Running CellDesigner™ Simulation with Control Panel

Quick Tutorial

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for CellDesigner Ver. 4.1

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Contents

Acknowledgements

- Rainer Machné and Christoph Flamm at University of Vienna for providing us a library version of SBML ODE Solver (SOSlib).
- Ralph Gauges, Sven Sahle and Ursula Kummer at University of Heidelberg for the development of a library version of COPASI.
- Frank Bergmann and Herbert Sauro at University of Washington for helping us support SBW-2.x on CellDesigner.
- Many thanks to the users who kindly provided us bug reports and feature requests!

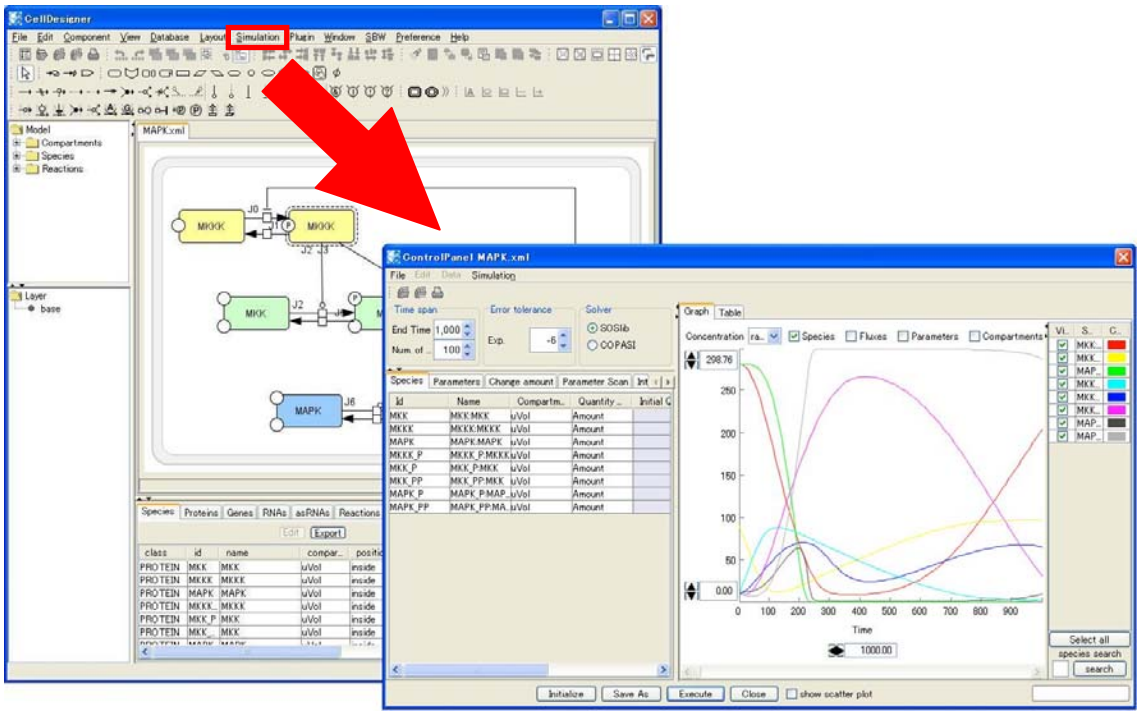
1. Introduction

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



Sample file used in this document:

This document uses a sample model “MAPK.xml” originally provided with SBML ODE Solver. When you install CellDesigner, MAPK.xml is deployed in the `/<your CellDesigner directory>/samples/` folder.

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

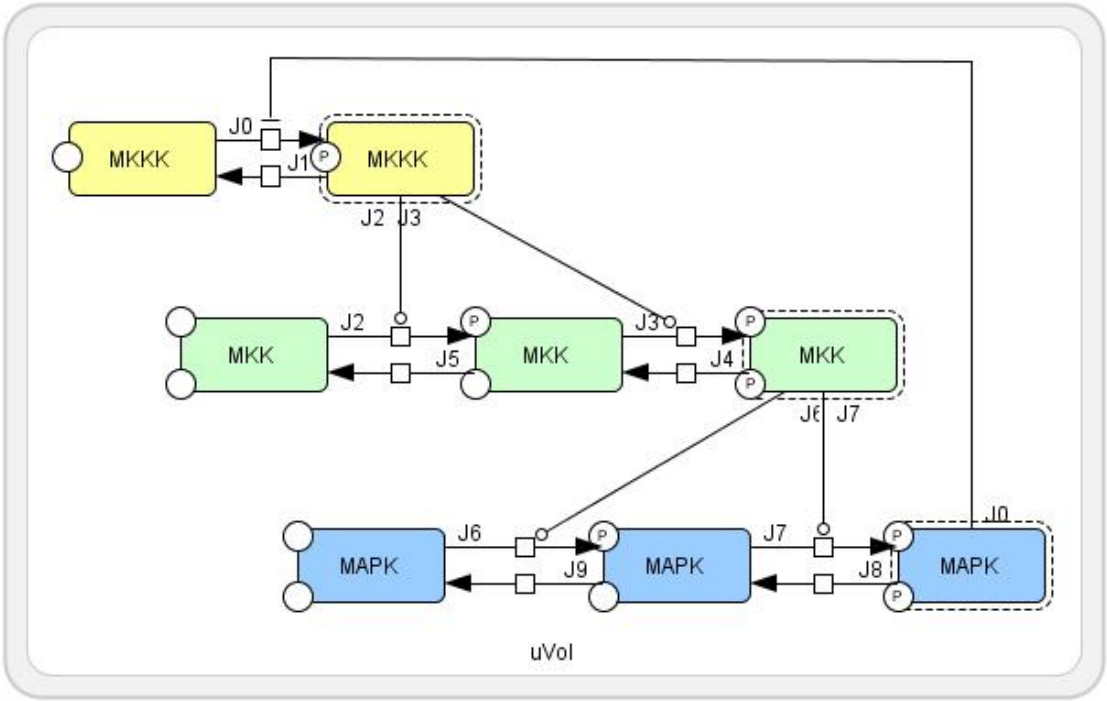
The model has been published in Kholodenko BN. Negative feedback and ultrasensitivity can bring about oscillations in the mitogen-activated protein kinase cascades. Eur. J. Biochem. 267: 1583-1588 (2000).

2. Quick Tutorial of Simulation

2.1 Before you start simulation

Throughout this tutorial, we will use MAPK.xml which can be found in the `<CellDesigner installation directory>/samples/` folder. All the formulae necessary for the simulation are already embedded in the Reactions. You can check the formulae in the CellDesigner's Reactions list.

→ See also: Startup Guide or CellDesigner Online Help.



KineticLaw

id	name	reactants	products	modifiers	math
J0	J0	MKKK	MKKK_P	MAPK_PP	V1 * MKKK / ((1 + pow(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

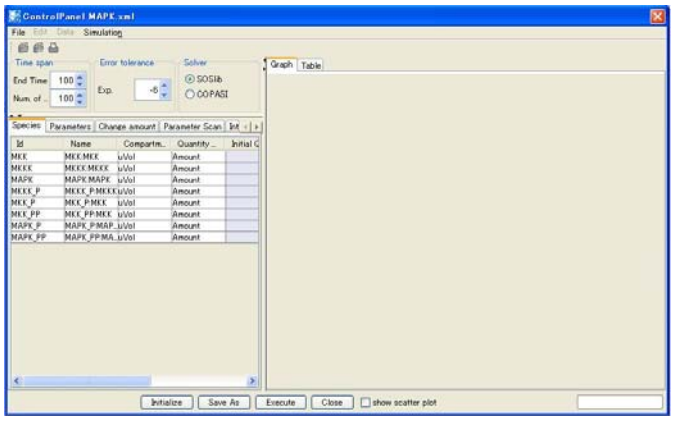
class	id	name	compartment	quantity type	initialQuantity
PROTEIN	MKK	MKK	uVol	Amount	280
PROTEIN	MKKK	MKKK	uVol	Amount	90
PROTEIN	MAPK	MAPK	uVol	Amount	280
PROTEIN	MKKK_P	MKKK	uVol	Amount	10
PROTEIN	MKK_P	MKK	uVol	Amount	10
PROTEIN	MKK_PP	MKK	uVol	Amount	10
PROTEIN	MAPK_P	MAPK	uVol	Amount	10
PROTEIN	MAPK_PP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

Parameters

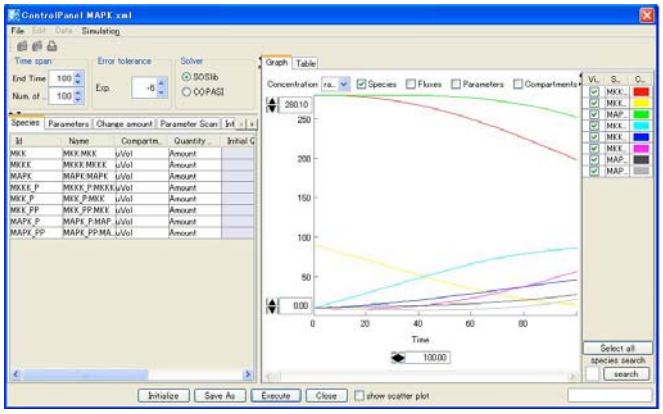
scope	id	name	value	units	constant
local:Reaction(J0)	V1		2.5		TRUE
local:Reaction(J0)	Ki		9		TRUE
local:Reaction(J0)	n		1		TRUE
local:Reaction(J0)	K1		10		TRUE
local:Reaction(J1)	V2		0.25		TRUE
local:Reaction(J1)	KK2		8		TRUE
local:Reaction(J2)	k3		0.025		TRUE
local:Reaction(J2)	KK3		15		TRUE
local:Reaction(J2)	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

2.2 To run a basic simulation:

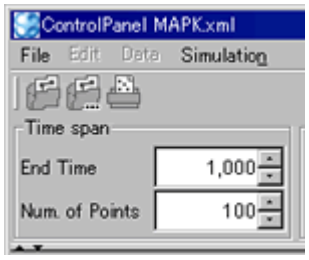
1. Open the sample file `MAPK.xml` in the `samples` folder.
2. In the Menu, select **Simulation** - **ControlPanel**.
3. The **ControlPanel** will open.



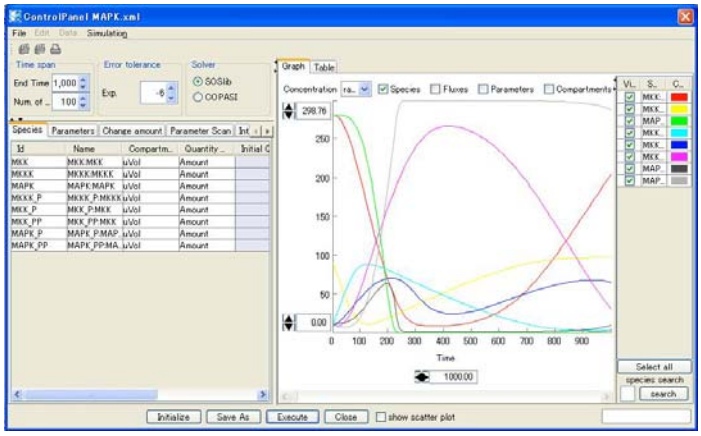
4. Click **Execute** button.
5. A graph will be drawn in the right window.



6. By default, the simulation **End Time** is set to "100" and **Num. of Points** to plot is "100". You can enter different values into **End Time** and **Num. of Points** to change these values.
7. Change **End Time** to "1000".

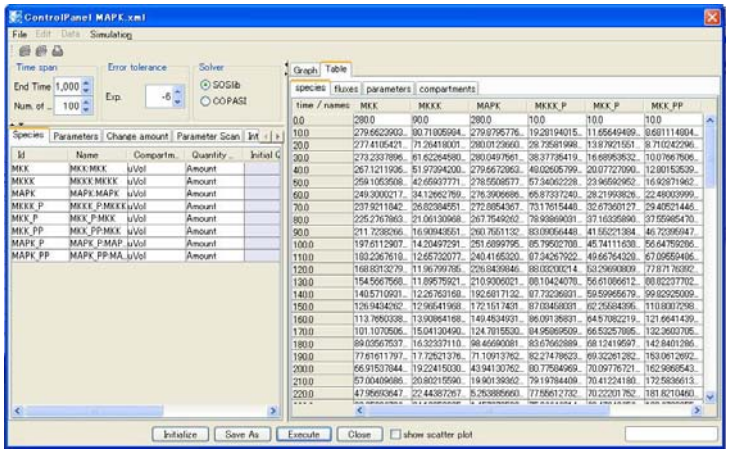


8. Click **Execute** button.
9. A graph is drawn with a longer time.



2.3 To view the values of the simulation results:

1. Click the **Table** Tab behind the **Graph** tab on the right panel.
2. You can view the results of the simulation in a table format. You can switch **species, fluxes, parameters** and **compartment** by clicking the relevant tabs.

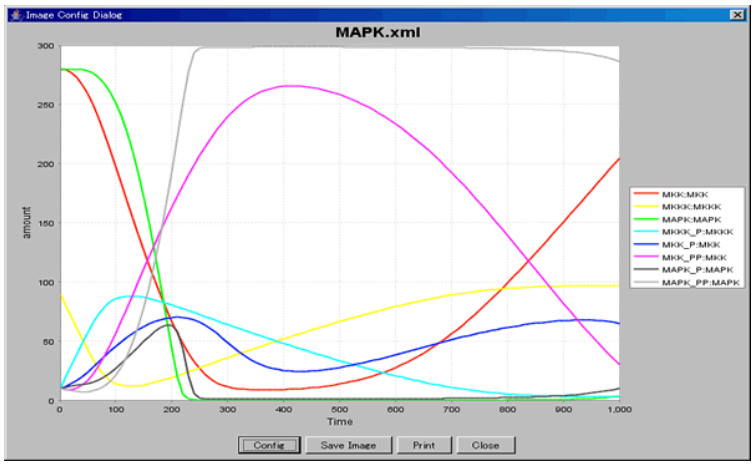


→ Note: You can copy the data from the table by specifying the area in the table. The data is treated as CSV format so you can paste it directly to the spreadsheet.

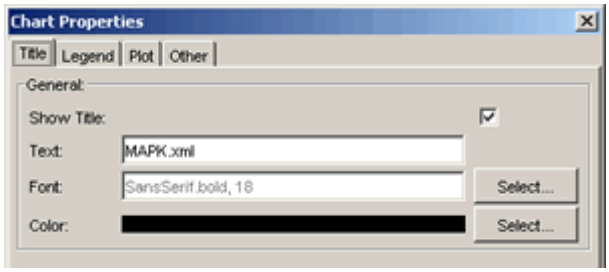
2.4 To save an image of the simulation result:

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".)

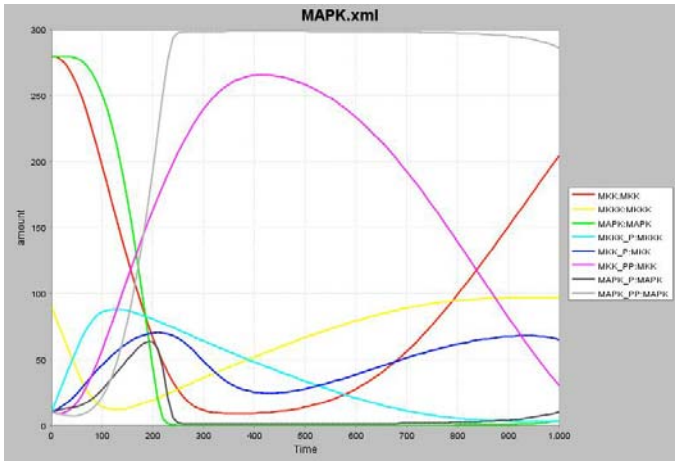
1. Select **Save Image / Print** from the **File** menu.
2. The **Image Config Dialog** pops up.



3. Select **Config** button to specify the graph items such as **Title**, **Legend** and **Plot** ranges.



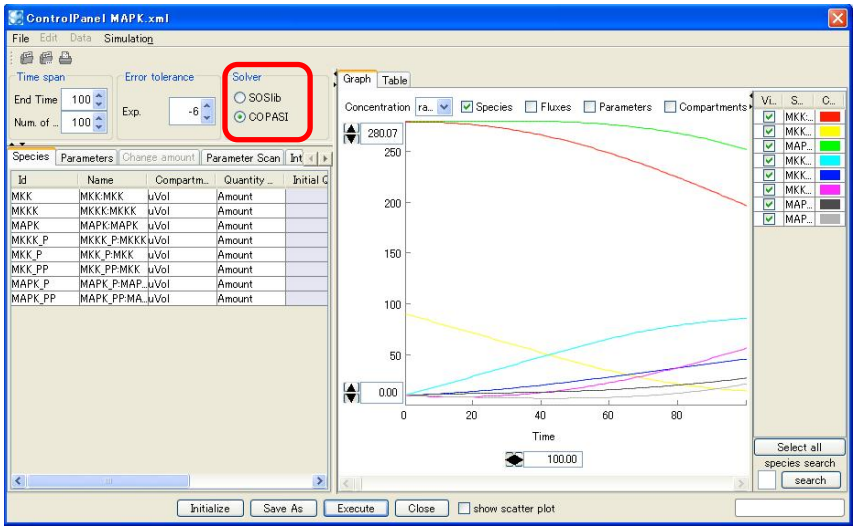
4. Click **OK**.
5. Select **Save Image** button, then select the file format and specify the file name for a graph image.



2.5 To change the solver to COPASI:

COPASI is a software application for simulation and analysis of biochemical networks. COPASI is free for non-commercial use. If you want to use COPASI with CellDesigner as a simulation solver, setup COPASI before you run the simulation.

1. Click the **COPASI** radio button.
2. Click **Execute**.



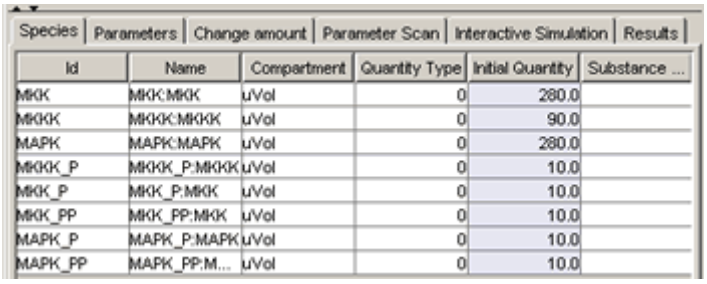
→ To install Copasi, see also README.txt or “Installation and Startup” section in CellDesigner’s Startup Guide,

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.

3.1 To change the initial quantity for Species:

1. Click the **Species** tab.

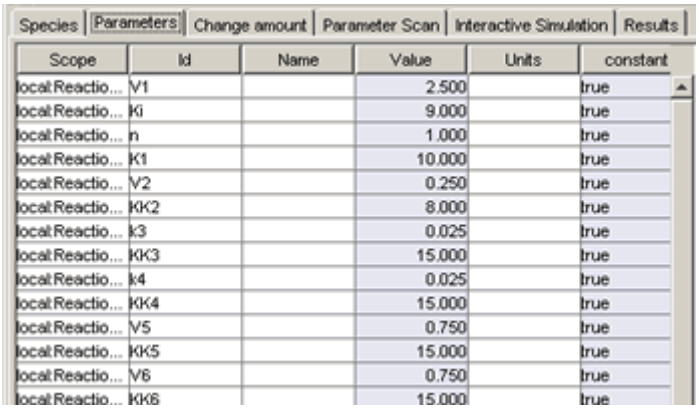


Id	Name	Compartment	Quantity Type	Initial Quantity	Substance ...
MKK	MKK:MKK	uVol	0	280.0	
MKKK	MKKK:MKKK	uVol	0	90.0	
MAPK	MAPK:MAPK	uVol	0	280.0	
MKKK_P	MKKK_P:MKKK	uVol	0	10.0	
MKK_P	MKK_P:MKK	uVol	0	10.0	
MKK_PP	MKK_PP:MKK	uVol	0	10.0	
MAPK_P	MAPK_P:MAPK	uVol	0	10.0	
MAPK_PP	MAPK_PP:M...	uVol	0	10.0	

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

3.2 To change the parameter values:

1. Click the **Parameters** tab.



Scope	Id	Name	Value	Units	constant
local:Reactio...	V1		2.500		true
local:Reactio...	Ki		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.

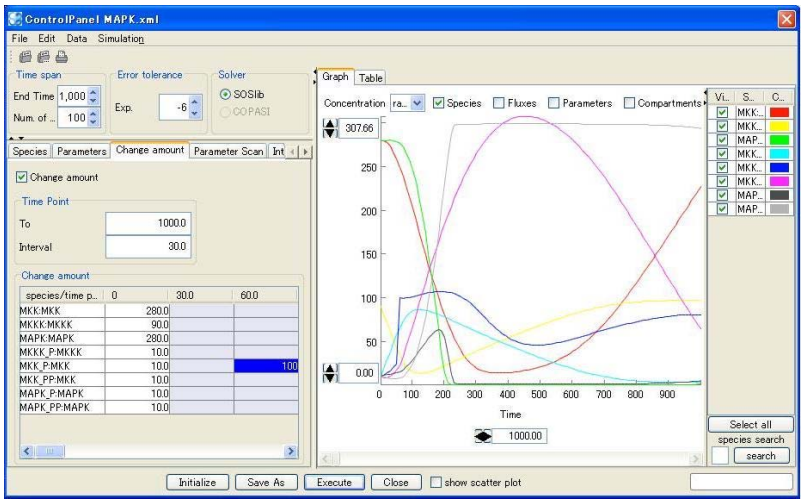
4. Change Amount for Simulation

In order to simulate the time course of Specie 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 at a specific time being changed to a desired value.

→ Note: COPASI does not support the Change Amount functionality.

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

1. Click the **Change amount** tab.
2. Check the **Change amount** checkbox.
3. In the **Change amount** matrix, enter the amount of Species at the time specified at the header row.



4. Click the **Execute** button.

4.2 To export and import the Change amount matrix:

The **Change amount** matrix can be edited by external software such as MS Excel by exporting the matrix to a CSV file. Conversely, a CSV file edited outside can be imported to ControlPanel.

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.

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.

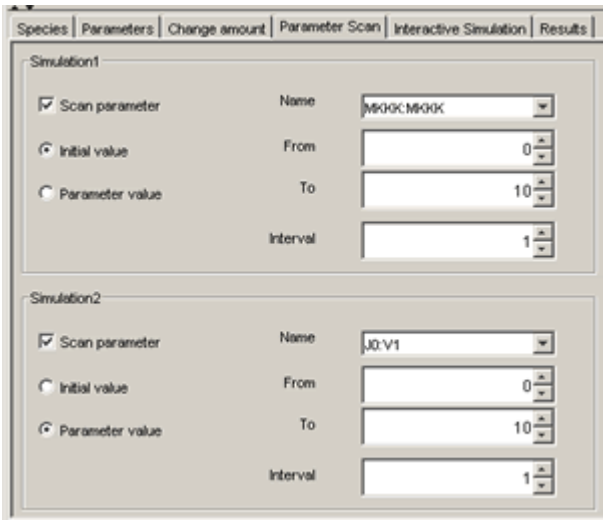
4. Select **Import** from the **Data** menu.
5. Select the file that you have just edited and click the **Open** button.

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.

5.1 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 **Name** 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.

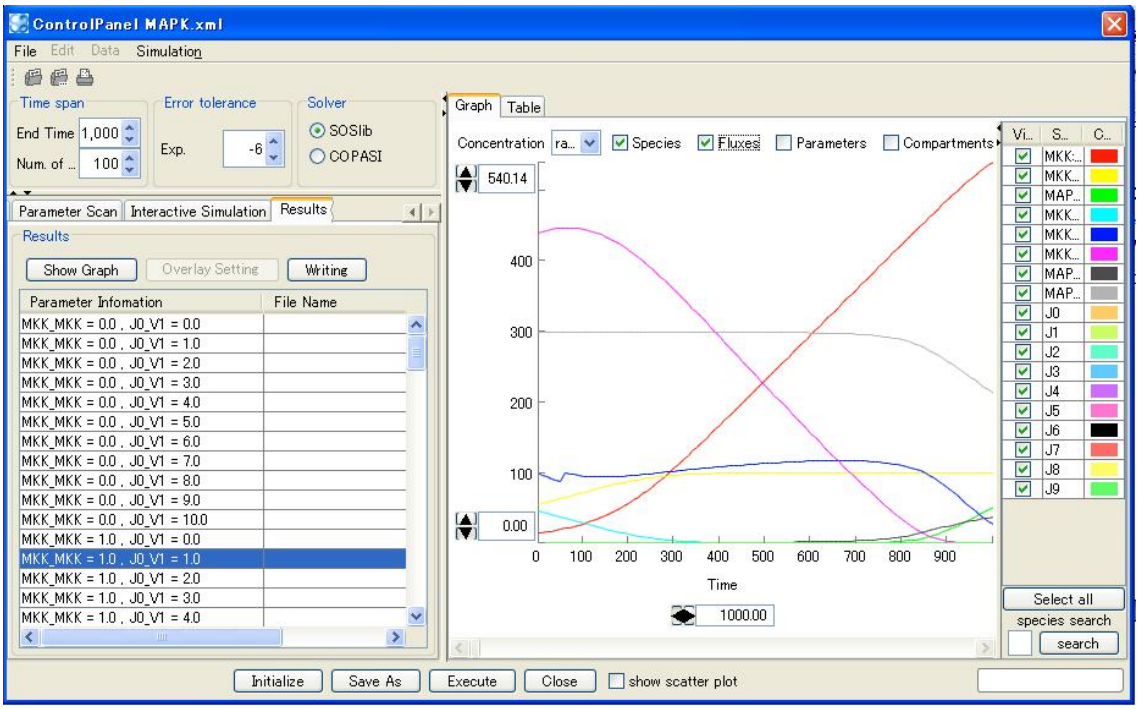


→ Note: In case you check two **Scan parameter** checkboxes, you can scan two parameters. The simulations are executed using the combination of the two parameters.

5.2 To see the results of parameter scan:

1. In the **Information** dialog saying "The simulation was completed" is displayed, click **OK**.
2. Click the blinking **Result** tab. (The right most tab)
3. Select the result you wish to see and click the **Show Graph** button.

→ Note: If you specify only one parameter on parameter scanning, you should specify Overlay Setting to view the graph.



5.3 To output the results of parameter scan:

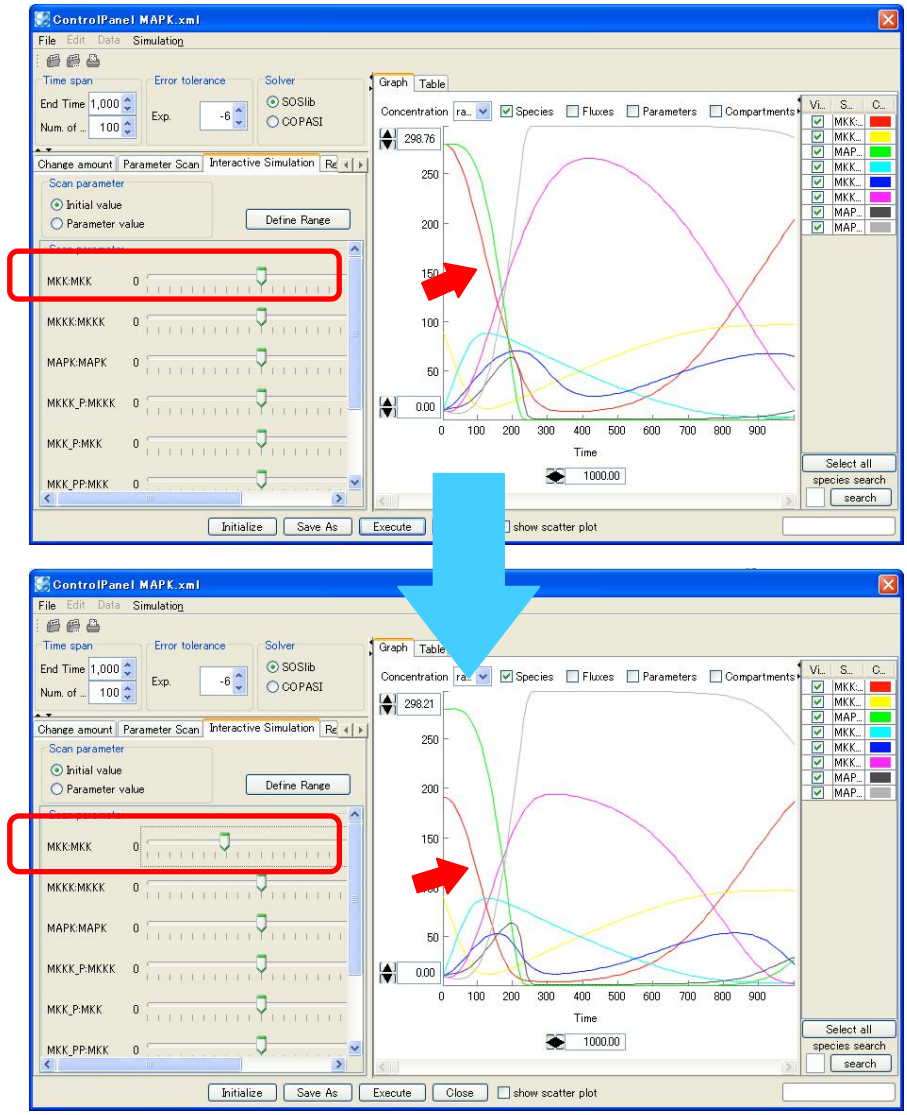
1. Click **Writing**.
2. Specify the file name and the directory to save the file.
3. The output of the parameter scan results will be saved in the text file format.

6. Interactive Simulation

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

6.1 To run interactive simulations:

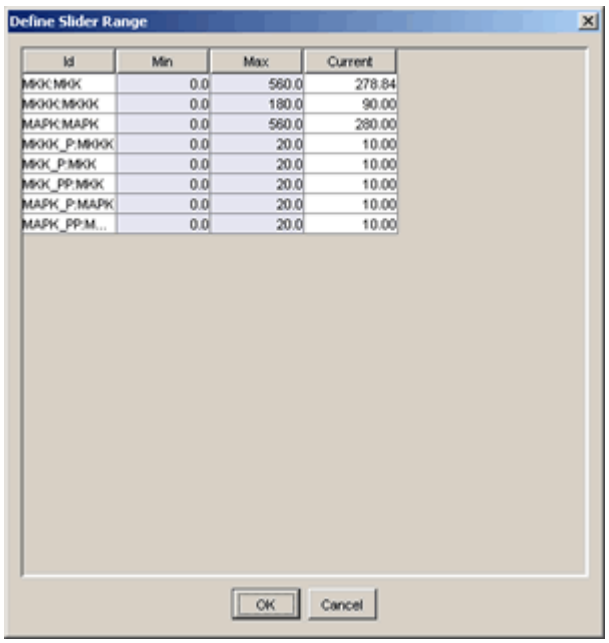
1. Click the **Interactive Simulation** tab.
2. Select the **Initial value** or **Parameter value** option.
3. To change a parameter, slide each slider bar or input a value into a box on the right side of the slider bar for the parameter.



→ Note: 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.

6.2 To change the data range of slider bars:

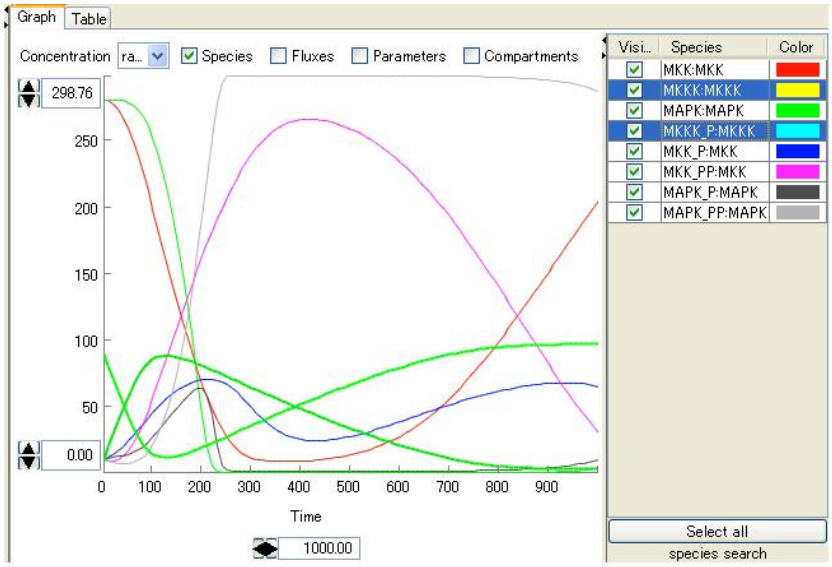
1. Click the **Define Range** button.
2. In the **Define Slider Range** dialog, change the minimum and maximum values and click the **OK** button.



7. Graph Area

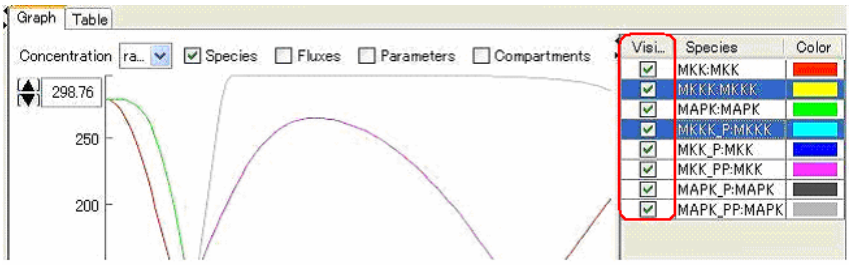
7.1 To highlight a Species in the Graph Area:

1. In the Control Panel, click **Graph** tab.
2. Click a cell in the **Species** column in the table.
3. The corresponding line in the **Graph** will be highlighted.
4. Next, click on a line in the **Graph**.
5. The corresponding table row on the right panel will be highlighted.



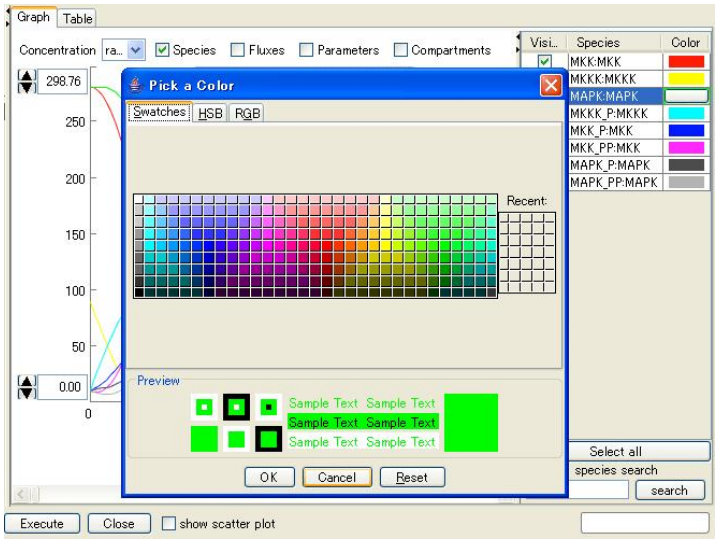
7.2 To show/hide Species displayed in the Graph Area:

1. In the Control Panel, click **Graph** tab.
2. Select/unselect checkboxes in the **Visible** column in the right panel.
3. The checked Species are displayed/hidden on the **Graph**.



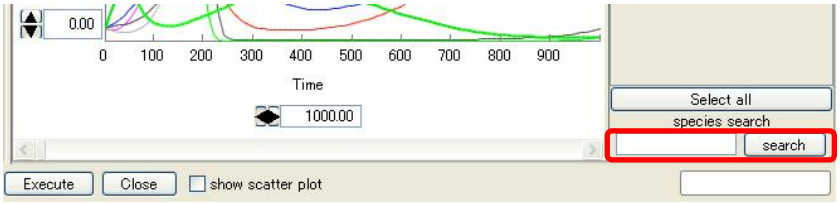
7.3 To change the line color of the graph:

1. In the Control Panel, click **Graph** tab.
2. Click a cell in the **Color** column on the right panel.
3. **Pick a Color** dialog appears.
4. Select a color and click the **OK** button.



7.4 To search for species:

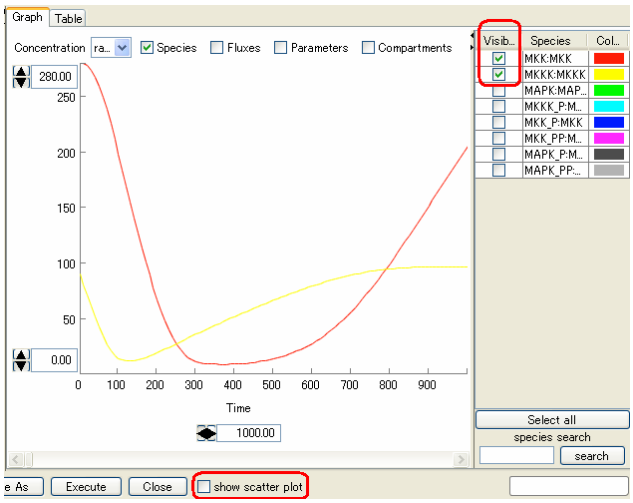
1. In the ControlPanel, in the **species search** textbox, enter your search word
2. Click **search**.



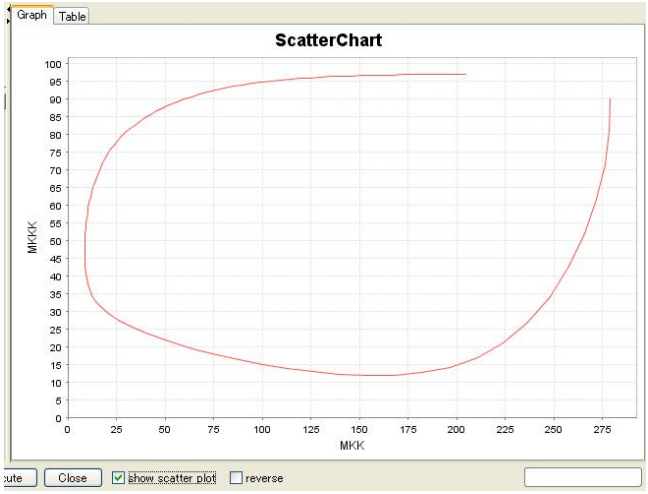
7.5 To convert the graph to a scatter plot:

You can convert the line chart to a scatter plot and compare the data of an arbitrary pair of Species.

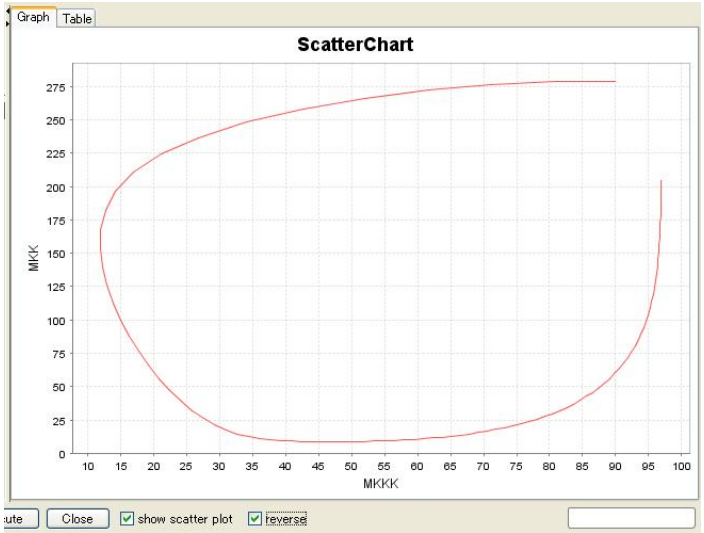
1. In the ControlPanel, select any two Species by ticking the checkboxes in the **Visible** column.
2. Observe that the graph has been reduced to two curves.
3. Tick the **show scatter plot**" checkbox.



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. Save/Open the Results of Simulation (File I/O)

The result of a simulation is stored in three file types:

- a model file (*.xml; SBML)
- a simulation condition file (*.sim)
- simulation result files (*.txt)

The model file (SBML) has a one-to-one correspondence with the simulation condition file (*.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）
```

8.1 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.

8.2 To open a result saved in files:

1. Select **Open** from the **File** menu of CellDesigner.
2. Select an SBML (.xml) file and click the **Open** button.
3. The corresponding conditon (.sim) file and result files (*.txt) are automatically imported so that you can start the ControlPanel and see the result.