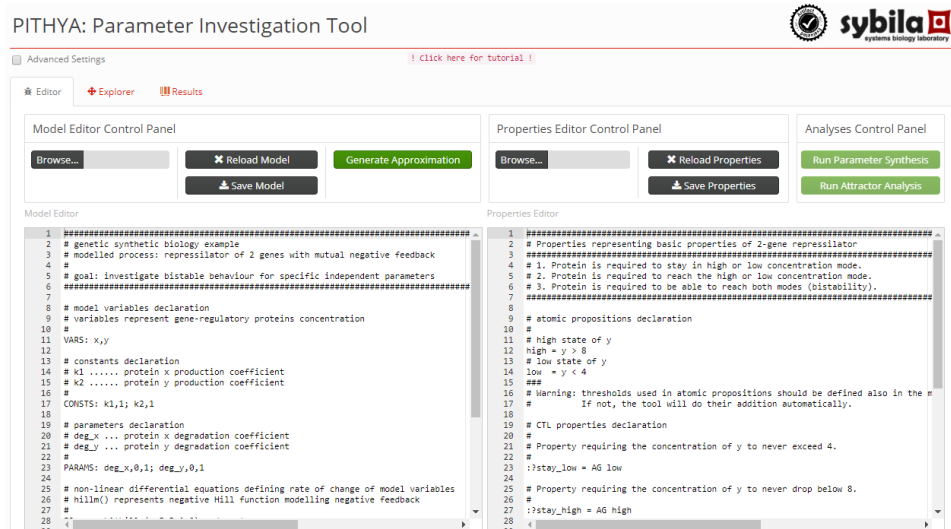


# Pithya Tutorial

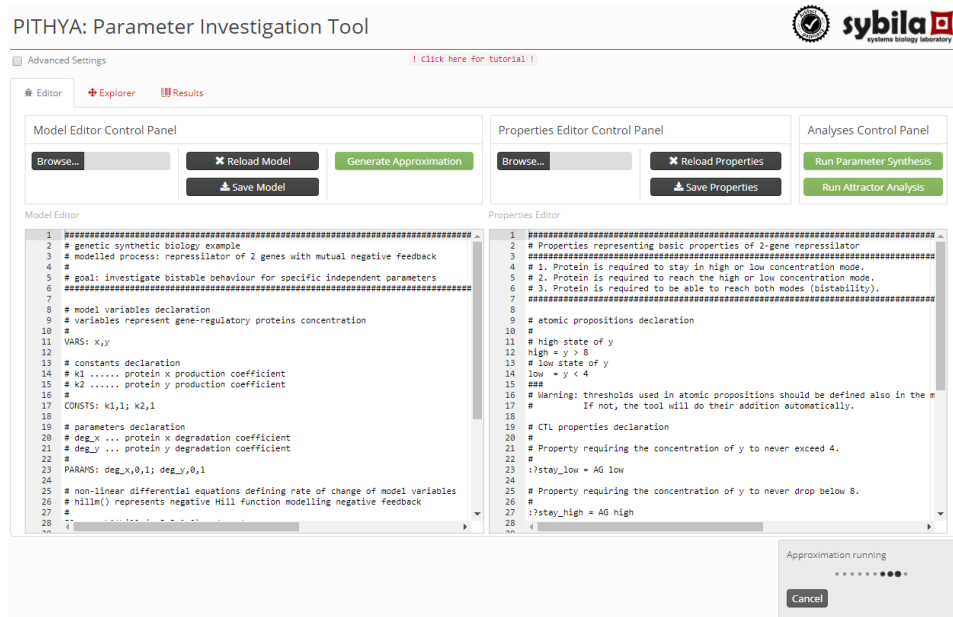
April 18, 2018

# First use

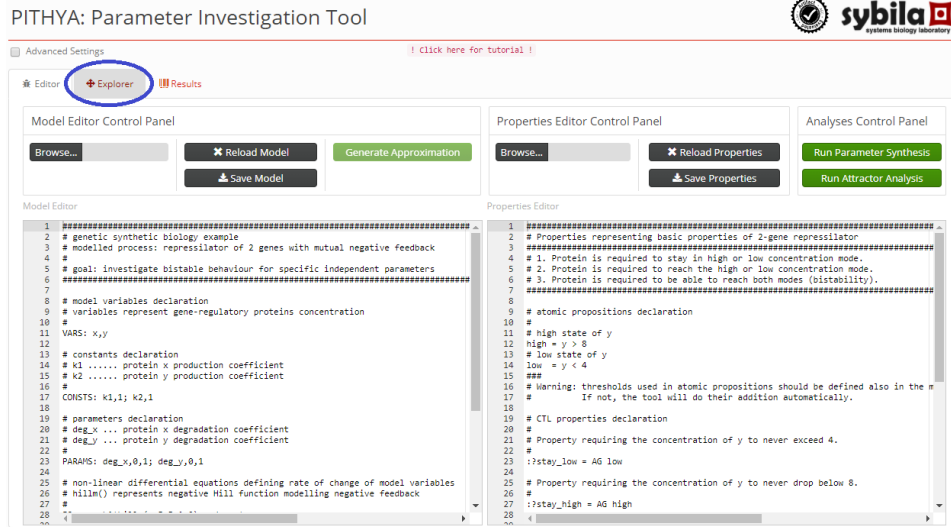
1. When you open Pithya GUI via a web browser you will see the very first panel called *Editor*. It allows loading, editing, and saving of model and property files. A demo model file along with a set of properties have already been loaded to ease your first use.



- First thing you have to do is to click on *Generate Approximation* button (the rich-green one). While the process is running, a notification is shown in the bottom right corner. This process will prepare the model for later analysis and is necessary for generation of transition state space which you will see in the next step.



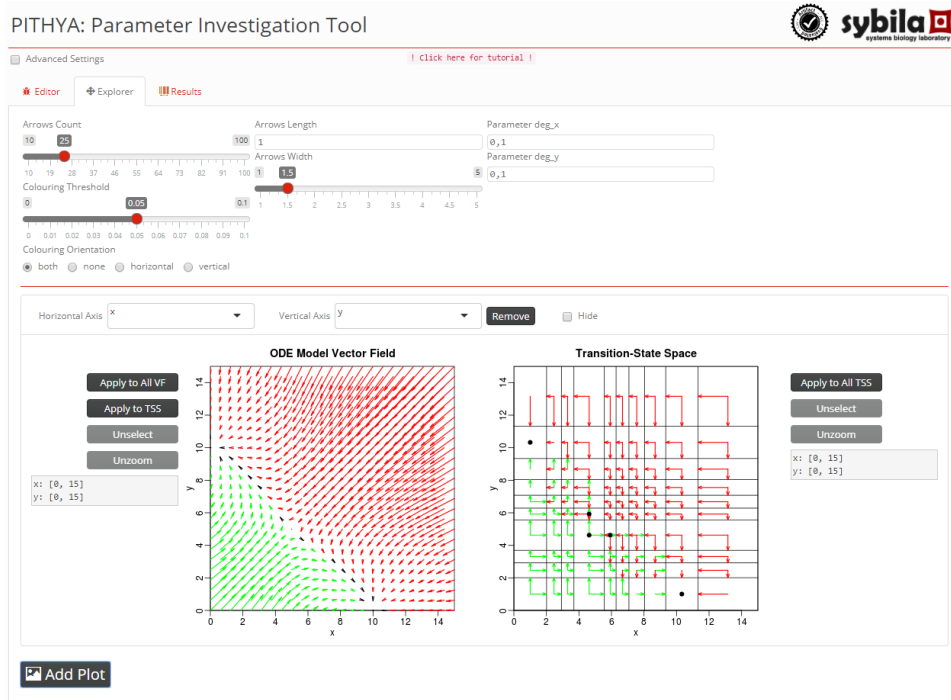
- When the approximation is finished, move to the next panel called *Explorer* by clicking on the tab with the corresponding name located at the top.



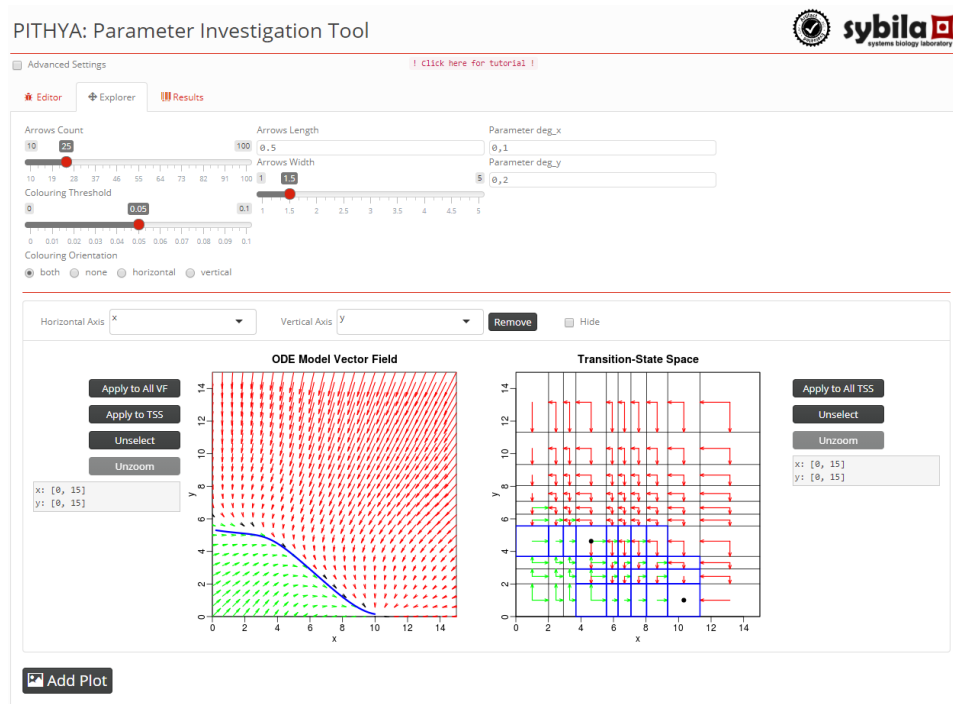
- Here you see the *Explorer* panel. In the upper part, there are several sliders which modify the appearance of plots (left), and input(s) for setting of model's parameter(s) (right).

In the lower part, you can see the first pair of plots — one with the vector field (left) and one with the transition state space (right) — together with associated buttons and other widgets. Above the plots are selectors for setting the axes, button for removing plots and checkbox for hiding them.

At the very bottom, there is one *Add Plot* button which you can use to add more such pairs of plots each with own setting controllers.

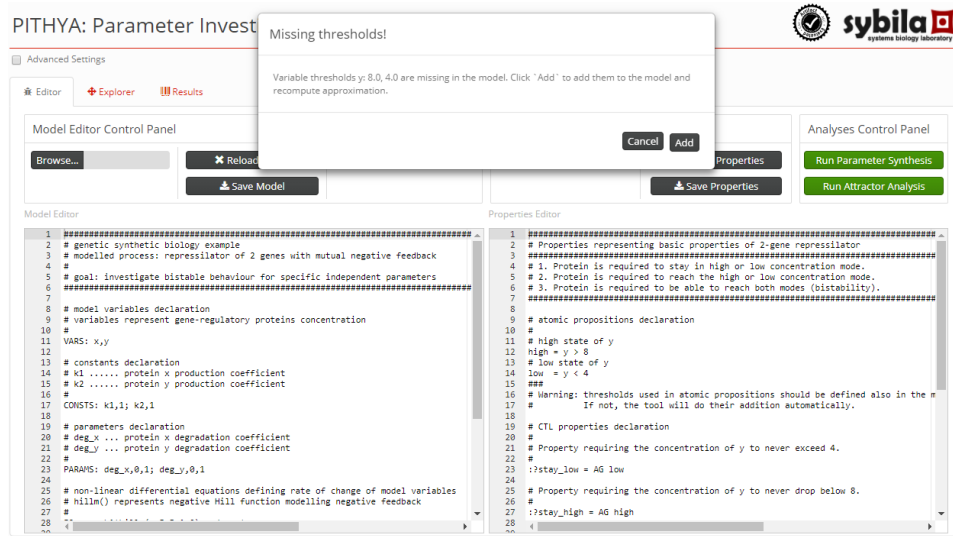


- Now, you can interact with the visualisation. Try to double-click inside the vector field and you will see a simulated trajectory of the model starting from this point. Double-clicking inside the transition state space produces a reachability set starting from the clicked state. Zooming is possible using the click-and-drag gesture. Use *Unzoom* button to reset your zoom position. Finally, try to change parameter(s) values or to adjust the selectors (for more information about their purpose, move your mouse over them and a tooltip will appear).




- Next step is to return to the *Editor* panel and start some analysis. In this tutorial, we decided to start with parameter synthesis by clicking on the *Run Parameter Synthesis* button (which is rich-green now due to the finished approximation as a necessary precondition).

Sometimes, your properties might use thresholds which are not part of the model. In that case, Pithya will notify you about inconsistency. By clicking the *Add* button you add all necessary thresholds directly to the model and a new run of approximation will be spawned (of course, you may refuse this by clicking the *Cancel* button).



- Now, the model and the properties are consistent so we can finally run the parameter synthesis process and then wait until the process is finished (watch the notification in the bottom right corner). The whole process can be time-consuming depending on the model/property combination. If you are interested, you have the opportunity to download an intermediate log file.

**PITHYA: Parameter Investigation Tool** 

Advanced Settings [Click here for tutorial](#)

Editor Explorer Results

**Model Editor Control Panel**

Browse... Reload Model Generate Approximation Save Model

**Properties Editor Control Panel**

Browse... Reload Properties Save Properties Run Parameter Synthesis Run Attractor Analysis

**Analyses Control Panel**

**Model Editor**

```

1 #####
2 # genetic synthetic biology example
3 # modelled process: repressor of 2 genes with mutual negative feedback
4 #
5 # goal: investigate bistable behaviour for specific independent parameters
6 #####
7
8 # model variables declaration
9 # variables represent gene-regulatory proteins concentration
10 #
11 VARS: x,y
12
13 # constants declaration
14 # k1 ..... protein x production coefficient
15 # k2 ..... protein y production coefficient
16 #
17 CONSTS: k1,1; k2,1
18
19 # parameters declaration
20 # deg_x ... protein x degradation coefficient
21 # deg_y ... protein y degradation coefficient
22 #
23 PARAMS: deg_x,0,1; deg_y,0,1
24
25 # non-linear differential equations defining rate of change of model variables
26 # hillm() represents negative Hill function modelling negative feedback
27
28 "

```

**Properties Editor**

```

1 #####
2 # Properties representing basic properties of 2-gene repressor
3 #####
4 # 1. Protein is required to stay in high or low concentration mode.
5 # 2. Protein is required to reach the high or low concentration mode.
6 # 3. Protein is required to be able to reach both modes (bistability).
7 #####
8
9 # atomic propositions declaration
10 #
11 # high state of y
12 high = y > 8
13 # low state of y
14 low = y < 4
15 ###
16 # Warning: thresholds used in atomic propositions should be defined also in the m
17 # If not, the tool will do their addition automatically.
18
19 # CTL properties declaration
20 #
21 # Property requiring the concentration of y to never exceed 4.
22 #
23 :?stay_low = AG low
24
25 # Property requiring the concentration of y to never drop below 8.
26 #
27 :?stay_high = AG high
28 <

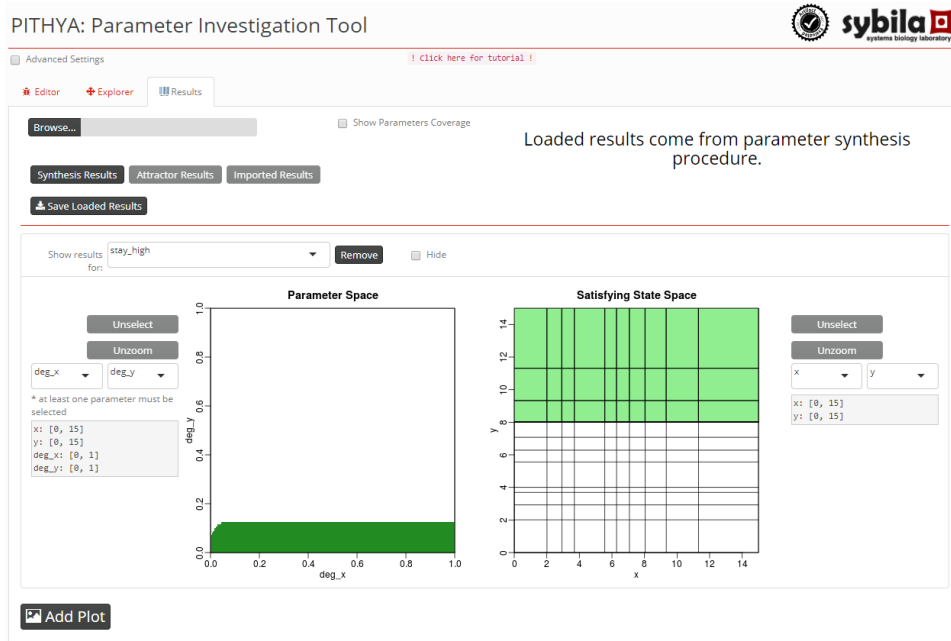
```

Parameter synthesis running  
Download log Cancel

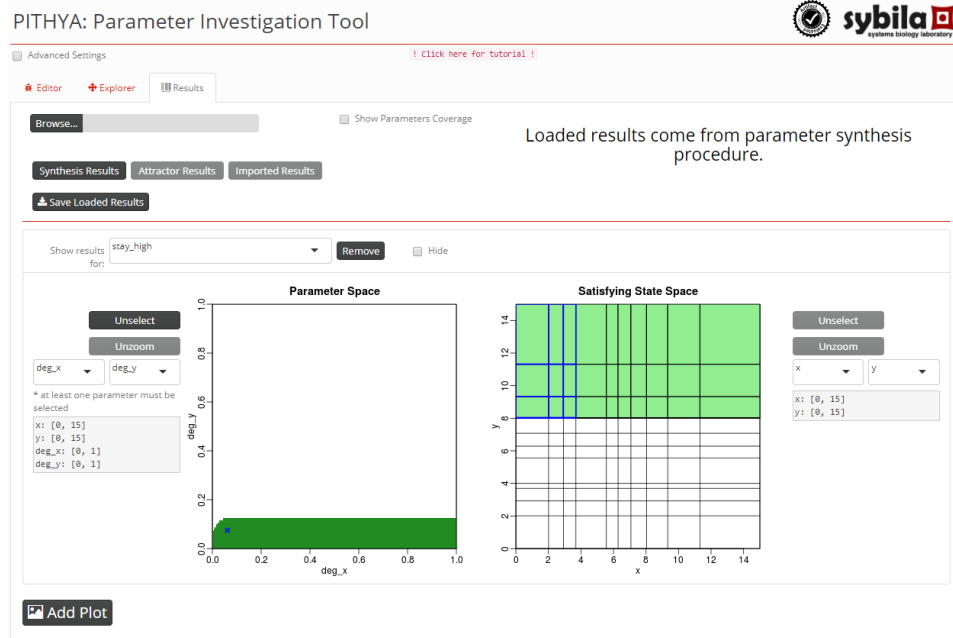


- Now, go to the last panel — called *Results* — where you can observe the results of the selected analysis. Here, the buttons for import and download of results are placed as well as three buttons for switching between different sources of result data. So far, only one — *Synthesis Results* — is activated. Notice that the first group of plots is shown automatically (also every time the source of data is changed).

At the bottom, you can add more plot groups using the *Add Plot* button. Each plot group consists of a plot representing the parameter space (left) displaying the regions that satisfy currently selected property and one representing the satisfying state space (right) displaying all states for which the property holds in at least one parameter valuation. Above them, there is a selector for choosing one of the properties previously checked during the parameter synthesis run, one button for removing whole group and one checkbox for hiding it. Right next to the plots, there are selectors for setting up the axes of the particular plot (with model variables for the satisfying state space and with parameters for the parameter space).



- It is possible to double-click inside both plots, but each with different effect. Double-clicking inside the left-hand plot will highlight (using blue color) the states which satisfy the formula under the selected parameter valuation. To cancel the selection, click the *Unselect* button next to the particular plot.

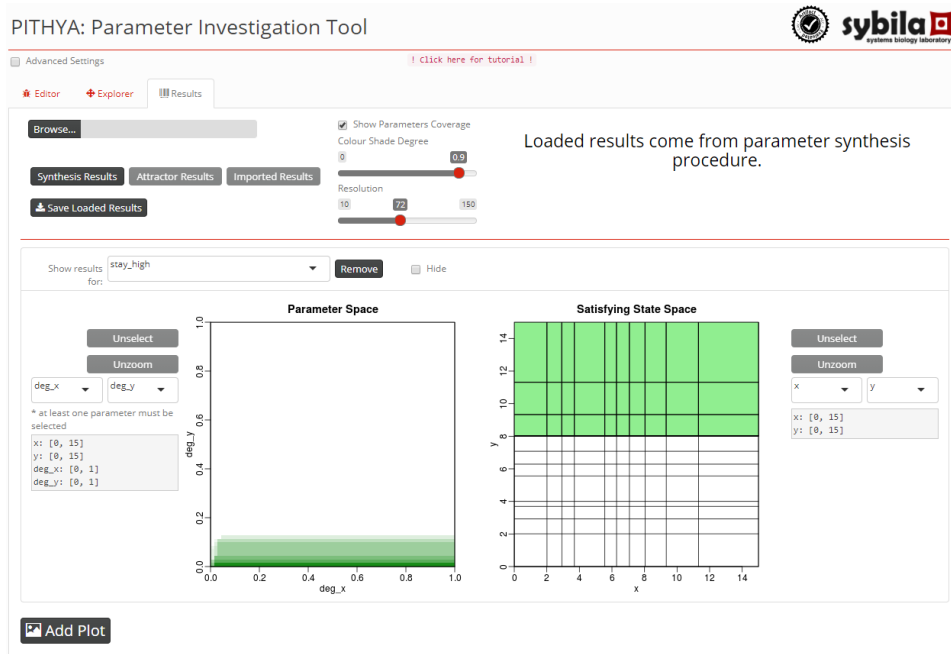


- Analogously, a state (or states) can be selected in the right-hand plot to show the satisfying parameter valuations. To cancel the selection click the *Unselect* button next to the particular plot.


#### PITHYA: Parameter Investigation Tool



11. An interesting feature is the *Show Parameter Coverage* checkbox right next to the *Browse...* button. It will redraw the parameter space plot in the shades of green colour according to the number of states which satisfy the selected property under a particular parameter region. The darker the shade, the more states satisfy the property and vice versa. This process is usually quite time-consuming so we advise precaution with its setting for large models.



12. Now, we can return on the *Editor* panel and run the attractor analysis. We can do that by clicking on the *Run Attractor Analysis* and wait until the process is finished. Notice the bottom right corner notification.

PITHYA: Parameter Investigation Tool 

Advanced Settings [! Click here for tutorial !](#)

Editor Explorer Results

Model Editor Control Panel

Browse... Reload Model Generate Approximation Save Model

Properties Editor Control Panel

Browse... Reload Properties Save Properties

Analyses Control Panel

Run Parameter Synthesis Run Attractor Analysis

Model Editor

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26 # hillm() represents negative Hill function modelling negative feedback
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28
29

```

Properties Editor

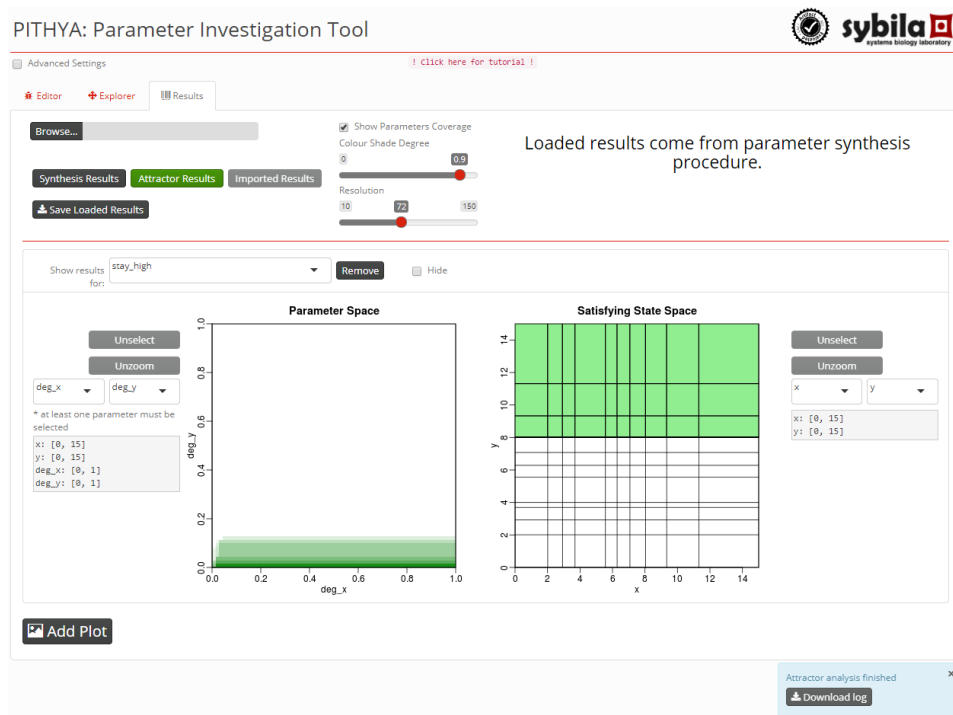
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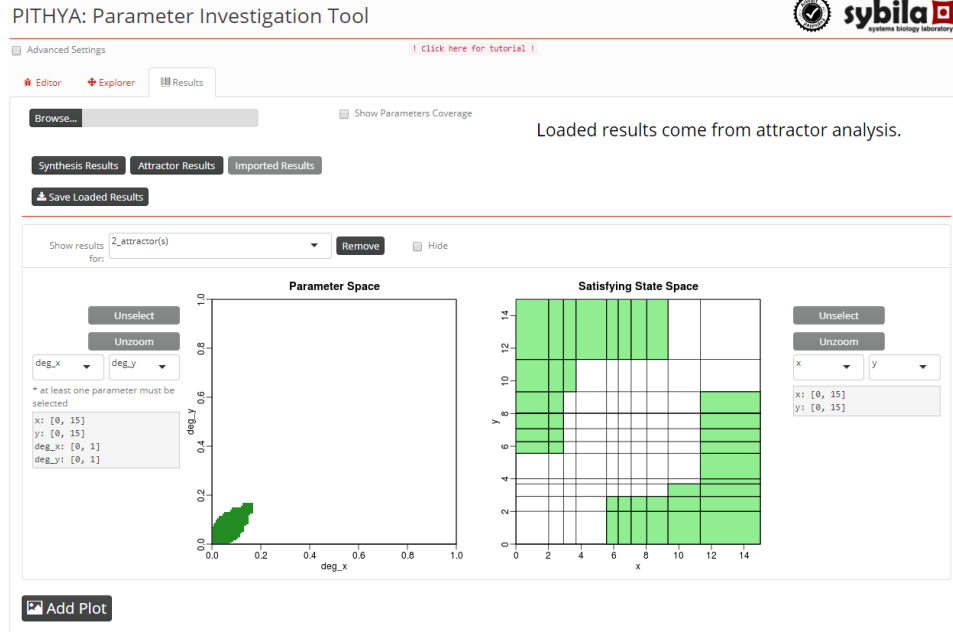
```

Attractor analysis running  
Download log Cancel

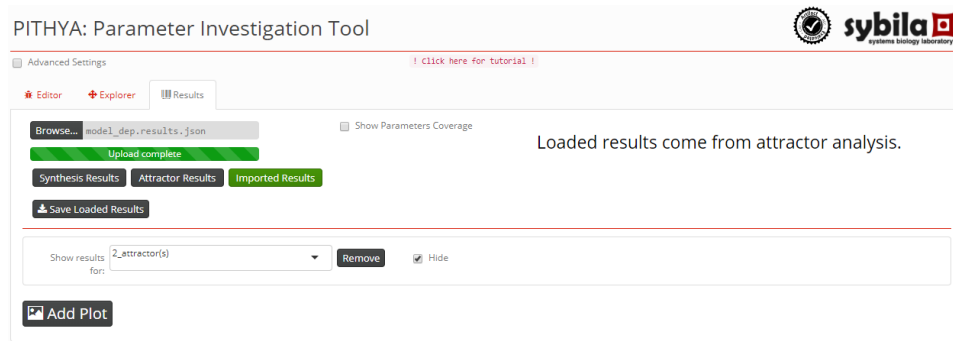
13. When the results are ready, you can flip to the *Results* panel again and observe the *Attractor Results* button being green now. Click on this button will load new source of data, which will discard the previously shown plot groups and show new results.



14. After the click, new group of plots will appear and the *Synthesis Results* button will turn black, meaning results are still available, but not shown. Now, you can interact with these results as with the previous one. Selectable properties represent the number of attractors in the model.



15. Finally, you can import your old results by clicking on the *Browse...* button which will turn the *Imported Results* button green, indicating the loaded data is prepared.





Whenever you edit the model file, the *Generate Approximation* button will turn rich-green in order to inform you that the results are outdated and the process needs recalculation. The same holds for the pair of the property file and the *Run Parameter Synthesis* button. After new approximation process is finished both buttons — *Run Parameter Synthesis* and *Run Attractor Analysis* — will turn rich-green for the same reason. Changes can be saved by the corresponding *Save Model/Properties* button or fully reset by the corresponding *Reload Model/Properties* button.