

Running CellDesigner™ Simulation with ControlPanel

Quick Tutorial

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- Frank Bergmann and Herbert Sauro at University of Washington for helping us support [SBW-2.x](#) on CellDesigner.
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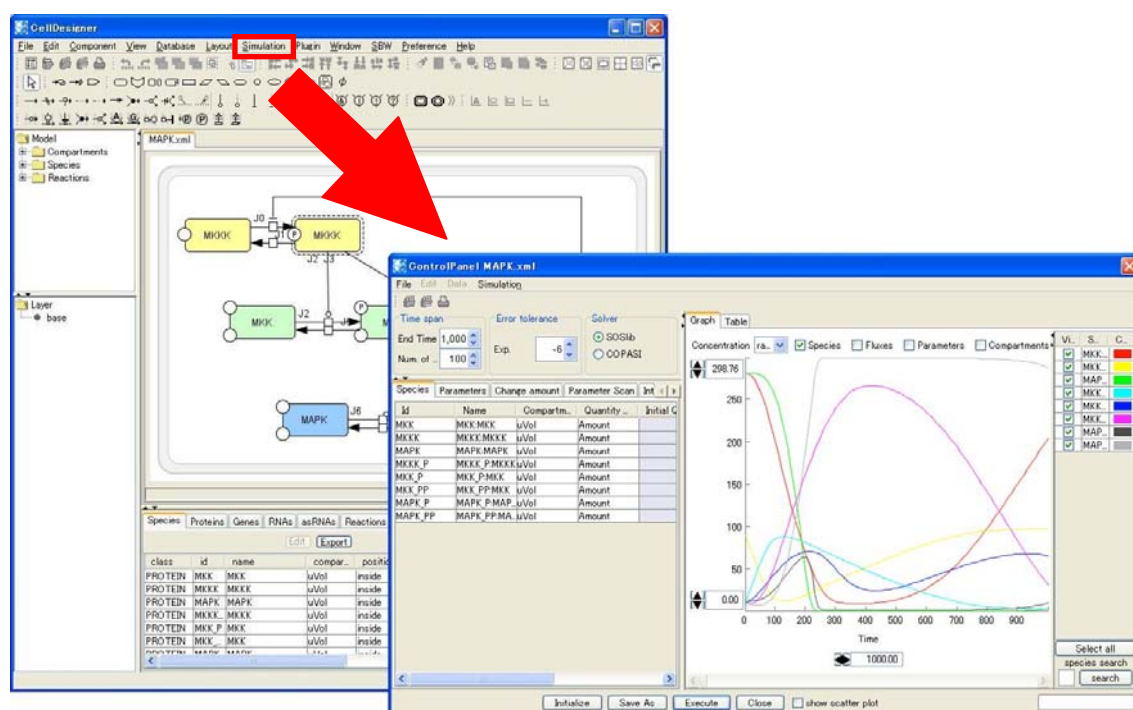
1. Introduction

The “Control Panel” is designed to assist the users to simulate directly from CellDesigner controlling the amounts and parameters of the Species.

Calling directly SBML ODE Solver (<http://www.tbi.univie.ac.at/~raim/odeSolver/>) from CellDesigner, ControlPanel enables you to specify the details of parameters, changing amount, conducting parameter search, and interactive simulation with intuitive manner.

You can also choose COPASI (<http://www.copasi.org/>) as an alternative solver.

See also: Startup Guide (Sections 7.1 & 7.5).



Sample file used in this document:

This document uses a sample model “MAPK.xml” provided with SBML ODE Solver.

This model has been slightly modified from a model obtained from <http://sbml.org/models/>.

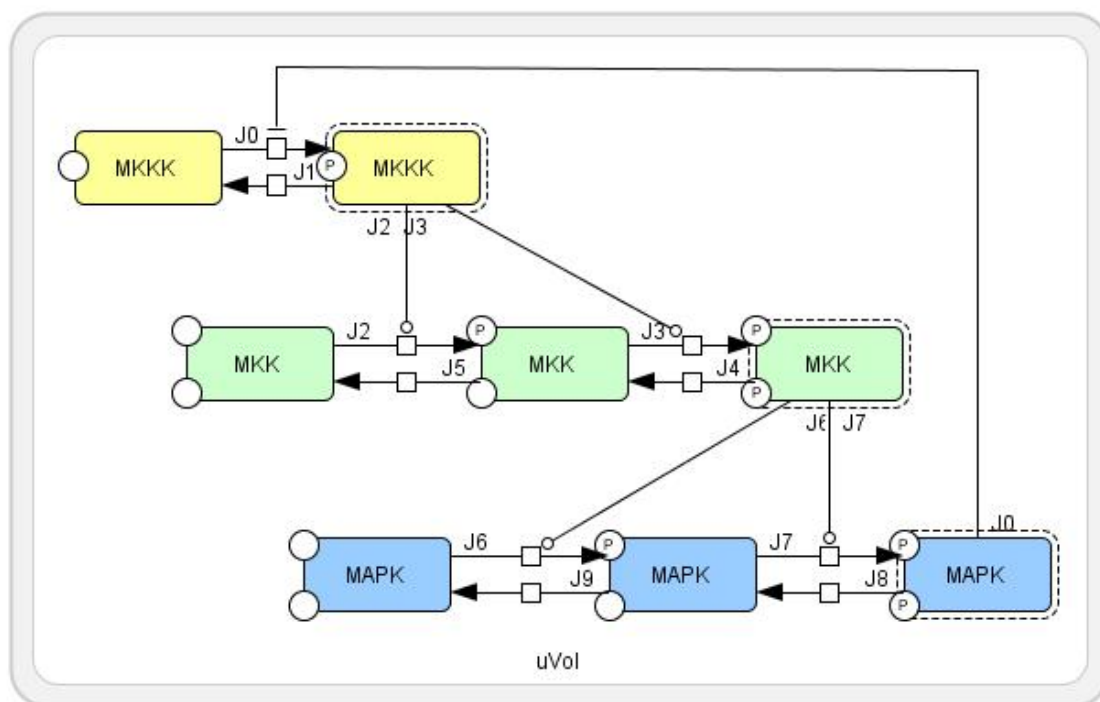
It has been published in Kholodenko BN. Negative feedback and ultrasensitivity can bring about oscillations in the mitogen-activated protein kinase cascades. Eur. J. Biochem. 267: 1583-1588 (2000).

2. Quick Tutorial of Simulation

Before you start simulation

Make sure you have the model with all the formulae necessary for the simulation have input to the reactions. You can check the KineticLaws in the reaction list:

See also: Startup Guide (Chapter 7) or CellDesigner Online Help.



KineticLaw

id	name	reactants	products	modifiers	math
J0	J0	MKKK	MKKK_P	MAPK_PP	$V1 * MKKK / ((1 + \text{pow}(\text{MAPK_PP} / Ki, n)) * (K1 + MKKK))$
J1	J1	MKKK_P	MKKK		$V2 * MKKK_P / (KK2 + MKKK_P)$
J2	J2	MKK	MKK_P	MKKK_P	$k3 * MKKK_P * MKK / (KK3 + MKK)$
J3	J3	MKK_P	MKK_PP	MKKK_P	$k4 * MKKK_P * MKK_P / (KK4 + MKK_P)$
J4	J4	MKK_PP	MKK_P		$V5 * MKK_PP / (KK5 + MKK_PP)$
J5	J5	MKK_P	MKK		$V6 * MKK_P / (KK6 + MKK_P)$
J6	J6	MAPK	MAPK_P	MKK_PP	$k7 * MKK_PP * MAPK / (KK7 + MAPK)$
J7	J7	MAPK_P	MAPK_PP	MKK_PP	$k8 * MKK_PP * MAPK_P / (KK8 + MAPK_P)$
J8	J8	MAPK_PP	MAPK_P		$V9 * MAPK_PP / (KK9 + MAPK_PP)$
J9	J9	MAPK_P	MAPK		$V10 * MAPK_P / (KK10 + MAPK_P)$

Species

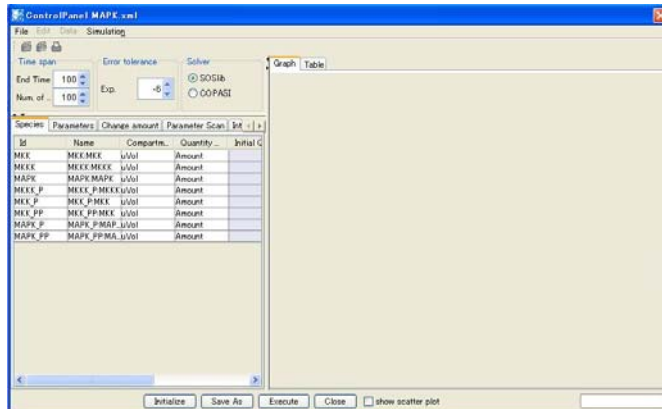
class	id	name	compartment	quantity type	initialQuantity
PROTEIN	MKK	MKK	uVol	Amount	280
PROTEIN	MKKK	MKKK	uVol	Amount	90
PROTEIN	MAPK	MAPK	uVol	Amount	280
PROTEIN	MKKK_P	MKKK	uVol	Amount	10
PROTEIN	MKK_P	MKK	uVol	Amount	10
PROTEIN	MKK_PP	MKK	uVol	Amount	10
PROTEIN	MAPK_P	MAPK	uVol	Amount	10
PROTEIN	MAPK_PP	MAPK	uVol	Amount	10

Parameters

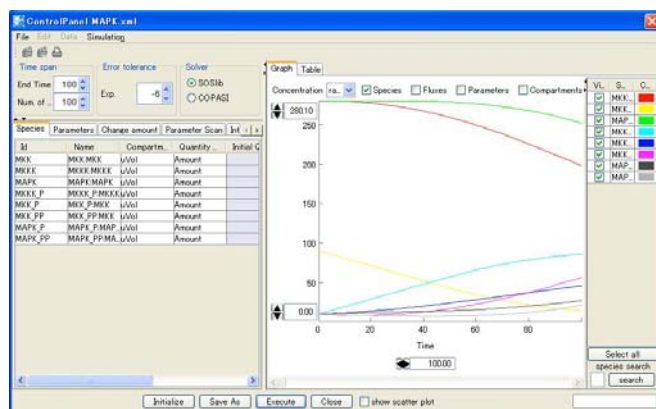
scope	id	name	value	units	constant
local:Reaction(J0)	V1		2.5		TRUE
local:Reaction(J0)	Ki		9		TRUE
local:Reaction(J0)	n		1		TRUE
local:Reaction(J0)	K1		10		TRUE
local:Reaction(J1)	V2		0.25		TRUE
local:Reaction(J1)	KK2		8		TRUE
local:Reaction(J2)	k3		0.025		TRUE
local:Reaction(J2)	KK3		15		TRUE
local:Reaction(J2)	V0	V0	111		TRUE
local:Reaction(J2)	K0	K0	1		TRUE
local:Reaction(J3)	k4		0.025		TRUE
local:Reaction(J3)	KK4		15		TRUE
local:Reaction(J4)	V5		0.75		TRUE
local:Reaction(J4)	KK5		15		TRUE
local:Reaction(J5)	V6		0.75		TRUE
local:Reaction(J5)	KK6		15		TRUE
local:Reaction(J6)	k7		0.025		TRUE
local:Reaction(J6)	KK7		15		TRUE
local:Reaction(J7)	k8		0.025		TRUE
local:Reaction(J7)	KK8		15		TRUE
local:Reaction(J8)	V9		0.5		TRUE
local:Reaction(J8)	KK9		15		TRUE
local:Reaction(J9)	V10		0.5		TRUE
local:Reaction(J9)	KK10		15		TRUE

To run a basic simulation:

1. Open a file to simulate by CellDesigner.
2. Select "ControlPanel" from the "Simulation" menu of CellDesigner.

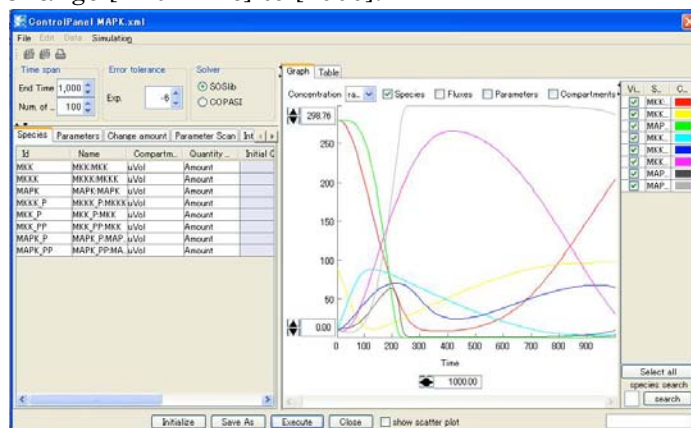
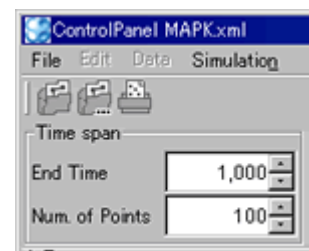


3. Click the "Execute" button on the bottom of the "ControlPanel".



By default, the simulation time end is set to 100 and number of points to plot is 100. You can enter values into "End Time" and "Num.of Points" to change these values.

4. Change [End Time] to [1000].



To view the values of the simulation results:

- Click the [Table] Tab behind the [Graph] tab on the right panel.

You can view the results of the simulation in the table format. You can switch [species] [fluxes] [parameters] and [compartment] by clicking the relevant tabs.

time / names	MKK	MKKK	MAPK	MKKK_P	MKK_P	MKK_PP
0.0	290.0	90.0	290.0	10.0	10.0	
10.0	279.6622903	90.71805904	279.6795776	19.28194015	11.65649499	3.681114804
20.0	277.4105421	71.26418001	260.0123660	29.73581998	13.97921501	9.710242296
30.0	273.2337896	61.62264580	260.0497061	38.37736419	16.68953632	10.07667606
40.0	267.1211906	51.97594200	279.6672063	40.02695799	20.07727090	12.80152639
50.0	259.1055906	42.65937771	278.5503677	67.34002228	23.94692462	16.42871962
60.0	249.3000217	34.12662769	276.3006966	69.8737240	28.2193826	22.49039999
70.0	237.9211842	26.82384051	272.8854367	73.17615440	32.67360127	29.40521446
80.0	225.2767863	21.06130968	267.7549262	76.93893031	37.16335860	37.55965470
90.0	211.7282366	16.8943851	260.7661132	80.09064448	41.55271384	46.7236947
100.0	197.6112907	14.20497591	251.689795	85.79552705	45.74111530	56.64755296
110.0	182.2367618	12.65732077	240.4165200	87.34267922	49.66754220	67.05659496
120.0	168.8013279	11.96799785	226.8439846	88.00000014	53.29690809	77.87176392
130.0	154.5657559	11.89575921	210.9300021	88.10424078	56.6106612	88.02237702
140.0	140.5710501	12.26767168	192.6917132	87.73286071	59.6995679	99.02925009
150.0	126.9434202	12.96541968	172.1617431	87.03408031	62.25684396	110.8007298
160.0	113.7880338	13.90864168	149.4834931	86.09139831	64.57082219	121.6641439
170.0	101.1070506	15.04130490	124.7015530	84.95895509	66.53257895	132.3603705
180.0	89.05567337	16.32337110	98.46649081	83.67603989	68.12418597	143.8481236
190.0	77.81611797	17.72821376	71.10913762	82.27478623	69.32381282	153.0612692
200.0	66.91537844	19.22415030	43.94130762	80.77584969	70.09776721	162.968543
210.0	57.0049686	20.80215590	19.90138362	79.19784409	70.41224180	172.5836613
220.0	47.95693647	22.44387267	5.753959990	77.56612732	70.22201752	181.8210490

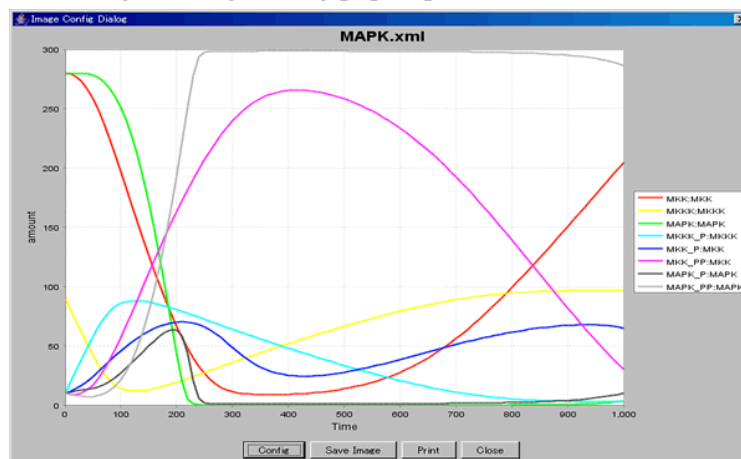
To save an image of the simulation result:

You can save the graph image into five types of graphical file format:

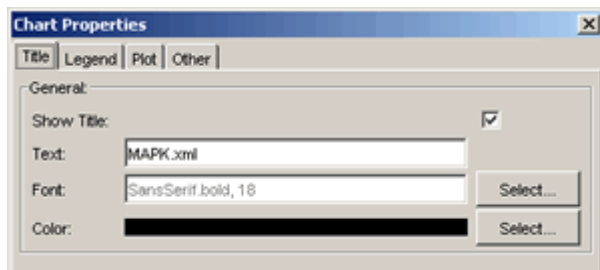
BMP, JPEG, PNG, TIFF, and PNM file format: (".bmp", ".jpg", ".png", ".tif" and ".pnm").

- Select "Save Image" from the "File" menu.

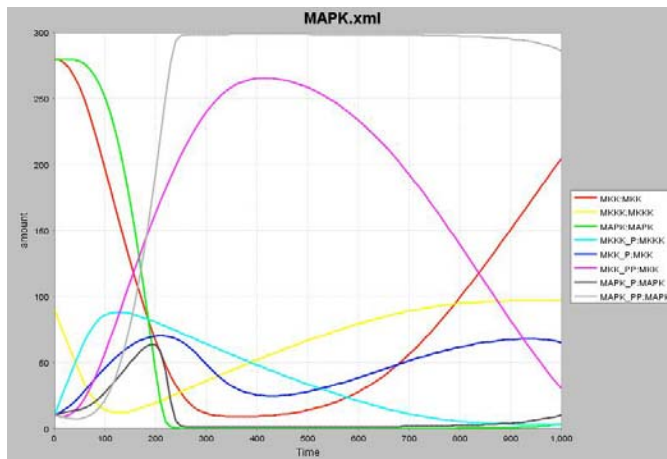
The Image Config Dialog pops up.



- Select "Config" button to specify the graph items such as title, legend and plot ranges.

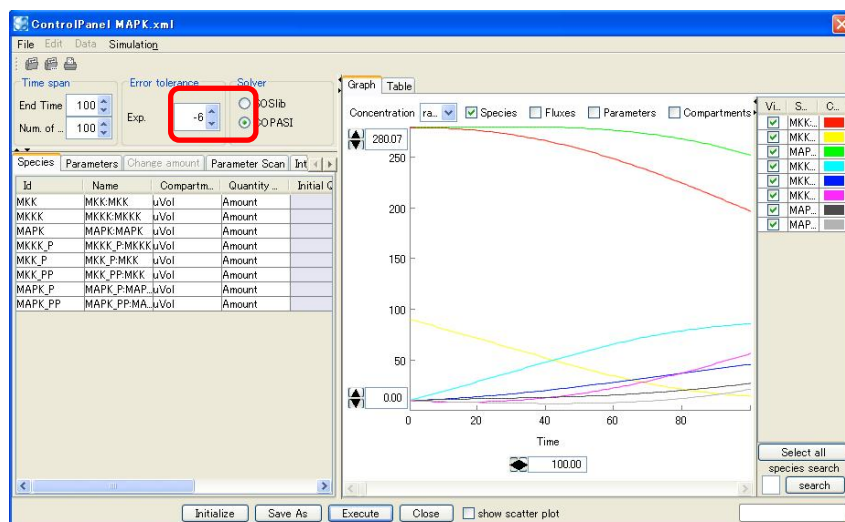


8. Select “Save Image” button, then select the file format and specify the file name for a graph image.



To change the solver to COPASI:

9. Click the “COPASI” radio button.
10. Click “Execute”.



3. Change the Initial Quantities of Species and Parameter Values

It is possible to run the simulation with the values in "Species" and "Parameters" tabs changed. The values changed in the "ControlPanel" are updated to the corresponding values in the "CellDesigner" itself.

To change the parameters for "Species":

1. Click the "Species" tab.

Species					
Id	Name	Compartment	Quantity Type	Initial Quantity	Substance ...
MKK	MKK:MKK	uVol	0	280.0	
MKKK	MKKK:MKKK	uVol	0	90.0	
MAPK	MAPK:MAPK	uVol	0	280.0	
MKKK_P	MKKK_P:MKKK	uVol	0	10.0	
MKK_P	MKK_P:MKK	uVol	0	10.0	
MKK_PP	MKK_PP:MKK	uVol	0	10.0	
MAPK_P	MAPK_P:MAPK	uVol	0	10.0	
MAPK_PP	MAPK_PP:MAPK	uVol	0	10.0	

2. Change the initial values by clicking each blue cell for the values to be modified.
3. Click the "Execute" button to run the simulation with the new parameters.

To change the parameter values:

1. Click the "Parameters" tab.

Parameters					
Scope	Id	Name	Value	Units	constant
local Reactio...	V1		2.500		true
local Reactio...	K1		9.000		true
local Reactio...	n		1.000		true
local Reactio...	K1		10.000		true
local Reactio...	V2		0.250		true
local Reactio...	KK2		8.000		true
local Reactio...	k3		0.025		true
local Reactio...	KK3		15.000		true
local Reactio...	k4		0.025		true
local Reactio...	KK4		15.000		true
local Reactio...	V5		0.750		true
local Reactio...	KK5		15.000		true
local Reactio...	V6		0.750		true
local Reactio...	KK6		15.000		true

2. Change the initial parameters by clicking each blue cell for the values to be modified.
3. Click the "Execute" button to run the simulation with the new parameters.

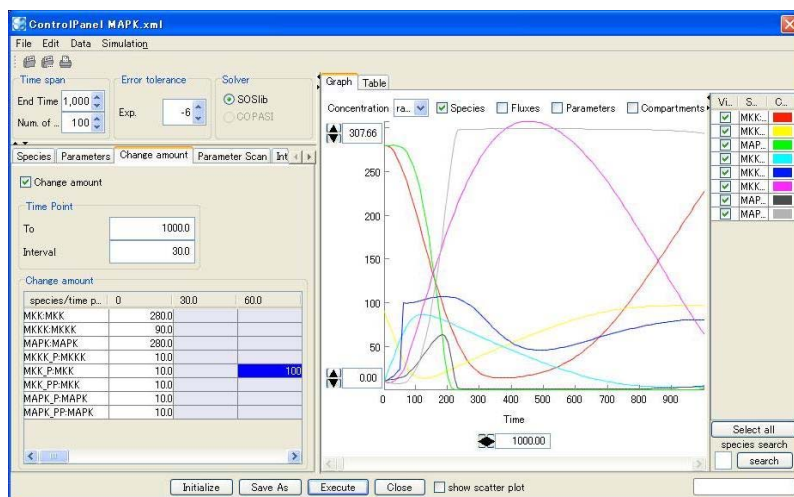
4. Change Amount for Simulation

In order to simulate the time course of "Species" resulting from forced expression of a gene/genes on a certain time, "ControlPanel" implements the "Change amount" functionality. By this functionality you can run a simulation with the amount of "Species" changed to a desired value on a specific time.

Note: COPASI does not support the Change Amount functionality.

To run simulation changing the amount of Species at specific time:

1. Click the "Change amount" tab.
2. Check the "Change amount" checkbox.
3. Input the amount of "Species" corresponding to the time specified at the header of the rows in the change amount matrix.
4. Click the "Execute" button.



The change amount matrix can be edited by external software such as MS Excel by exporting the matrix to a CSV file. The CSV file edited outside can be imported to "ControlPanel".

To export and import the Change amount matrix:

1. Select "Export" from the "Data" menu.
2. Enter a file name and click the "Save" button.
(A CSV file will be created with the specified file name.)
3. Open the CSV file using other software such as MS Excel, edit values, and save them.
4. Select "Import" from the "Data" menu.
5. Select the file that you have just edited and click the "Open" button.

Span	100			
Step	30			
species/time point	0	30	60	90
MKKK	90			
MKKK_P	10			
MKK	280			
MKK_P	10		100	
MKK_PP	10			
MAPK	280			
MAPK_P	10			
MAPK_PP	10			

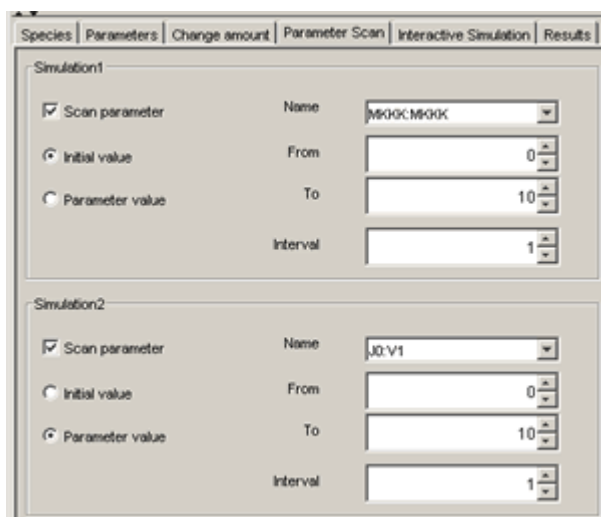
e.g. an example of .CSV file exported from Control Panel.

5. Parameter Scan

You can run simulations in a batch job to scan parameters. By setting the range and interval of each parameter to scan, "ControlPanel" runs the simulation with each parameter changing within the specified range with the value incremented by the specified interval.

To scan parameters:

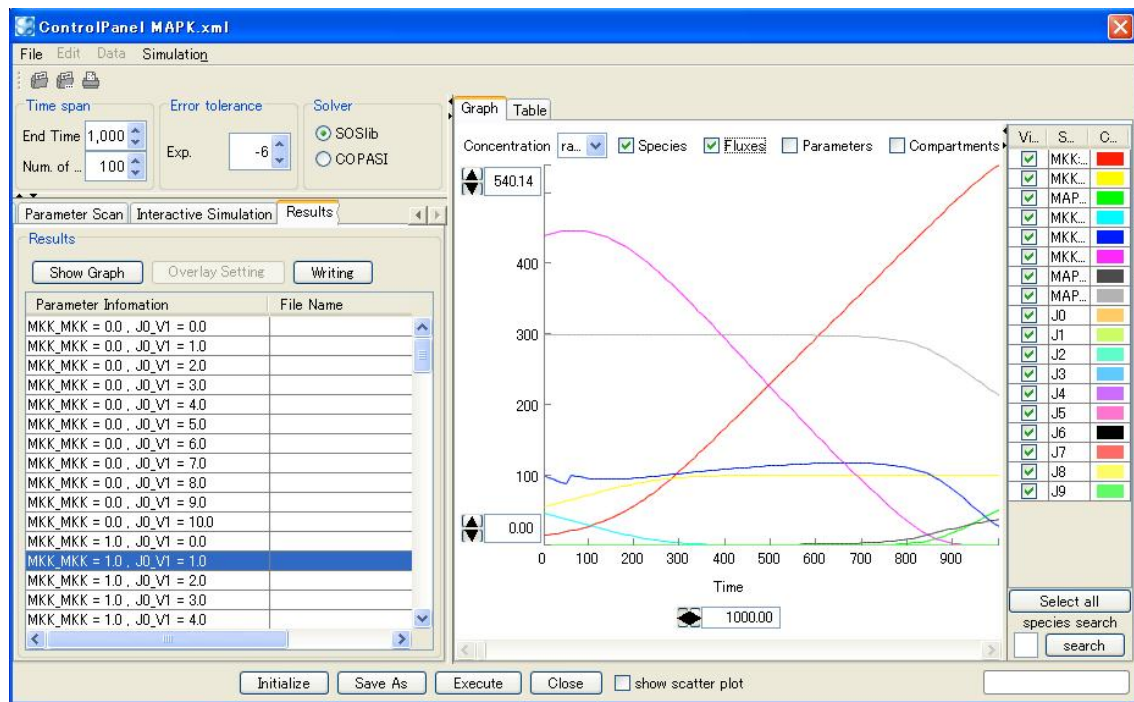
1. Click the "Parameter Scan" tab.
2. Check the "Scan parameter" checkbox.
3. Select the "Initial value" or "Parameter value" option.
4. Select the name of a parameter to change from the list.
5. Input values into "From", "To", and "Interval" for a parameter scan, which correspond to the start value, the end value, and the interval respectively.
6. Click [Execute] button to start simulation scanning the specified parameters.



In case you check two "Scan parameter" checkboxes, you can scan two parameters. The simulations are executed using the combination of the two parameters.

To see the results of parameter scan:

1. When the message "The simulation was completed" is displayed, click the blinking "Result" tab.
2. Select the result you wish to see and click the "Show Graph" button.

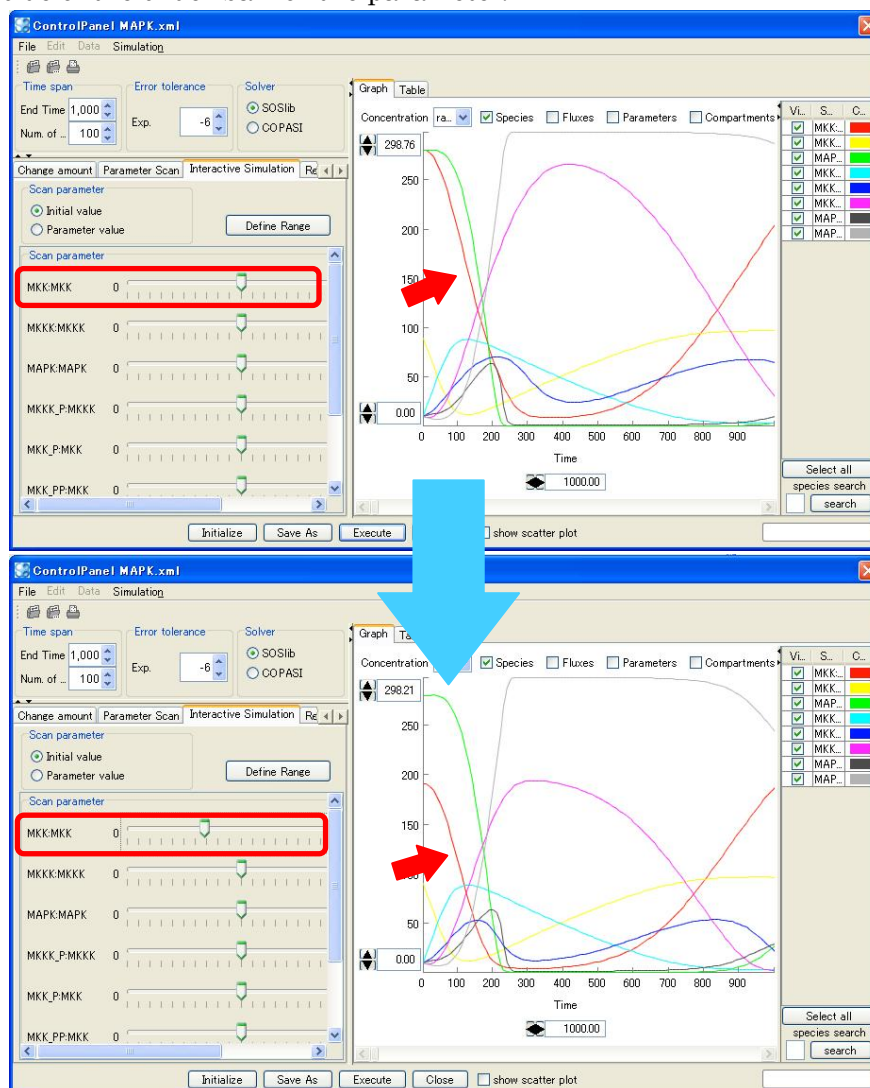


6. Interactive Simulation

"ControlPanel" allow you to see real-time results of simulations. You should use "Interactive simulation" for this purpose.

To run interactive simulations:

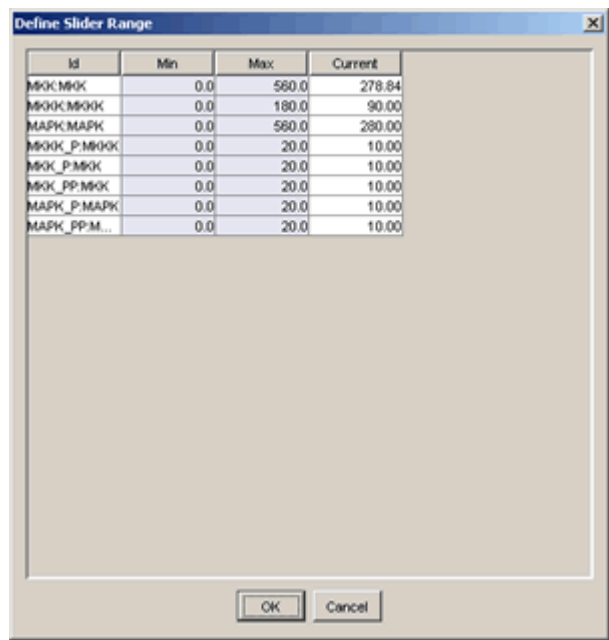
1. Click the "Interactive Simulation" tab.
2. Select the "Initial value" or "Parameter value" option.
3. To change a parameter, slide each slider bar or input a value into a box on the right side of the slider bar for the parameter.



The minimum and maximum values of slider bar were automatically defined based on the initial values of SBML. However, you can change the data range of slider bars.

To change the data range of slider bars:

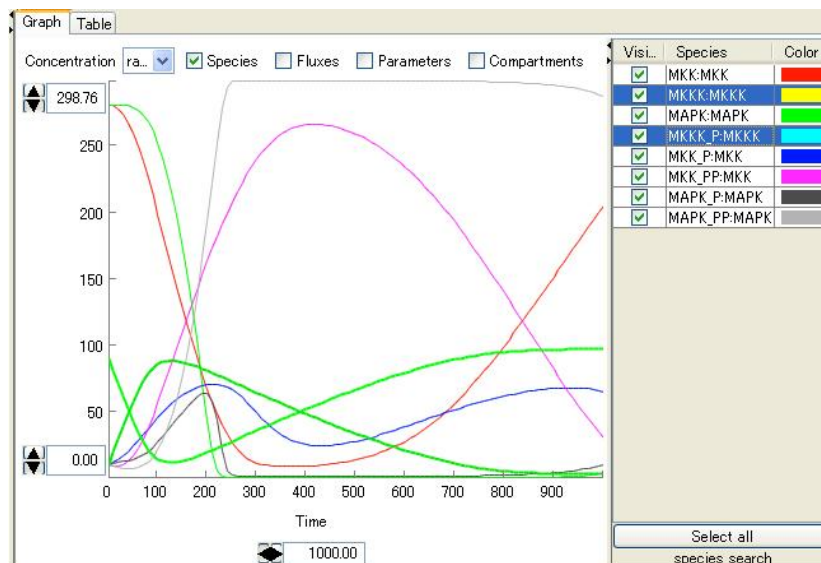
- 1. Click the "Define Range" button.
- 2. Change the minimum and maximum values and click the "OK" button.



7. Plot area

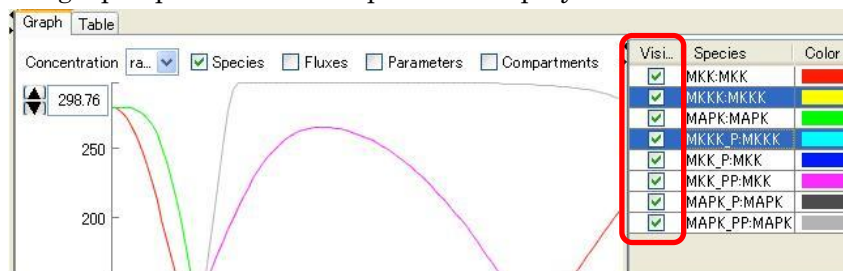
To highlight a plot and a node:

- Click a cell of the "Species" column in the right panel
(the corresponding plot will be highlighted).
- Click on a plot
(the corresponding table data on the right panel will be highlighted).



To change the graphs plot displayed in the plot area:

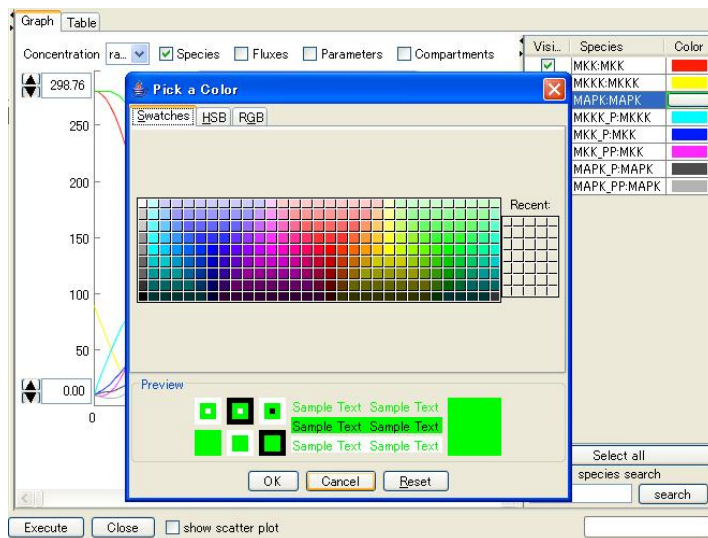
1. Check checkboxes in the "Visible" column in the right panel.
2. The graphs plot of checked species is displayed.



Note: [Select All] / [Unselect All] toggle button is available for batch operation. (just above the search button)

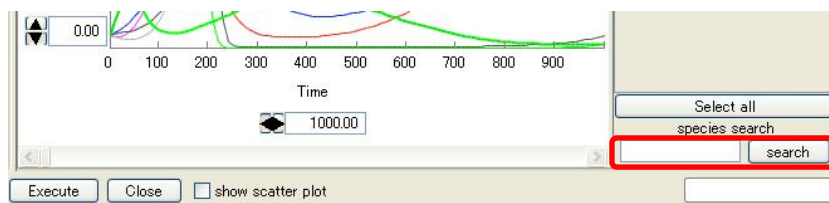
To change the color of a plot:

1. Click a cell in the "Color" column on the right panel.
("Pick a color" dialog appears)
2. Select a color and click the "OK" button.



Search for Species:

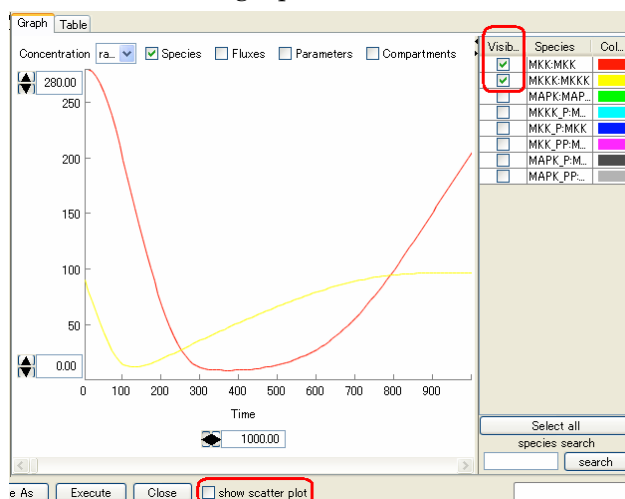
To search for a specific "Species", enter a keyword into "species search" textbox located on the lower right portion of "ControlPanel", and click the "search" button.



Show Scatter Plot:

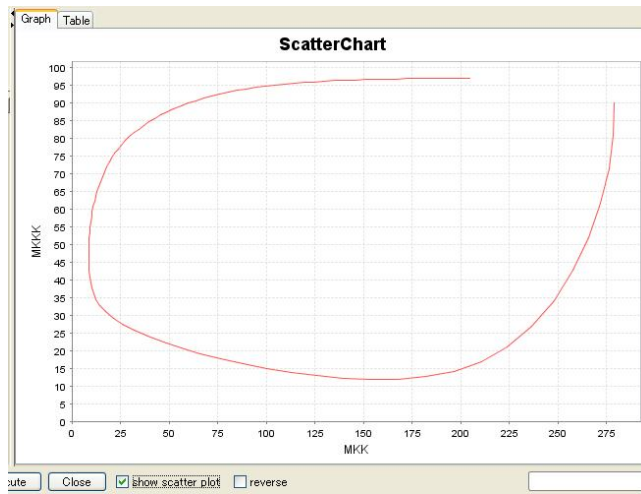
You can plot and compare the data of an arbitrary pair of Species.

1. In the ControlPanel, select any two Species by ticking the checkboxes in the "Visible" column.
2. Observe that the graph has been reduced to two curves.

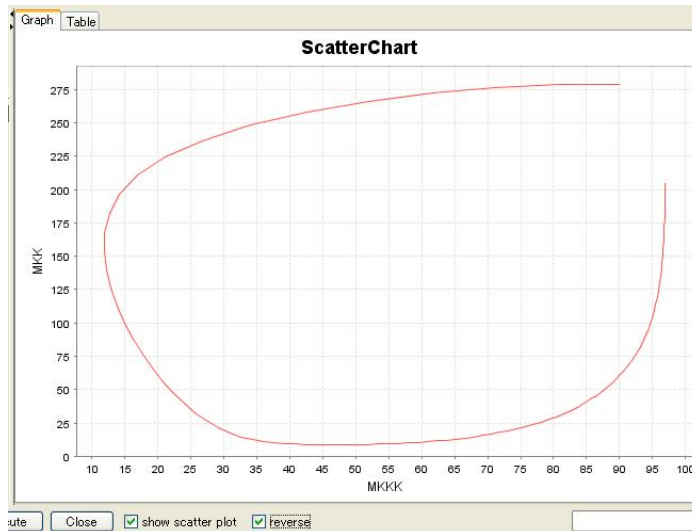


3. Tick the "show scatter plot" checkbox.

4. Observe that in the new graph the x-axis does not indicate time series any more.



5. Select the “reverse” checkbox to change the x- and y- axes.



8. File I/O

The result of a simulation is stored in three types of file: the model to be used (SBML), the parameters to be set (*.sim), and the simulation result (*.txt). The model (SBML) has a one-to-one correspondence with the parameters (*.sim). For example, if you stored the results of two simulations run by model1.xml and newmodel.xml into the "models" directory, the contents of the directory will be:

```
[models]
+-----model1.xml (SBML)
+-----model1.sim (parameters setting for the model 1)
+-----[model1] (the result folder for the model 1)
          +-----result1.txt (simulation result 1)
          +-----result2.txt (simulation result 2)
          +
          .....
+-----newmodel.xml (a new model)
+-----newmodel.sim (parameters setting for the new model)
+-----[newmodel] (the result folder for the new model)
          +-----result1.txt (simulation result 1)
          +-----result2.txt (simulation result 2)
```

To save a simulation result into files:

1. Select "Save As" from the "File" menu of "ControlPanel".
2. Enter the file name for a simulation result and click the "save" button.
3. Then three types of file having extensions ".xml", ".sim", and ".txt" are created.

To open a result saved in files:

1. Select "Open" from the File menu of CellDesigner.
2. Select "SBML file" and click the "open" button.
3. The corresponding ".sim" file and result files are automatically imported, so you can start the "ControlPanel" and see the result.