WTAC Computational Systems Biology for Complex Human Disease 21-26 of April 2024

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The Importance of Interoperability

Objectives

Objective 1: Search for a pathway of interest, download the file in the proper format (sbml, xml), and use the appropriate tool to open it, modify it, and save it (CellDesigner).

Objective 2: Use CaSQ to create an executable file (Boolean model) in different formats (sbml qual and JSON) and complementary files containing different information (sif files).

Objective 3: Import the sbml qual file in two different simulation platforms and perform preliminary experiments (simulations).

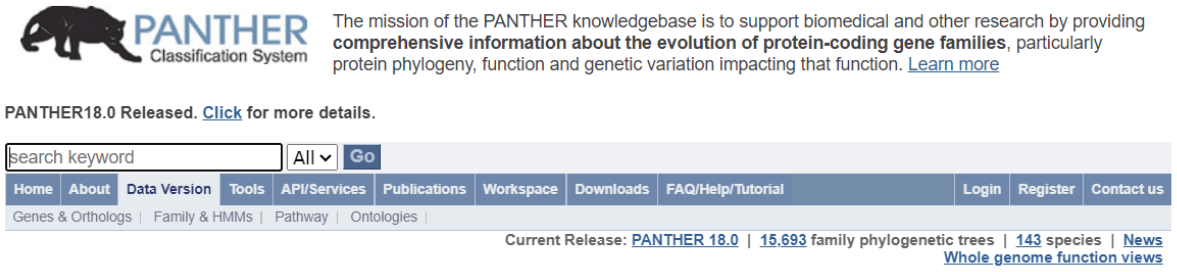
Objective 4: Import the JSON file to a different platform (BMA)

This tutorial links the different model types (static, process description, activity flow, dynamic, and executable) and the tools shown in the course. Each simulation platform has its own detailed tutorial. The purpose here is to focus on interoperability and provide participants with a quick guide to help them in their projects.

Finding a pathway of interest

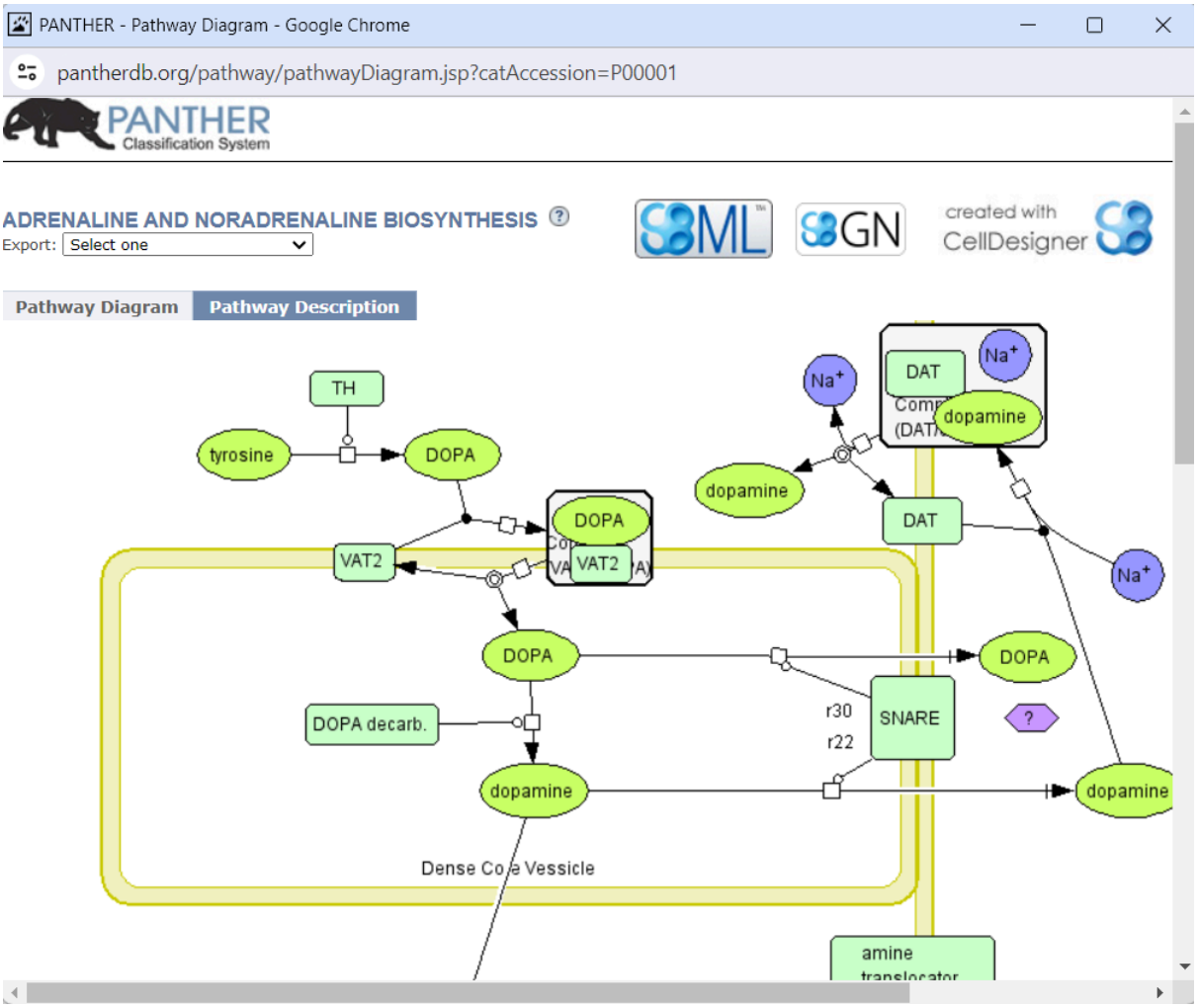
Please go to the Pather DB database
https://www.pantherdb.org/

Then, search for the pathway list by clicking on the Data version tab



Then click on Pathway
And subsequently, click on List of Pathways

Select the pathway Adrenaline and noradrenaline biosynthesis by clicking on it

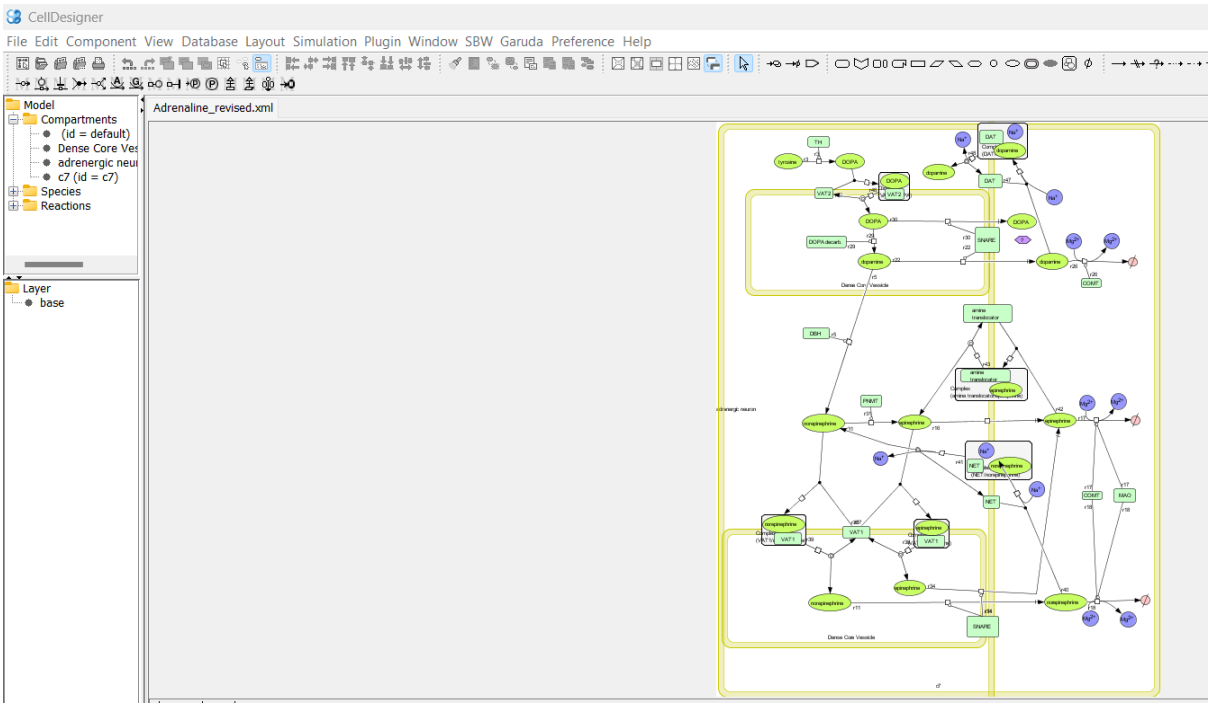


Spend some time to understand the pathway and read the pathway description

Export the pathway in SBML format and save it to your session.
You will notice that it has an xml suffix.

Visualising and modifying the diagram using Cell Designer

Open the Cell Designer tool and open the file.
Select a compartment and surround the graph. Save the file as Adrenaline_revised.xml to your session.



Creating an executable model

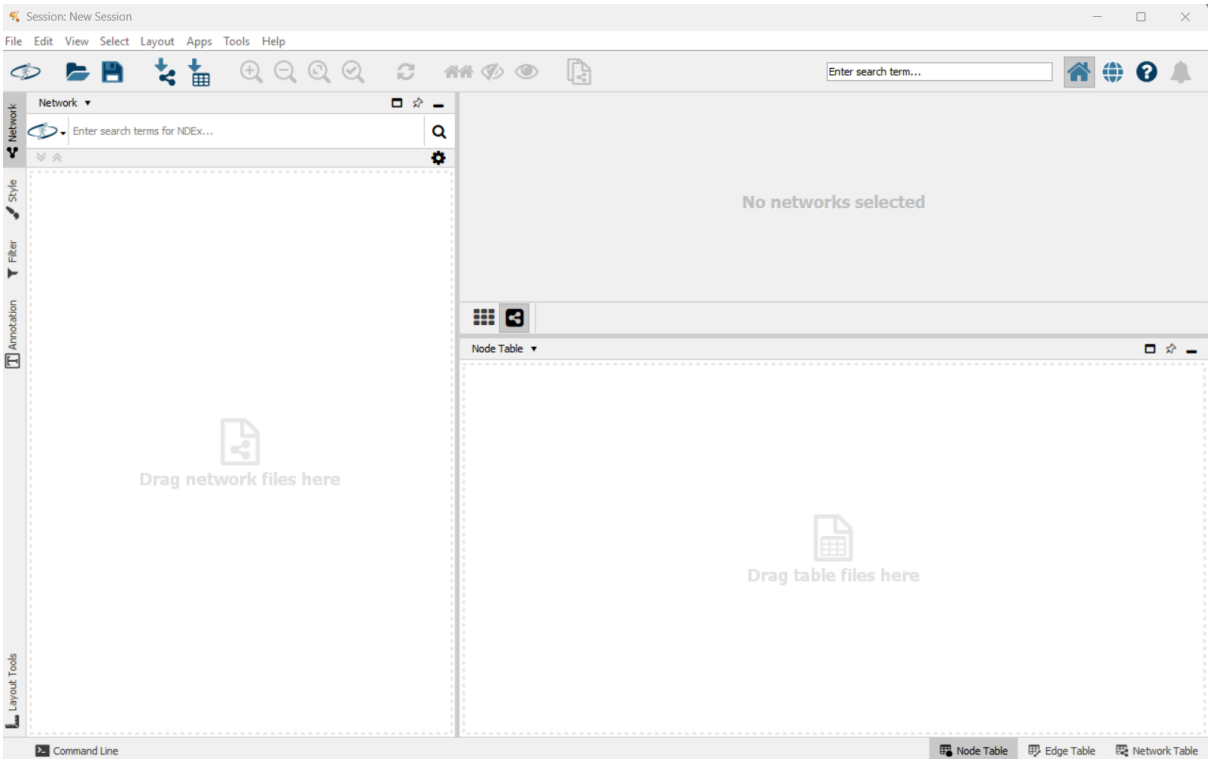
Now open your terminal and type

casq -s Adrenaline_revised/xml Adrenaline_revised.sbml
(here is an example where the drag and drop of the files to the terminal creates the right path automatically)

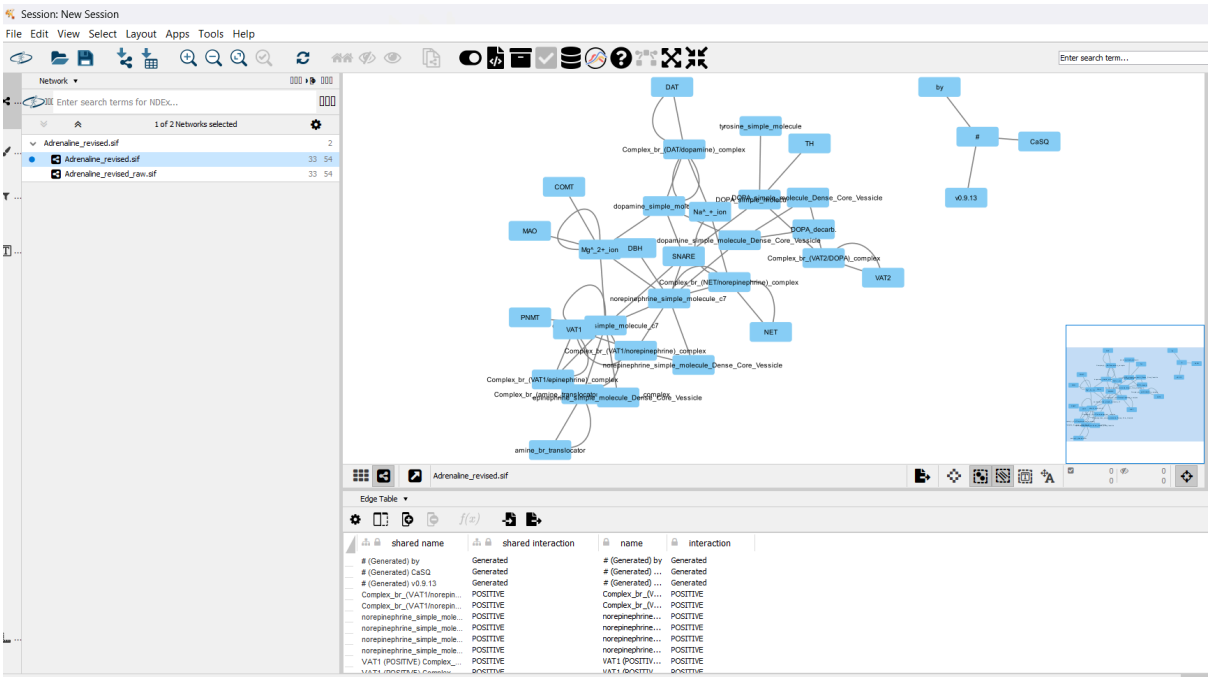
```
C:\Users\aelec> casq -s C:\Users\aelec\Desktop\Adrenaline_revised.xml C:\Users\aelec\Desktop\Adrenaline_revised.sbml
```

This will produce a series of files (sif, raw_sif, sbml).
Look at the sif files and determine what they contain (open them with a text editor).

You can also import your sif files to Cytoscape. Open Cytoscape
(Open the terminal in your VM session, type Cytoscape and hit enter.
Cytoscape will launch a session.



Then click Import network from file and select the Adrenaline_revised.sif file
Then click again and import the Adrenaline_revised.sif file.



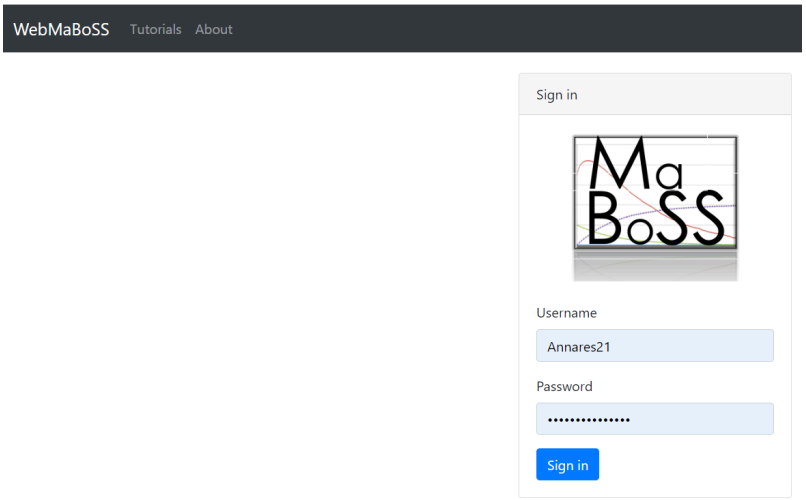
What do you observe?

Using web-based simulation platforms to do *in-silico* experiments

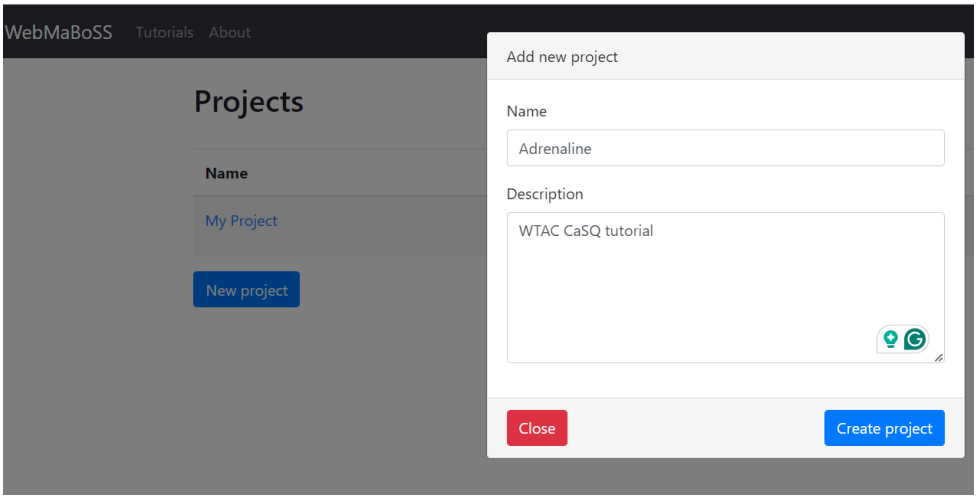
WebMaBoSS

Go to the WebMaBoSS site:
https://webmaboss.vincent-noel.fr/login/

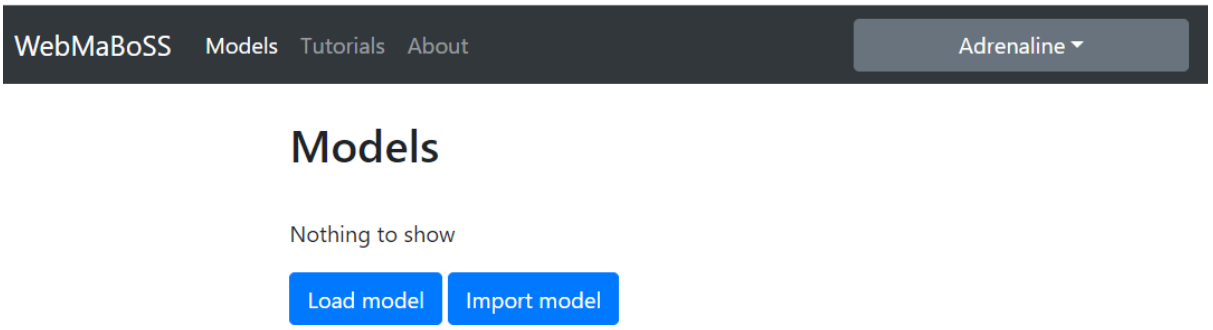
Login to your session:



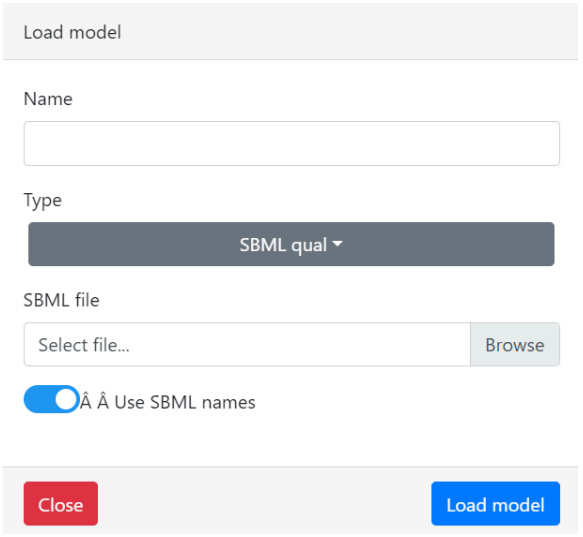
Create a project:

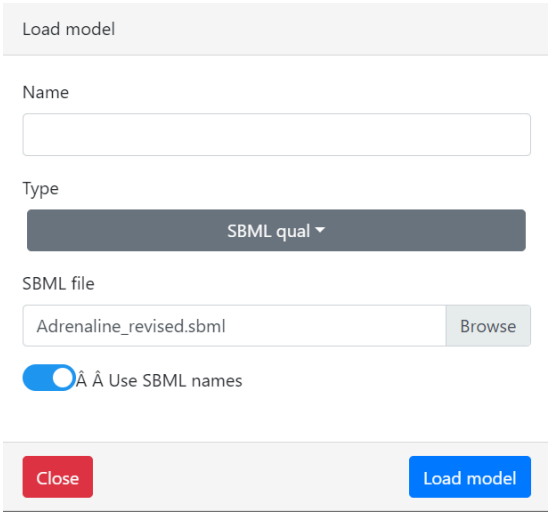


Now go to your newly created project space and load the Adrenaline_revised.sbml file

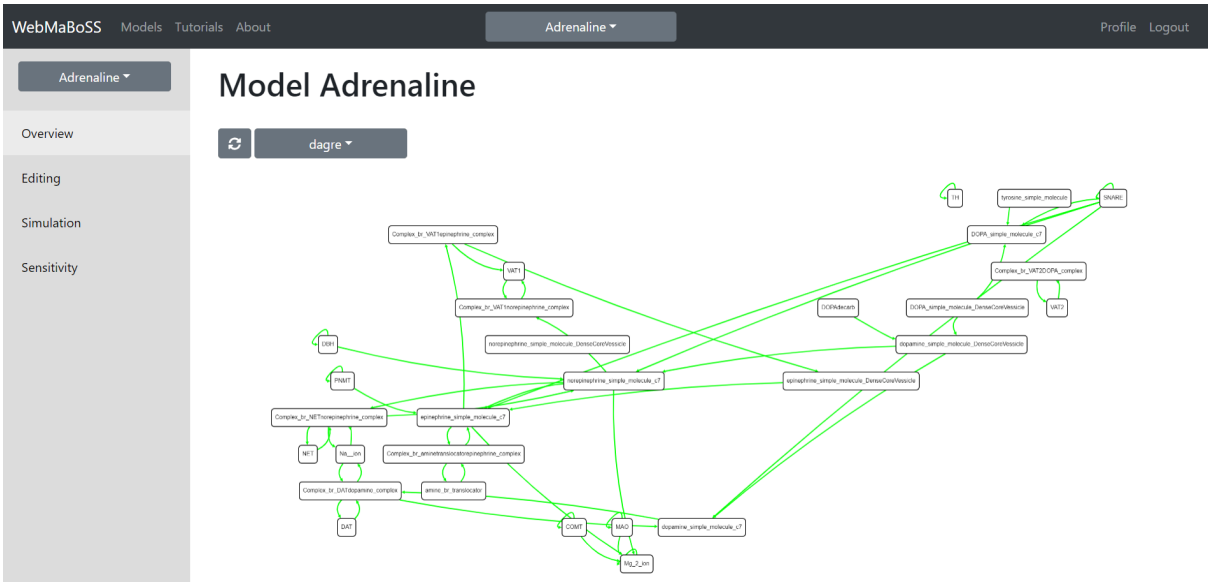


Click on Load model and then select SBML qual. Using the browse button, find your model and upload it—don't forget to name it!



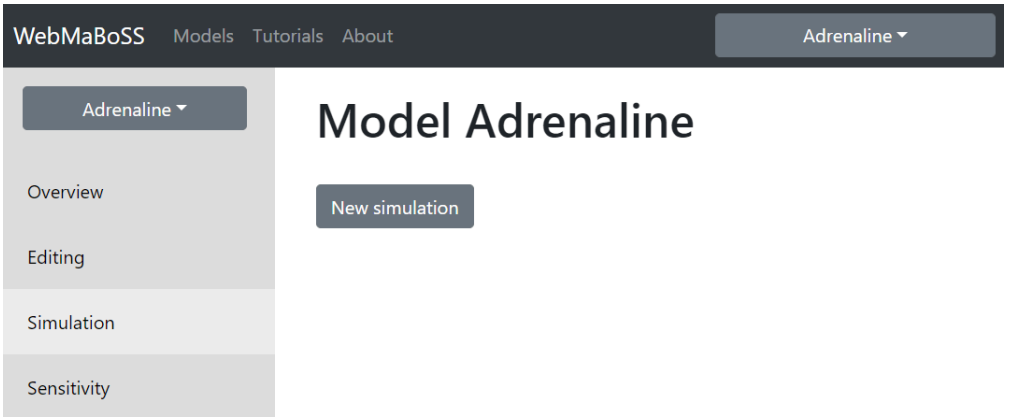


Now click on your model and see it

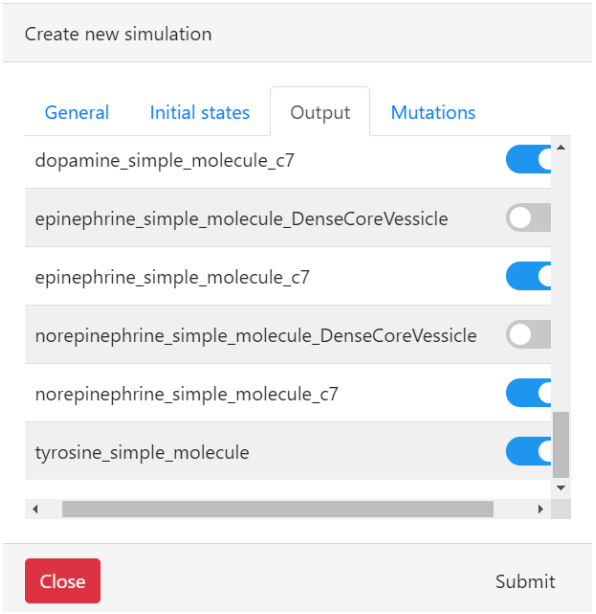


What do you observe? Compare this to the graph you see in Cell Designer (xml).
Compare this graph to the one you see in Cytoscape (sif).

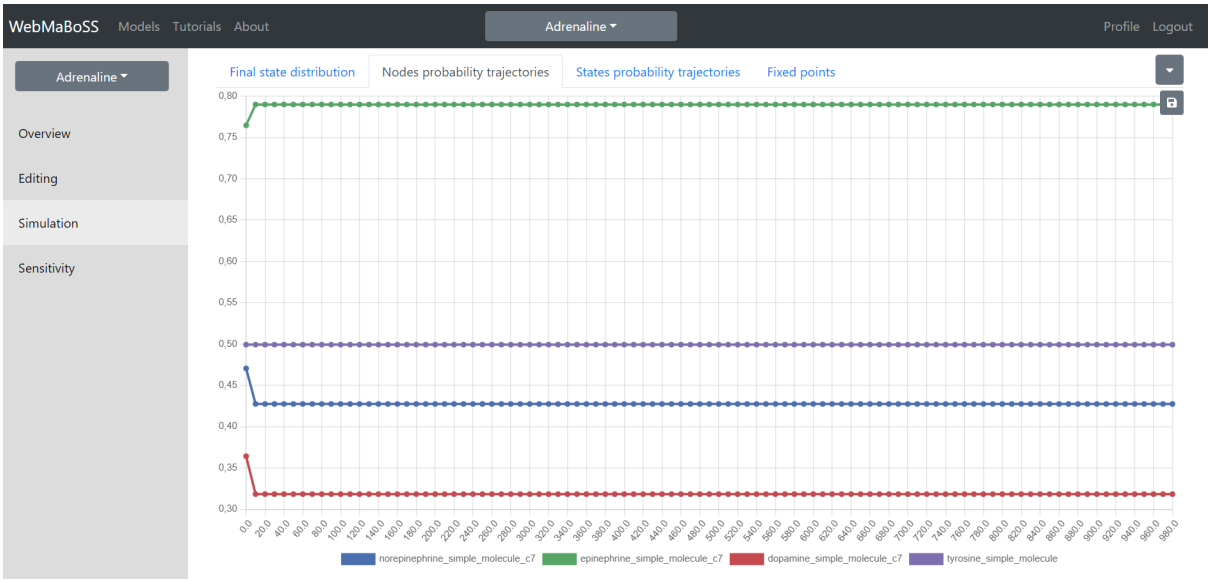
Now click on the simulation button and then to New simulation



Leave the initial states at default configuration where all nodes have 50% activity and select as outputs only the four simple molecules:
Dopamine, norepinephrine, tyrosine, epinephrine. Then hit submit



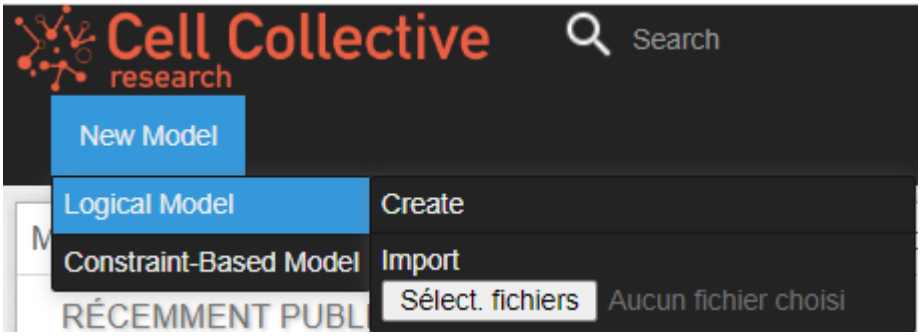
Observe the nodes' probability trajectories - what do you make of it?



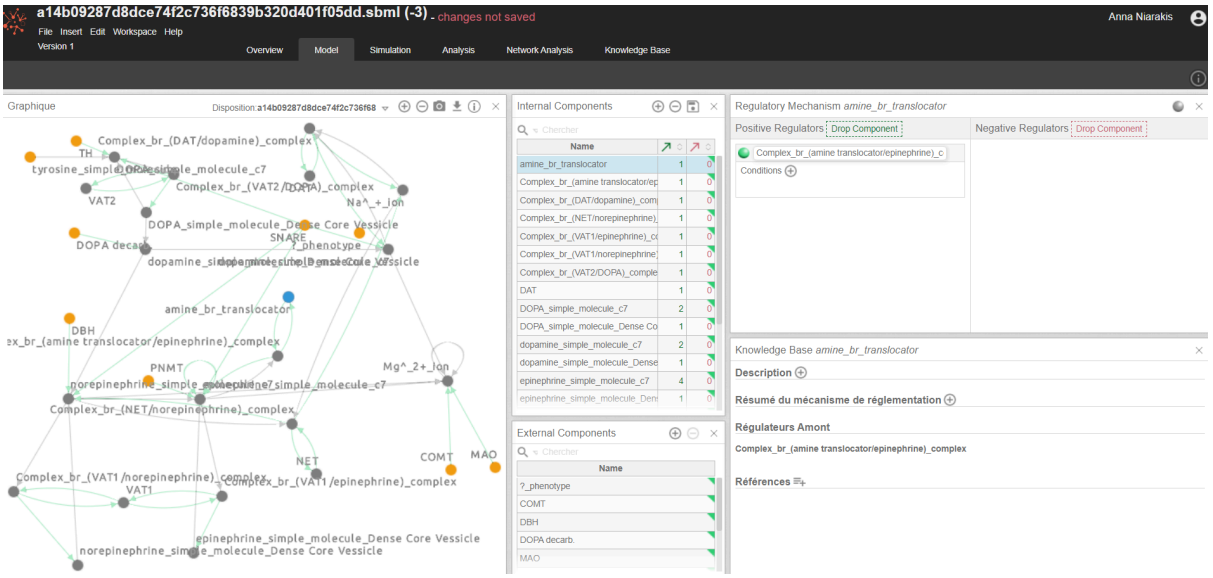
Cell Collective

Login to your Cell Collective account
https://research.cellcollective.org/?dashboard=true#

Then click on the left upper panel New model, select Logical model and import

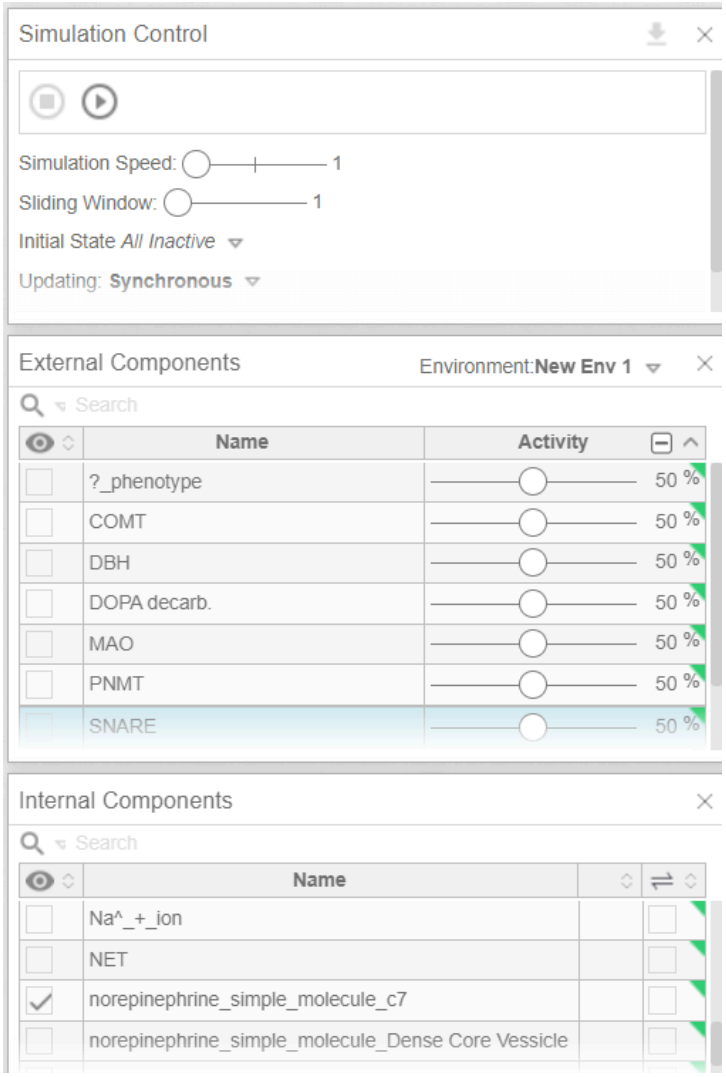


Choose your Adrenaline_revised.sbml file to import

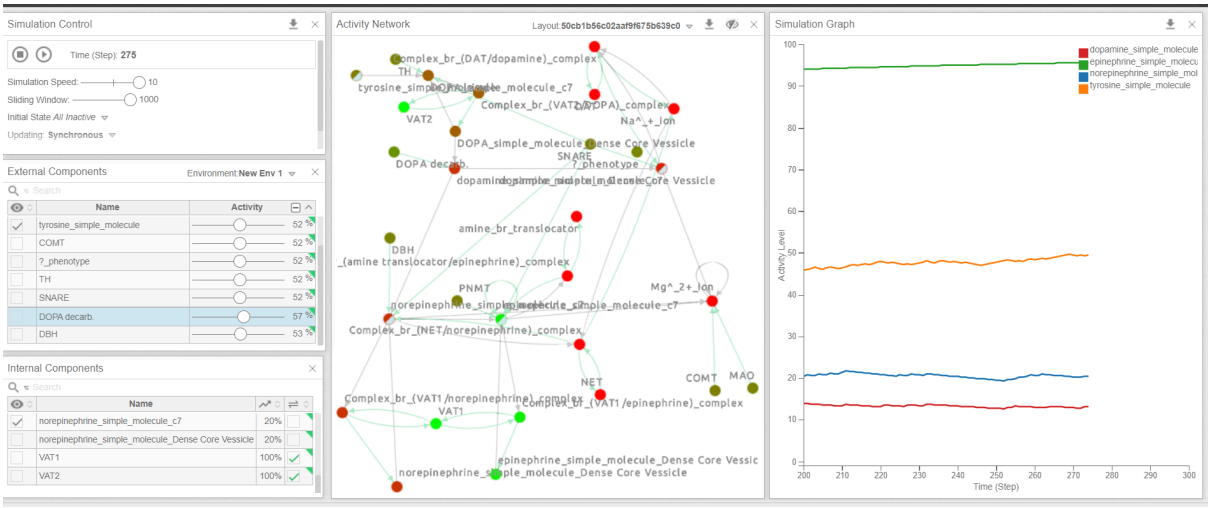


Change the model name to Adrenaline_revised_CC and go to the Simulation tab

Here, you have a different way of simulating your model (detailed CC tutorial follows)
In the simulation control panel, set the external components to 50% and click below the eye icon on the internal components for the simple molecules:
Dopamine, norepinephrine, epinephrine, and under the external components for tyrosine



Also, put as always active VAT1 and 2 and set the simulation speed and sliding window at max.Then launch the simulation.



What do you observe?
Are these results comparable with the ones obtained previously? Feel free to play around with the model and the platform.

BMA

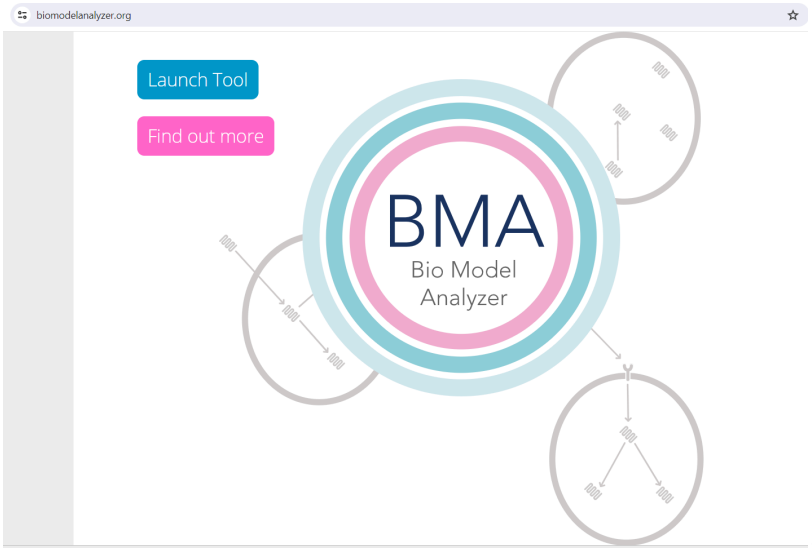
Now go back to your teminal and type
casq -b adrenaline_revised.xml adrenaline_revised.json

Here is an example with paths

```
C:\Users\aelec> casq -b C:\Users\aelec\Desktop\Adrenaline_revised.xml C:\Users\aelec\Desktop\Adrenaline_revised.json
```

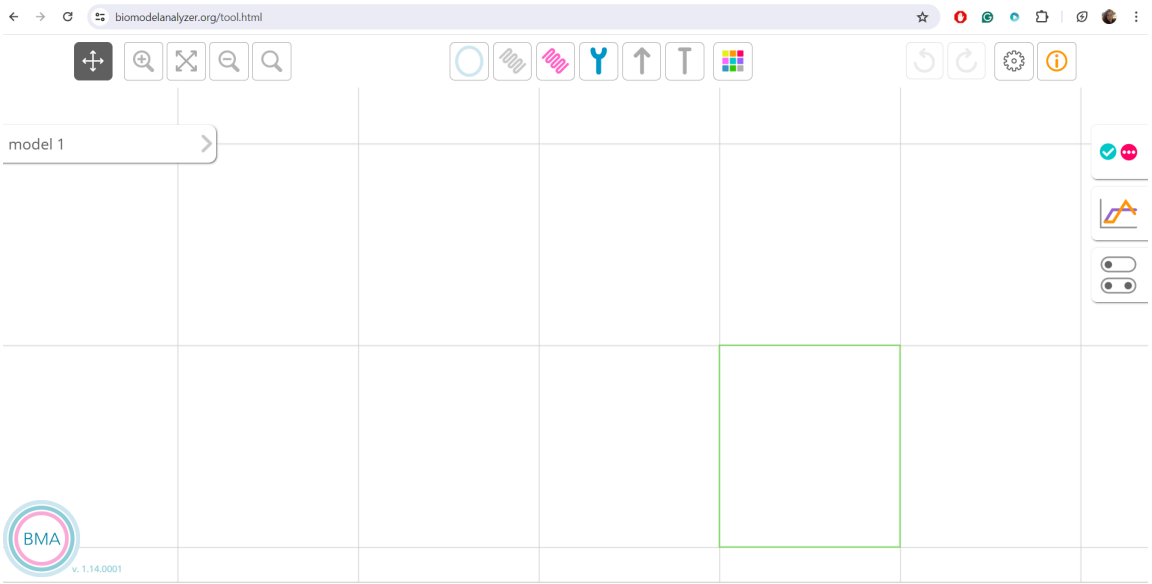
You should have now created your json file

Go now to
https://biomodelanalyzer.org/

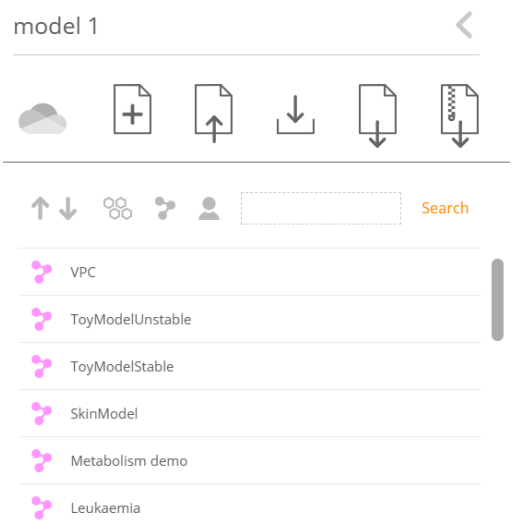


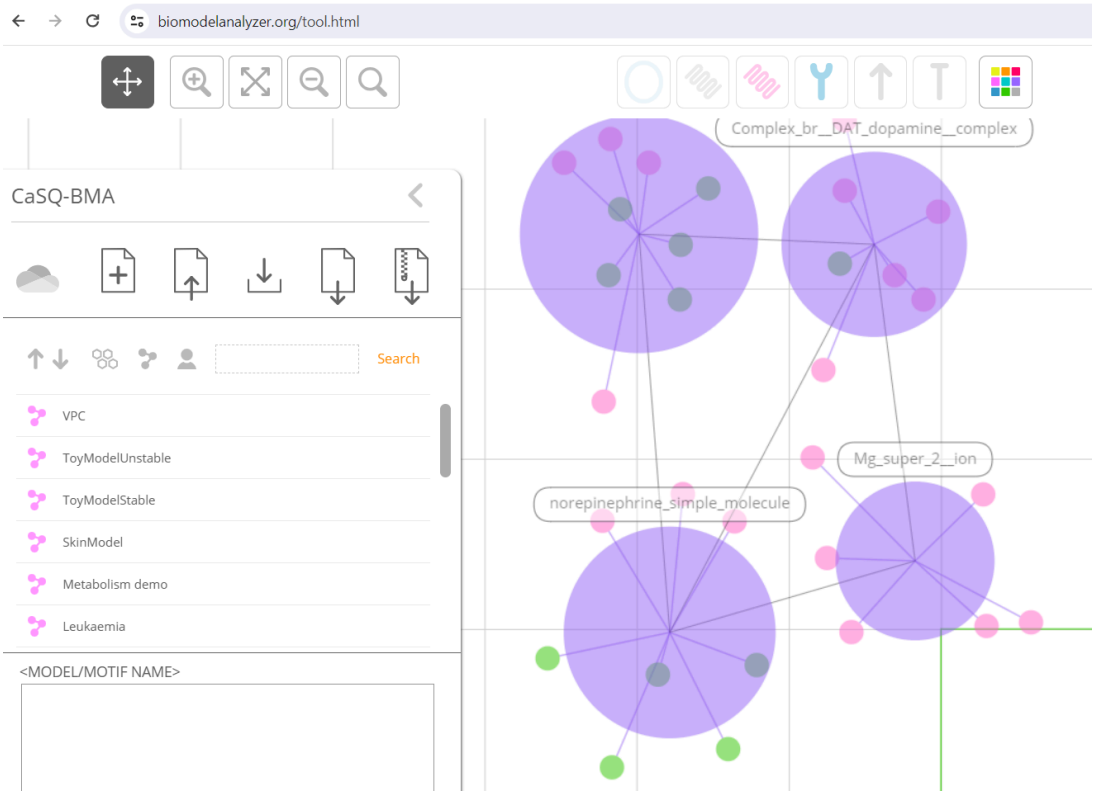
and launch the tool

Click on model1



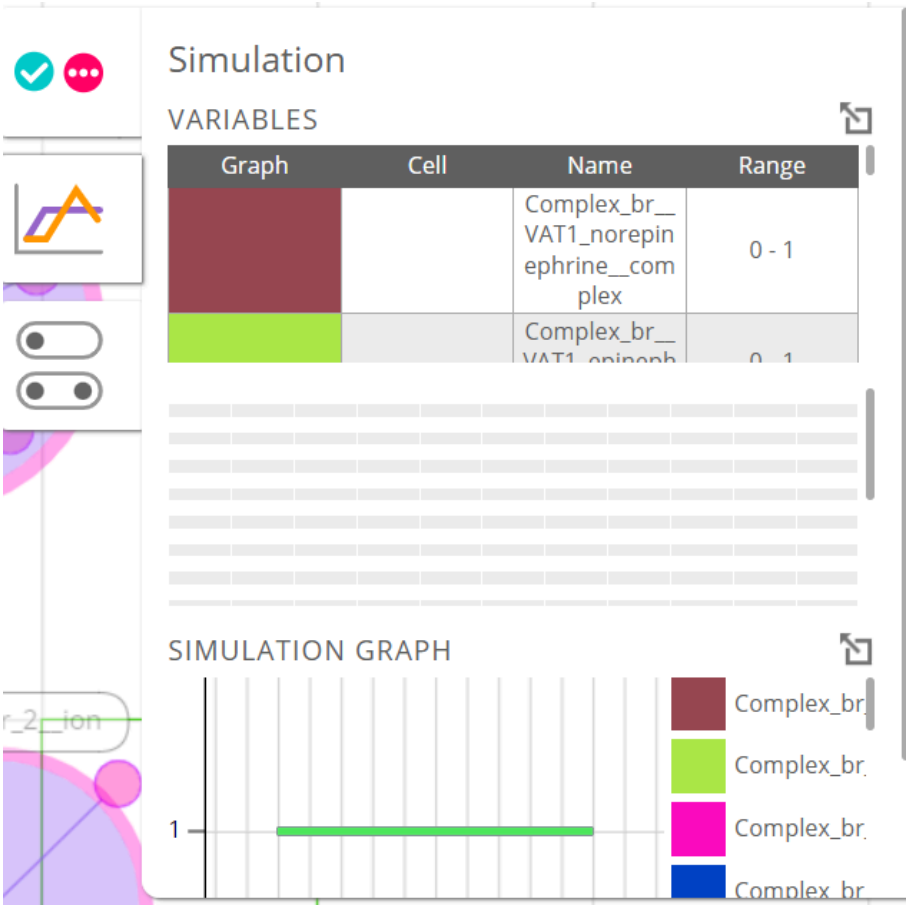
And import your newly generated json file





Click now on the simulation panel (the second button below)

The below panel will now appear on the screen:



Click on the arrow in the upper right on the variables panel

You can now imitate or randomise the initial conditions of the previous simulations.
Choose to see only the simple molecules in the graph
Here is an example:

Simulation Progression

Randomise

Graph		Name	Range		Initial Value									
		Complex_br__VAT1_...	0	1	1		0	0	0	0	0	0	0	0	0	0
		Complex_br__VAT1_...	0	1	1		0	0	0	0	0	0	0	0	0	0
		Complex_br__NET_n...	0	1	0		0	0	0	0	0	0	0	0	0	0
		Complex_br__amine...	0	1	0		0	0	0	0	0	0	0	0	0	0
		Complex_br__VAT2_...	0	1	0		0	0	0	0	0	0	0	0	0	0
		Complex_br__DAT_d...	0	1	0		0	0	0	0	0	0	0	0	0	0
		TH	0	1	0		1	1	1	1	1	1	1	1	1	1
		DOPA_decarb.	0	1	0		1	1	1	1	1	1	1	1	1	1
		DBH	0	1	0		1	1	1	1	1	1	1	1	1	1
		PNMT	0	1	0		1	1	1	1	1	1	1	1	1	1
	✓	tyrosine_simple_mol...	0	1	0		1	1	1	1	1	1	1	1	1	1
		DOPA_simple_molec...	0	1	0		0	1	1	1	1	1	1	1	1	1
	✓	dopamine_simple_m...	0	1	0		0	0	0	0	0	0	0	0	0	0
	✓	norepinephrine_sim...	0	1	0		0	1	0	0	0	0	0	0	0	0
	✓	epinephrine_simple_...	0	1	0		0	1	1	1	1	1	1	1	1	1
		NET	0	1	0		0	0	0	0	0	0	0	0	0	0
		VAT1	0	1	0		1	0	0	0	0	0	0	0	0	0
		SNARE	0	1	0		1	1	1	1	1	1	1	1	1	1
	✓	norepinephrine_sim...	0	1	0		1	0	0	0	0	0	0	0	0	0
		amine_br_translocat	0	1	0		0	0	0	0	0	0	0	0	0	0

EXPORT CSV | - 10 | STEPS: 10 | + 10 | Run

Simulation Graph