CMB - Helmholtz Zentrum München

iVUN 1.1

Case Study Tutorial

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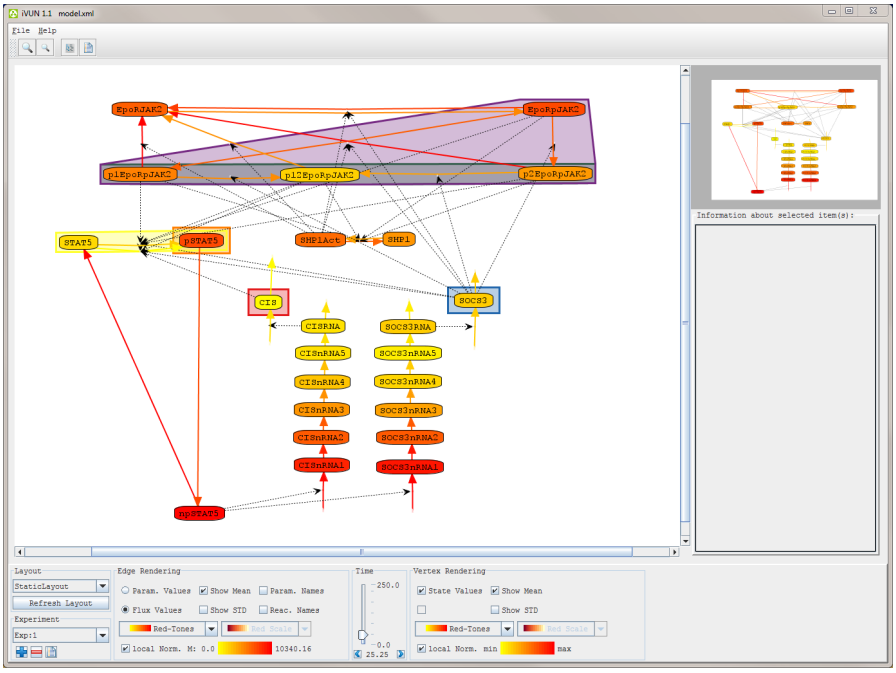
Preparation of Analysis

1 Preparation of Analysis

1. Open iVUN by double click or via the command line java iVUN.jar
2. Load SBML model: `File > Open > Network (SBML) ...> model.xml`
3. Generate own layout (see documentation) or load layout: `File > Open > Layout ...> layout.layout`. The view can be scaled using the magnifier (top left) or using the scroll wheel of the mouse and shifted using the small visualization (top right) or the sliders of the graph view. To improve the visualization, we recommend to suppress the parameter and reaction names by unchecking the respective boxes in the Edge Rendering menu (bottom middle).
4. Load parameter sample: `File > Open > Parameters ...> parameter_sample_log10.txt` Load fluxes, states and outputs for the 6 experimental conditions:
   a) *Experimental condition 1:*
      i. Load data for the first experimental condition: `File > Open > Complete Exp. (Y,V,X) ...> condition_1`.
      ii. Choose the default percentiles: lower percentile = 5%, upper percentile = 95%.
   b) *Experimental condition 2, 3, 4, 5 and 6:*
      i. Add experimental conditions by pressing the blue plus sign in the Experiment menu (bottom left).
      ii. Load data for the second experimental condition: `File > Open > Complete Exp. (Y,V,X) ...> condition_2`.

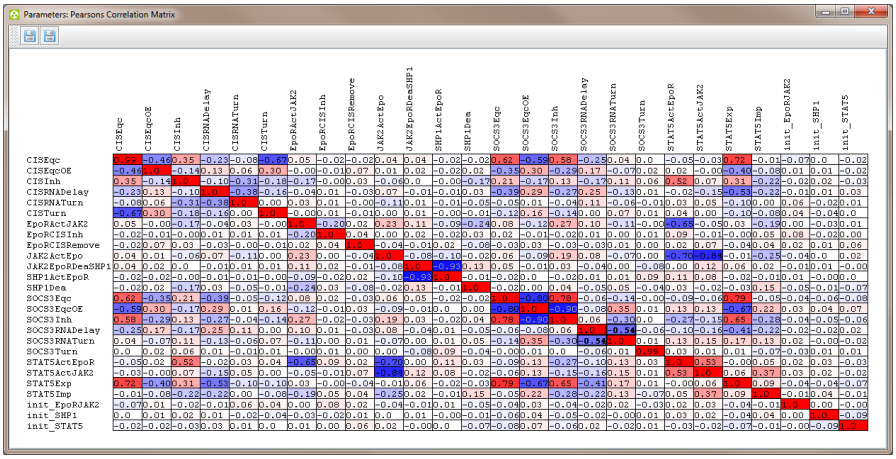
   Repeat 4(b)i and 4(b)ii for the experimental conditions 3, 4, 5 and 6.

2 Figure 3A



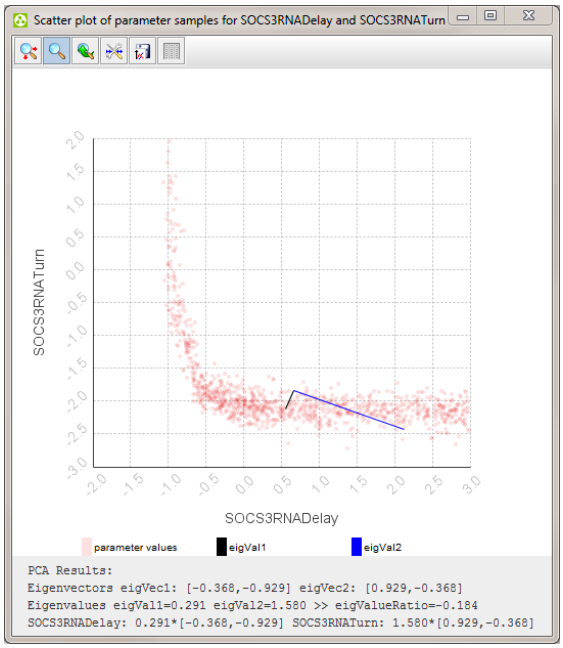
1. Select Exp:1 from the drop-down menu in the Experiment menu (bottom left).
2. Change the settings in Edge Rendering menu (bottom middle) to:
   - Flux Values → true
   - Show Mean → true
   - Show STD → false
   - local Norm. → true
   - color map → Red-Tones
3. Change the settings in Vertex Rendering menu (bottom right) to:
   - Conc. Values → true
   - Show Mean → true
   - Show STD → false
   - local Norm. → true
   - color map → Red-Tones
4. Move the time slider (bottom middle) to 25.25.

3 Figure 3B



1. Select an edge by left-click.
2. Open the drop-down menu for the selected edge by right-click.
3. Open the table view of the Pearson correlation matrix by left-click on the fifth entry `Show correlation matrix: parameters`.

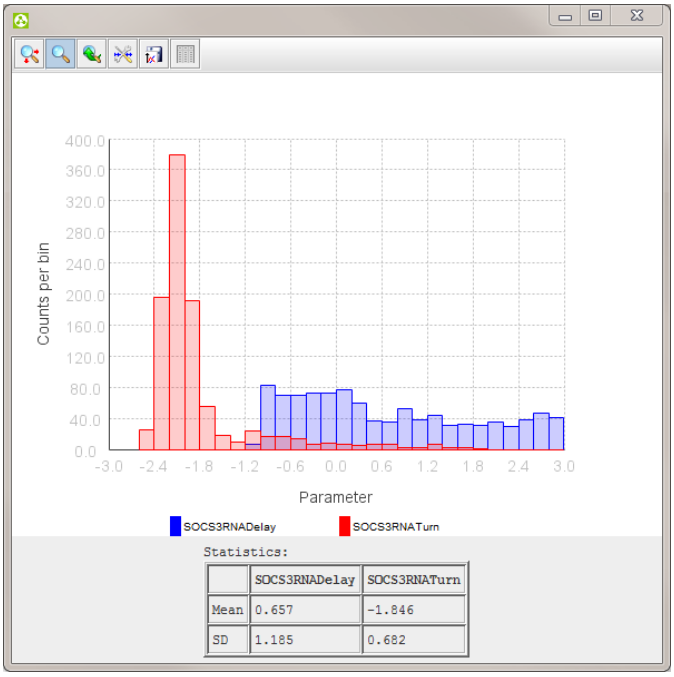
4 Figure 3C - Scatterplot



1. Select in the Pearson correlation matrix one of the cells belonging to the SOCS3RNADelay and SOCS3RNATurn by left-click.

2. Open the drop-down menu for the selected element by right-click.
3. Open the corresponding scatterplot by left-click on `Show scatterplot`.
4. To change the axis scaling, e.g., SOCS3RNADelay $\rightarrow \log_{10}$(SOCS3RNADelay), use the fourth button ( ).

5 Figure 3C - Histogram

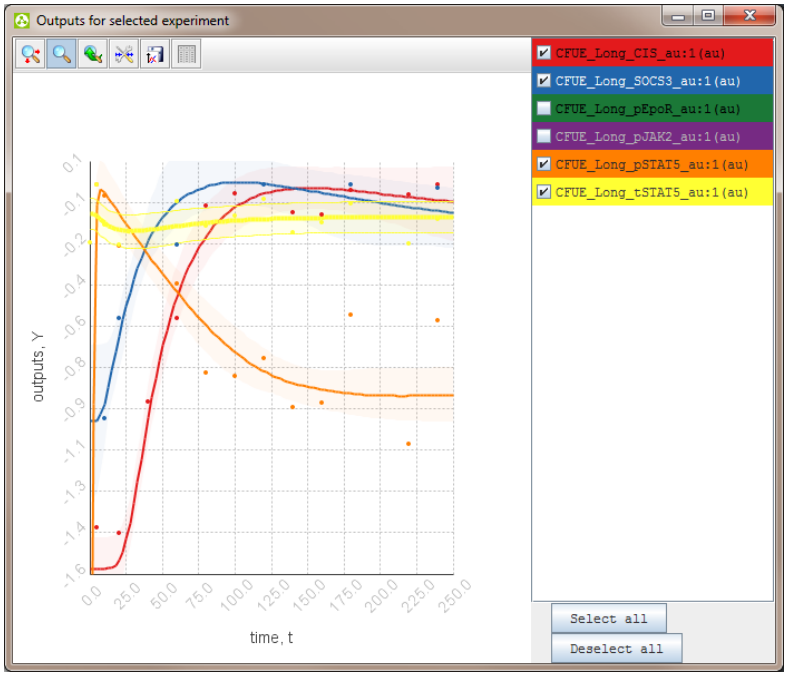


1. Select in the Pearson correlation matrix one of the cells belonging to the SOCS3RNADelay and SOCS3RNATurn by left-click.
2. Open the drop-down menu for the selected element by right-click.
3. Open the corresponding histograms by left-click on > `Show histogram`.

6 Figure 4A

Equivalent to Figure 3A but for three different time points $(0, 10.1$, and $50.5)$. The dynamics can be animated by keeping the forward or backward button in the Time menu pressed.

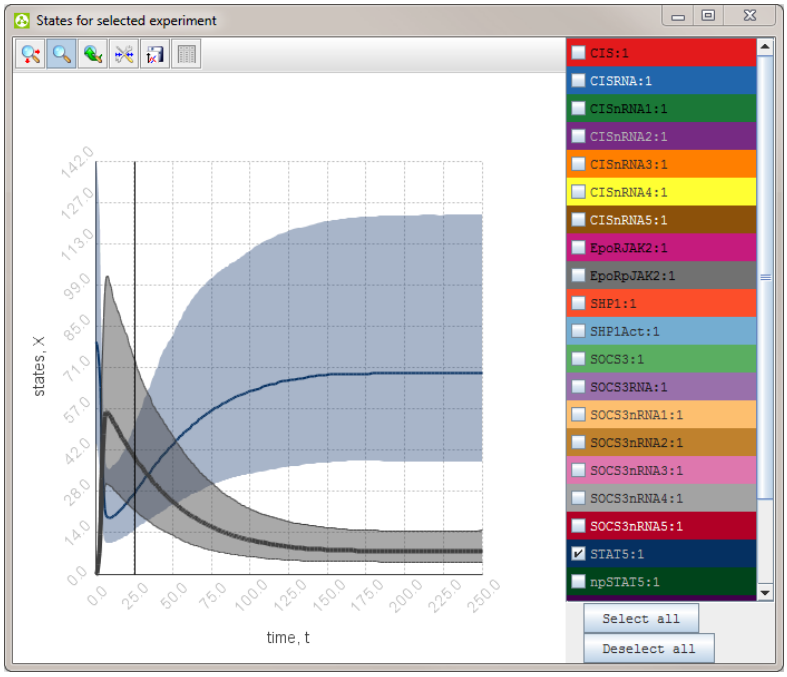
7 Figure 4B



1. Select one of the states (vertices) which influence at least one output (is contained in one of the colored regions) by left-click.
2. Open the drop-down menu for the selected vertex by right-click.
3. Open the line plot for the output of the selected experiment by left-click on: `Show line/dot plot: output > time series of current exp..`
4. Deselect the two outputs CFUE_Long_pEpoR_au and CFUE_Long_pJAK2_au.

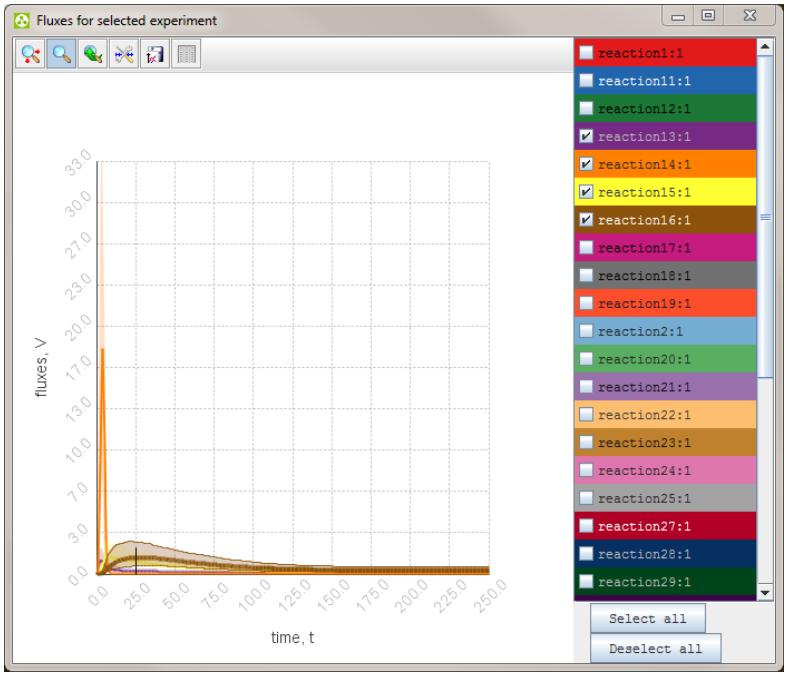
(Remark: Keep the window open to obtain Figure 4C.)

8 Figure 4C



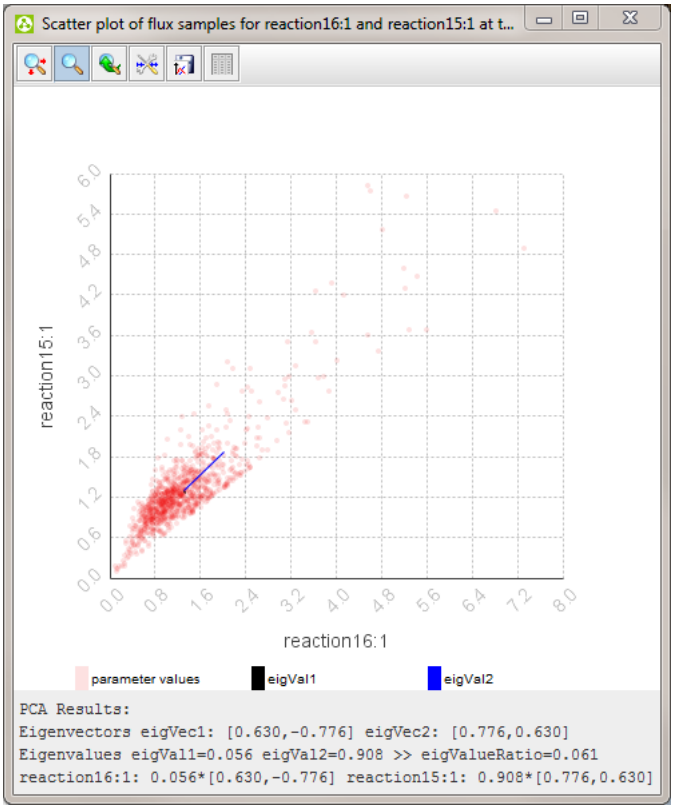
1. Select one state (vertex) in the graph view by left-click.
2. Open the drop-down menu for the selected vertex by right-click.
3. Open the line plot for the states by left-click on: `Show line plot: states > time series of current exp.`.
4. Deselect all states (by pressing the button `Deselect all` below the check boxes).
5. In the line plot for the outputs, select by left-click the trajectory of CFUE_Long_tSTAT5_au. This results automatically in the selection of STAT5 and pSTAT5 in the line plot of the states. Alternatively, you can also directly select STAT5 and pSTAT5, however, this requires that you already know that the output CFUE_Long_tSTAT5_au depends on these two states.

9 Figure 4D



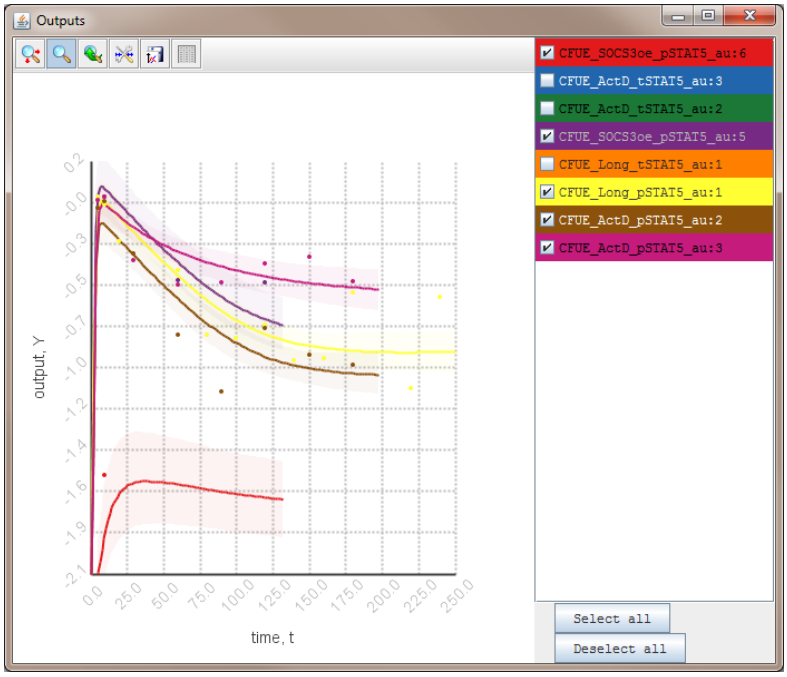
1. Select one reaction (edge) in the graph view by left-click.
2. Open the drop-down menu for the selected edge by right-click.
3. Open the line plot for the fluxes by left-click on: `Show line plot: fluxes > time series of current exp..`
4. Deselect all reactions (by pressing the button below the check boxes).
5. Select reactions 13, 14, 15 and 16. These reactions are directly involved in STAT5 activation and transport.

10 Figure 4E



1. Move the time slider in the Time menu (bottom middle) to 16.16.
2. Select in the graph view reaction 15 and 16 by keeping the shift-button pressed. You may therefore enable the reaction names for edge labeling again by selecting the check box `Reac. Names` in the Edge Rendering menu.
3. Open the drop-down menu for the selected edges by right-click on one of them.
4. Open the scatter plot of the corresponding flux samples by left-click on: `Show scatter plot: fluxes (reaction15,reaction16) at` $t = 16.16$.
5. To change the axis scaling use the fourth button ( ).

11 Figure 4F



1. Select the state pSTAT5 in the graph view by left-click.
2. Open the drop-down menu for the selected vertex by right-click.
3. Open the line plot for between experiment comparison by left-click on: `Show line/dot plot: outputs > compare time series of experiments`.
4. Deselect the tSTAT5 outputs.