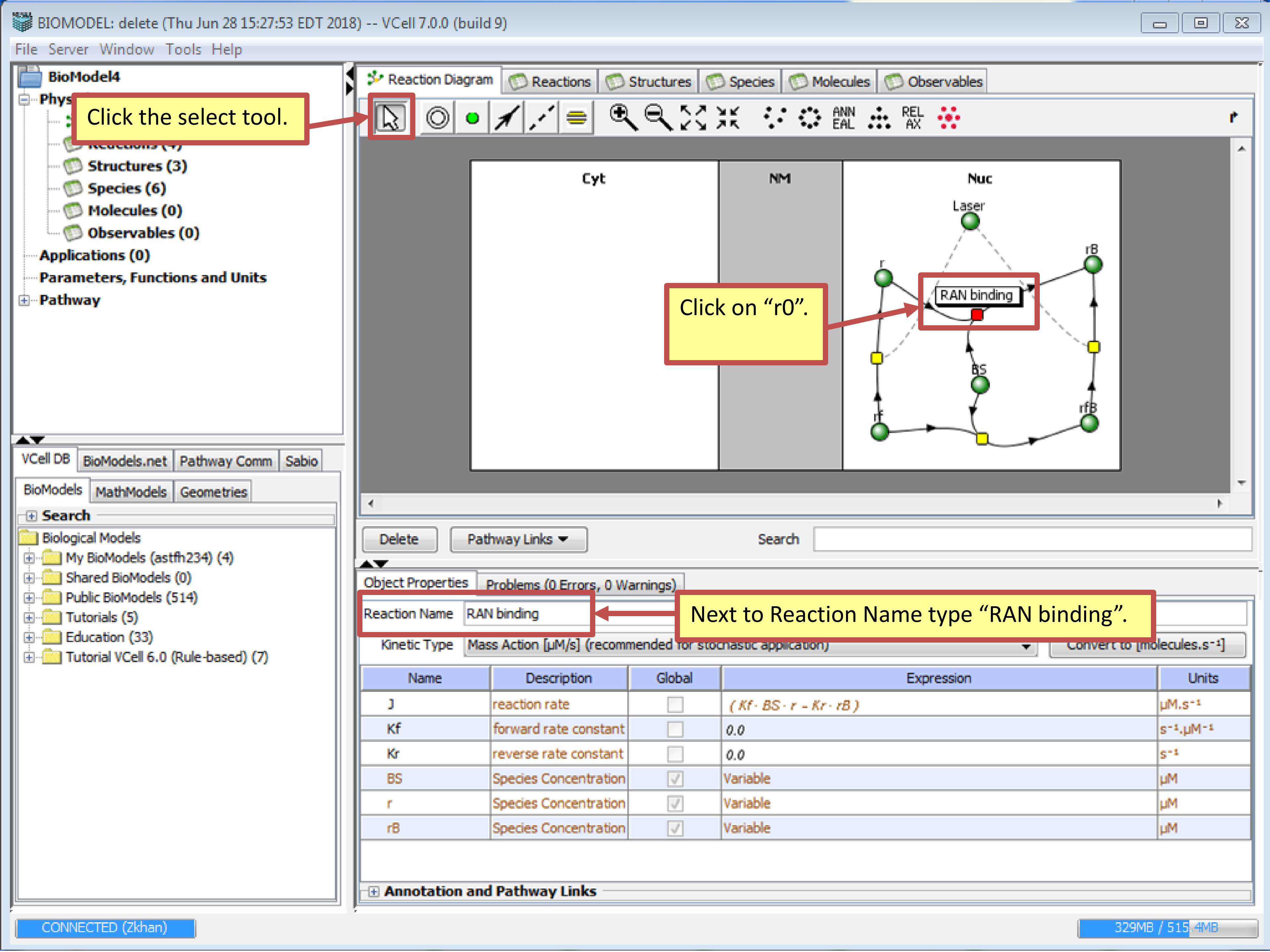
Annotation: Light Source

Species: **Laser**

Problems (0 Errors, 0 Warnings)

CONNECTED (Zkhan)

329MB / 5154MB



Click the select tool.

Click on “r0”.

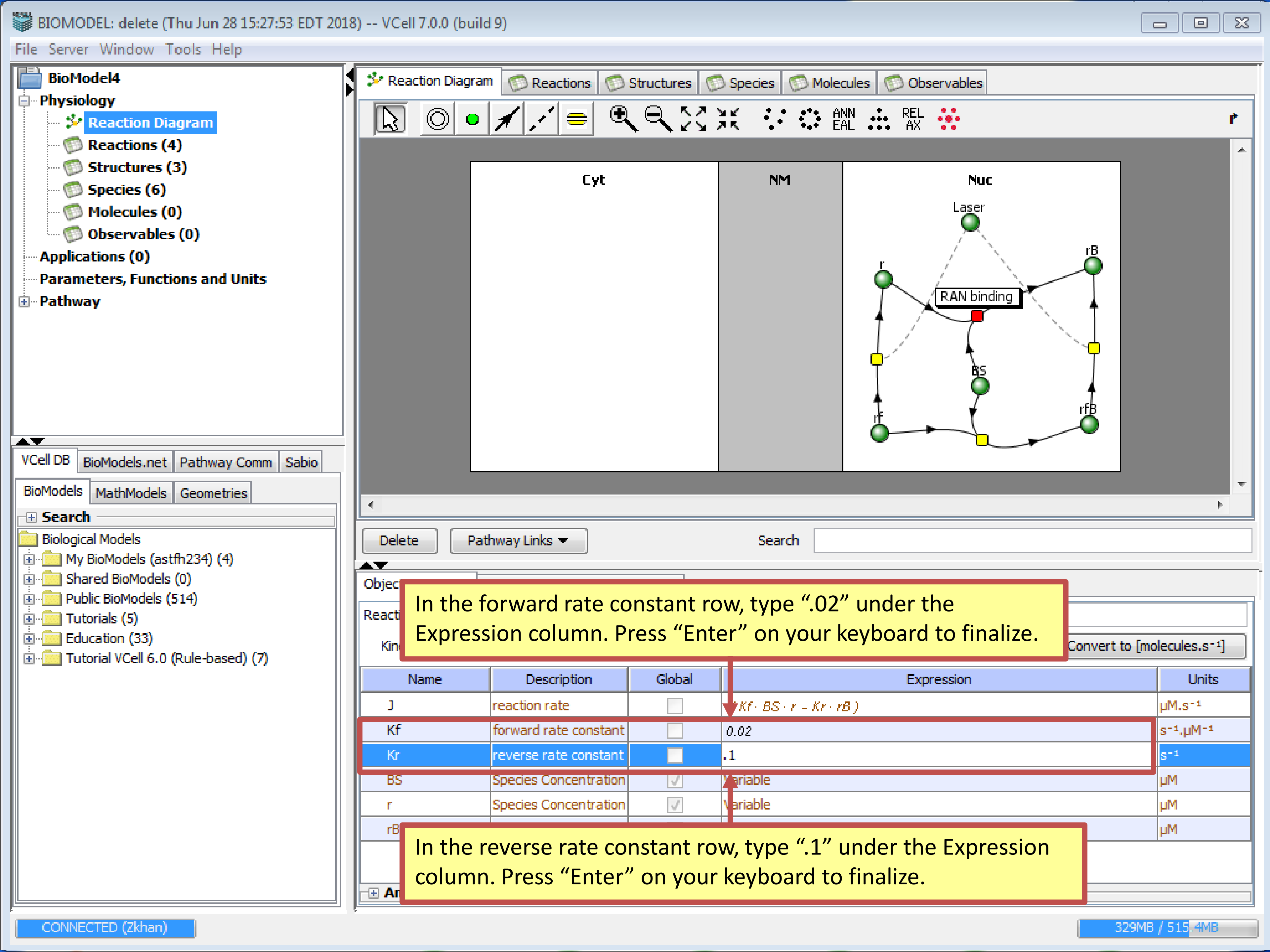
Next to Reaction Name type “RAN binding”.

Reaction Name: RAN binding

Kinetic Type: Mass Action [µM/s] (recommended for stochastic application)

Convert to [molecules.s^{-1}]

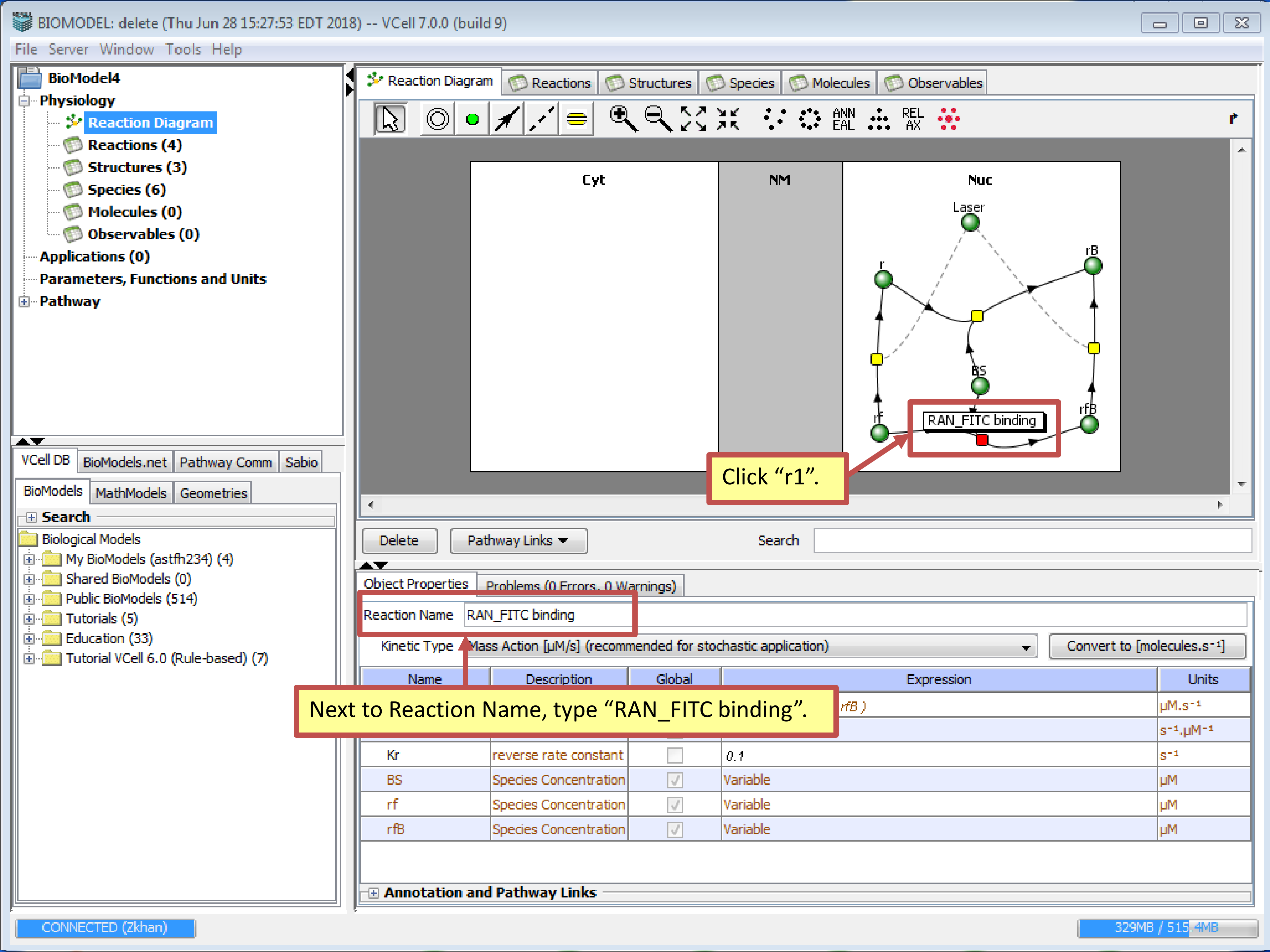
Name	Description	Global	Expression	Units
J	reaction rate	☐	(Kf · BS · r - Kr · rB)	$\mu M.s^{-1}$
Kf	forward rate constant	☐	0.0	$s^{-1}.\mu M^{-1}$
Kr	reverse rate constant	☐	0.0	s^{-1}
BS	Species Concentration	☑	Variable	µM
r	Species Concentration	☑	Variable	µM
rB	Species Concentration	☑	Variable	µM



In the forward rate constant row, type ".02" under the Expression column. Press "Enter" on your keyboard to finalize.

Name	Description	Global	Expression	Units
J	reaction rate	☐	(Kf · BS · r – Kr · rB)	µM.s^{-1}
Kf	forward rate constant	☐	0.02	s^{-1}.µM^{-1}
Kr	reverse rate constant	☐	.1	s^{-1}
BS	Species Concentration	☑	ariable	µM
r	Species Concentration	☑	ariable	µM
rB				µM

In the reverse rate constant row, type ".1" under the Expression column. Press "Enter" on your keyboard to finalize.



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Click “r1”.

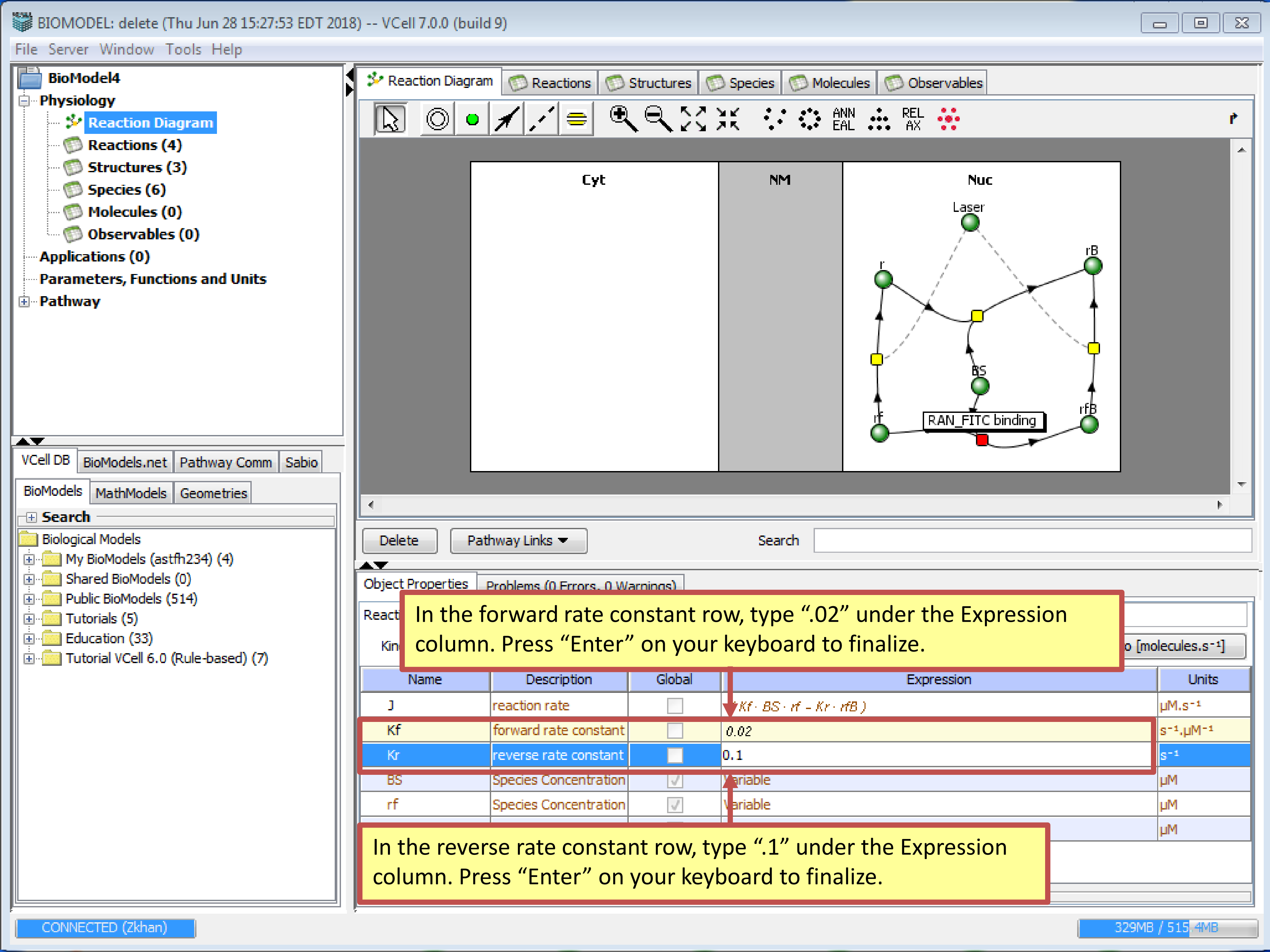
Reaction Name: RAN_FITC binding

Kinetic Type: Mass Action [μM/s] (recommended for stochastic application)

Convert to [molecules.s⁻¹]

Name	Description	Global	Expression	Units
			rfB)	μM.s⁻¹
				s⁻¹.μM⁻¹
Kr	reverse rate constant	☐	0.1	s⁻¹
BS	Species Concentration	☑	Variable	μM
rf	Species Concentration	☑	Variable	μM
rfB	Species Concentration	☑	Variable	μM

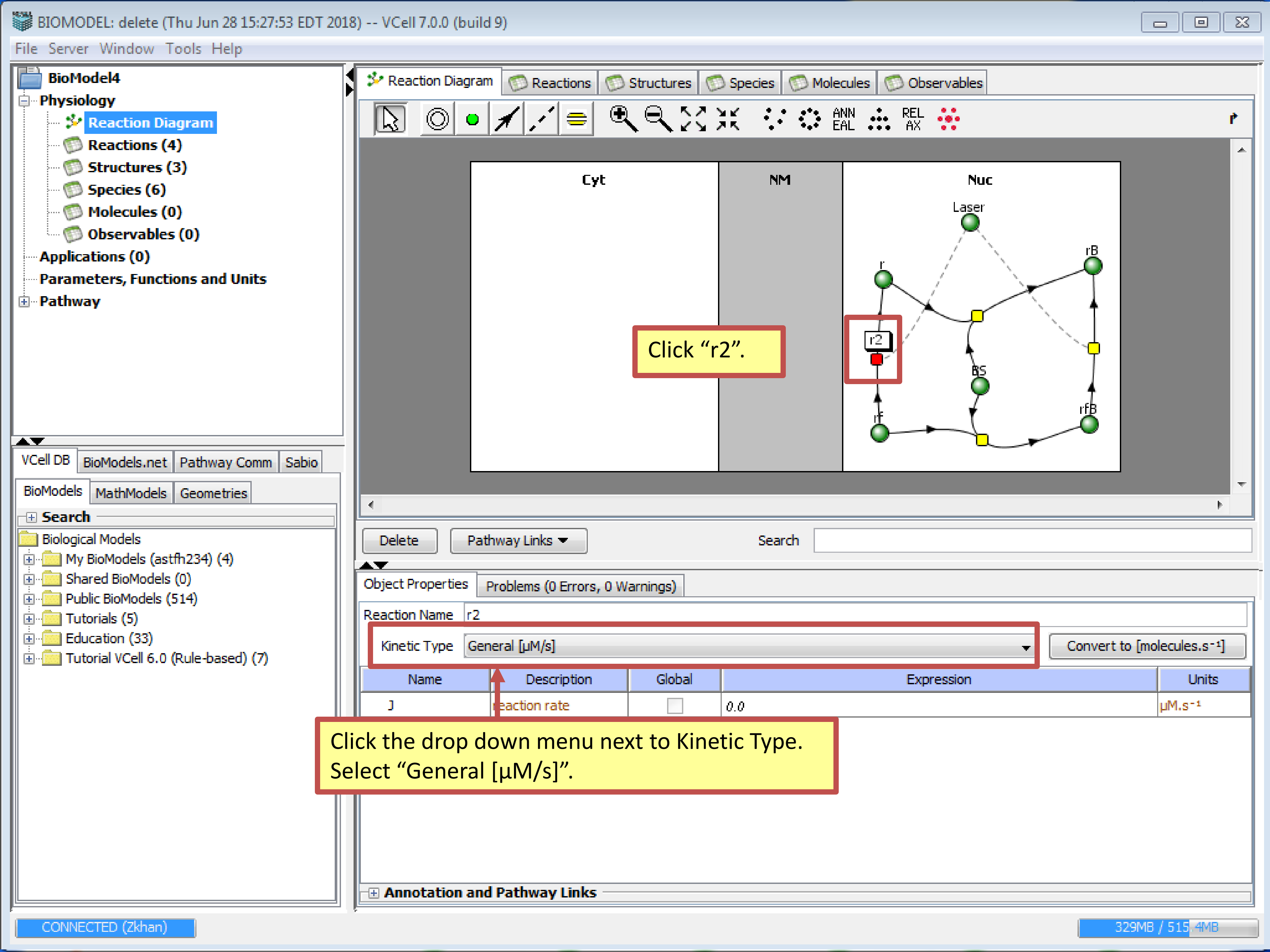
Next to Reaction Name, type “RAN_FITC binding”.



In the forward rate constant row, type ".02" under the Expression column. Press "Enter" on your keyboard to finalize.

Name	Description	Global	Expression	Units
J	reaction rate	☐	(Kf · BS · rf – Kr · rfB)	$\mu M.s^{-1}$
Kf	forward rate constant	☐	0.02	$s^{-1}.\mu M^{-1}$
Kr	reverse rate constant	☐	0.1	s^{-1}
BS	Species Concentration	☑	Variable	μM
rf	Species Concentration	☑	Variable	μM
				μM

In the reverse rate constant row, type ".1" under the Expression column. Press "Enter" on your keyboard to finalize.



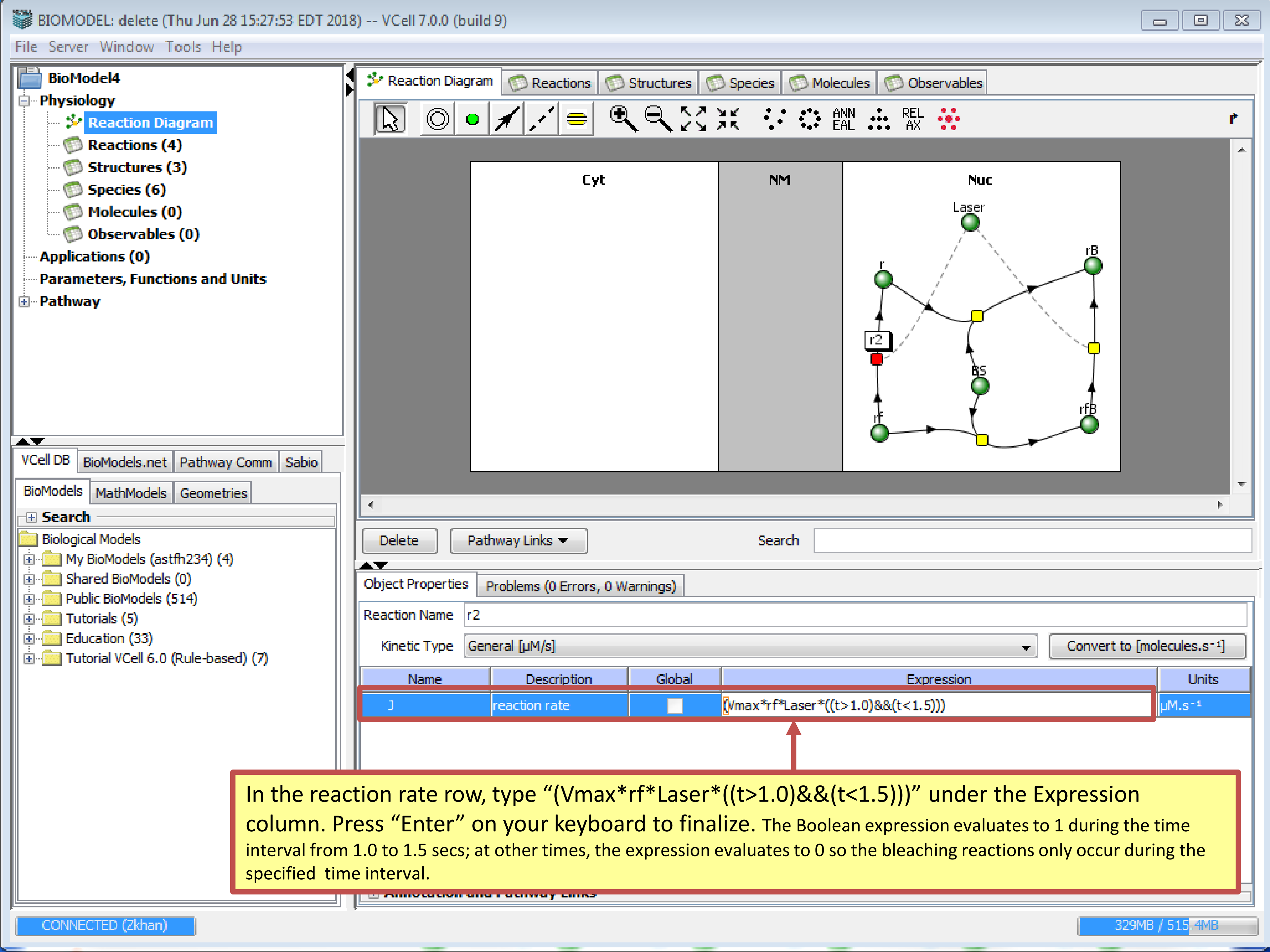
Click “r2”.

Reaction Name r2

Kinetic Type General [µM/s]

Name	Description	Global	Expression	Units
J	reaction rate	☐	0.0	$\mu M.s^{-1}$

Click the drop down menu next to Kinetic Type. Select “General [µM/s]”.

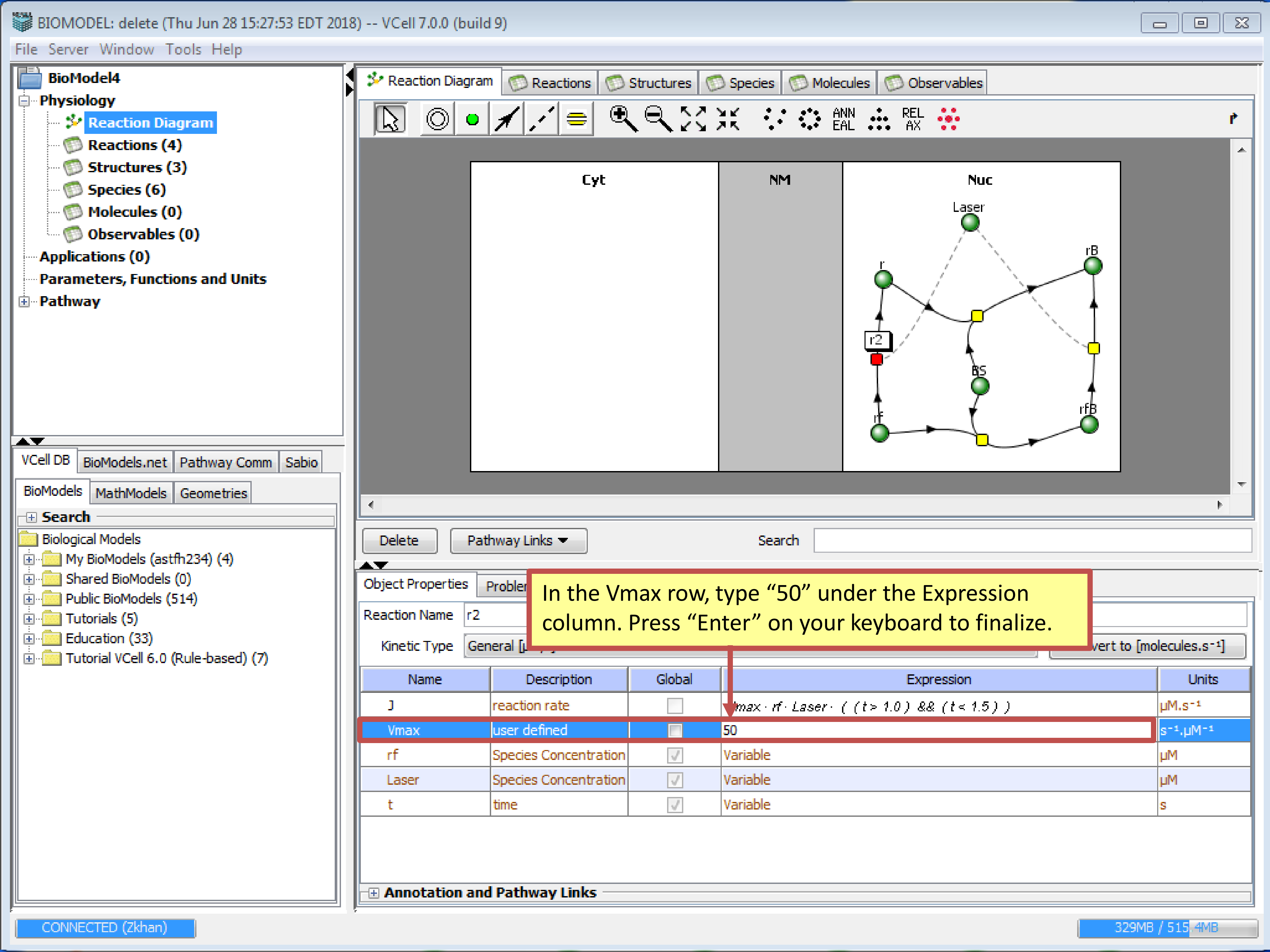


Reaction Name: r2

Kinetic Type: General [µM/s]

Name	Description	Global	Expression	Units
J	reaction rate	☐	(Vmax*rf*Laser*((t>1.0)&&(t<1.5)))	µM.s^{-1}

In the reaction rate row, type "(Vmax*rf*Laser*((t>1.0)&&(t<1.5)))" under the Expression column. Press "Enter" on your keyboard to finalize. The Boolean expression evaluates to 1 during the time interval from 1.0 to 1.5 secs; at other times, the expression evaluates to 0 so the bleaching reactions only occur during the specified time interval.



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In the Vmax row, type “50” under the Expression column. Press “Enter” on your keyboard to finalize.

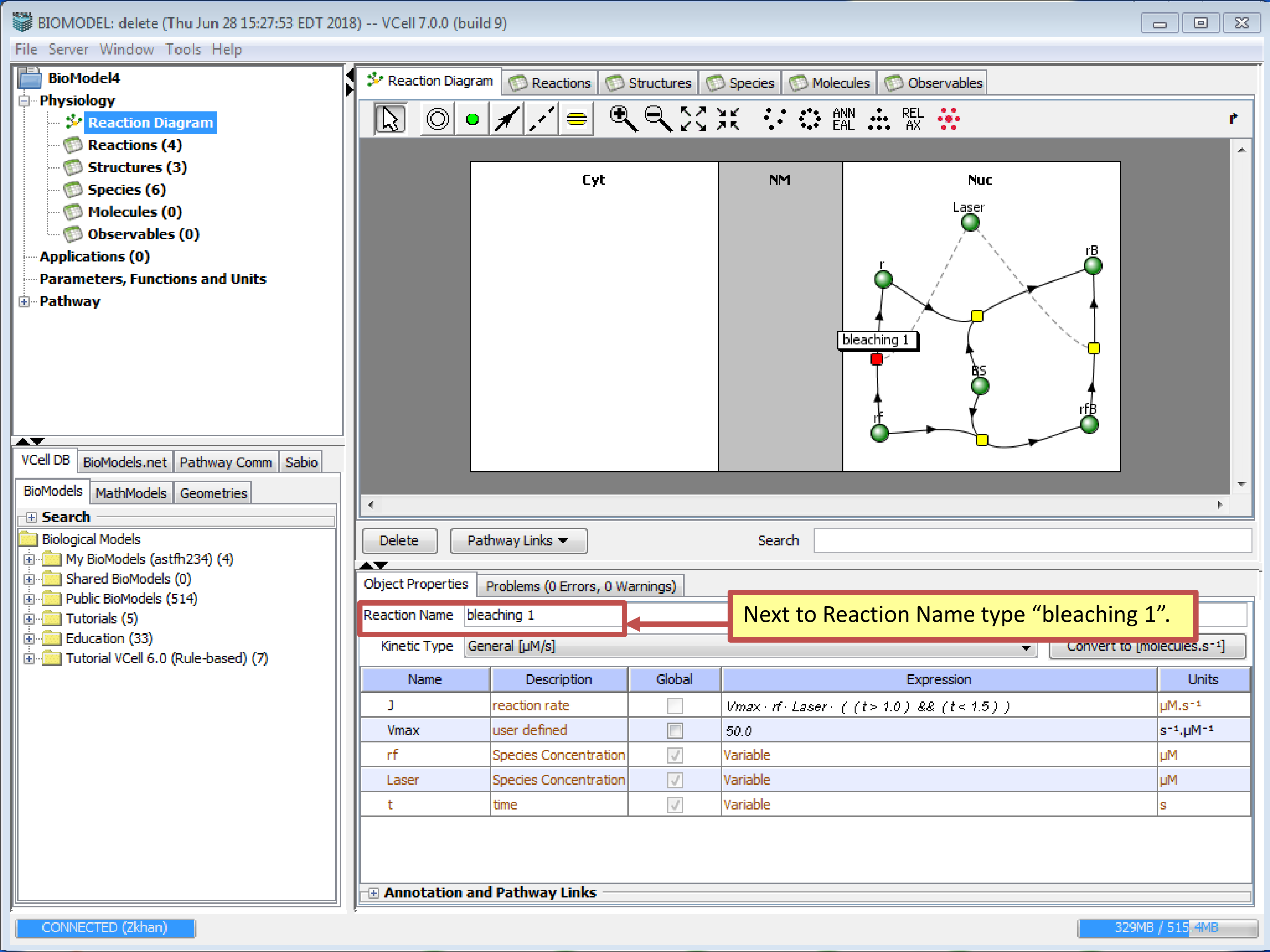
Reaction Name: r2

Kinetic Type: General [

vert to [molecules.s^{-1}]

Name	Description	Global	Expression	Units
J	reaction rate	☐	max · rf · Laser · ((t > 1.0) && (t < 1.5))	$\mu M.s^{-1}$
Vmax	user defined	☐	50	$s^{-1}.\mu M^{-1}$
rf	Species Concentration	☑	Variable	μM
Laser	Species Concentration	☑	Variable	μM
t	time	☑	Variable	s

Annotation and Pathway Links

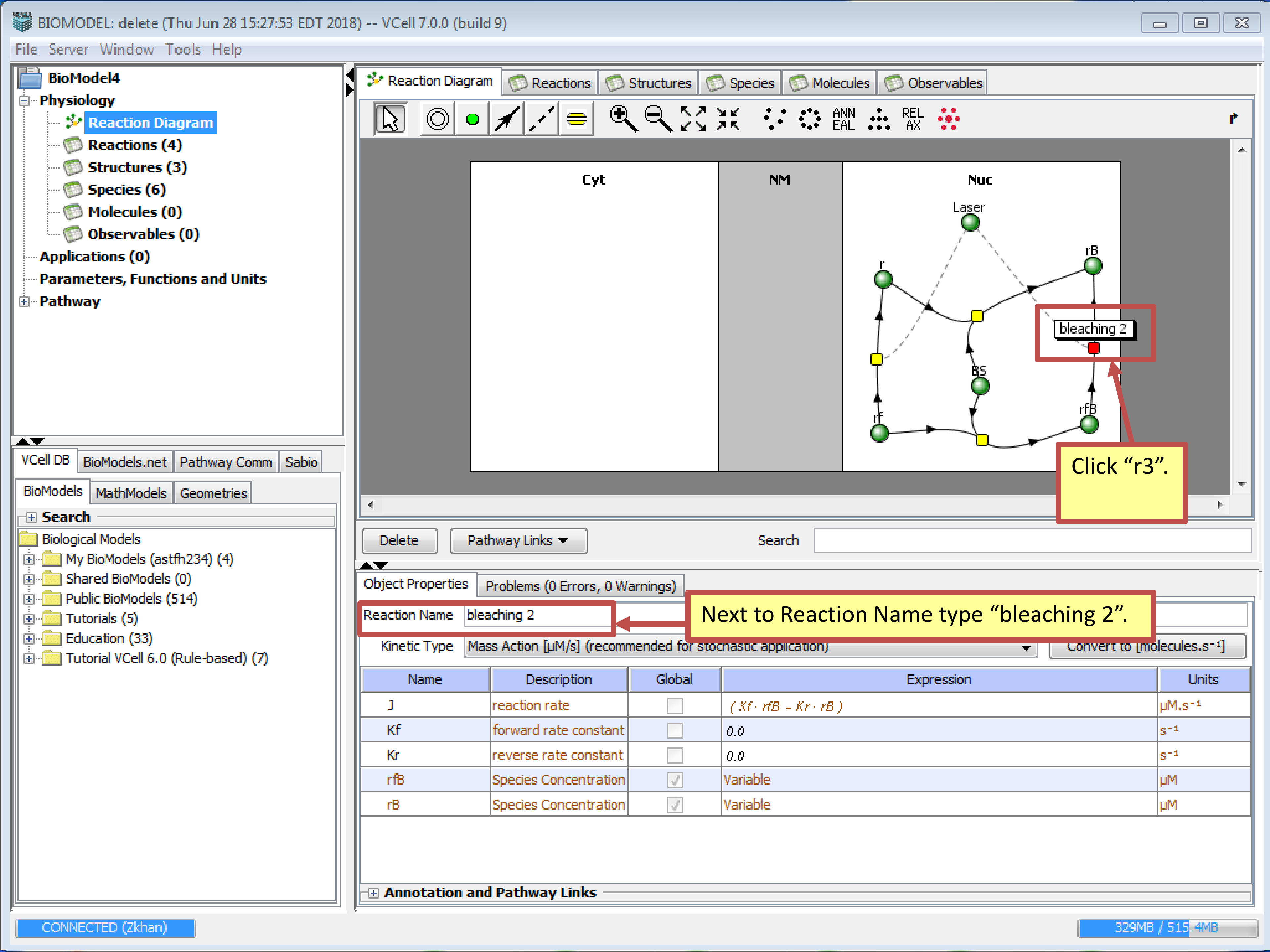


Next to Reaction Name type “bleaching 1”.

Reaction Name: bleaching 1

Kinetic Type: General [µM/s]

Name	Description	Global	Expression	Units
J	reaction rate	☐	Vmax · rf · Laser · ((t > 1.0) && (t < 1.5))	µM.s⁻¹
Vmax	user defined	☐	50.0	s⁻¹.µM⁻¹
rf	Species Concentration	☑	Variable	µM
Laser	Species Concentration	☑	Variable	µM
t	time	☑	Variable	s



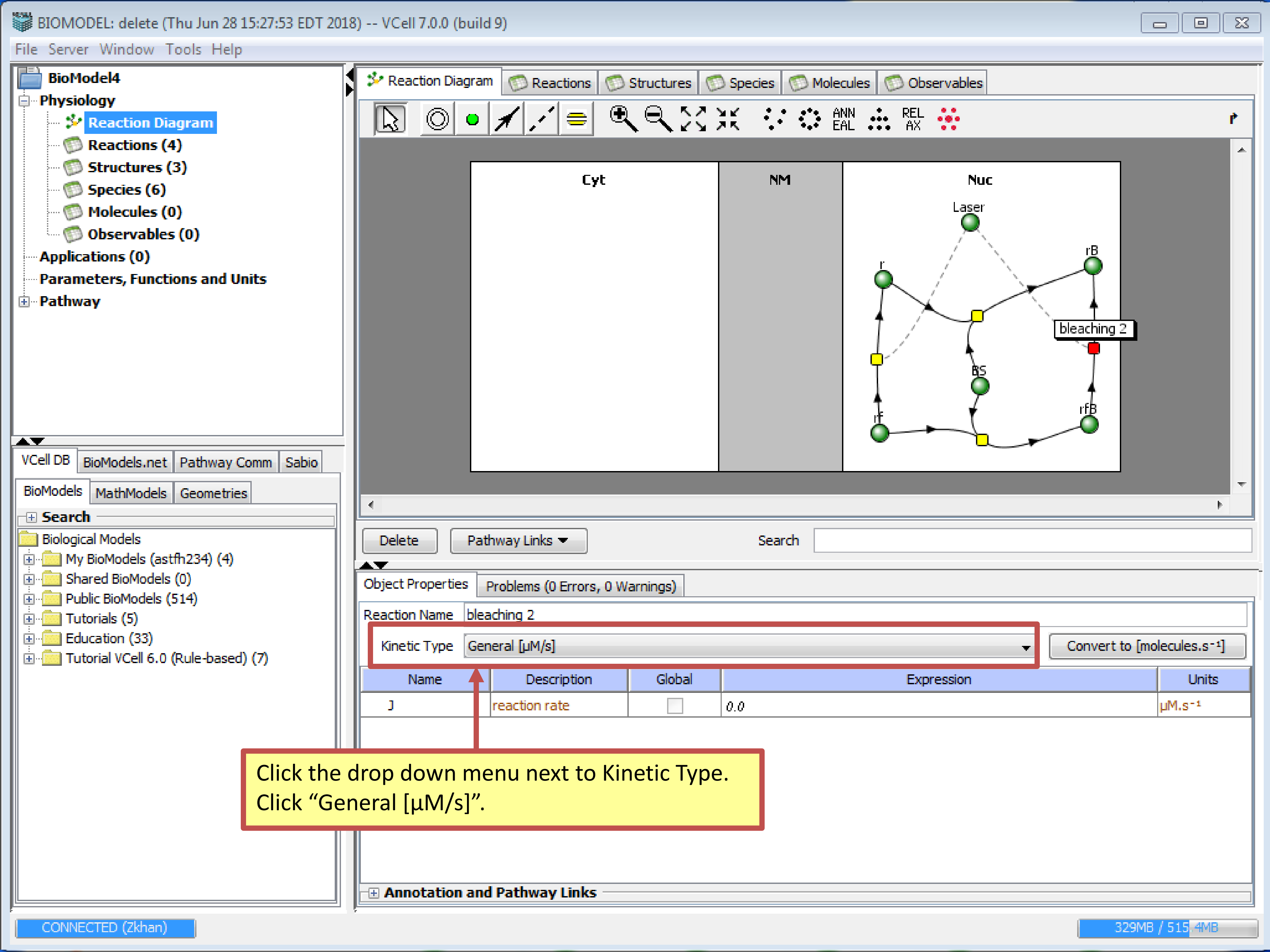
Click “r3”.

Next to Reaction Name type “bleaching 2”.

Reaction Name: bleaching 2

Kinetic Type: Mass Action [µM/s] (recommended for stochastic application)

Name	Description	Global	Expression	Units
J	reaction rate	☐	$(Kf \cdot rfB - Kr \cdot rB)$	$\mu M.s^{-1}$
Kf	forward rate constant	☐	0.0	s^{-1}
Kr	reverse rate constant	☐	0.0	s^{-1}
rfB	Species Concentration	☑	Variable	µM
rB	Species Concentration	☑	Variable	µM

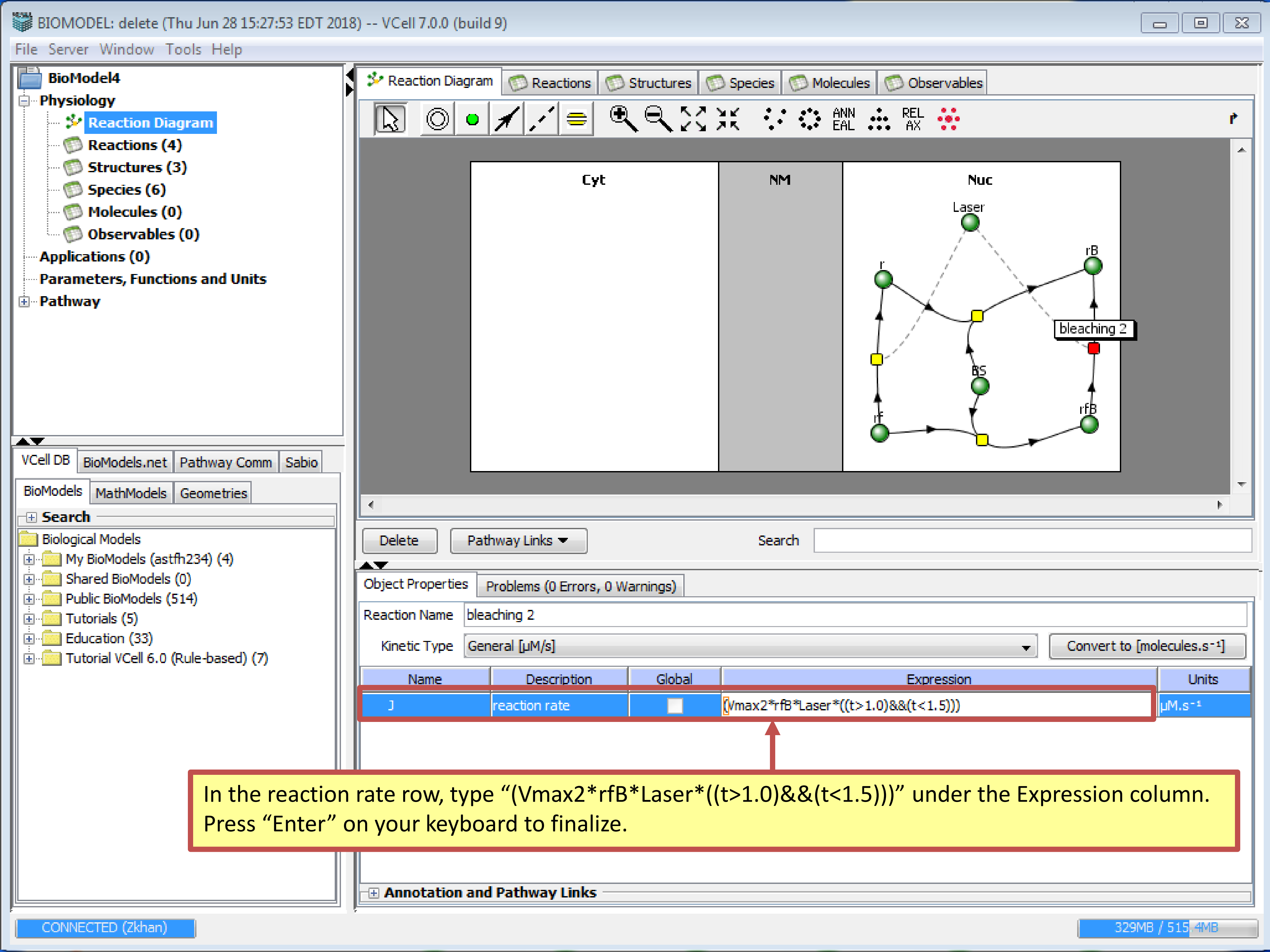


Reaction Name: bleaching 2

Kinetic Type: General [µM/s]

Name	Description	Global	Expression	Units
J	reaction rate	☐	0.0	$\mu M.s^{-1}$

Click the drop down menu next to Kinetic Type.
Click “General [µM/s]”.

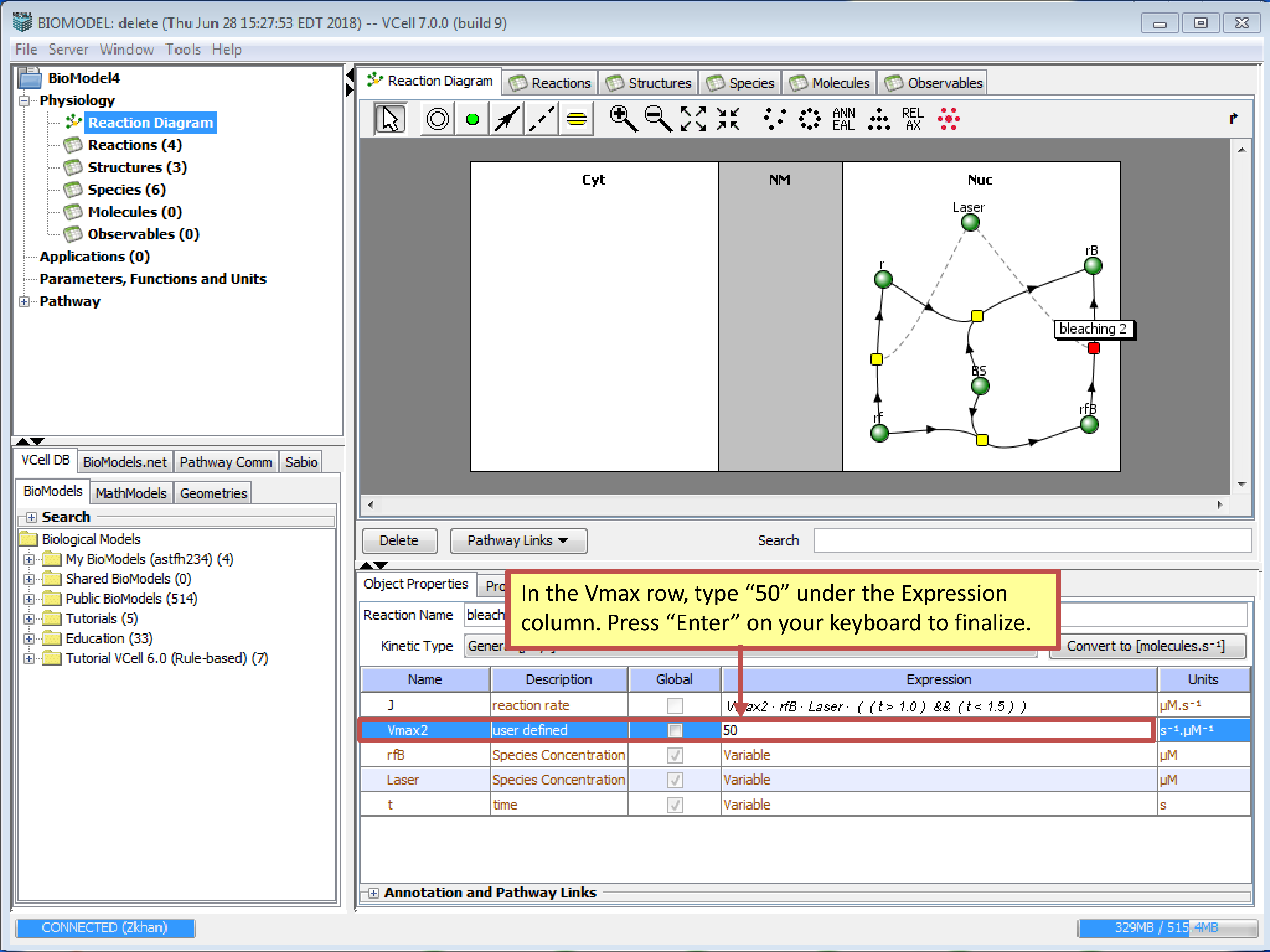


Reaction Name: bleaching 2

Kinetic Type: General [µM/s]

Name	Description	Global	Expression	Units
J	reaction rate	☐	(Vmax2*rfB*Laser*((t>1.0)&&(t<1.5)))	µM.s⁻¹

In the reaction rate row, type "(Vmax2*rfB*Laser*((t>1.0)&&(t<1.5)))" under the Expression column. Press "Enter" on your keyboard to finalize.

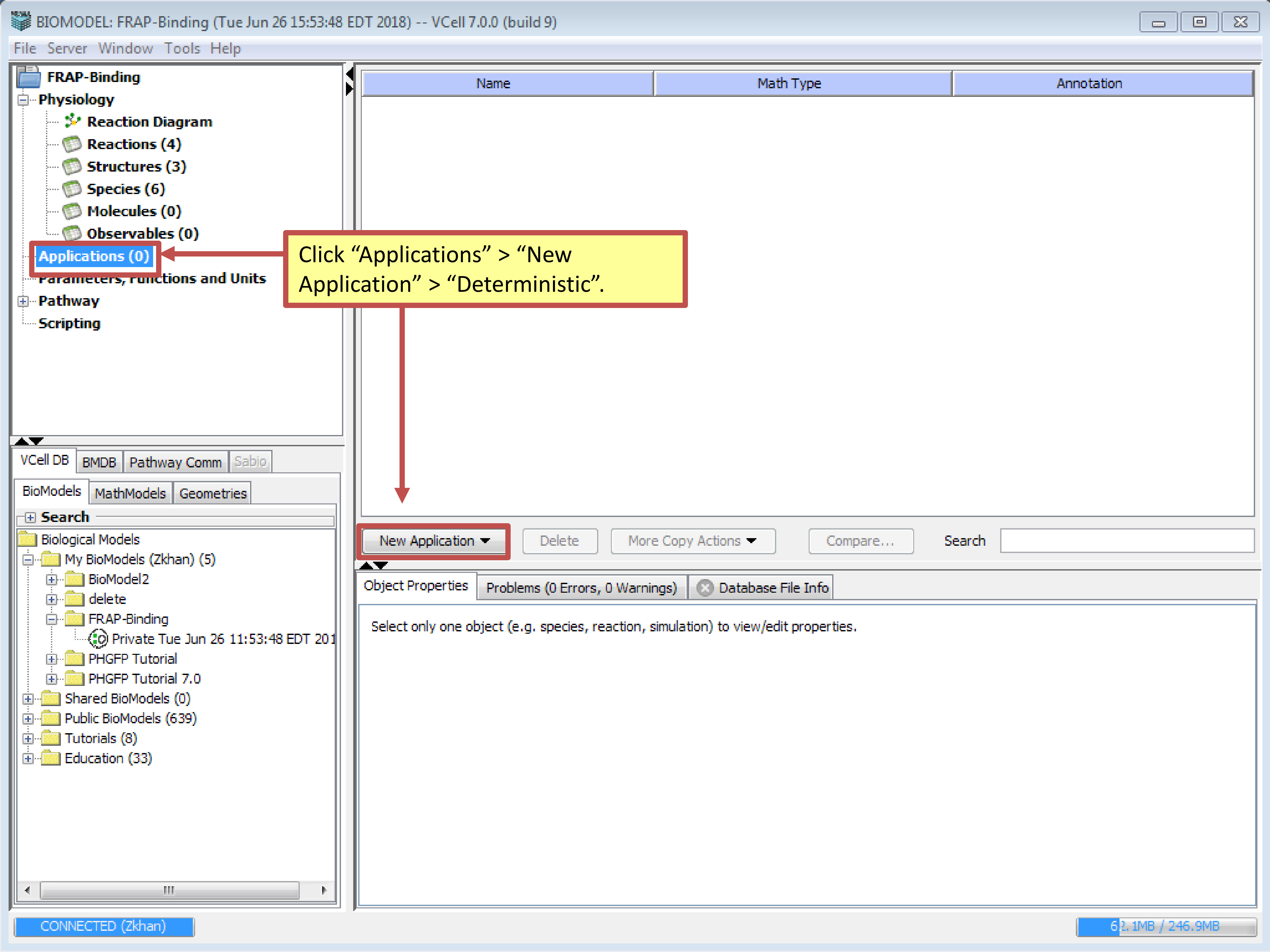


In the Vmax row, type “50” under the Expression column. Press “Enter” on your keyboard to finalize.

Reaction Name: bleach

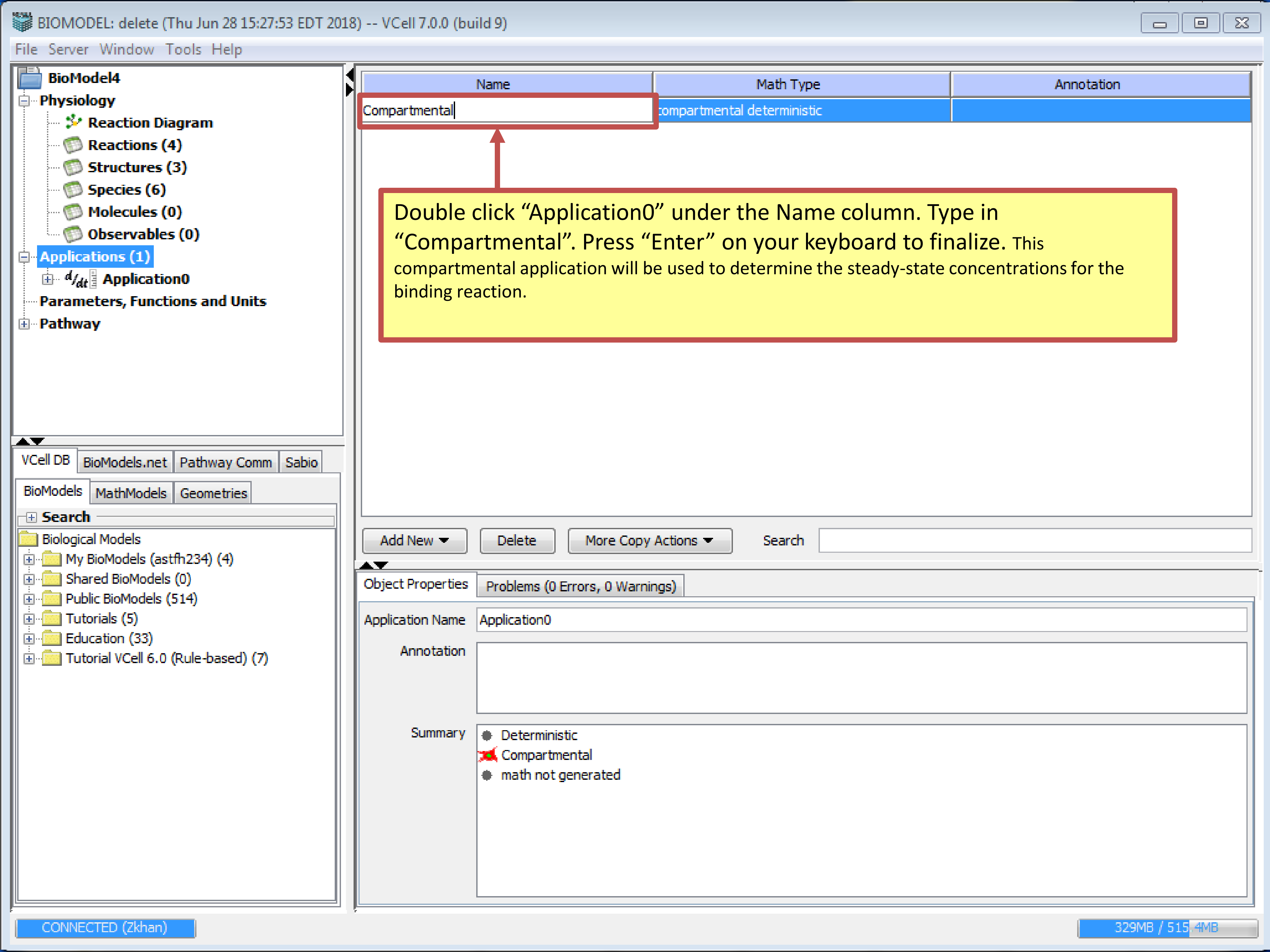
Kinetic Type: Gener

Name	Description	Global	Expression	Units
J	reaction rate	☐	Vmax2 · rfB · Laser · ((t > 1.0) && (t < 1.5))	µM.s⁻¹
Vmax2	user defined	☐	50	s⁻¹.µM⁻¹
rfB	Species Concentration	☑	Variable	µM
Laser	Species Concentration	☑	Variable	µM
t	time	☑	Variable	s



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

Click “Applications” > “New Application” > “Deterministic”.



BIOMODEL: delete (Thu Jun 28 15:27:53 EDT 2018) -- VCell 7.0.0 (build 9)

Double click “Application0” under the Name column. Type in “Compartmental”. Press “Enter” on your keyboard to finalize. This compartmental application will be used to determine the steady-state concentrations for the binding reaction.

Name	Math Type	Annotation
Compartmental	compartmental deterministic	

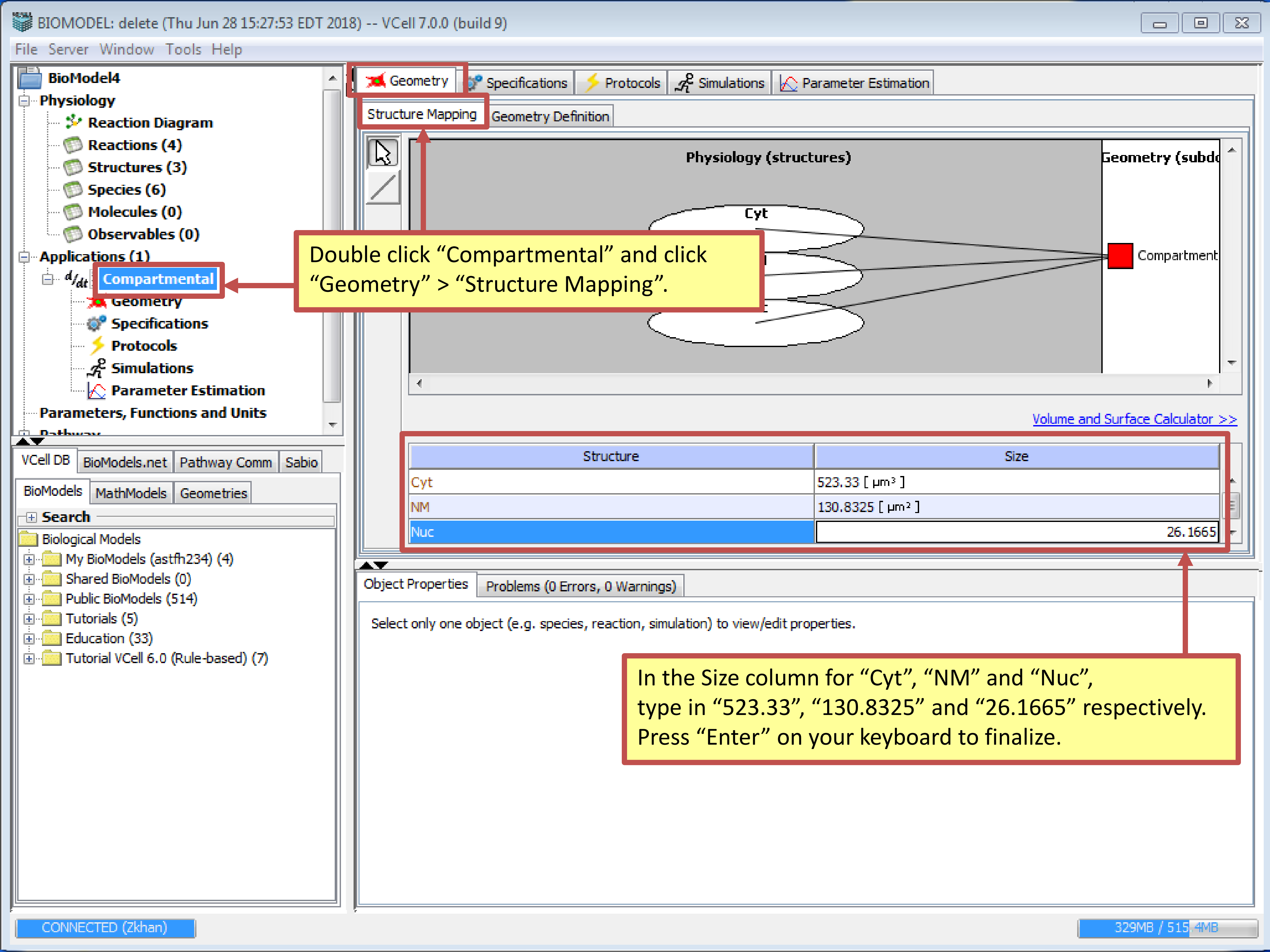
Application Name: Application0

Annotation:

Summary:
- Deterministic
- Compartmental
- math not generated

CONNECTED (Zkhan)

329MB / 515.4MB

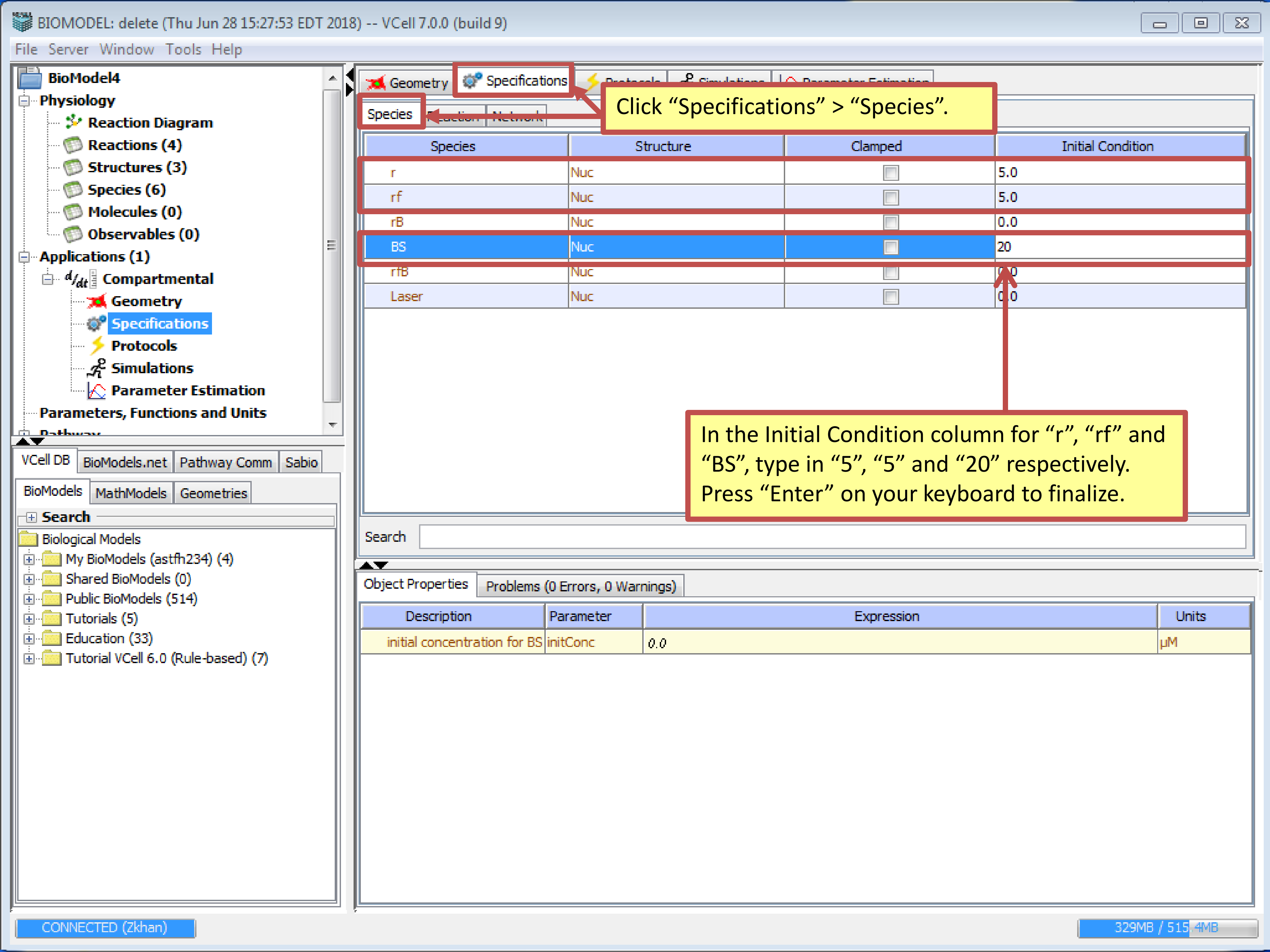


Double click “Compartmental” and click “Geometry” > “Structure Mapping”.

Structure	Size
Cyt	523.33 [µm³]
NM	130.8325 [µm²]
Nuc	26.1665

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

In the Size column for “Cyt”, “NM” and “Nuc”, type in “523.33”, “130.8325” and “26.1665” respectively. Press “Enter” on your keyboard to finalize.

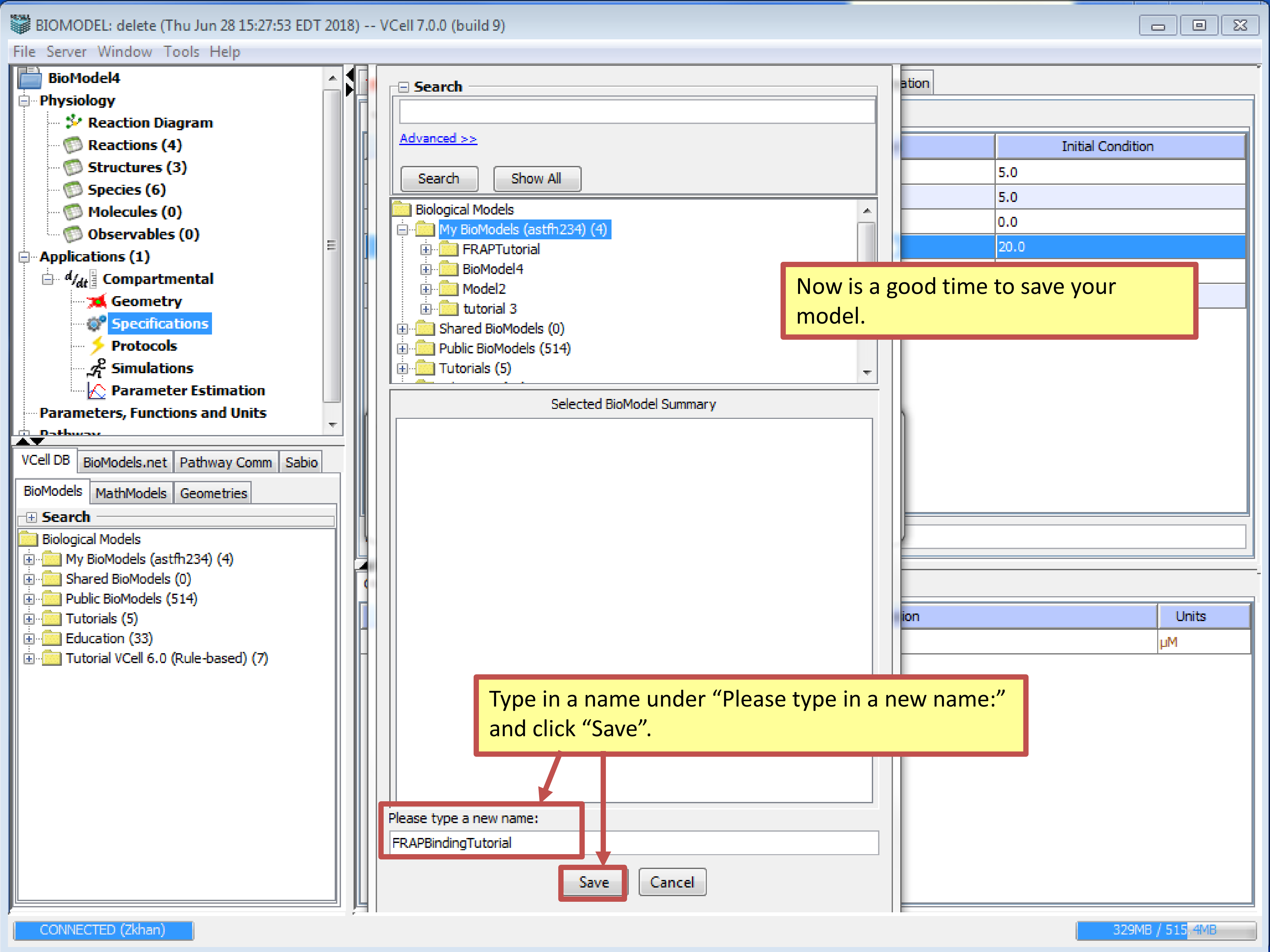


Click “Specifications” > “Species”.

Species	Structure	Clamped	Initial Condition
r	Nuc	☐	5.0
rf	Nuc	☐	5.0
rB	Nuc	☐	0.0
BS	Nuc	☐	20
rfB	Nuc	☐	0.0
Laser	Nuc	☐	0.0

In the Initial Condition column for “r”, “rf” and “BS”, type in “5”, “5” and “20” respectively. Press “Enter” on your keyboard to finalize.

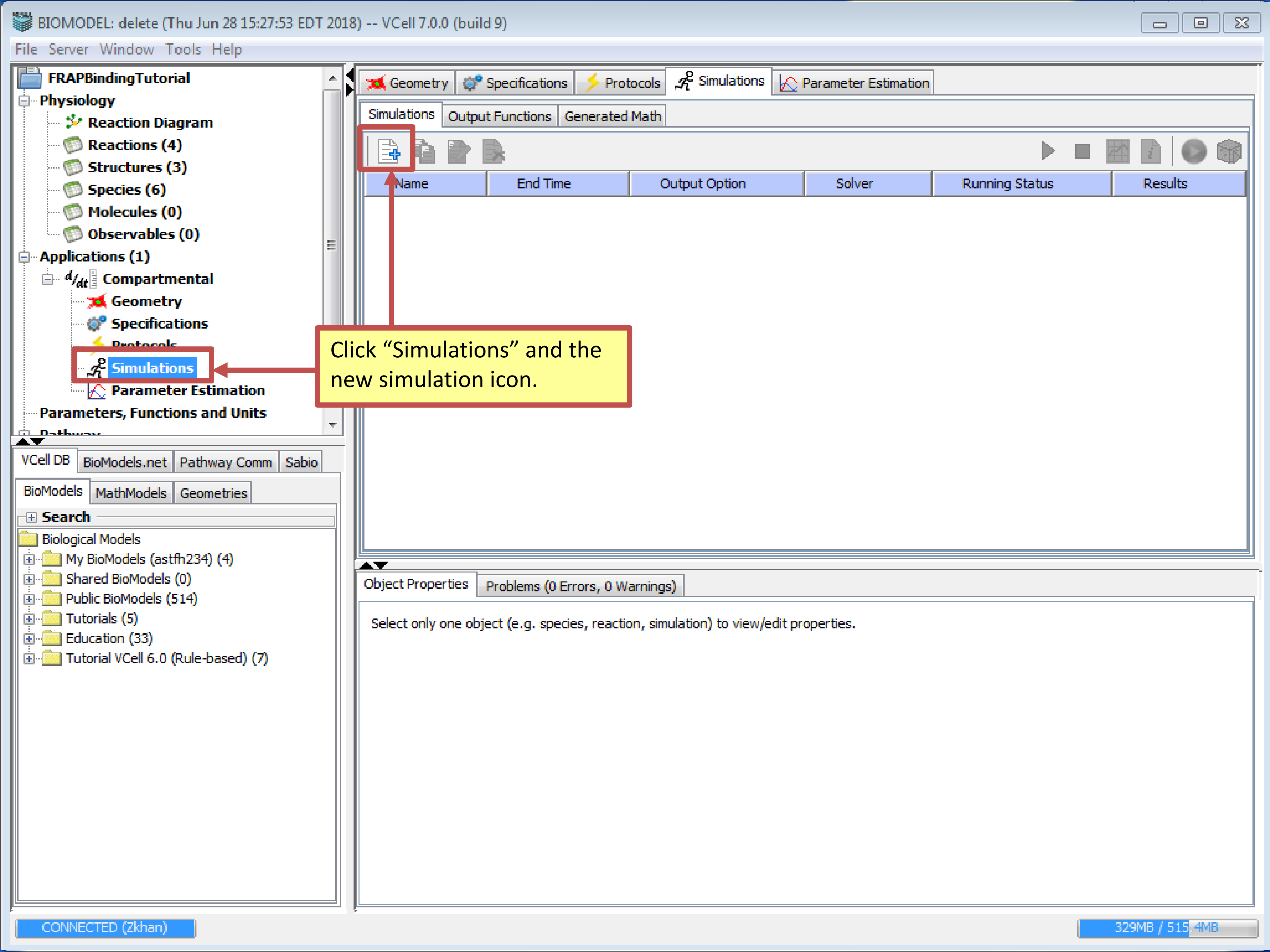
Description	Parameter	Expression	Units
initial concentration for BS	initConc	0.0	μM



Please type a new name: FRAPBindingTutorial

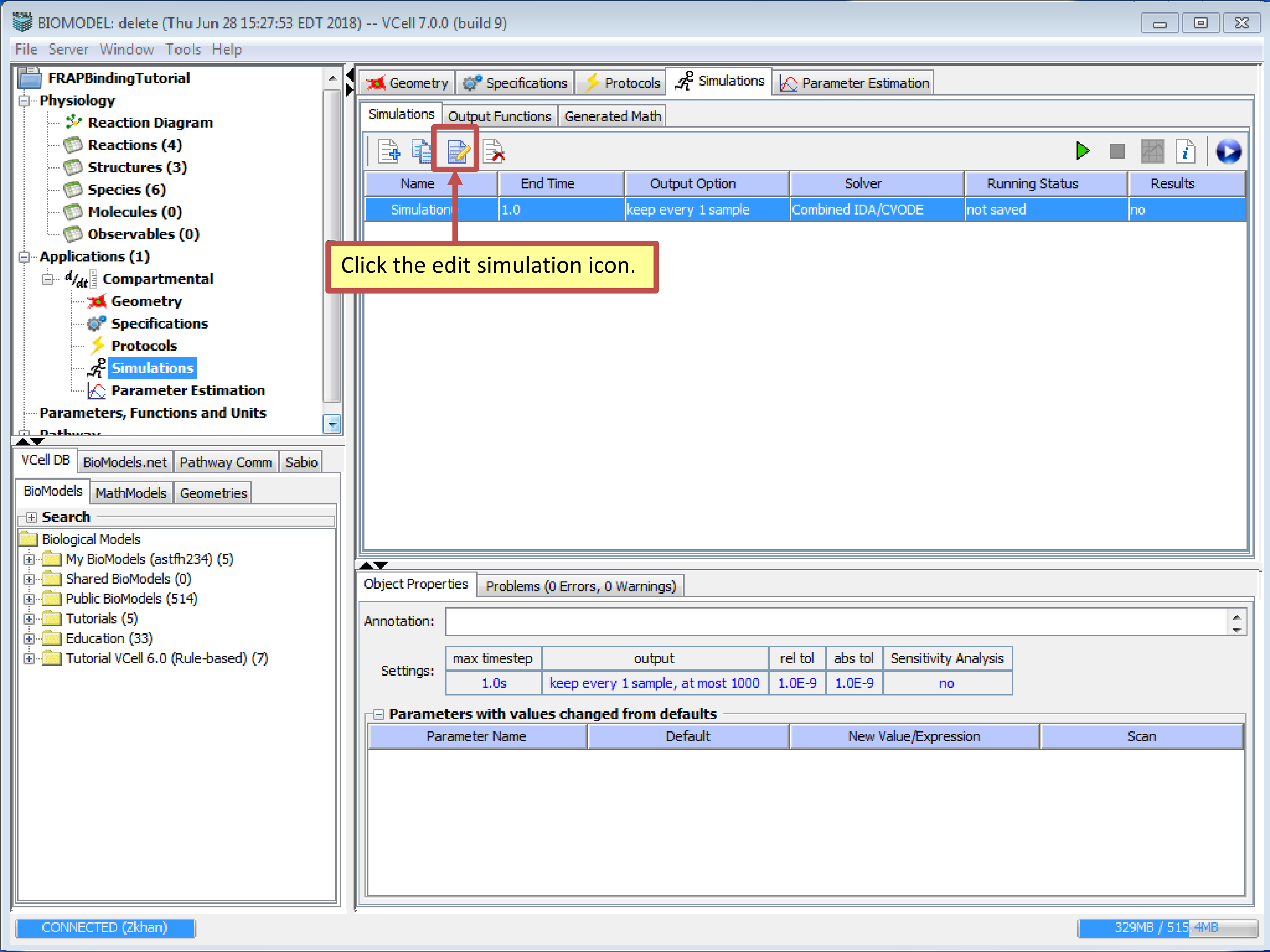
Now is a good time to save your model.

Type in a name under “Please type in a new name:” and click “Save”.



Click “Simulations” and the new simulation icon.

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



Click the edit simulation icon.

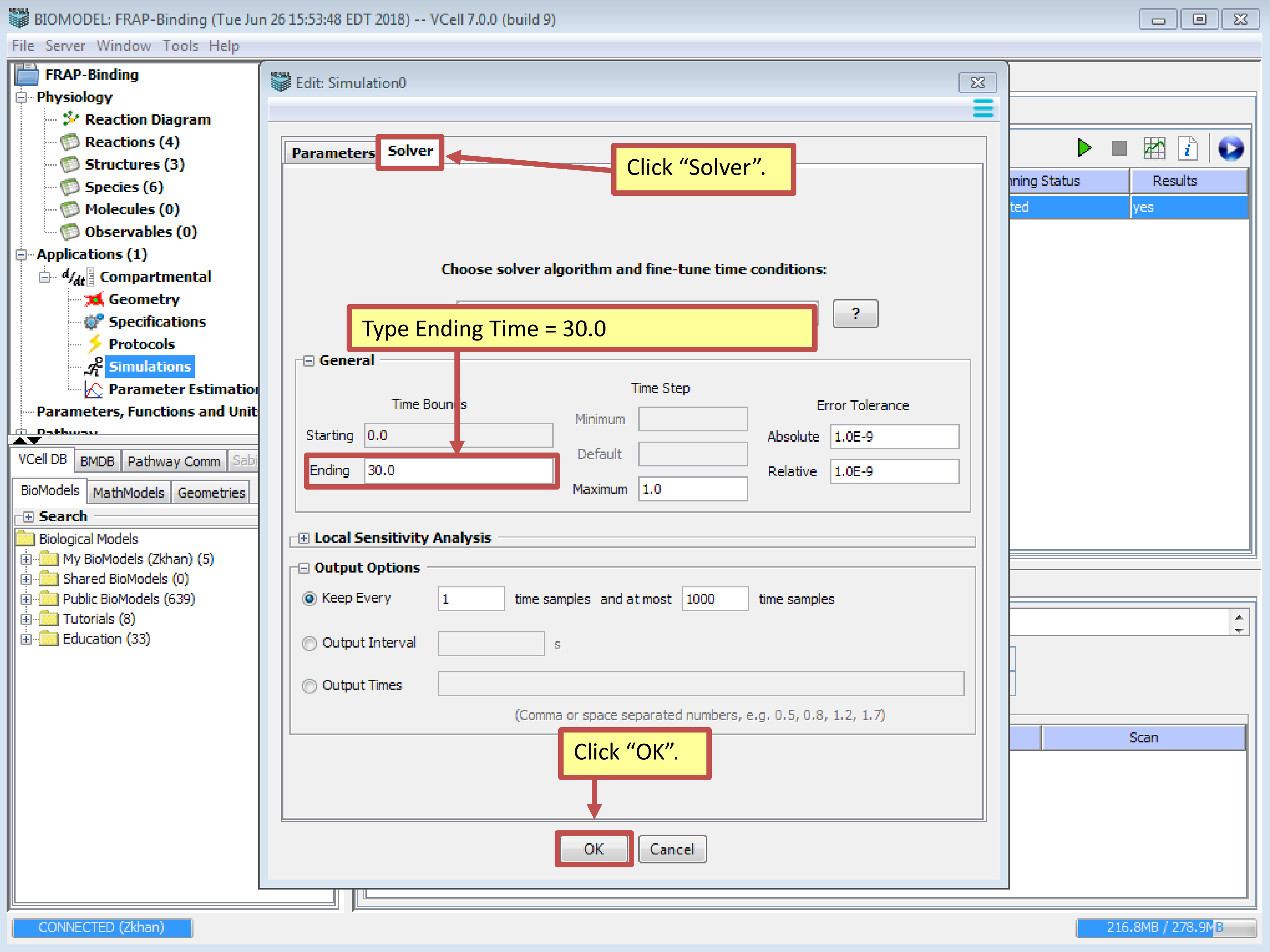
Name	End Time	Output Option	Solver	Running Status	Results
Simulation	1.0	keep every 1 sample	Combined IDA/CVODE	not saved	no

Settings:

max timestep	output	rel tol	abs tol	Sensitivity Analysis
1.0s	keep every 1 sample, at most 1000	1.0E-9	1.0E-9	no

Parameters with values changed from defaults

Parameter Name	Default	New Value/Expression	Scan



Click "Solver".

Type Ending Time = 30.0

Click "OK".

Choose solver algorithm and fine-tune time conditions:

General

Time Bounds
Starting 0.0
Ending 30.0

Time Step
Minimum
Default
Maximum 1.0

Error Tolerance
Absolute 1.0E-9
Relative 1.0E-9

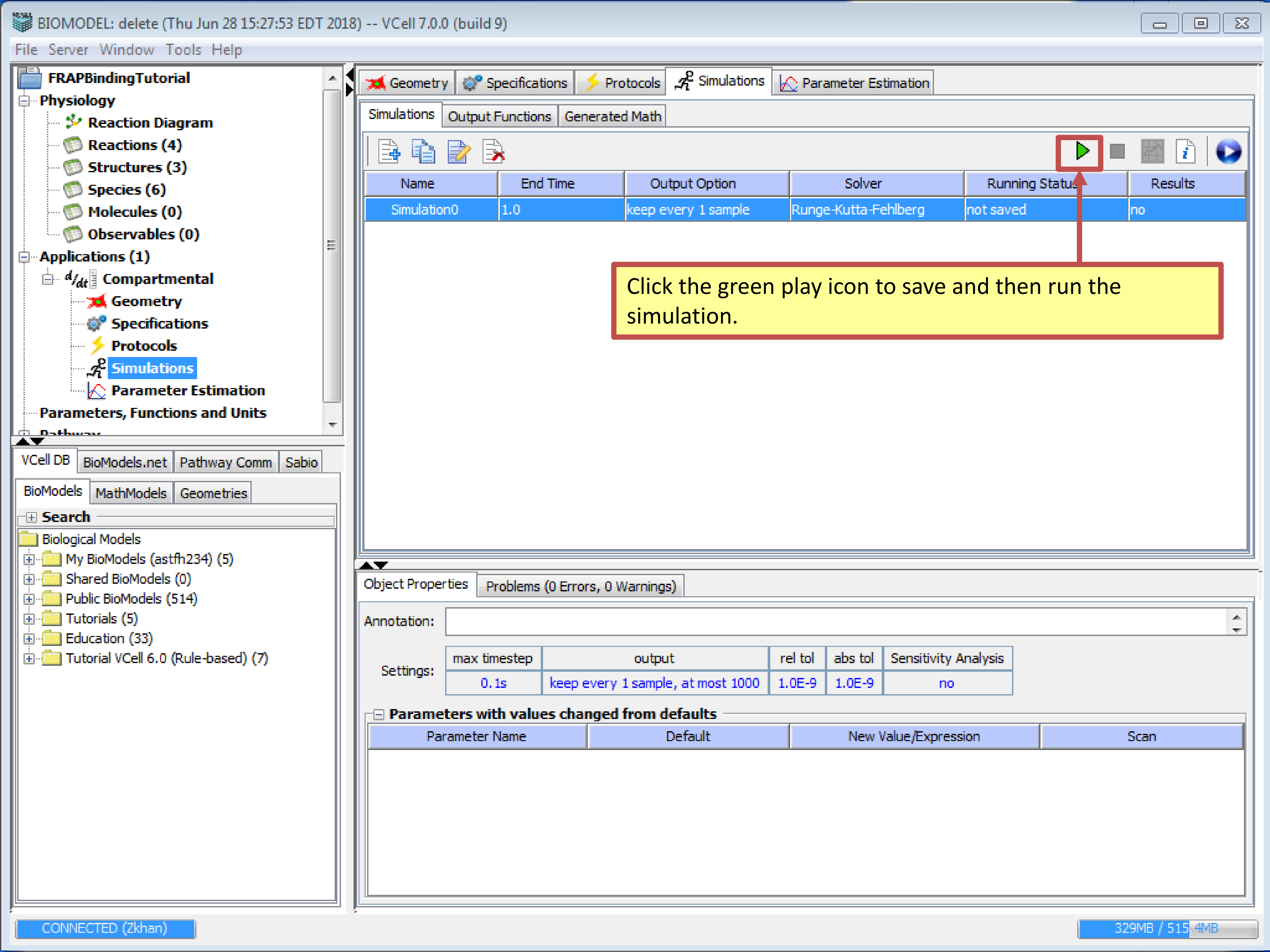
Output Options

● Keep Every 1 time samples and at most 1000 time samples

○ Output Interval s

○ Output Times

(Comma or space separated numbers, e.g. 0.5, 0.8, 1.2, 1.7)

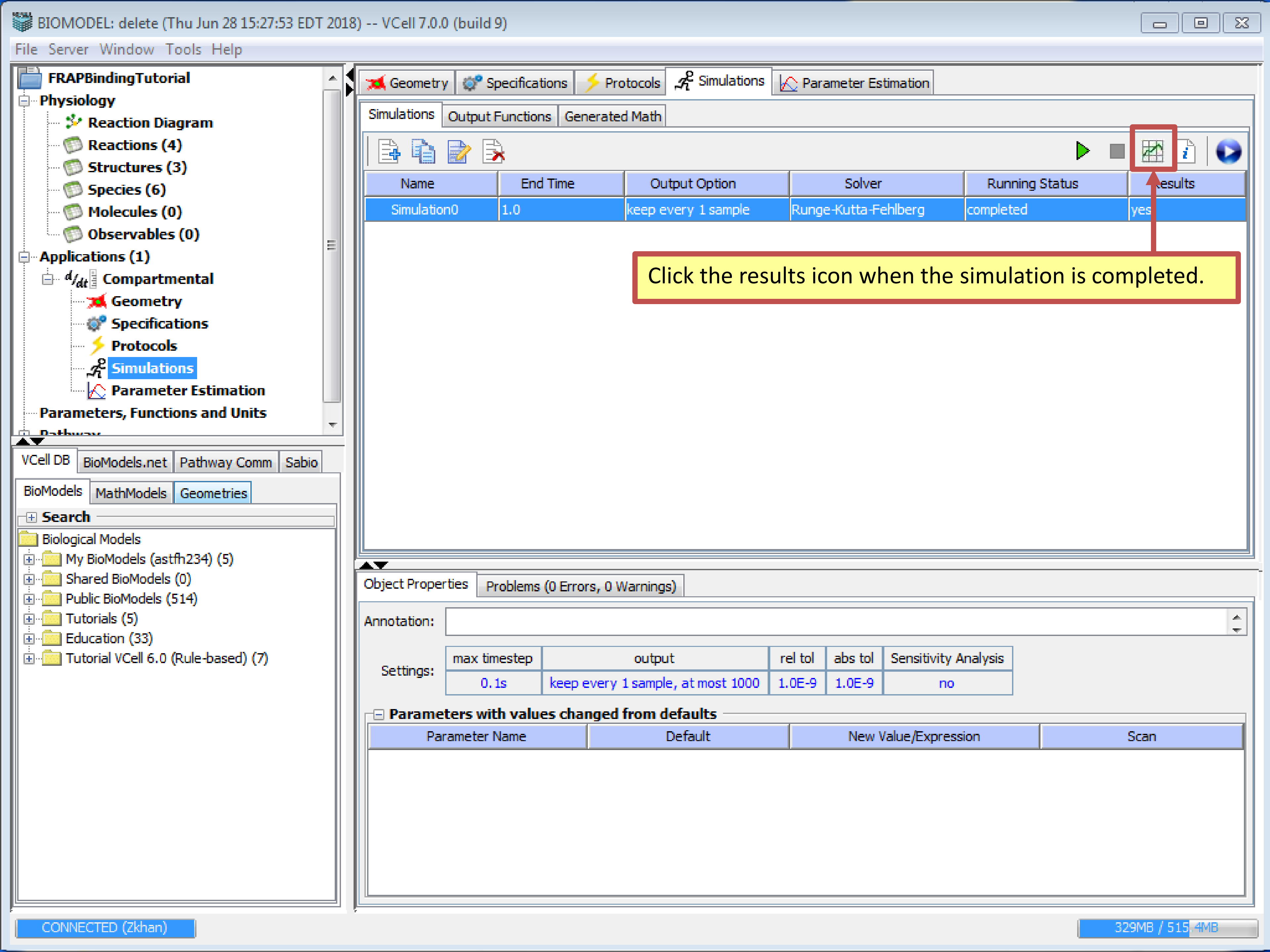


Name	End Time	Output Option	Solver	Running Status	Results
Simulation0	1.0	keep every 1 sample	Runge-Kutta-Fehlberg	not saved	no

Click the green play icon to save and then run the simulation.

max timestep	output	rel tol	abs tol	Sensitivity Analysis
0.1s	keep every 1 sample, at most 1000	1.0E-9	1.0E-9	no

Parameter Name	Default	New Value/Expression	Scan

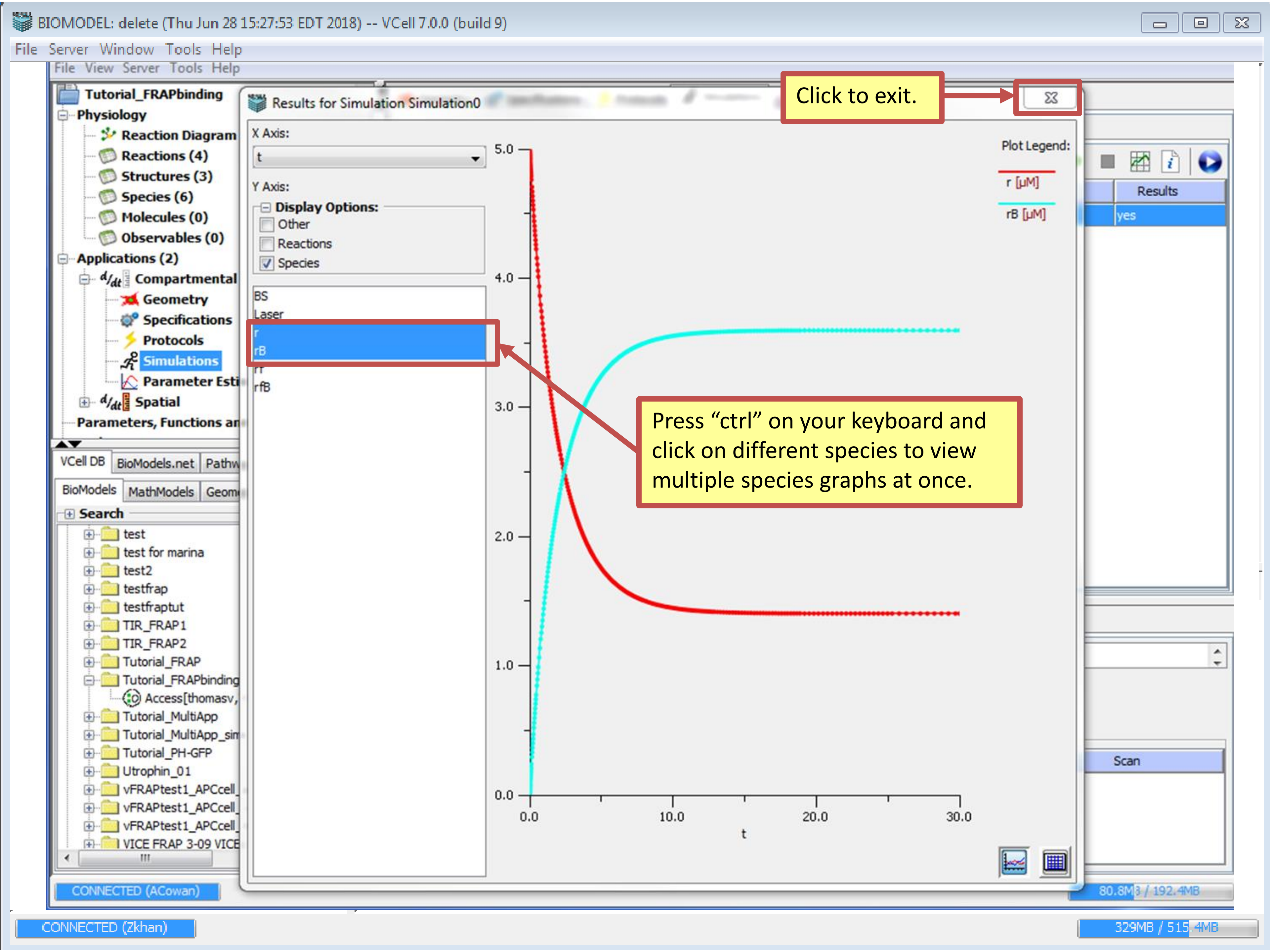


Name	End Time	Output Option	Solver	Running Status	Results
Simulation0	1.0	keep every 1 sample	Runge-Kutta-Fehlberg	completed	yes

Click the results icon when the simulation is completed.

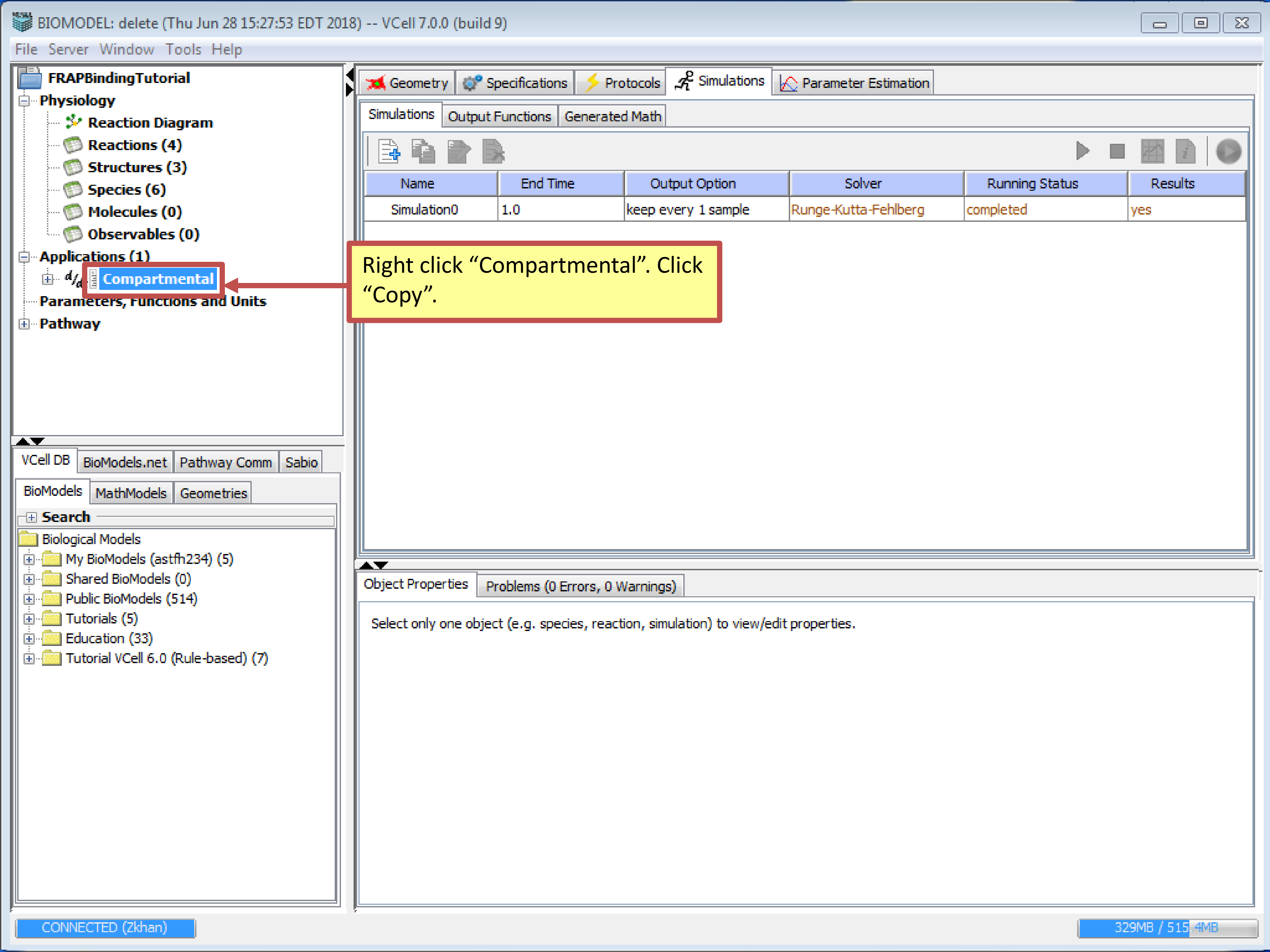
max timestep	output	rel tol	abs tol	Sensitivity Analysis
0.1s	keep every 1 sample, at most 1000	1.0E-9	1.0E-9	no

Parameter Name	Default	New Value/Expression	Scan



Click to exit.

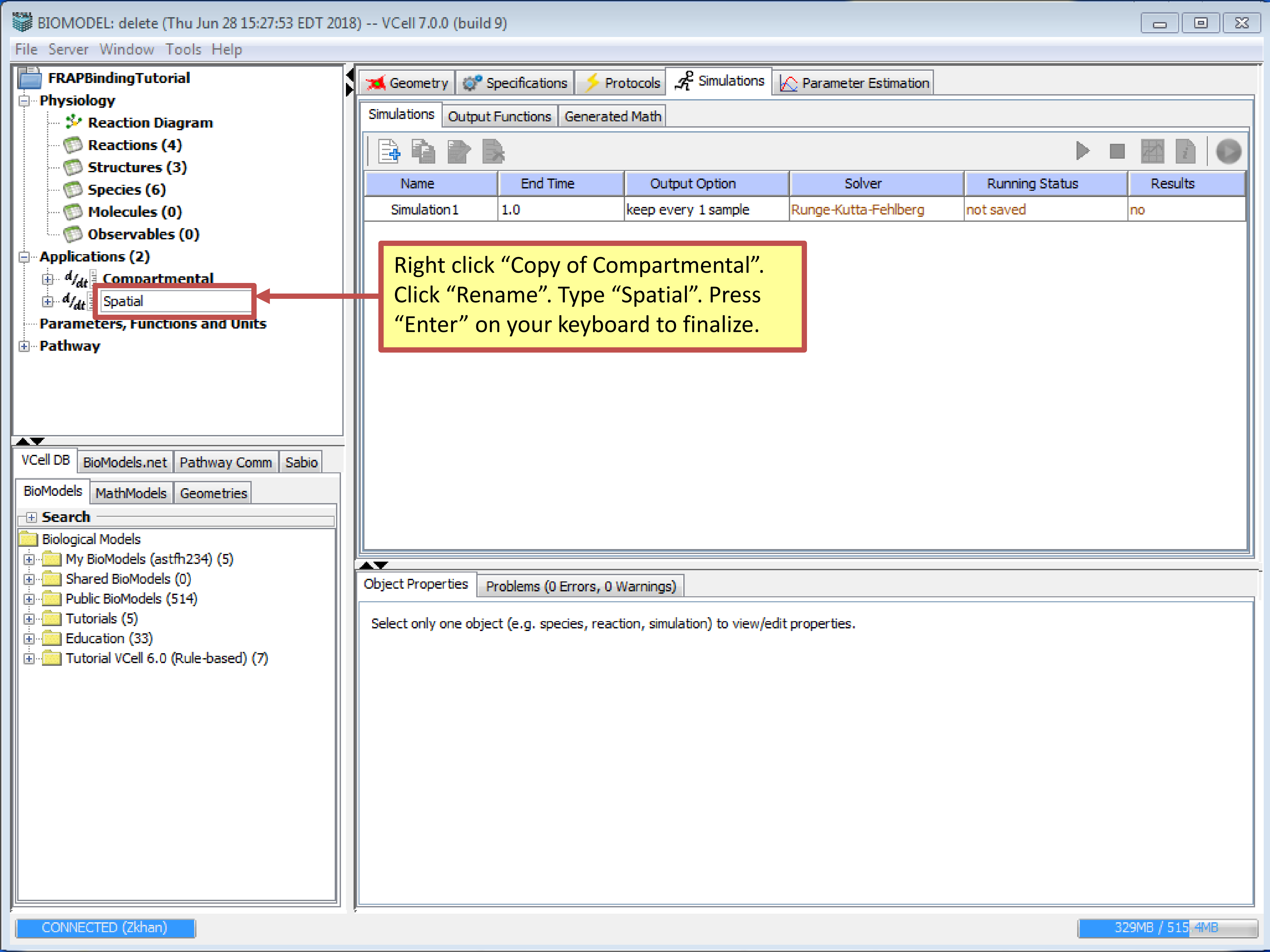
Press “ctrl” on your keyboard and click on different species to view multiple species graphs at once.



Name	End Time	Output Option	Solver	Running Status	Results
Simulation0	1.0	keep every 1 sample	Runge-Kutta-Fehlberg	completed	yes

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

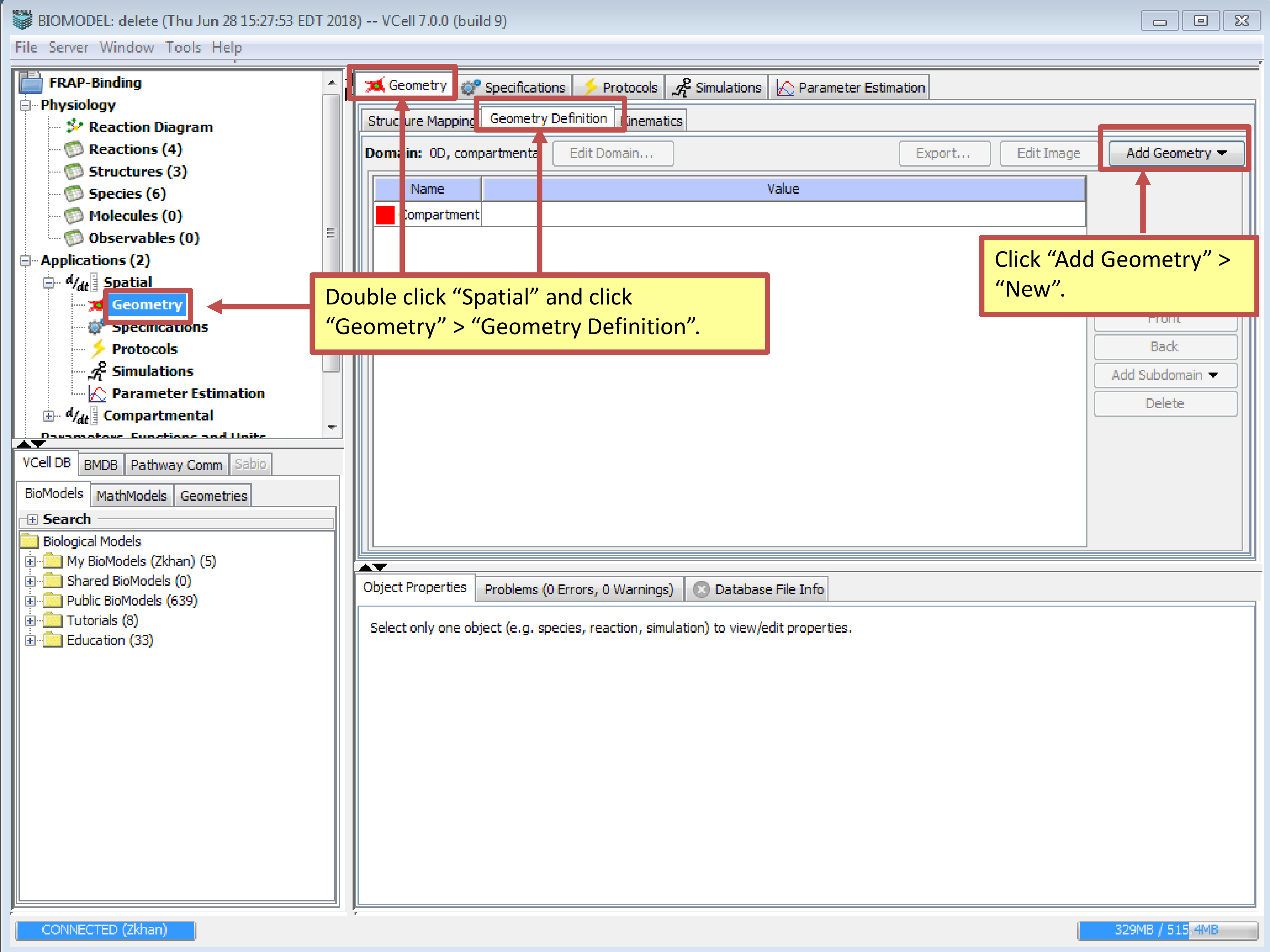
Right click “Compartmental”. Click “Copy”.



Name	End Time	Output Option	Solver	Running Status	Results
Simulation1	1.0	keep every 1 sample	Runge-Kutta-Fehlberg	not saved	no

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

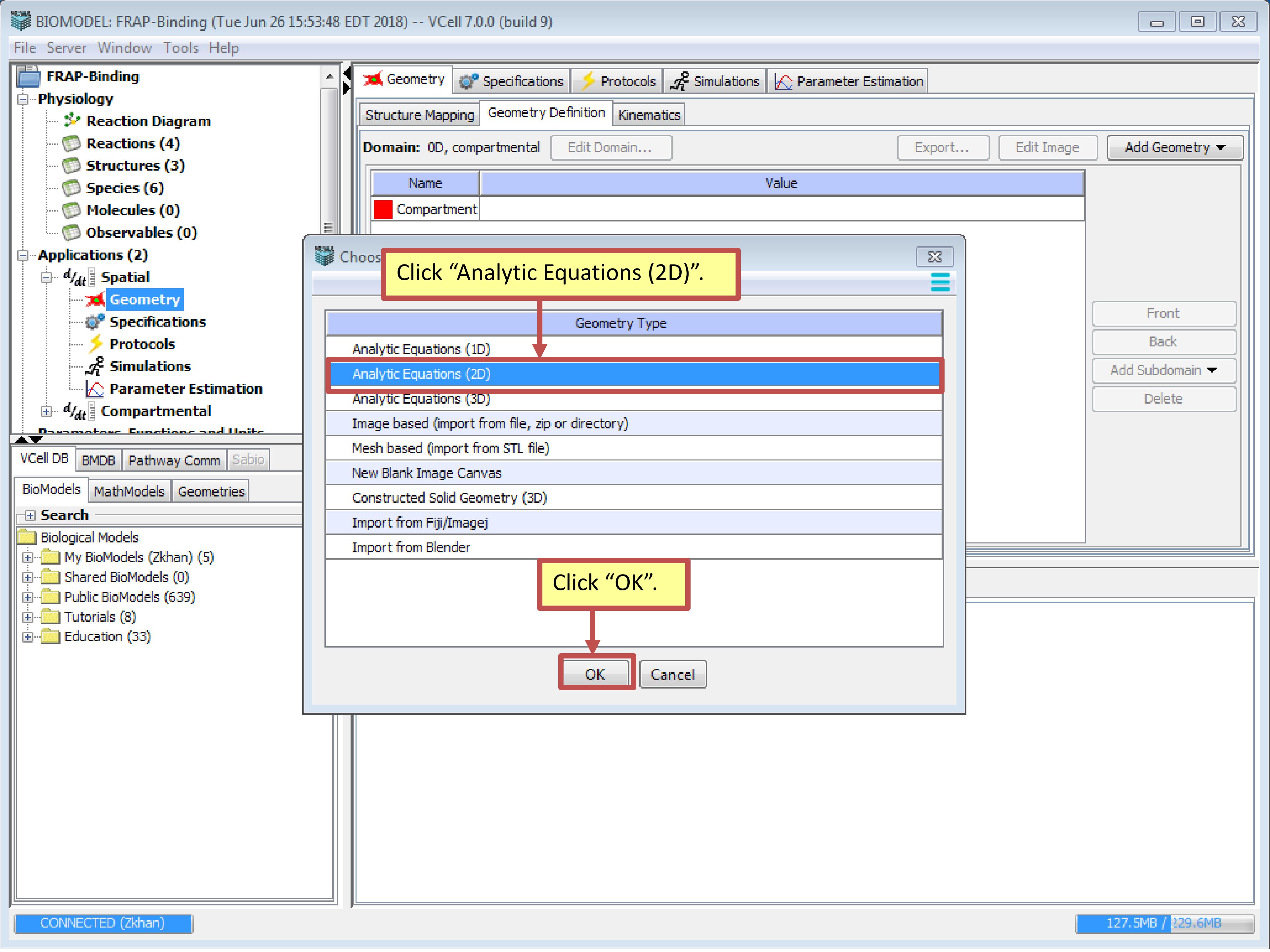
Right click “Copy of Compartmental”. Click “Rename”. Type “Spatial”. Press “Enter” on your keyboard to finalize.



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

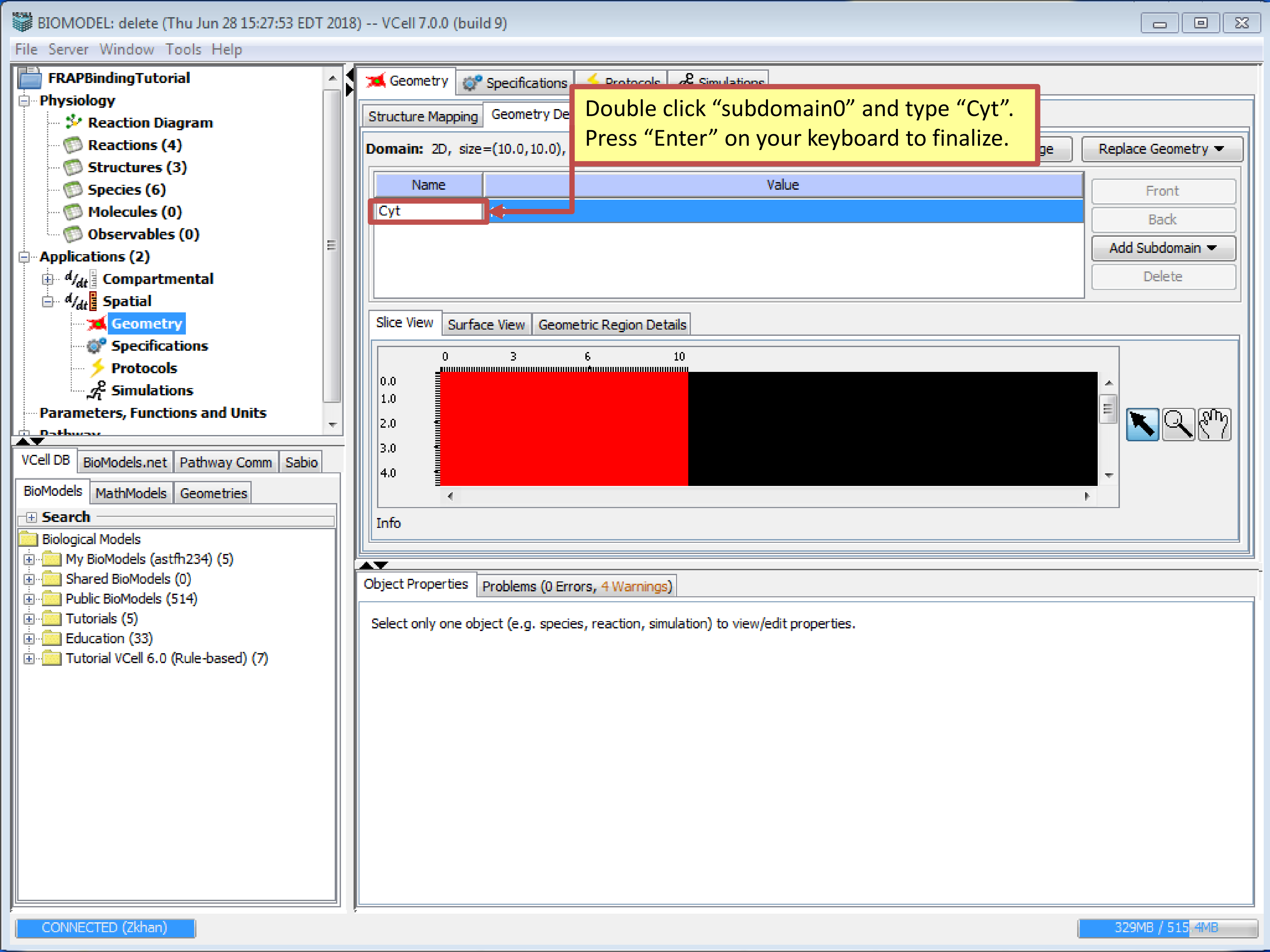
Double click “Spatial” and click “Geometry” > “Geometry Definition”.

Click “Add Geometry” > “New”.



Click “Analytic Equations (2D)”.

Click “OK”.



Double click “subdomain0” and type “Cyt”. Press “Enter” on your keyboard to finalize.

BIOMODEL: delete (Thu Jun 28 15:27:53 EDT 2018) -- VCell 7.0.0 (build 9)

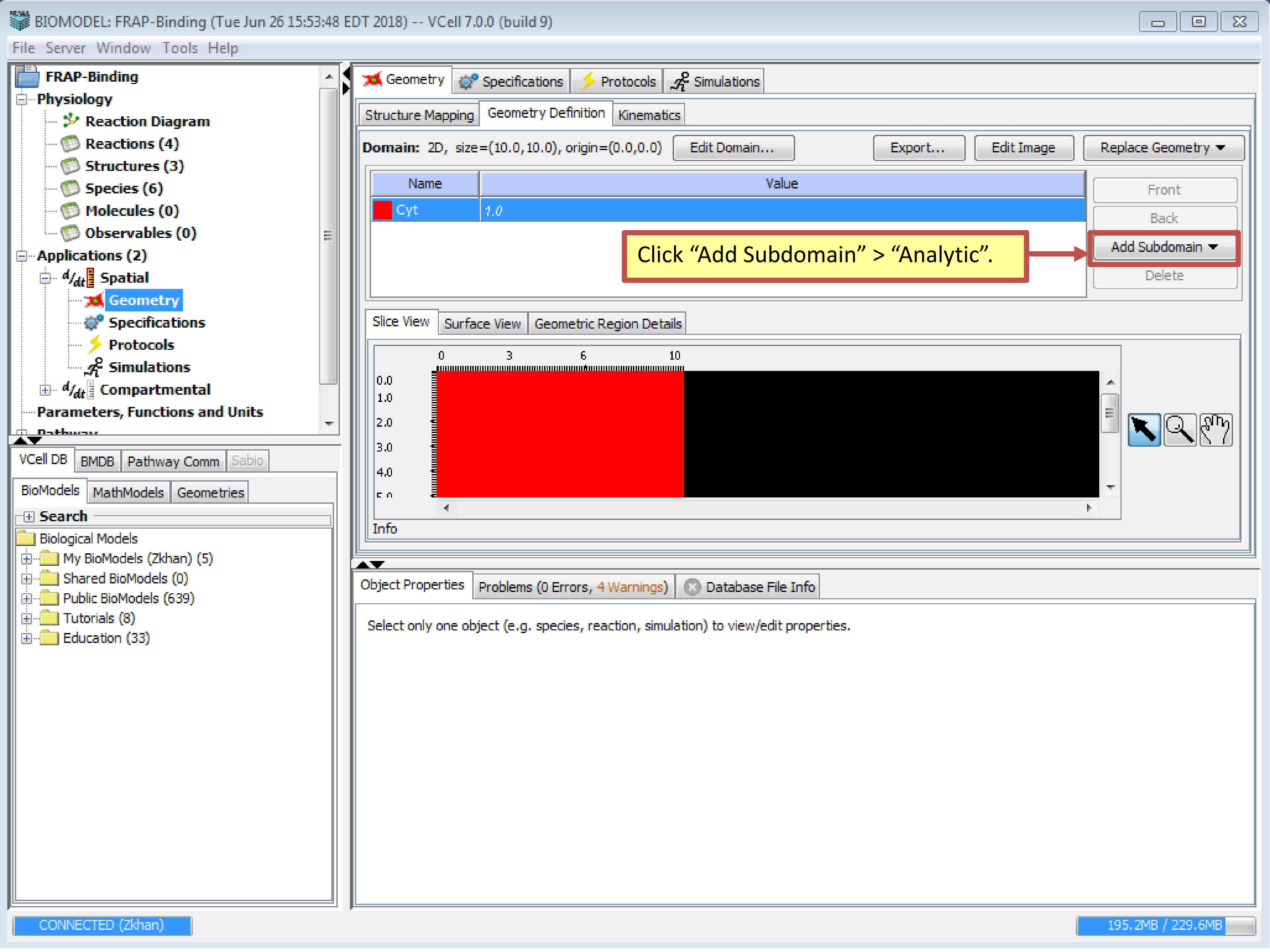
Domain: 2D, size=(10.0,10.0),

Name	Value
Cyt	

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

CONNECTED (Zkhan)

329MB / 515.4MB



BIOMODEL: FRAP-Binding (Tue Jun 26 15:53:48 EDT 2018) -- VCell 7.0.0 (build 9)

Domain: 2D, size=(10.0,10.0), origin=(0.0,0.0)

Name	Value
🟥 Cyt	1.0

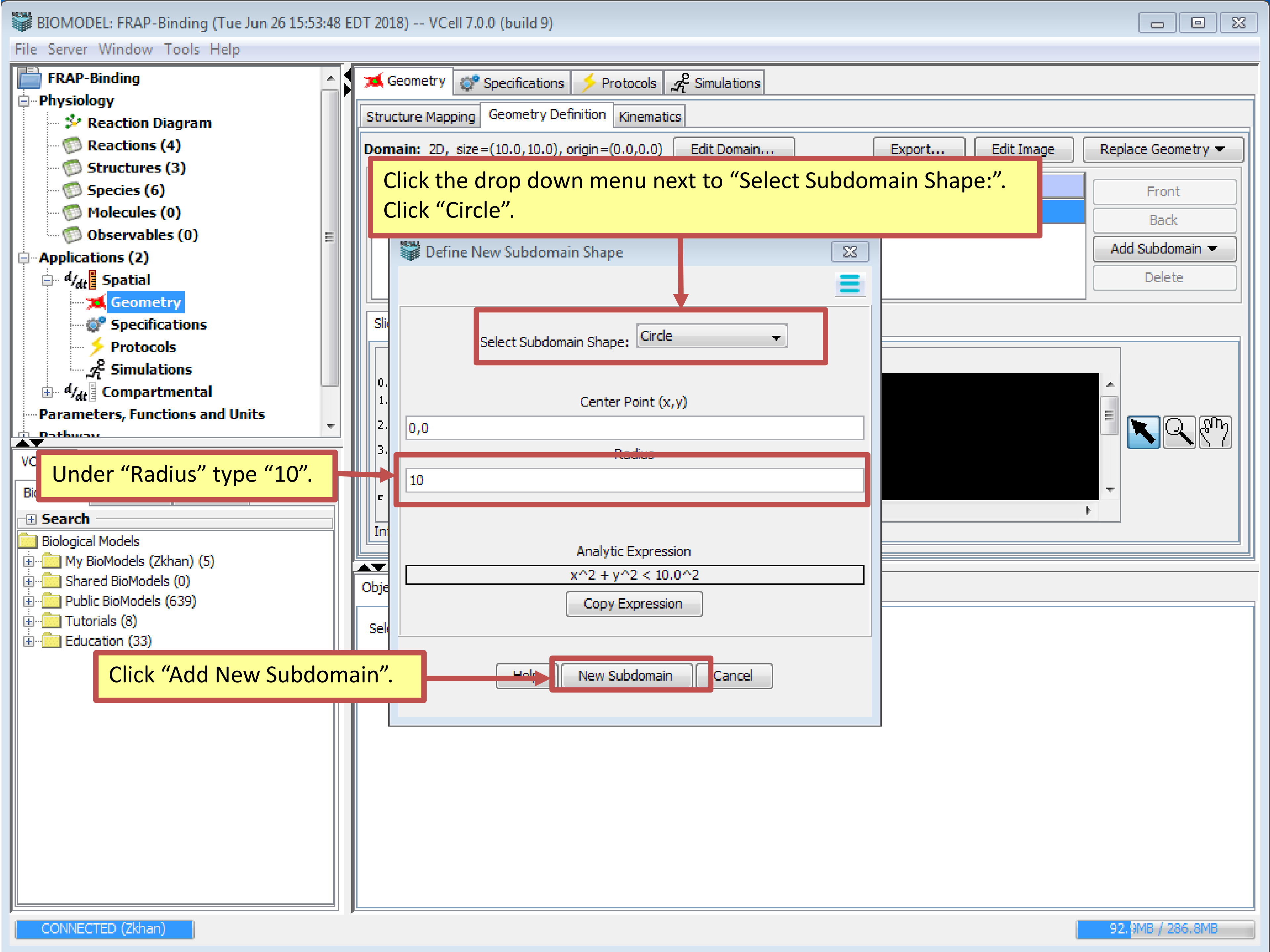
Click “Add Subdomain” > “Analytic”.

Problems (0 Errors, 4 Warnings)

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

CONNECTED (Zkhan)

195.2MB / 229.6MB



BIOMODEL: FRAP-Binding (Tue Jun 26 15:53:48 EDT 2018) -- VCell 7.0.0 (build 9)

Domain: 2D, size=(10.0,10.0), origin=(0.0,0.0)

Click the drop down menu next to “Select Subdomain Shape:”. Click “Circle”.

Define New Subdomain Shape

Select Subdomain Shape: Circle

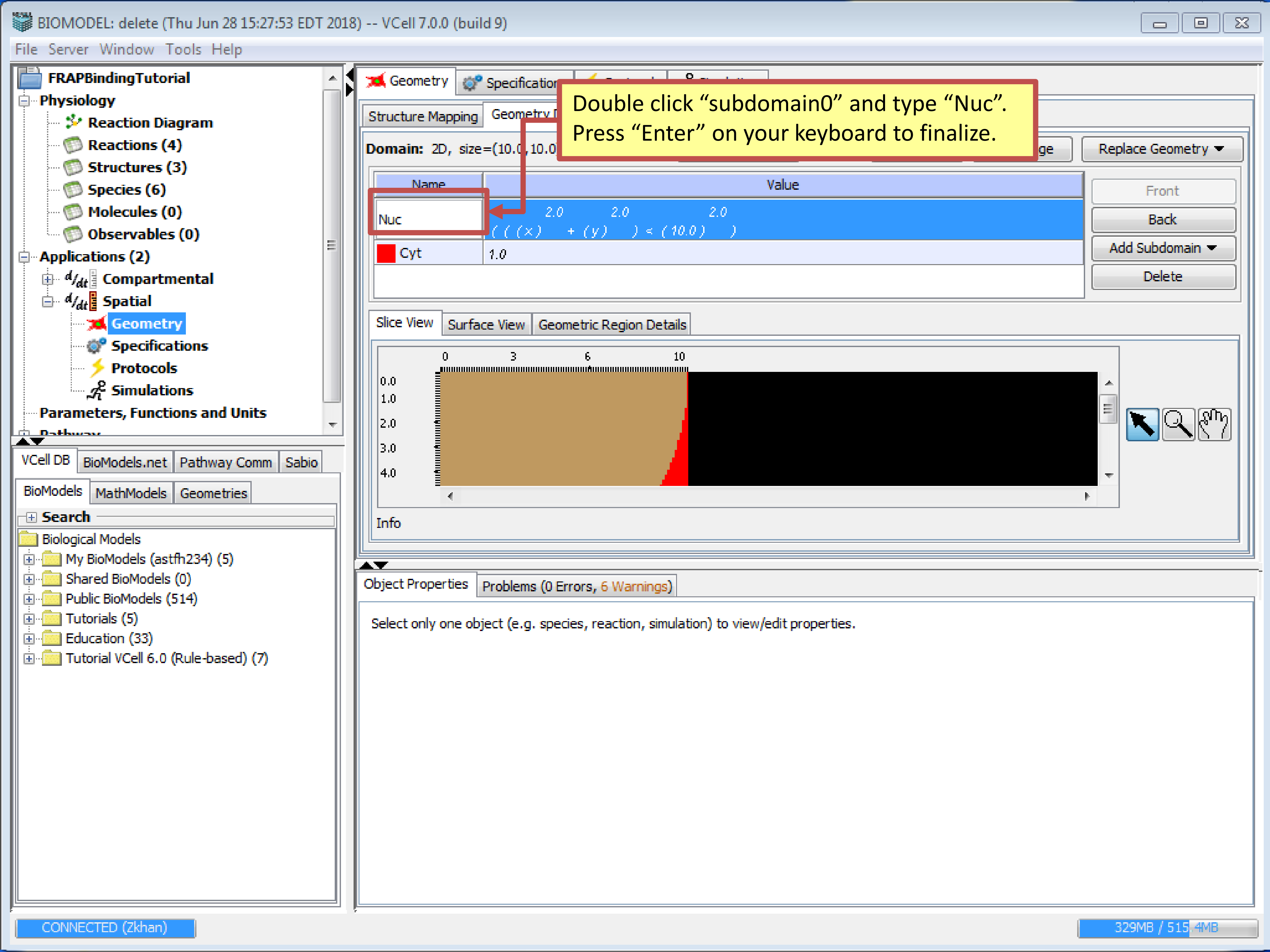
Center Point (x,y): 0,0

Radius: 10

Analytic Expression: x^2 + y^2 < 10.0^2

Under “Radius” type “10”.

Click “Add New Subdomain”.

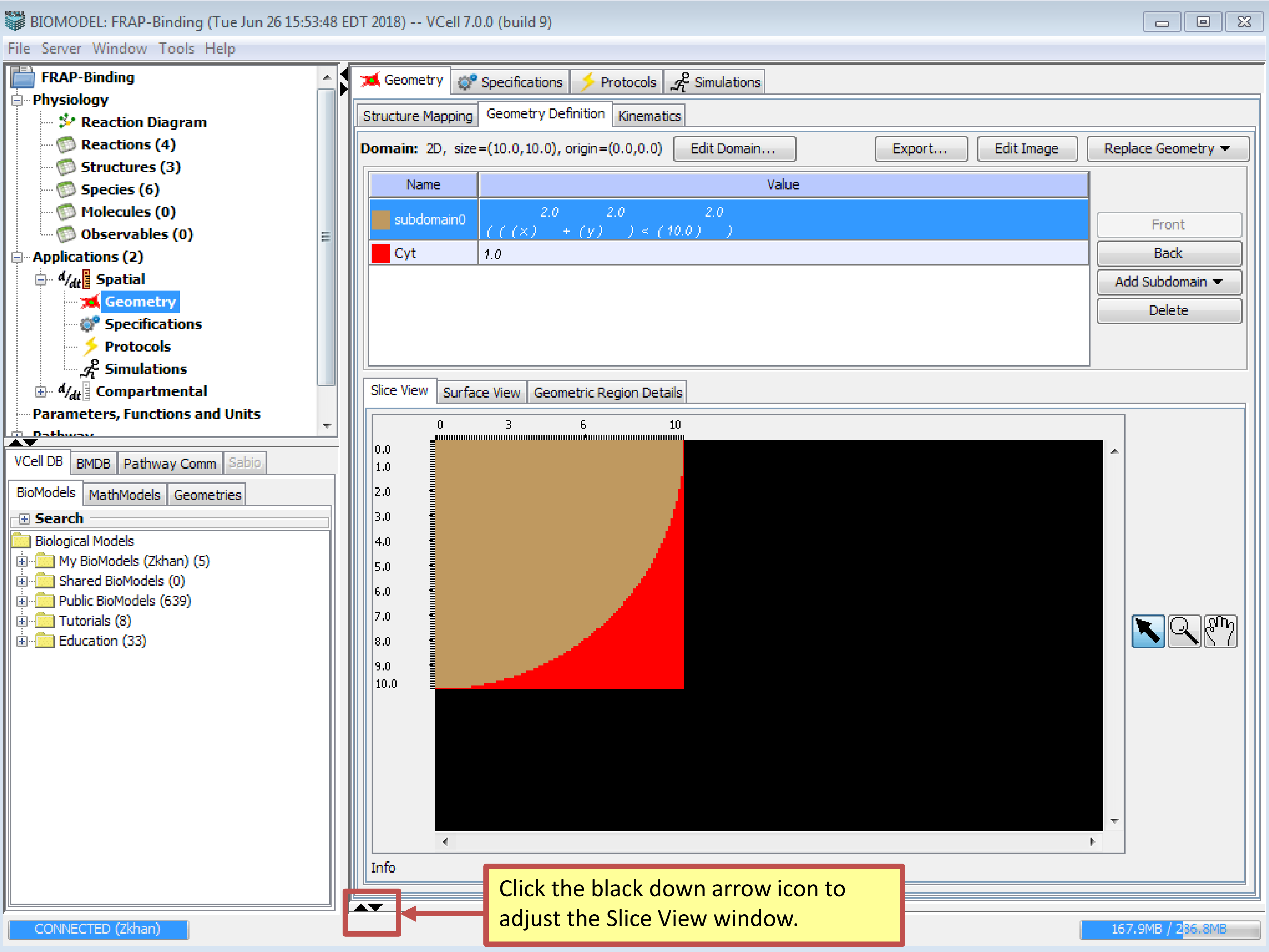


Double click “subdomain0” and type “Nuc”. Press “Enter” on your keyboard to finalize.

Domain: 2D, size=(10.0, 10.0

Name	Value
Nuc	$((x)^{2.0} + (y)^{2.0}) < (10.0)^{2.0}$
🟥 Cyt	1.0

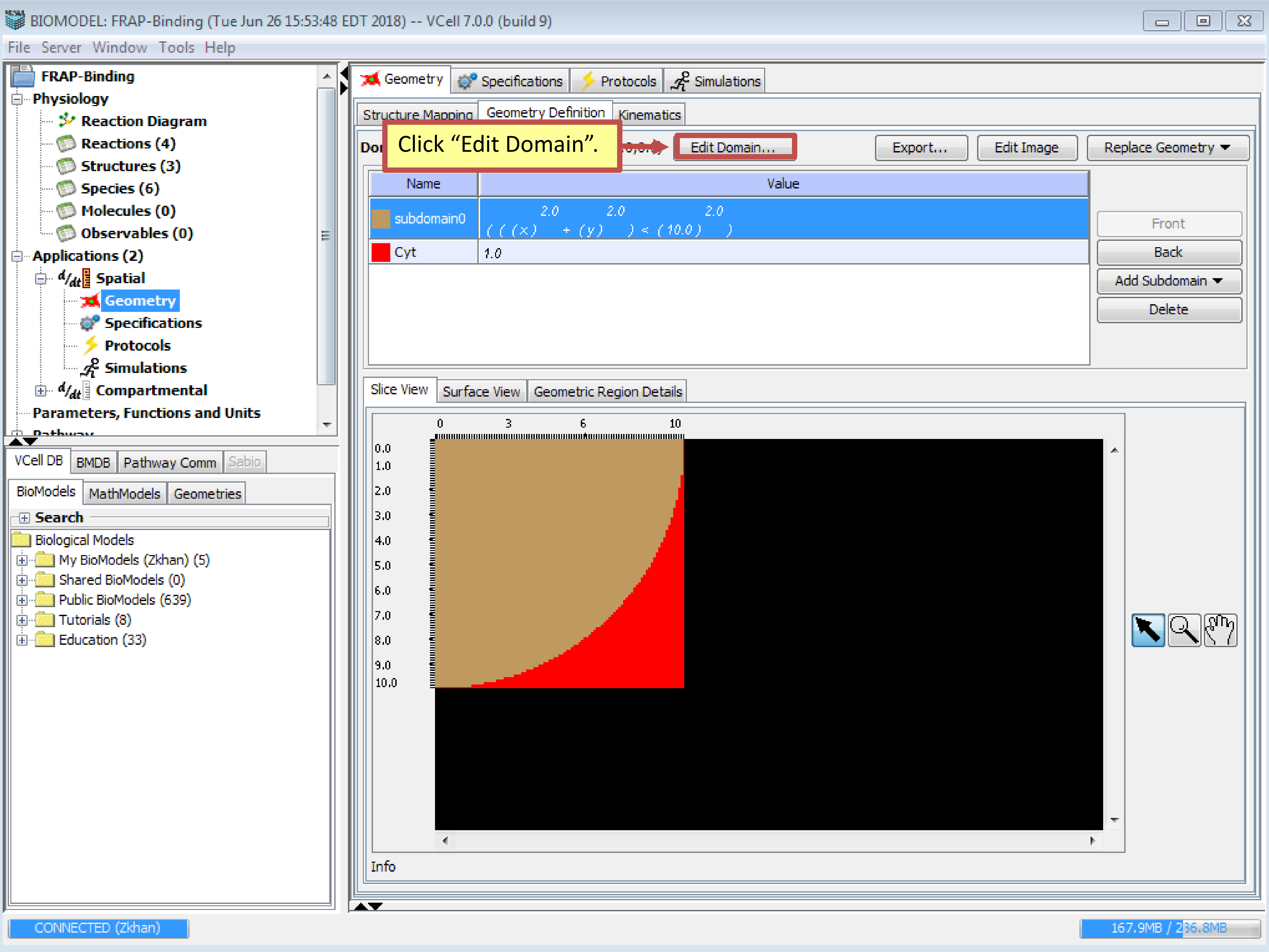
Select only one object (e.g. species, reaction, simulation) to view/edit properties.



Domain: 2D, size=(10.0,10.0), origin=(0.0,0.0)

Name	Value
subdomain0	$((x)^{2.0} + (y)^{2.0}) < (10.0)^{2.0}$
Cyt	1.0

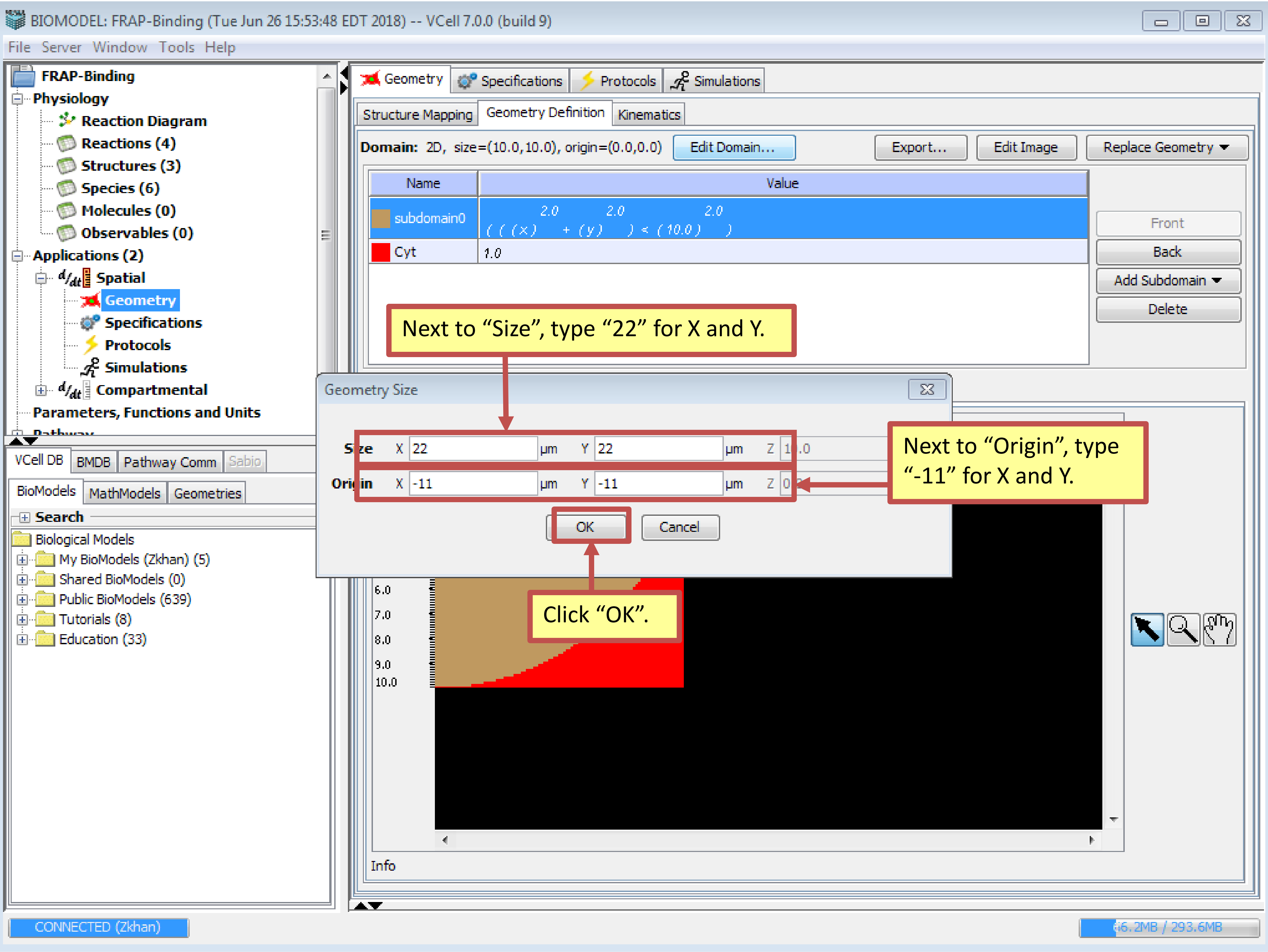
Click the black down arrow icon to adjust the Slice View window.



Click “Edit Domain”.

BIOMODEL: FRAP-Binding (Tue Jun 26 15:53:48 EDT 2018) -- VCell 7.0.0 (build 9)

Name	Value
subdomain0	$((x)^{2.0} + (y)^{2.0}) < (10.0)^{2.0}$
Cyt	1.0



Domain: 2D, size=(10.0,10.0), origin=(0.0,0.0)

Name	Value
subdomain0	$((x)^{2.0} + (y)^{2.0}) < (10.0)^{2.0}$
Cyt	1.0

Geometry Size

Size X 22 µm Y 22 µm Z 10.0

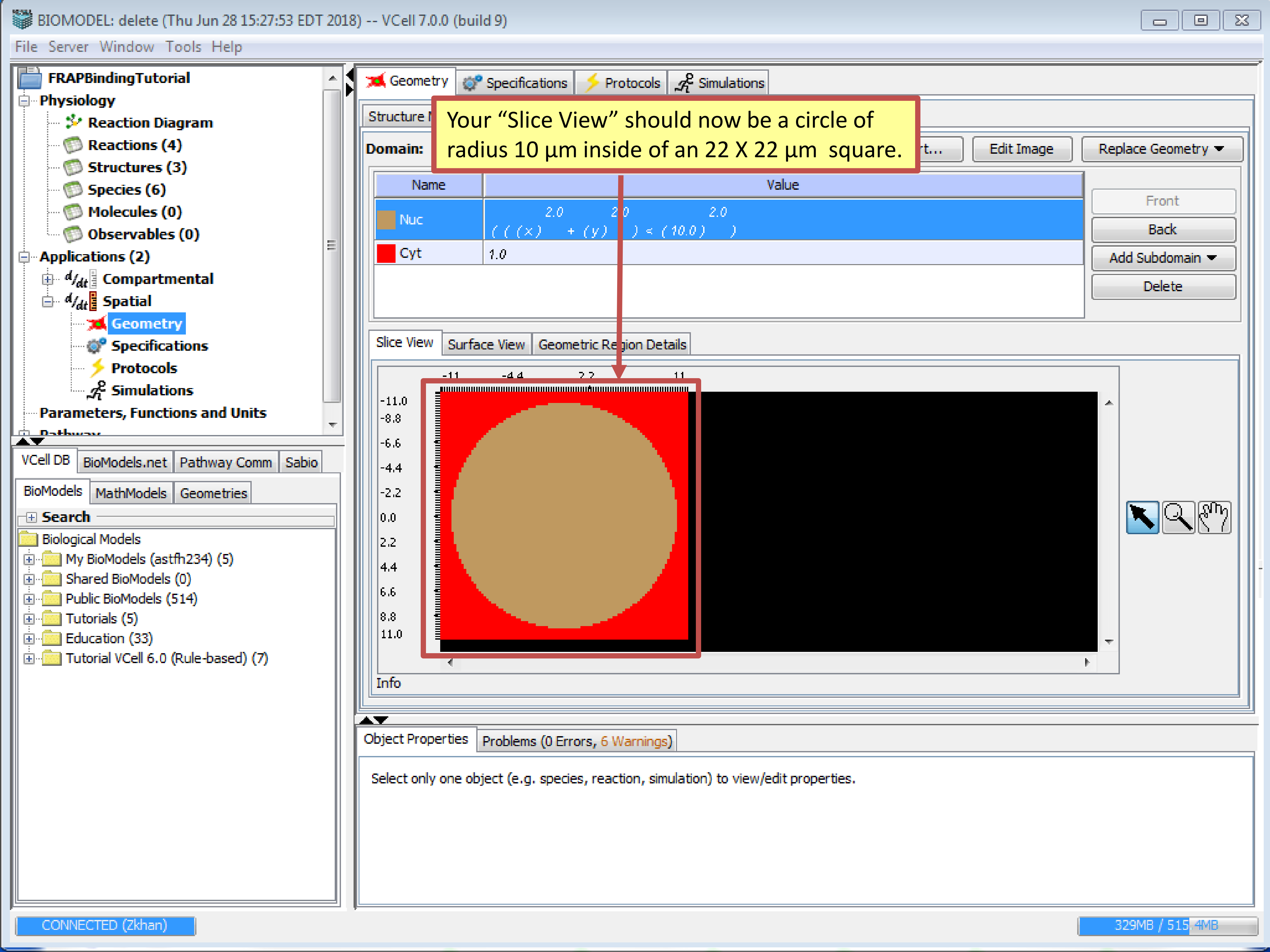
Origin X -11 µm Y -11 µm Z 0

OK Cancel

Next to "Size", type "22" for X and Y.

Next to "Origin", type "-11" for X and Y.

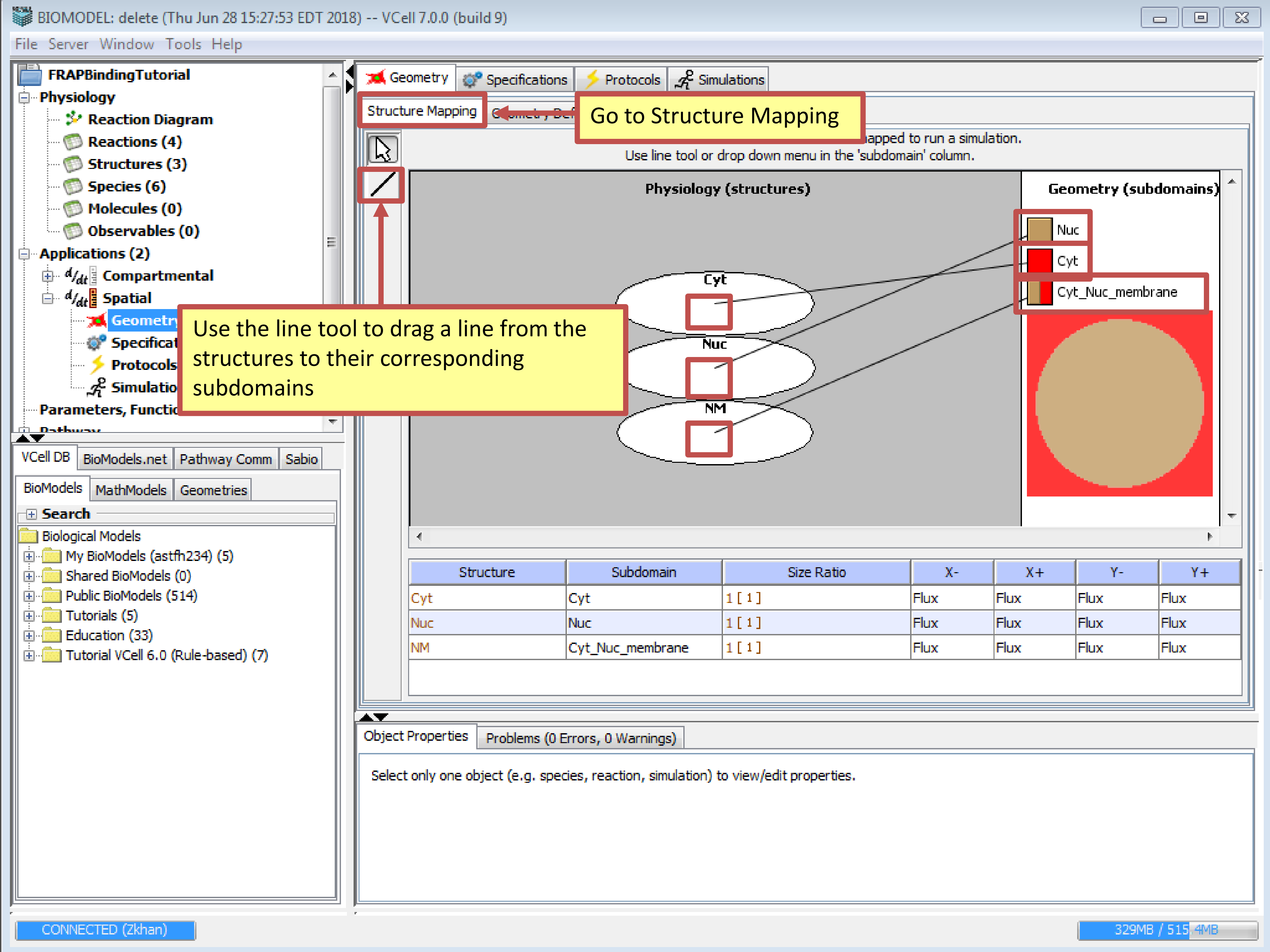
Click "OK".



Your “Slice View” should now be a circle of radius 10 µm inside of an 22 X 22 µm square.

Name	Value
Nuc	$(((x)^{2.0} + (y)^{2.0}) < (10.0)^{2.0})$
Cyt	1.0

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



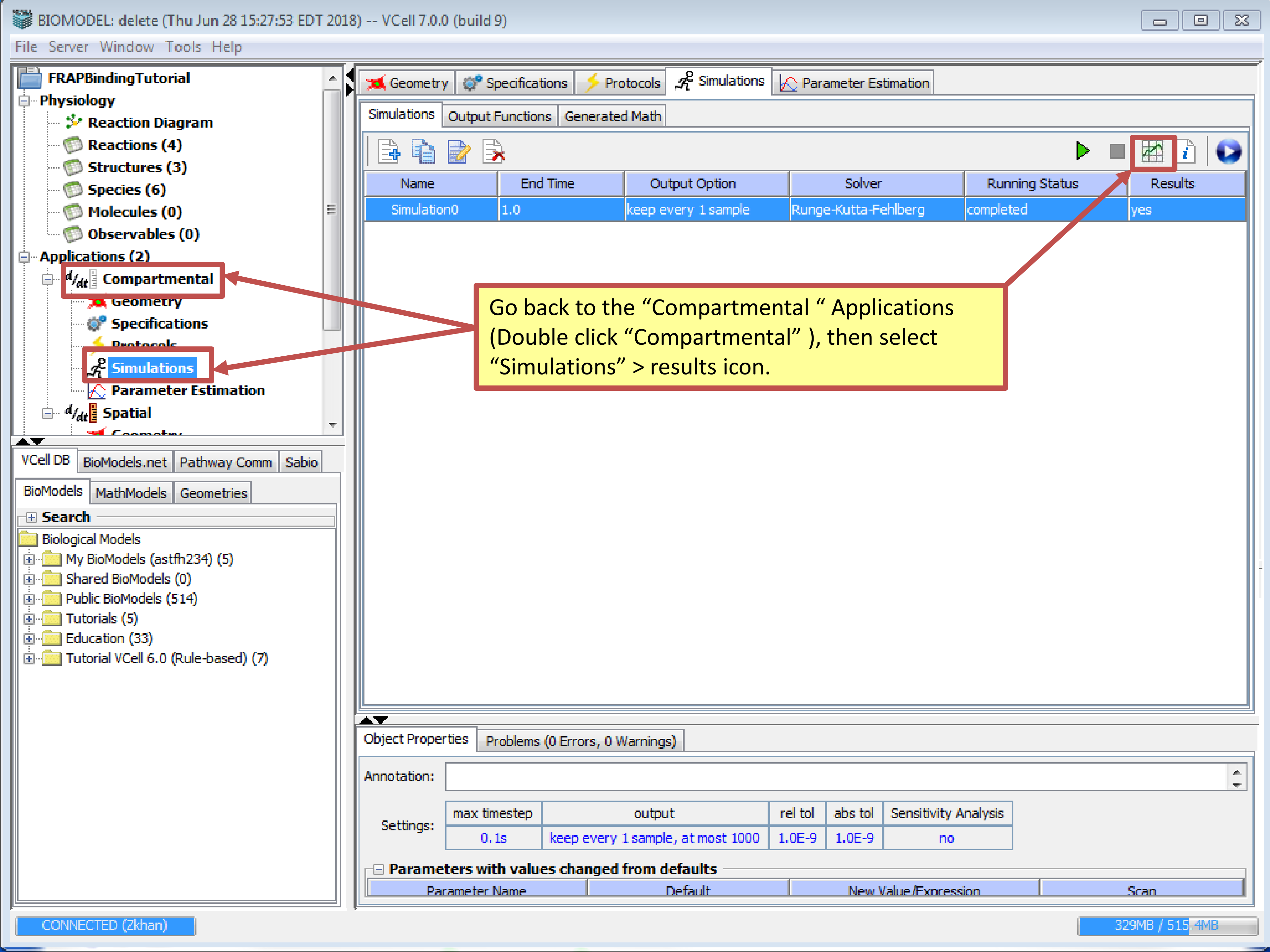
Go to Structure Mapping

Use the line tool to drag a line from the structures to their corresponding subdomains

apped to run a simulation.
Use line tool or drop down menu in the 'subdomain' column.

Structure	Subdomain	Size Ratio	X-	X+	Y-	Y+
Cyt	Cyt	1 [1]	Flux	Flux	Flux	Flux
Nuc	Nuc	1 [1]	Flux	Flux	Flux	Flux
NM	Cyt_Nuc_membrane	1 [1]	Flux	Flux	Flux	Flux

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



Go back to the “Compartmental “ Applications (Double click “Compartmental”), then select “Simulations” > results icon.

Name	End Time	Output Option	Solver	Running Status	Results
Simulation0	1.0	keep every 1 sample	Runge-Kutta-Fehlberg	completed	yes

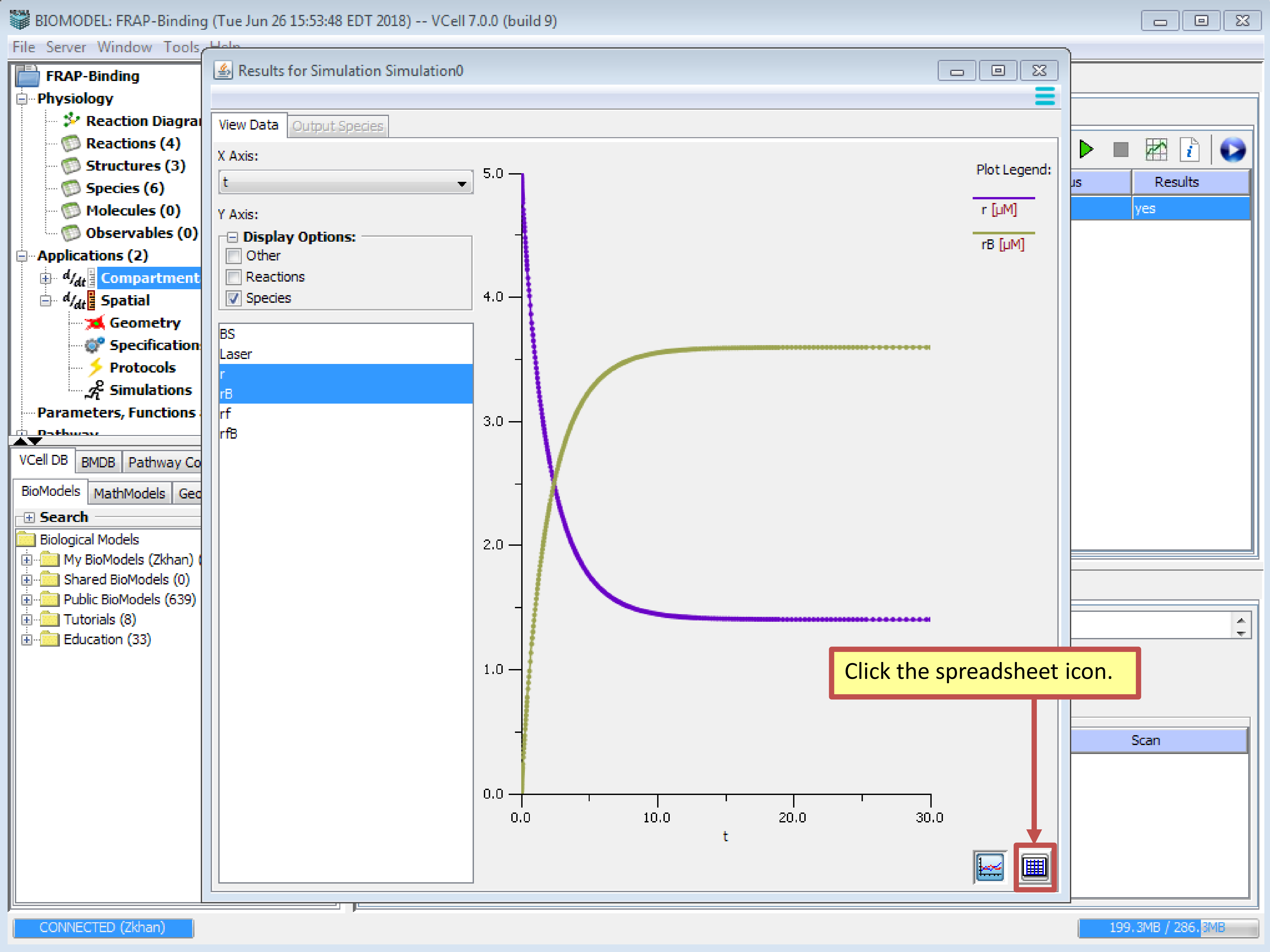
Annotation:

Settings:

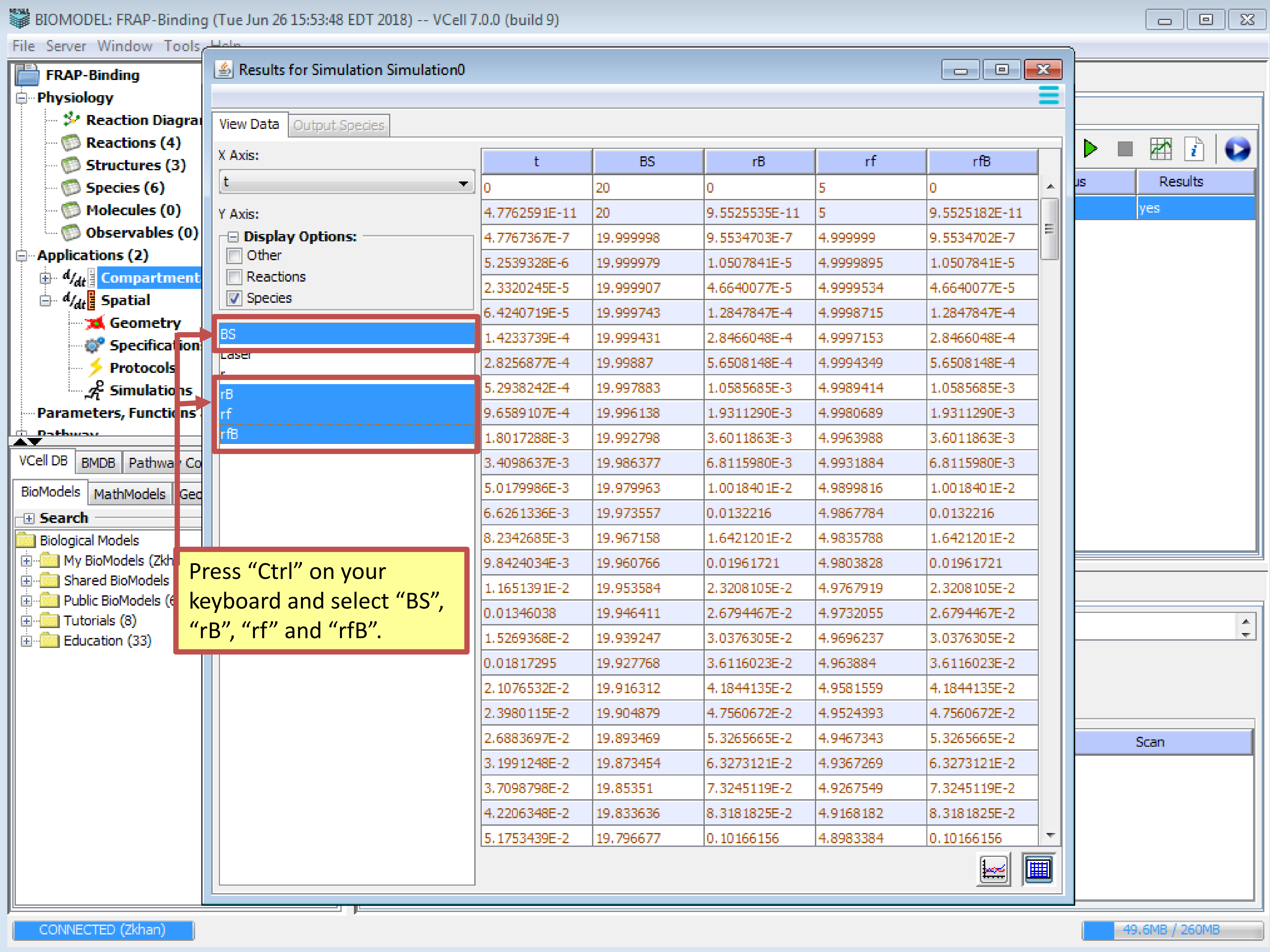
max timestep	output	rel tol	abs tol	Sensitivity Analysis
0.1s	keep every 1 sample, at most 1000	1.0E-9	1.0E-9	no

Parameters with values changed from defaults

Parameter Name	Default	New Value/Expression	Scan



Click the spreadsheet icon.



X Axis: t

Y Axis:

Display Options:

☐ Other

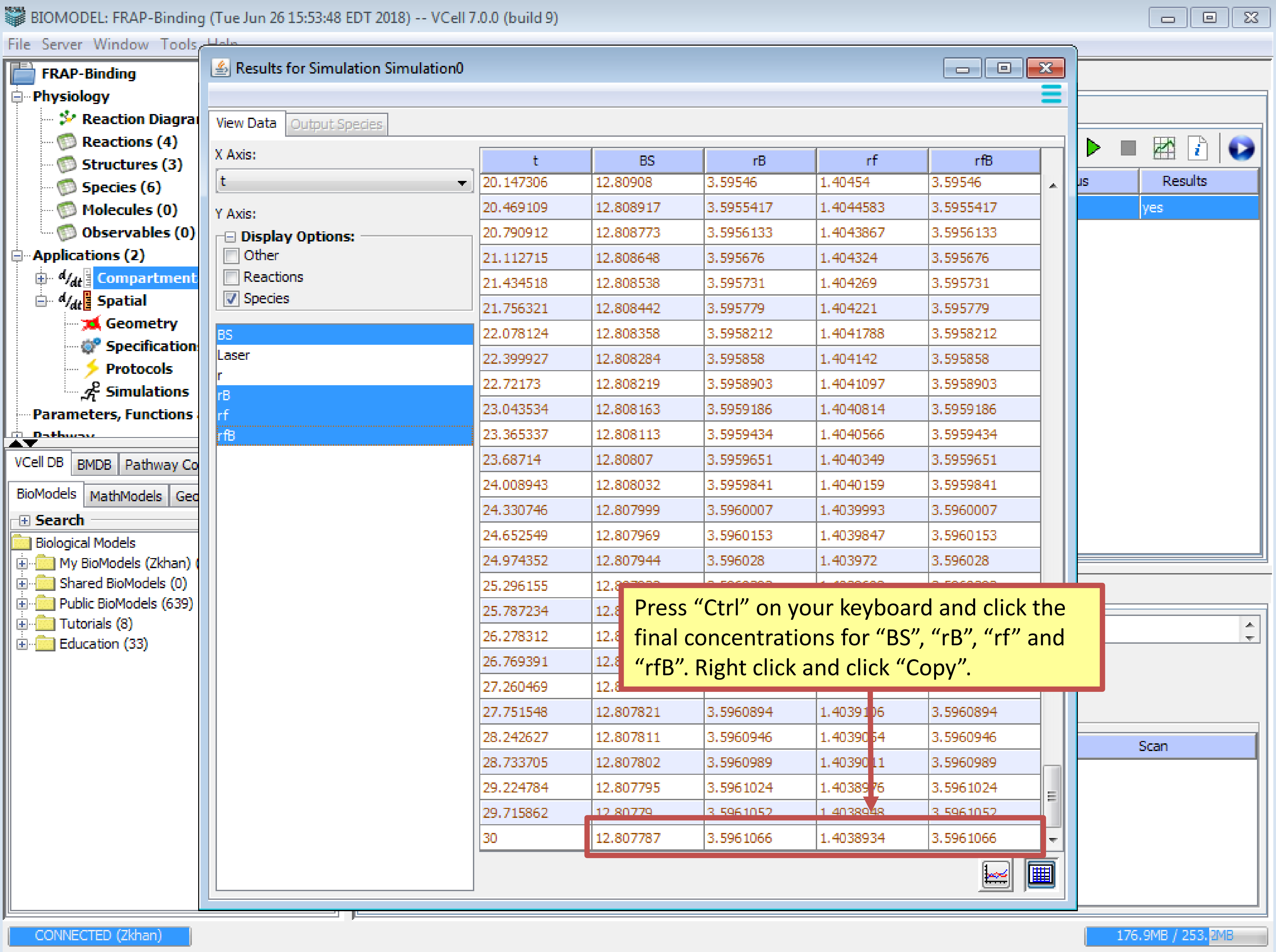
☐ Reactions

☑ Species

BS
Laser
r
rB
rf
rfB

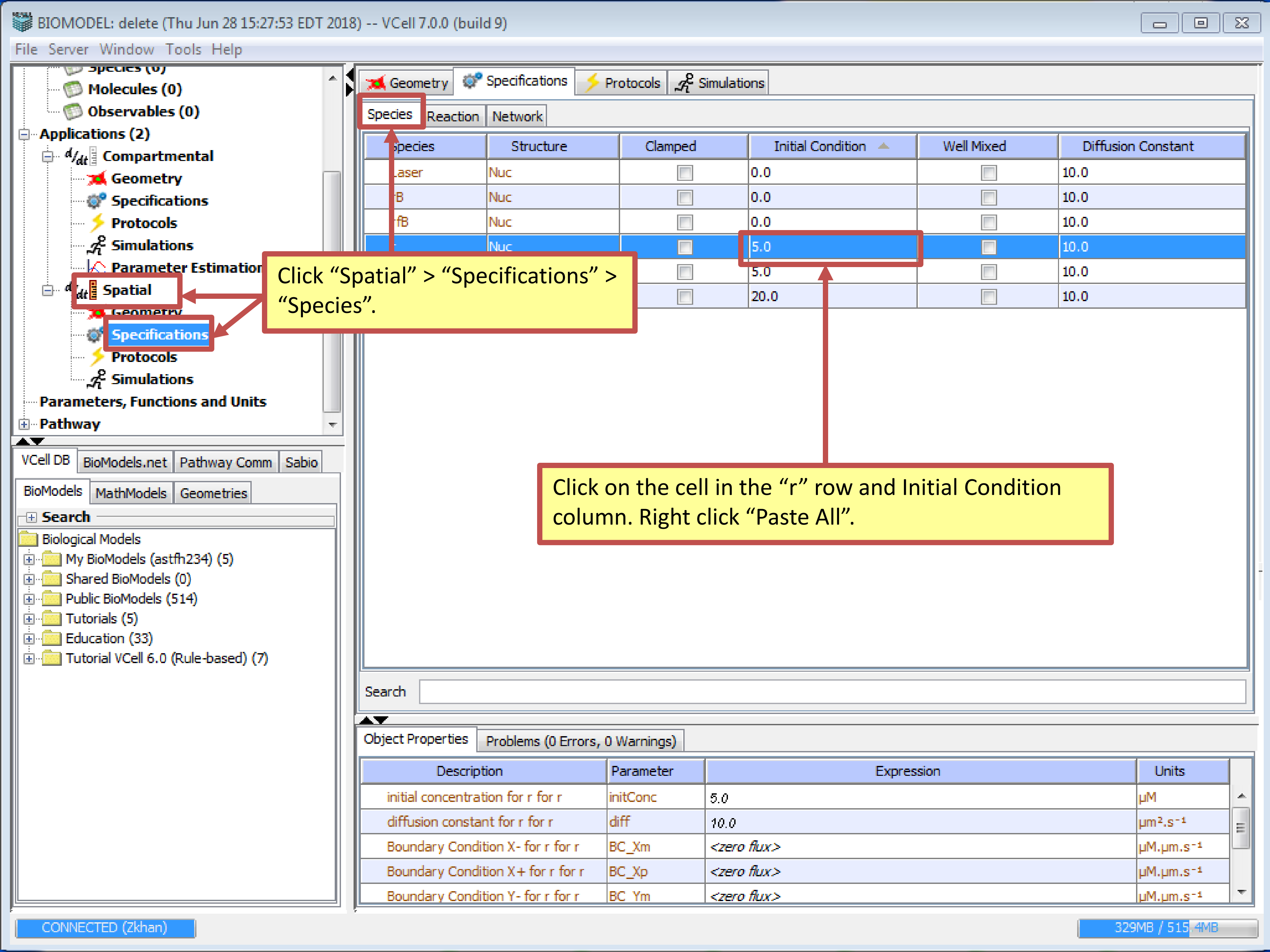
t	BS	rB	rf	rfB
0	20	0	5	0
4.7762591E-11	20	9.5525535E-11	5	9.5525182E-11
4.7767367E-7	19.999998	9.5534703E-7	4.999999	9.5534702E-7
5.2539328E-6	19.999979	1.0507841E-5	4.9999895	1.0507841E-5
2.3320245E-5	19.999907	4.6640077E-5	4.9999534	4.6640077E-5
6.4240719E-5	19.999743	1.2847847E-4	4.9998715	1.2847847E-4
1.4233739E-4	19.999431	2.8466048E-4	4.9997153	2.8466048E-4
2.8256877E-4	19.99887	5.6508148E-4	4.9994349	5.6508148E-4
5.2938242E-4	19.997883	1.0585685E-3	4.9989414	1.0585685E-3
9.6589107E-4	19.996138	1.9311290E-3	4.9980689	1.9311290E-3
1.8017288E-3	19.992798	3.6011863E-3	4.9963988	3.6011863E-3
3.4098637E-3	19.986377	6.8115980E-3	4.9931884	6.8115980E-3
5.0179986E-3	19.979963	1.0018401E-2	4.9899816	1.0018401E-2
6.6261336E-3	19.973557	0.0132216	4.9867784	0.0132216
8.2342685E-3	19.967158	1.6421201E-2	4.9835788	1.6421201E-2
9.8424034E-3	19.960766	0.01961721	4.9803828	0.01961721
1.1651391E-2	19.953584	2.3208105E-2	4.9767919	2.3208105E-2
0.01346038	19.946411	2.6794467E-2	4.9732055	2.6794467E-2
1.5269368E-2	19.939247	3.0376305E-2	4.9696237	3.0376305E-2
0.01817295	19.927768	3.6116023E-2	4.963884	3.6116023E-2
2.1076532E-2	19.916312	4.1844135E-2	4.9581559	4.1844135E-2
2.3980115E-2	19.904879	4.7560672E-2	4.9524393	4.7560672E-2
2.6883697E-2	19.893469	5.3265665E-2	4.9467343	5.3265665E-2
3.1991248E-2	19.873454	6.3273121E-2	4.9367269	6.3273121E-2
3.7098798E-2	19.85351	7.3245119E-2	4.9267549	7.3245119E-2
4.2206348E-2	19.833636	8.3181825E-2	4.9168182	8.3181825E-2
5.1753439E-2	19.796677	0.10166156	4.8983384	0.10166156

Press “Ctrl” on your keyboard and select “BS”, “rB”, “rf” and “rfB”.



t	BS	rB	rf	rfB
20.147306	12.80908	3.59546	1.40454	3.59546
20.469109	12.808917	3.5955417	1.4044583	3.5955417
20.790912	12.808773	3.5956133	1.4043867	3.5956133
21.112715	12.808648	3.595676	1.404324	3.595676
21.434518	12.808538	3.595731	1.404269	3.595731
21.756321	12.808442	3.595779	1.404221	3.595779
22.078124	12.808358	3.5958212	1.4041788	3.5958212
22.399927	12.808284	3.595858	1.404142	3.595858
22.72173	12.808219	3.5958903	1.4041097	3.5958903
23.043534	12.808163	3.5959186	1.4040814	3.5959186
23.365337	12.808113	3.5959434	1.4040566	3.5959434
23.68714	12.80807	3.5959651	1.4040349	3.5959651
24.008943	12.808032	3.5959841	1.4040159	3.5959841
24.330746	12.807999	3.5960007	1.4039993	3.5960007
24.652549	12.807969	3.5960153	1.4039847	3.5960153
24.974352	12.807944	3.596028	1.403972	3.596028
25.296155	12.8[illegible]	[illegible]	[illegible]	[illegible]
25.787234	12.8[illegible]	[illegible]	[illegible]	[illegible]
26.278312	12.8[illegible]	[illegible]	[illegible]	[illegible]
26.769391	12.8[illegible]	[illegible]	[illegible]	[illegible]
27.260469	12.8[illegible]	[illegible]	[illegible]	[illegible]
27.751548	12.807821	3.5960894	1.4039[illegible]06	3.5960894
28.242627	12.807811	3.5960946	1.40390[illegible]4	3.5960946
28.733705	12.807802	3.5960989	1.40390[illegible]1	3.5960989
29.224784	12.807795	3.5961024	1.40389[illegible]6	3.5961024
29.715862	12.80779	3.5961052	1.4038948	3.5961052
30	12.807787	3.5961066	1.4038934	3.5961066

Press “Ctrl” on your keyboard and click the final concentrations for “BS”, “rB”, “rf” and “rfB”. Right click and click “Copy”.

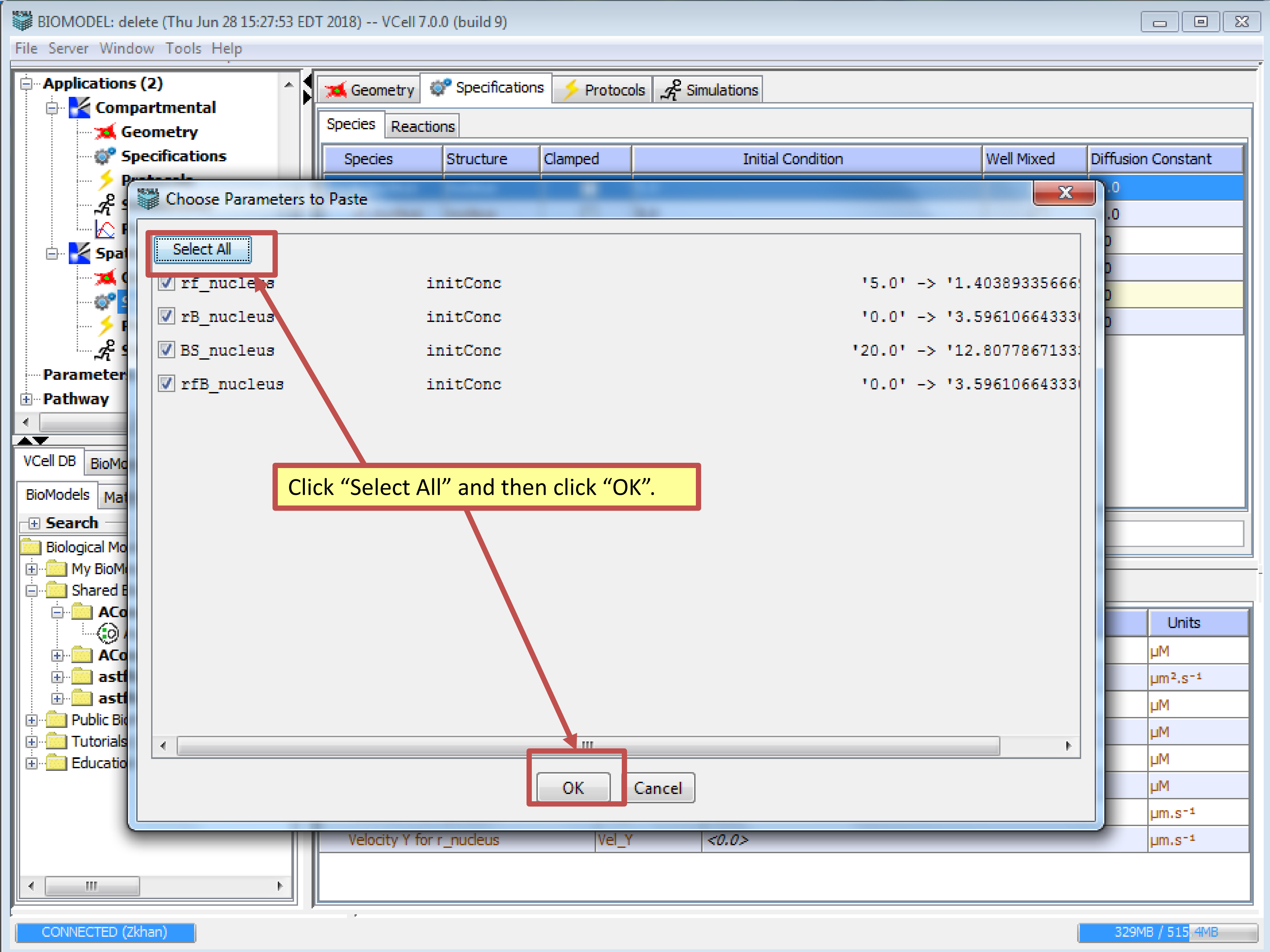


Click “Spatial” > “Specifications” > “Species”.

Click on the cell in the “r” row and Initial Condition column. Right click “Paste All”.

Species	Structure	Clamped	Initial Condition	Well Mixed	Diffusion Constant
Laser	Nuc	☐	0.0	☐	10.0
B	Nuc	☐	0.0	☐	10.0
fB	Nuc	☐	0.0	☐	10.0
	Nuc	☐	5.0	☐	10.0
		☐	5.0	☐	10.0
		☐	20.0	☐	10.0

Description	Parameter	Expression	Units
initial concentration for r for r	initConc	5.0	µM
diffusion constant for r for r	diff	10.0	µm².s⁻¹
Boundary Condition X- for r for r	BC_Xm	<zero flux>	µM.µm.s⁻¹
Boundary Condition X+ for r for r	BC_Xp	<zero flux>	µM.µm.s⁻¹
Boundary Condition Y- for r for r	BC_Ym	<zero flux>	µM.µm.s⁻¹



BIOMODEL: delete (Thu Jun 28 15:27:53 EDT 2018) -- VCell 7.0.0 (build 9)

Choose Parameters to Paste

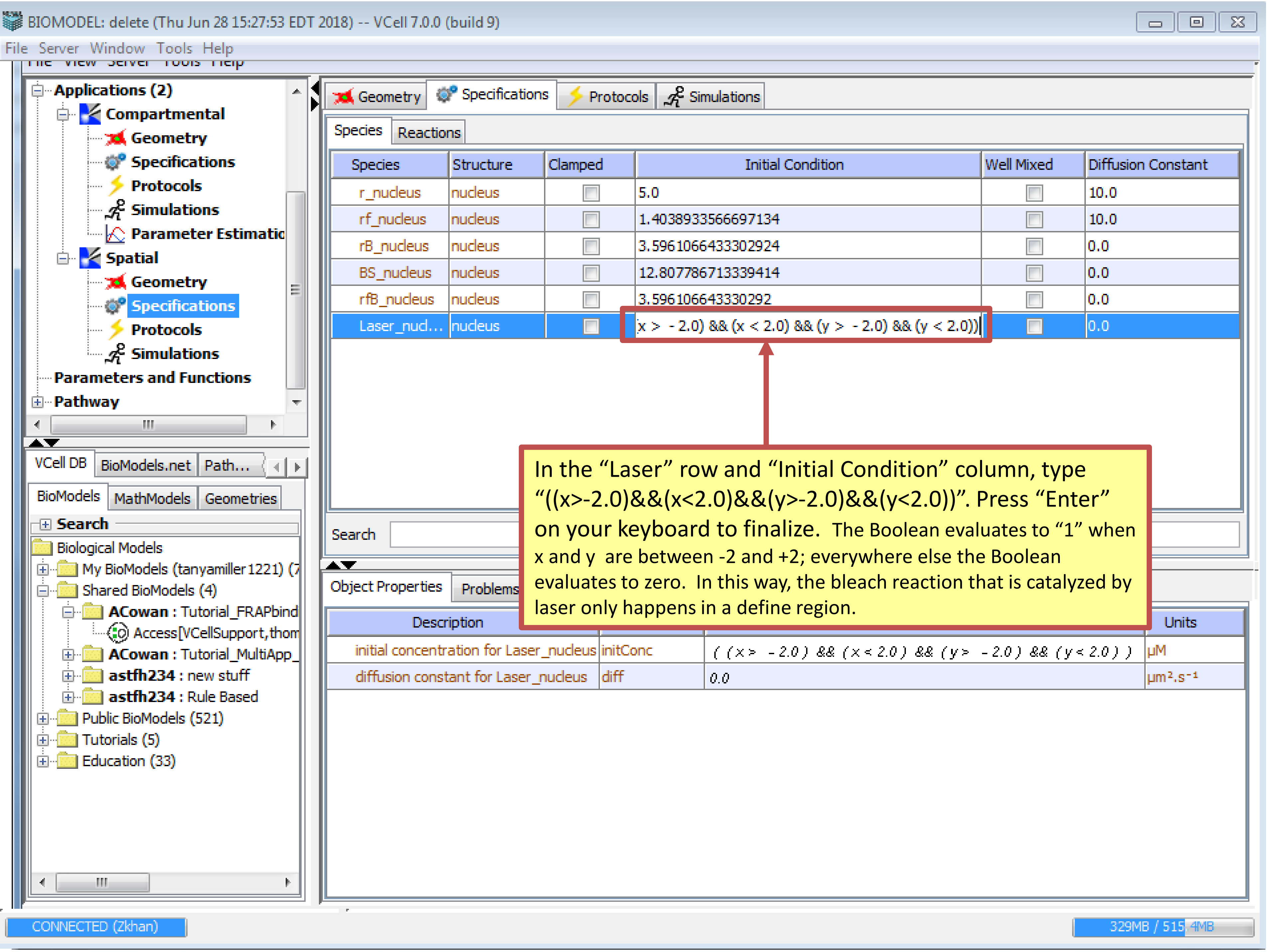
☑ rf_nucleus initConc '5.0' -> '1.40389335666

☑ rB_nucleus initConc '0.0' -> '3.59610664333

☑ BS_nucleus initConc '20.0' -> '12.8077867133

☑ rfB_nucleus initConc '0.0' -> '3.59610664333

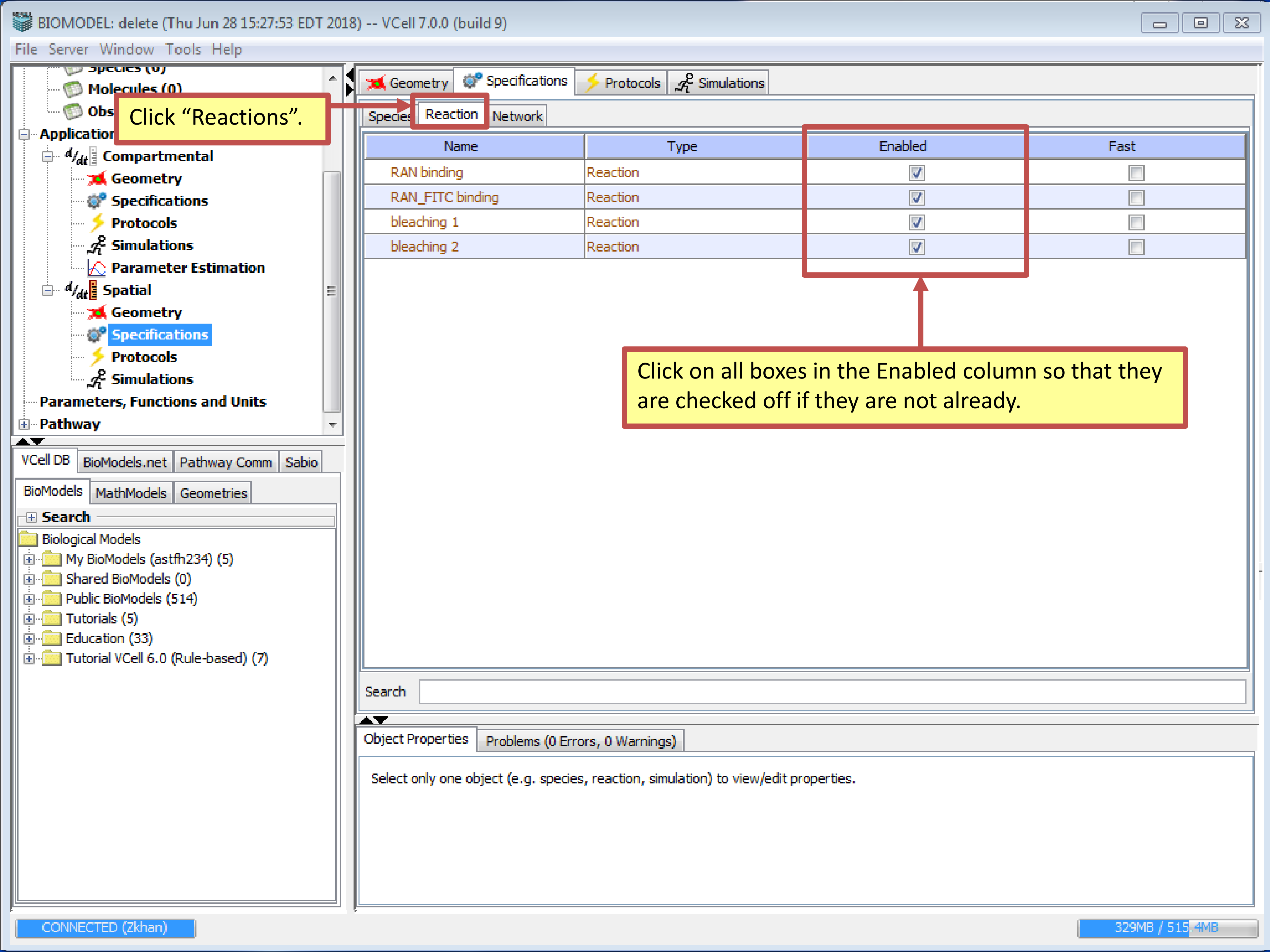
Click “Select All” and then click “OK”.



Species	Structure	Clamped	Initial Condition	Well Mixed	Diffusion Constant
r_nucleus	nucleus	☐	5.0	☐	10.0
rf_nucleus	nucleus	☐	1.4038933566697134	☐	10.0
rB_nucleus	nucleus	☐	3.5961066433302924	☐	0.0
BS_nucleus	nucleus	☐	12.807786713339414	☐	0.0
rfB_nucleus	nucleus	☐	3.596106643330292	☐	0.0
Laser_nucl…	nucleus	☐	x > - 2.0) && (x < 2.0) && (y > - 2.0) && (y < 2.0))	☐	0.0

In the "Laser" row and "Initial Condition" column, type "((x>-2.0)&&(x<2.0)&&(y>-2.0)&&(y<2.0))". Press "Enter" on your keyboard to finalize. The Boolean evaluates to "1" when x and y are between -2 and +2; everywhere else the Boolean evaluates to zero. In this way, the bleach reaction that is catalyzed by laser only happens in a define region.

Description			Units
initial concentration for Laser_nucleus	initConc	((x > - 2.0) && (x < 2.0) && (y > - 2.0) && (y < 2.0))	μM
diffusion constant for Laser_nucleus	diff	0.0	$\mu m^2.s^{-1}$

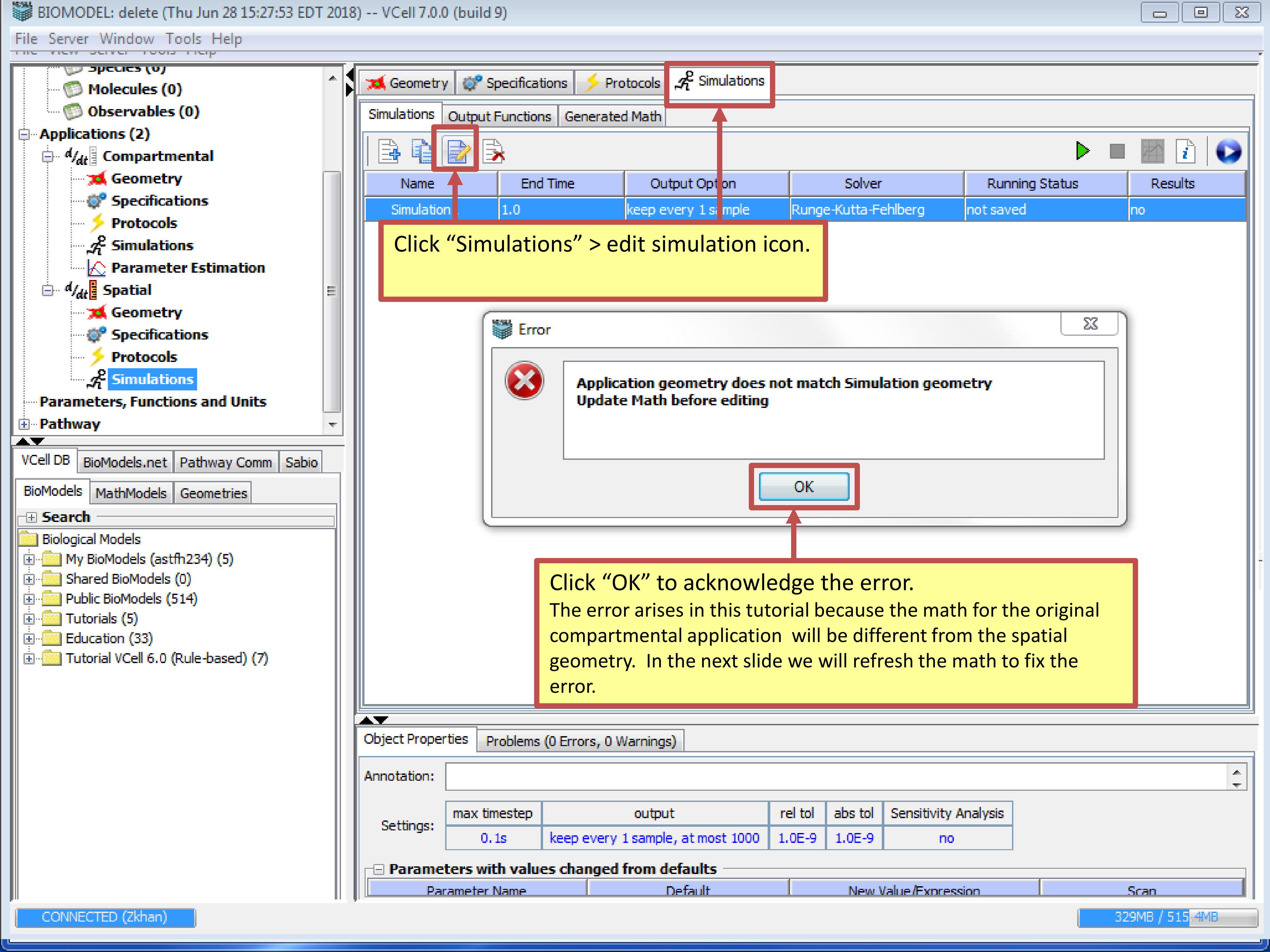


Click “Reactions”.

Name	Type	Enabled	Fast
RAN binding	Reaction	☑	☐
RAN_FITC binding	Reaction	☑	☐
bleaching 1	Reaction	☑	☐
bleaching 2	Reaction	☑	☐

Click on all boxes in the Enabled column so that they are checked off if they are not already.

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



Name	End Time	Output Option	Solver	Running Status	Results
Simulation	1.0	keep every 1 sample	Runge-Kutta-Fehlberg	not saved	no

Click “Simulations” > edit simulation icon.

Error

Application geometry does not match Simulation geometry
Update Math before editing

OK

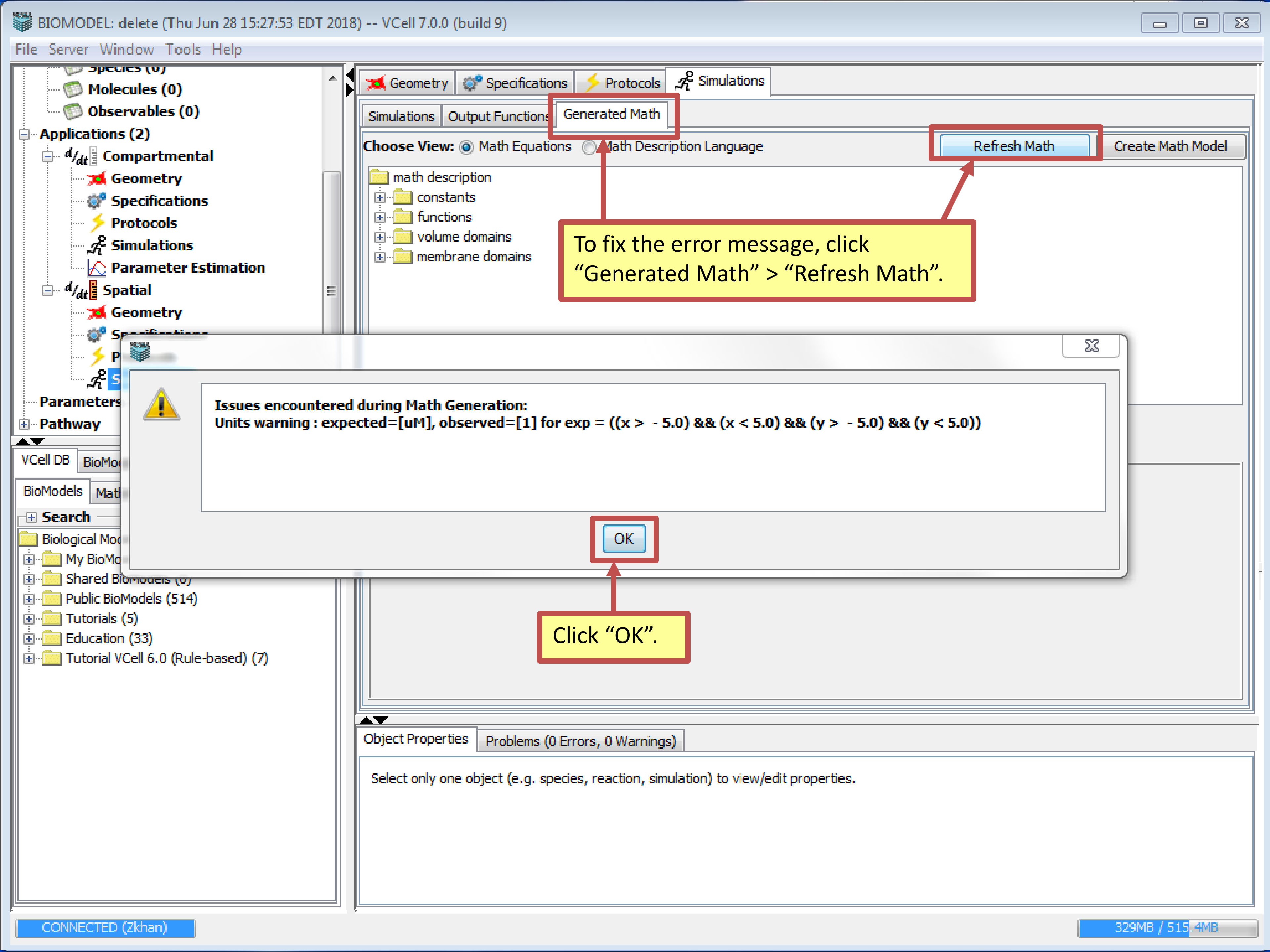
Click “OK” to acknowledge the error.
The error arises in this tutorial because the math for the original compartmental application will be different from the spatial geometry. In the next slide we will refresh the math to fix the error.

Annotation:

Settings:

max timestep	output	rel tol	abs tol	Sensitivity Analysis
0.1s	keep every 1 sample, at most 1000	1.0E-9	1.0E-9	no

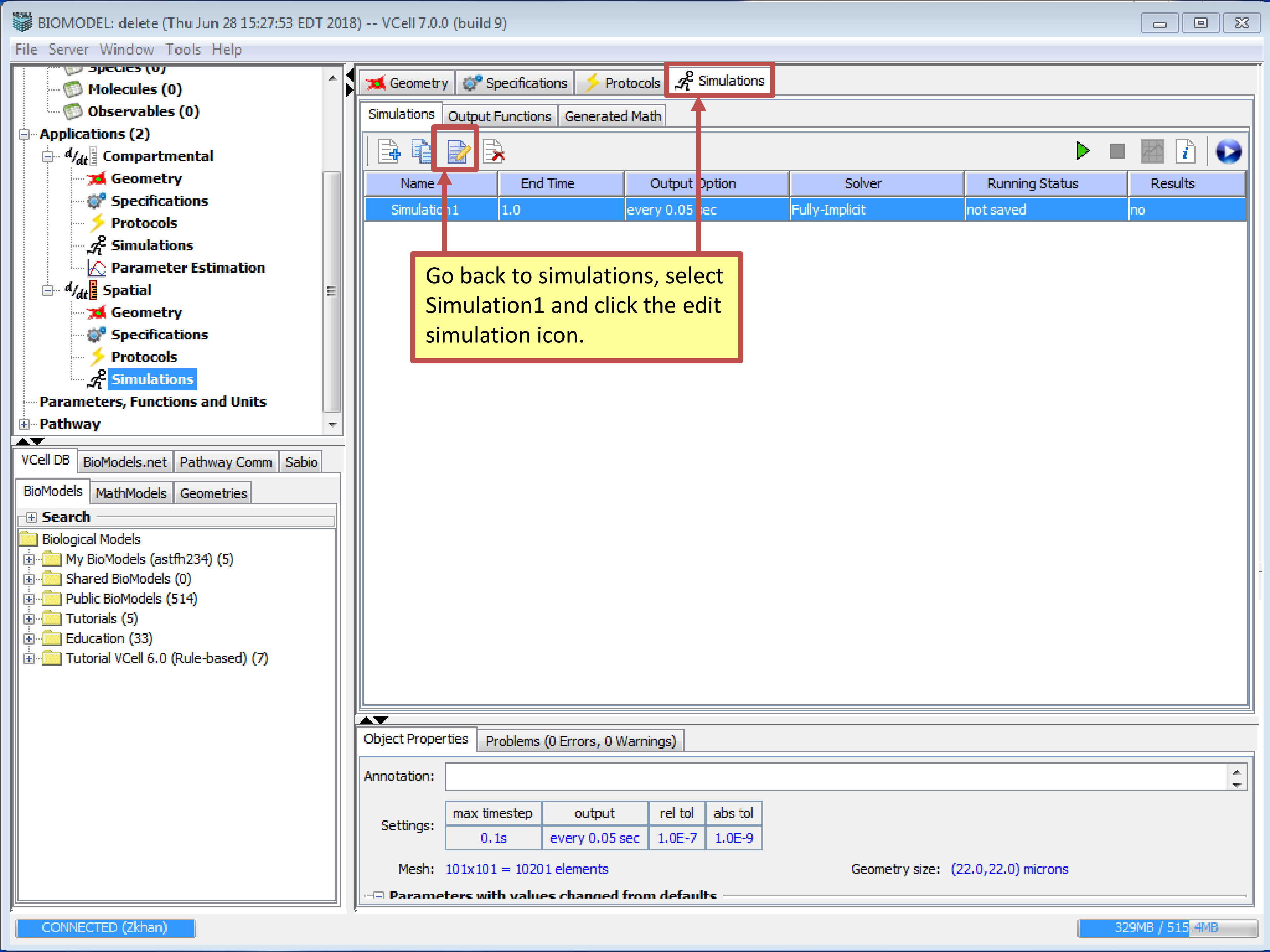
Parameter Name	Default	New Value/Expression	Scan



Issues encountered during Math Generation:
Units warning : expected=[uM], observed=[1] for exp = ((x > - 5.0) && (x < 5.0) && (y > - 5.0) && (y < 5.0))

To fix the error message, click "Generated Math" > "Refresh Math".

Click "OK".



Name	End Time	Output Option	Solver	Running Status	Results
Simulation1	1.0	every 0.05 sec	Fully-Implicit	not saved	no

Go back to simulations, select Simulation1 and click the edit simulation icon.

Annotation:

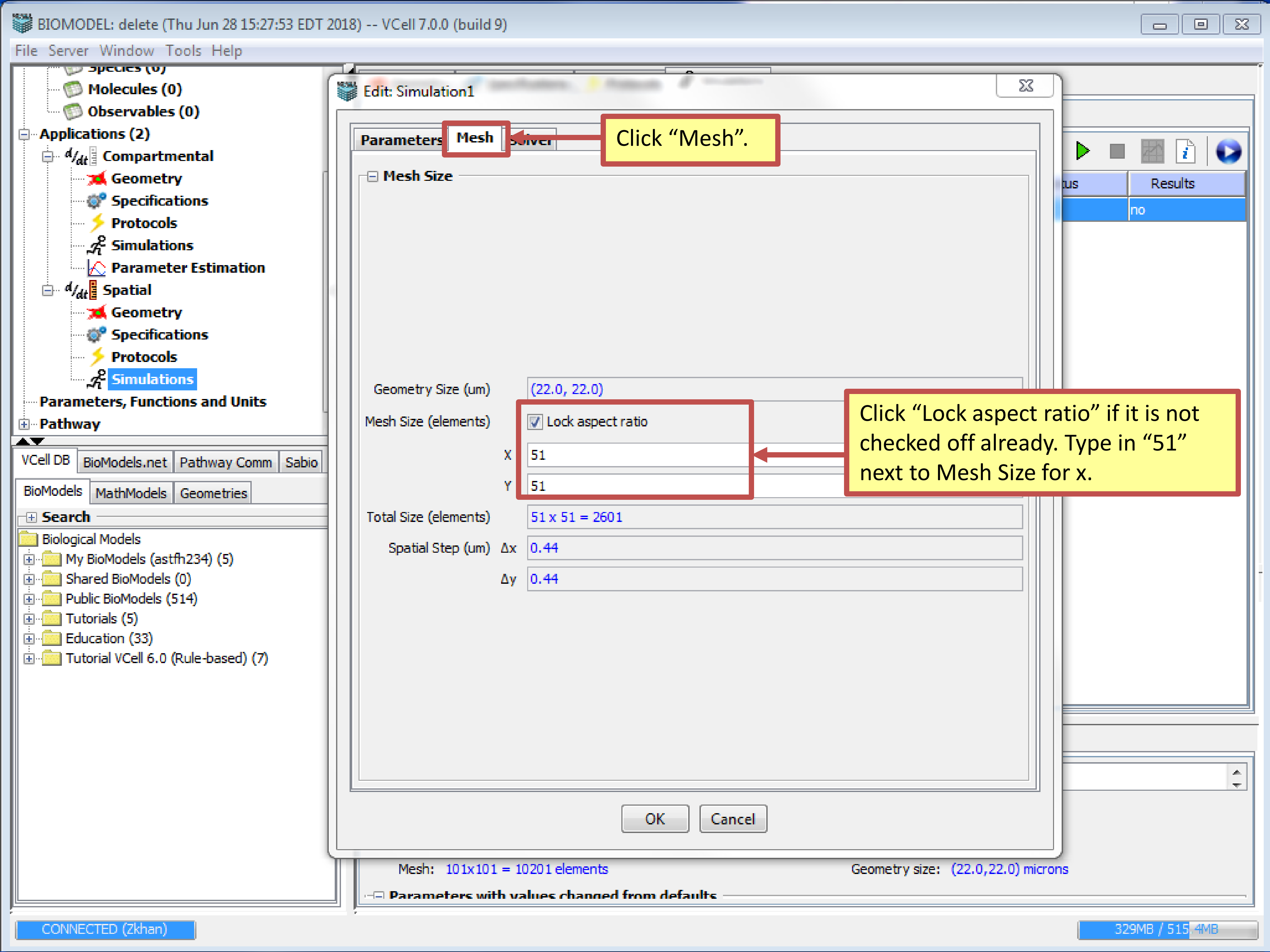
Settings:

max timestep	output	rel tol	abs tol
0.1s	every 0.05 sec	1.0E-7	1.0E-9

Mesh: 101x101 = 10201 elements

Geometry size: (22.0,22.0) microns

Parameters with values changed from defaults



Click “Mesh”.

Geometry Size (um) (22.0, 22.0)

Mesh Size (elements) ☑ Lock aspect ratio

X 51

Y 51

Total Size (elements) 51 x 51 = 2601

Spatial Step (um) Δx 0.44

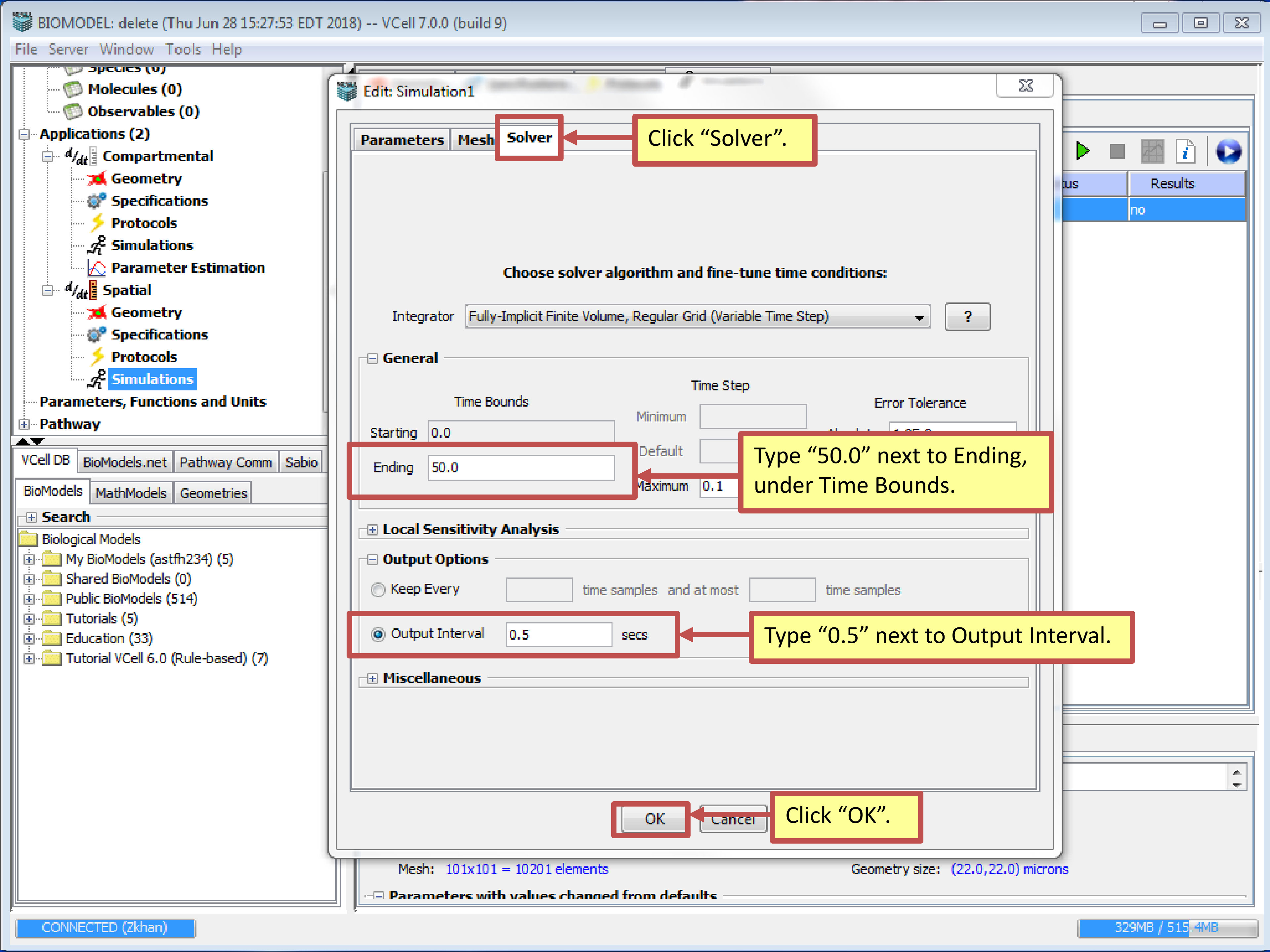
Δy 0.44

Click “Lock aspect ratio” if it is not checked off already. Type in “51” next to Mesh Size for x.

Mesh: 101x101 = 10201 elements

Geometry size: (22.0,22.0) microns

Parameters with values changed from defaults



Choose solver algorithm and fine-tune time conditions:

Integrator: Fully-Implicit Finite Volume, Regular Grid (Variable Time Step)

General

Time Bounds		Time Step		Error Tolerance
Starting	0.0	Minimum		
Ending	50.0	Default		
		Maximum	0.1	

Output Options

○ Keep Every ___ time samples and at most ___ time samples

● Output Interval 0.5 secs

Mesh: 101x101 = 10201 elements Geometry size: (22.0,22.0) microns

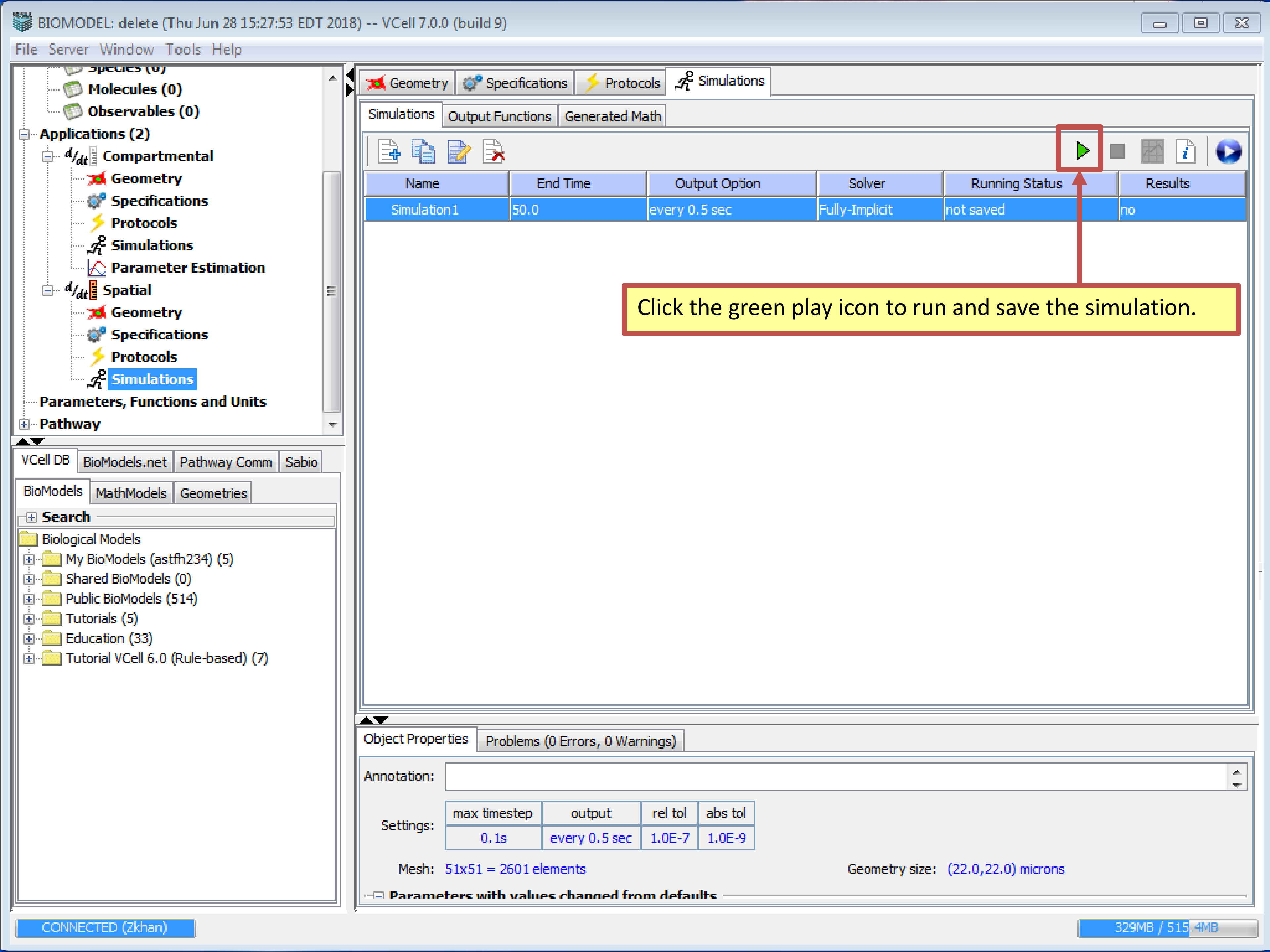
Parameters with values changed from defaults

Click “Solver”.

Type “50.0” next to Ending, under Time Bounds.

Type “0.5” next to Output Interval.

Click “OK”.



Name	End Time	Output Option	Solver	Running Status	Results
Simulation1	50.0	every 0.5 sec	Fully-Implicit	not saved	no

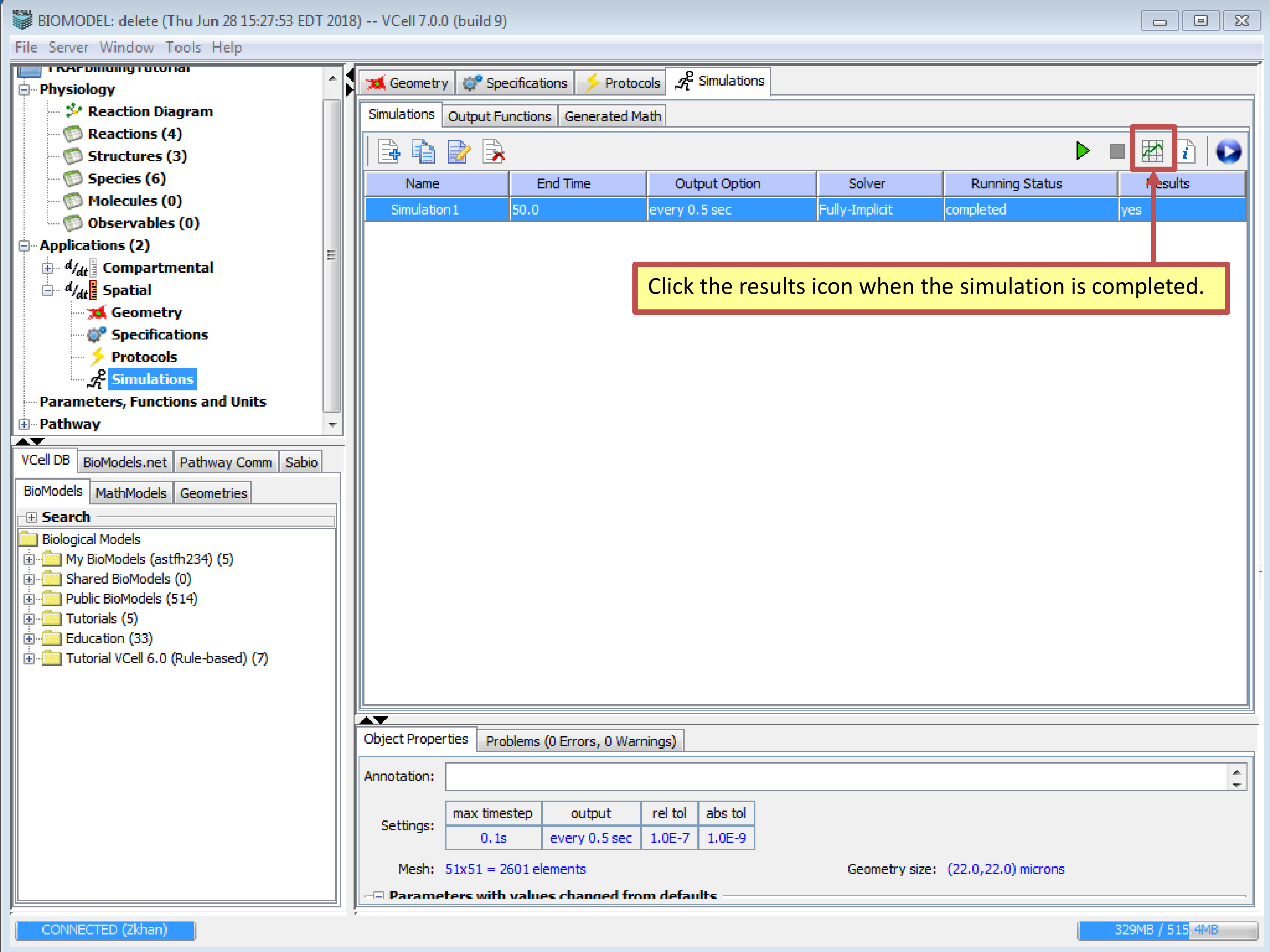
Click the green play icon to run and save the simulation.

Settings:

max timestep	output	rel tol	abs tol
0.1s	every 0.5 sec	1.0E-7	1.0E-9

Mesh: 51x51 = 2601 elements

Geometry size: (22.0,22.0) microns



Name	End Time	Output Option	Solver	Running Status	Results
Simulation1	50.0	every 0.5 sec	Fully-Implicit	completed	yes

Click the results icon when the simulation is completed.

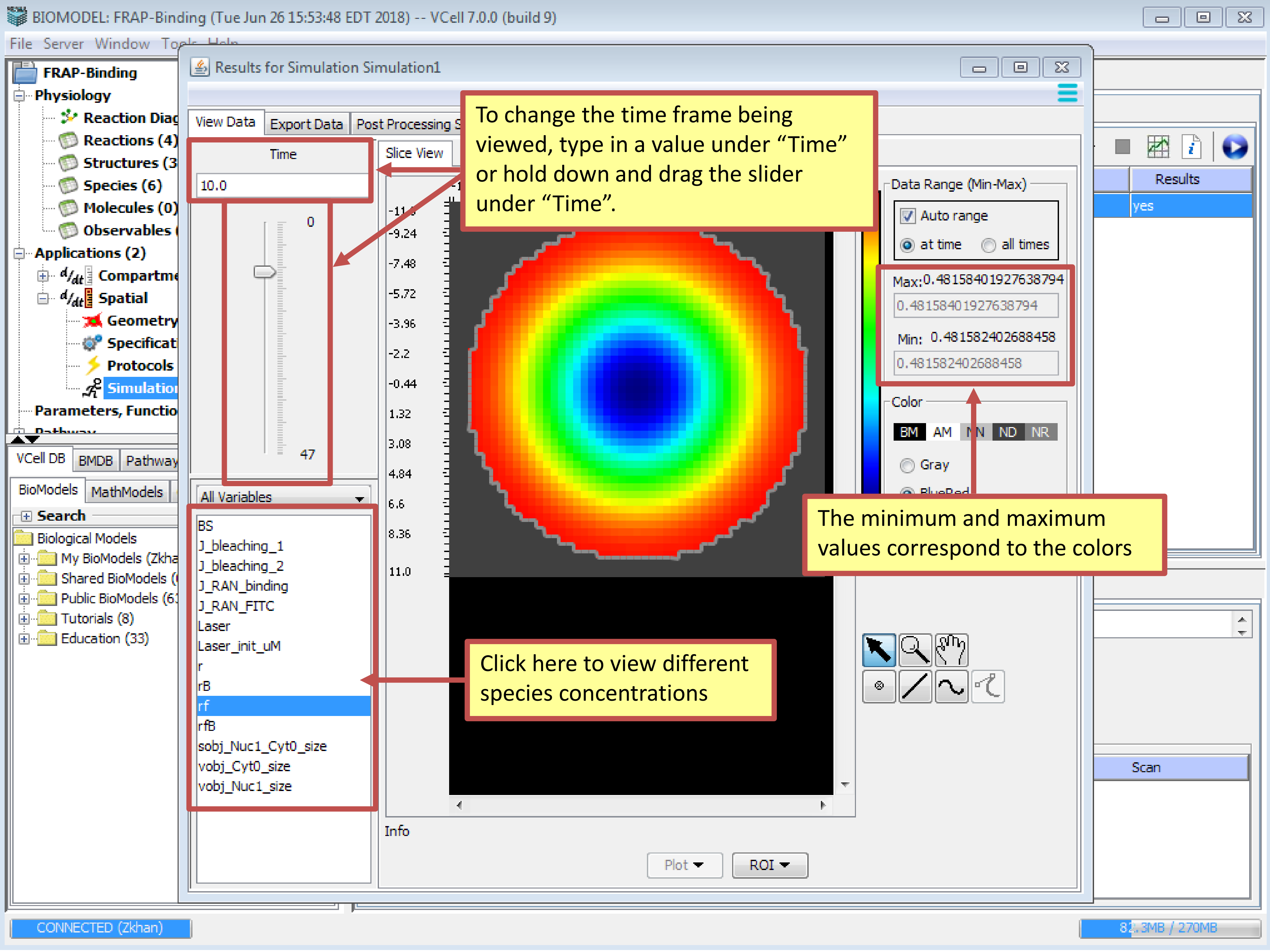
Annotation:

Settings:

max timestep	output	rel tol	abs tol
0.1s	every 0.5 sec	1.0E-7	1.0E-9

Mesh: 51x51 = 2601 elements

Geometry size: (22.0,22.0) microns



BIOMODEL: FRAP-Binding (Tue Jun 26 15:53:48 EDT 2018) -- VCell 7.0.0 (build 9)

Results for Simulation Simulation1

Time: 10.0

Data Range (Min-Max)

☑ Auto range

● at time ○ all times

Max: 0.48158401927638794

Min: 0.481582402688458

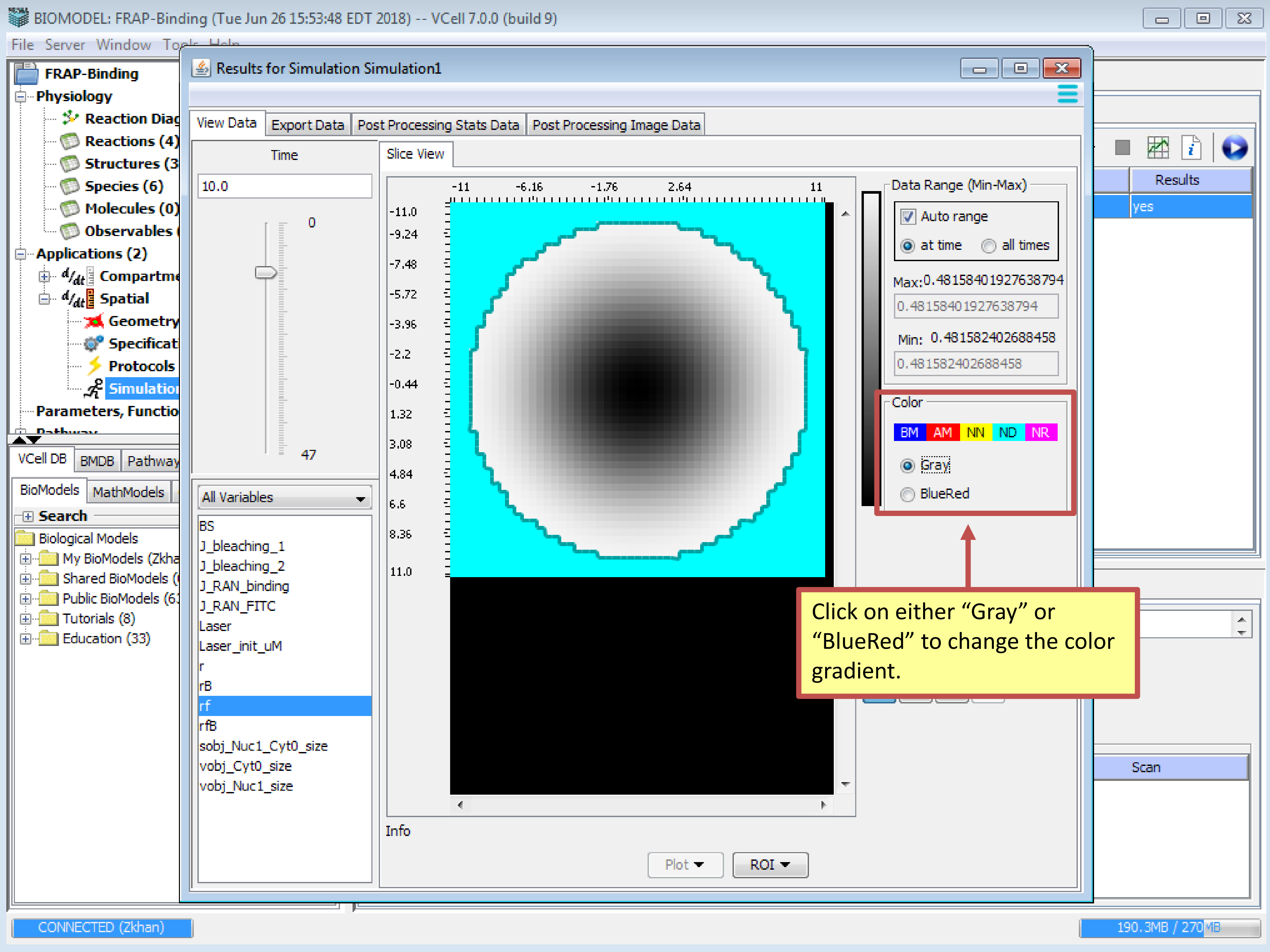
To change the time frame being viewed, type in a value under “Time” or hold down and drag the slider under “Time”.

The minimum and maximum values correspond to the colors

Click here to view different species concentrations

CONNECTED (Zkhan)

81.3MB / 270MB



BIOMODEL: FRAP-Binding (Tue Jun 26 15:53:48 EDT 2018) -- VCell 7.0.0 (build 9)

Results for Simulation Simulation1

Time: 10.0

Data Range (Min-Max)

☑ Auto range

● at time ○ all times

Max: 0.48158401927638794

Min: 0.481582402688458

Color

BM AM NN ND NR

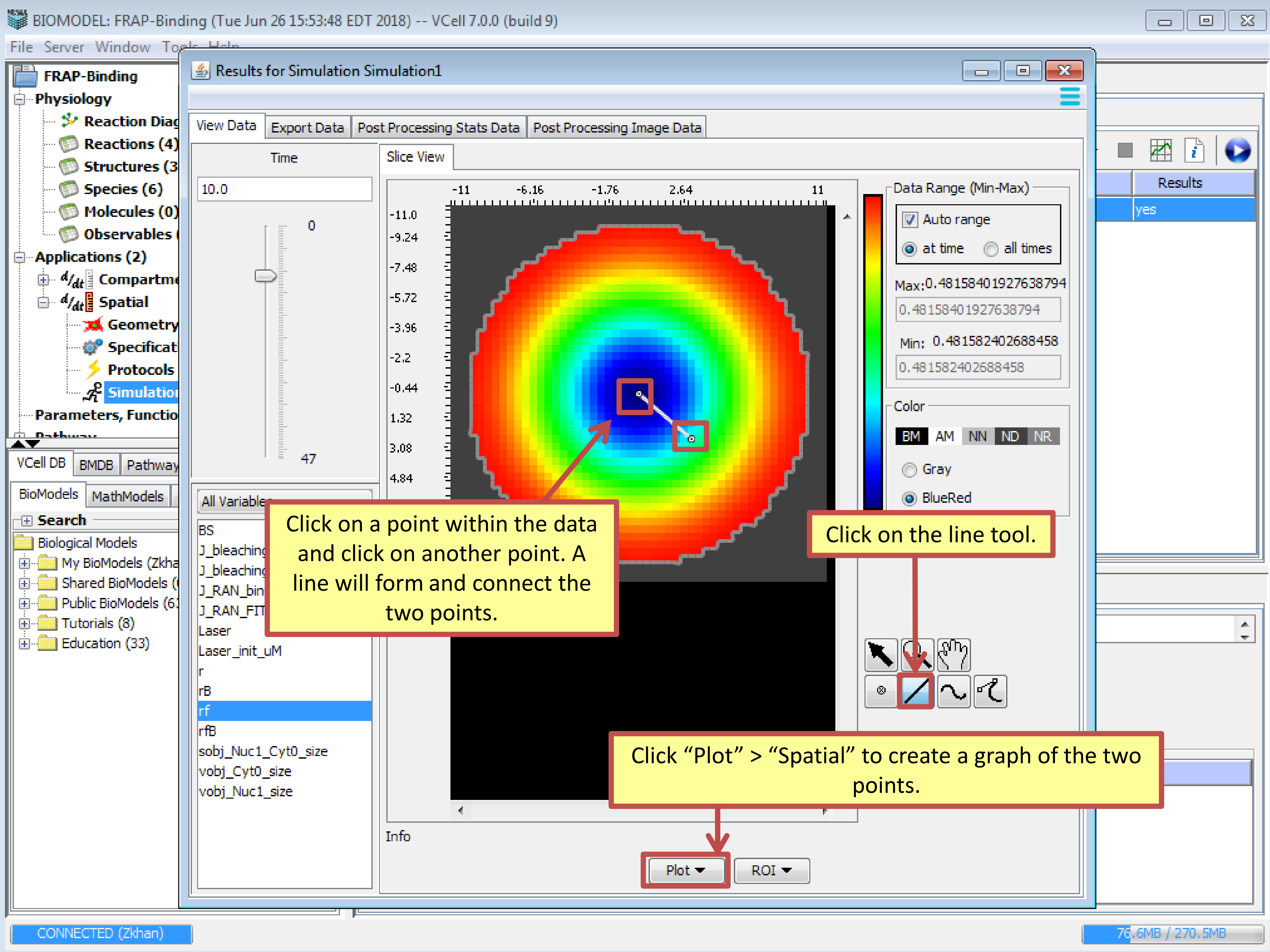
● Gray

○ BlueRed

CONNECTED (Zkhan)

190.3MB / 270MB

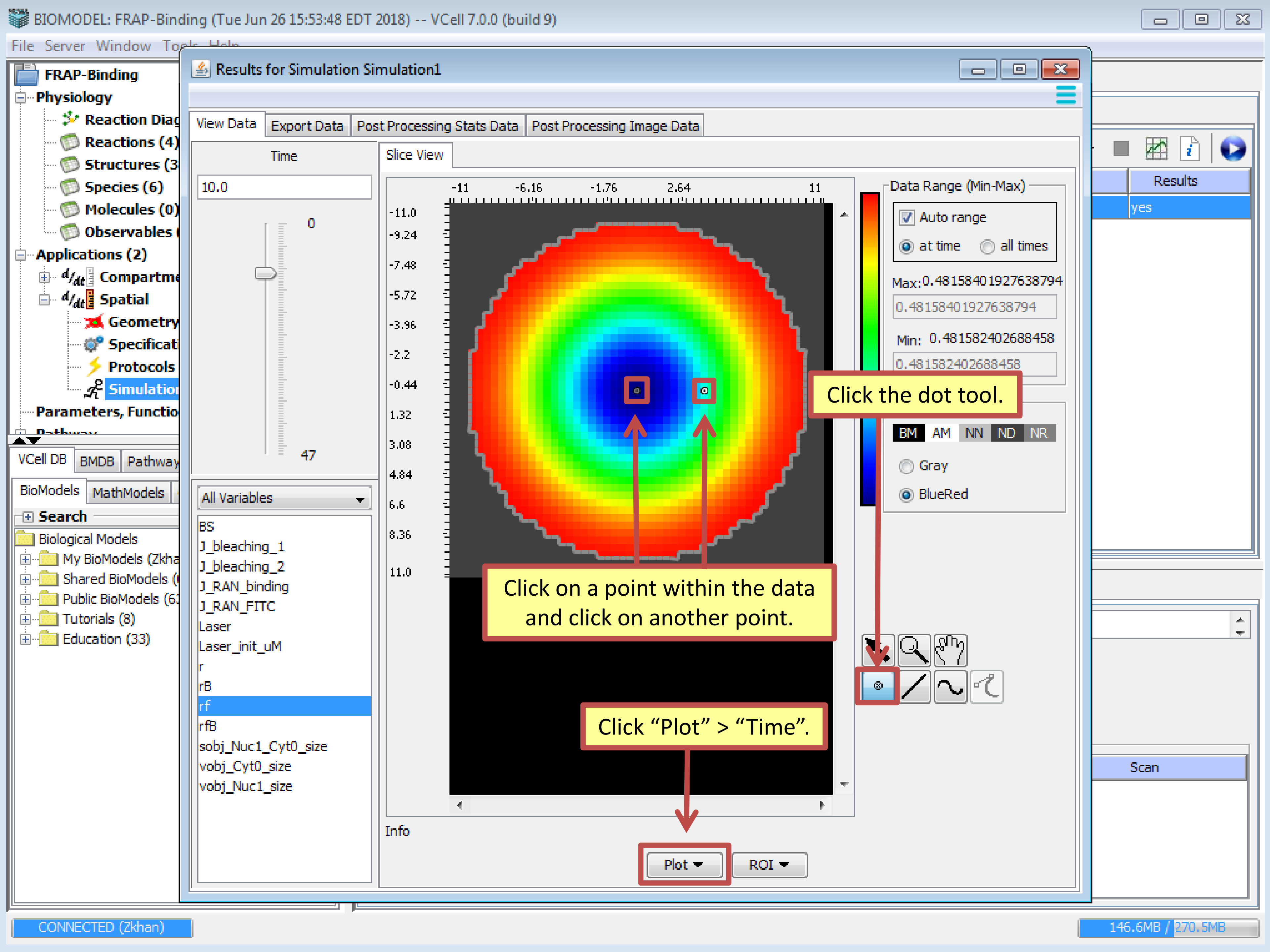
Click on either “Gray” or “BlueRed” to change the color gradient.



Click on a point within the data and click on another point. A line will form and connect the two points.

Click on the line tool.

Click “Plot” > “Spatial” to create a graph of the two points.



BIOMODEL: FRAP-Binding (Tue Jun 26 15:53:48 EDT 2018) -- VCell 7.0.0 (build 9)

Results for Simulation Simulation1

Time: 10.0 (slider 0 – 47)

All Variables

- BS
- J_bleaching_1
- J_bleaching_2
- J_RAN_binding
- J_RAN_FITC
- Laser
- Laser_init_uM
- r
- rB
- rf
- rfB
- sobj_Nuc1_Cyt0_size
- vobj_Cyt0_size
- vobj_Nuc1_size

Data Range (Min-Max)

☑ Auto range

● at time ○ all times

Max: 0.48158401927638794

0.48158401927638794

Min: 0.481582402688458

0.481582402688458

○ Gray

● BlueRed

Results: yes

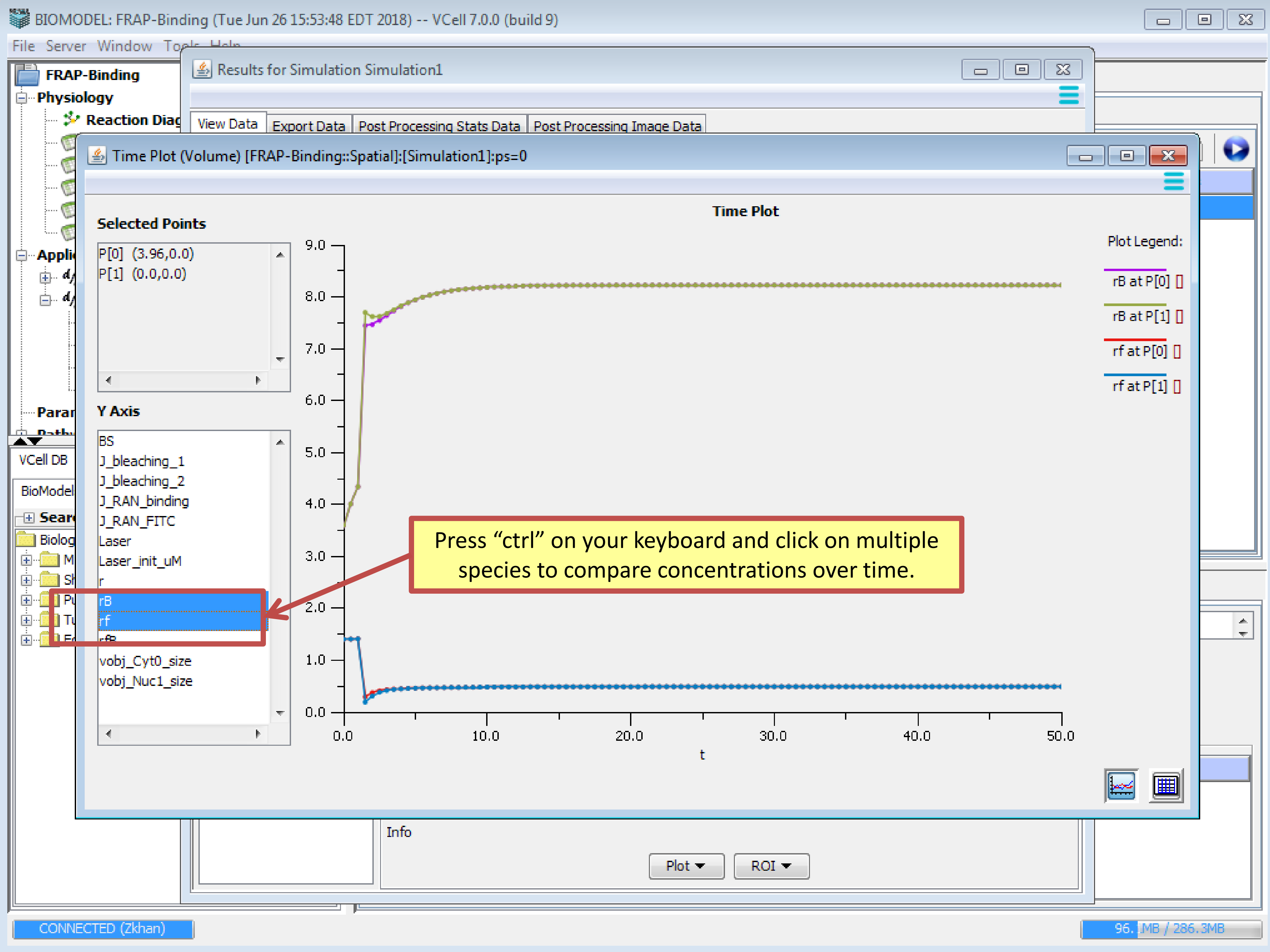
CONNECTED (Zkhan)

146.6MB / 270.5MB

Click the dot tool.

Click on a point within the data and click on another point.

Click “Plot” > “Time”.



Press “ctrl” on your keyboard and click on multiple species to compare concentrations over time.

Acknowledgements

The following students worked on this tutorial:

Tanya Miller (2015) – Pomperaug High School
Nathan Schaumburger (2017) – Hall High School
Arundeep Singh (2018) – Sport and Medical Sciences Academy
Zaiba Khan (2018) – East Windsor High School

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