

# Applying the Scientific Method to Simulation Experiments



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# Scientific Method

***Scientific method*** – body of techniques for investigating ***phenomena*** and acquiring new ***knowledge***, as well as for ***correcting and integrating*** previous knowledge.

# Models

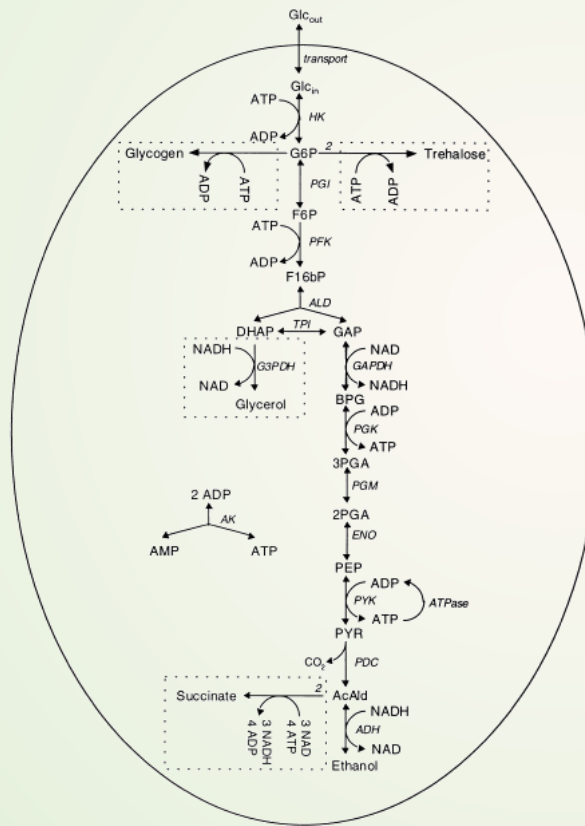


Fig. 1. Scheme of the model. Reactions in boxes show the branches introduced in the extended model. GAP, *GraP*; DHAP, glyceraldehyde phosphate; BPG, 1,3*GriP*; 3PGA, 3*GriP*; 2PGA, 2*GriP*; PEP, phospho-enol-pyruvate; GAPDH, *GraPDH*.

$$d[\text{Glc}_{\text{in}}]/dt = v_{\text{transport}} - v_{\text{HK}} \quad (6)$$

$$d[\text{G6P}]/dt = v_{\text{HK}} - v_{\text{PGI}} - 2v_{\text{trehalose}} - v_{\text{glycogen}} \quad (7)$$

$$d[\text{F6P}]/dt = v_{\text{PGI}} - v_{\text{PFK}} \quad (8)$$

$$d[\text{F1,6bP}_2]/dt = v_{\text{PFK}} - v_{\text{ALD}} \quad (9)$$

$$d[\text{Trio-P}]/dt = 2v_{\text{ALD}} - v_{\text{GraPDH}} (-v_{\text{glycerol}}) \quad (10)$$

$$d[\text{BPG}]/dt = v_{\text{GraPDH}} - v_{\text{PGK}} \quad (11)$$

$$d[3\text{GriP}]/dt = v_{\text{PGK}} - v_{\text{PGM}} \quad (12)$$

$$d[2\text{GriP}]/dt = v_{\text{PGM}} - v_{\text{ENO}} \quad (13)$$

$$d[\text{phosphoenolpyruvate}]/dt = v_{\text{ENO}} - v_{\text{PYK}} \quad (14)$$

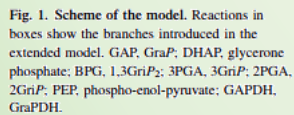
$$d[\text{PYR}]/dt = v_{\text{PYK}} - v_{\text{PDC}} \quad (15)$$

$$d[\text{AcAld}]/dt = v_{\text{PDC}} - v_{\text{ADH}} (-2v_{\text{succinate}}) \quad (16)$$

$$dP/dt = -v_{\text{HK}} - v_{\text{PFK}} + v_{\text{PGK}} + v_{\text{PYK}} - v_{\text{ATPase}} \\ (-v_{\text{trehalose}} - v_{\text{glycogen}} - 4v_{\text{succinate}}) \quad (17)$$

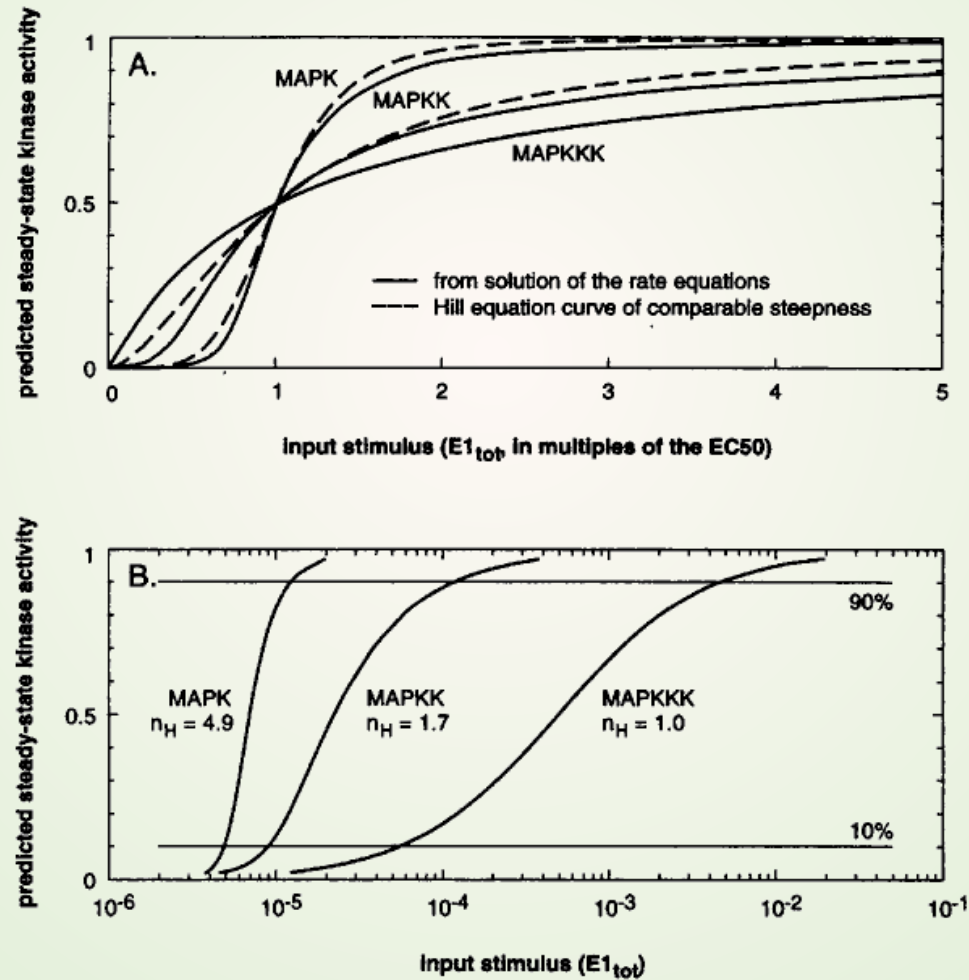
$$d[\text{NADH}]/dt = v_{\text{GraPDH}} - v_{\text{ADH}} (-v_{\text{glycerol}} + 3v_{\text{succinate}}) \quad (18)$$

$$d[\text{NAD}]/dt = -d[\text{NADH}]/dt \quad (19)$$



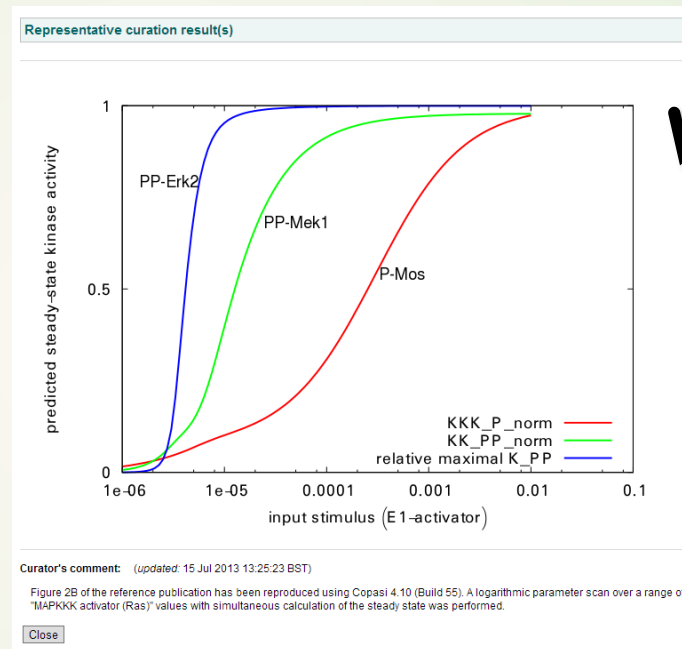
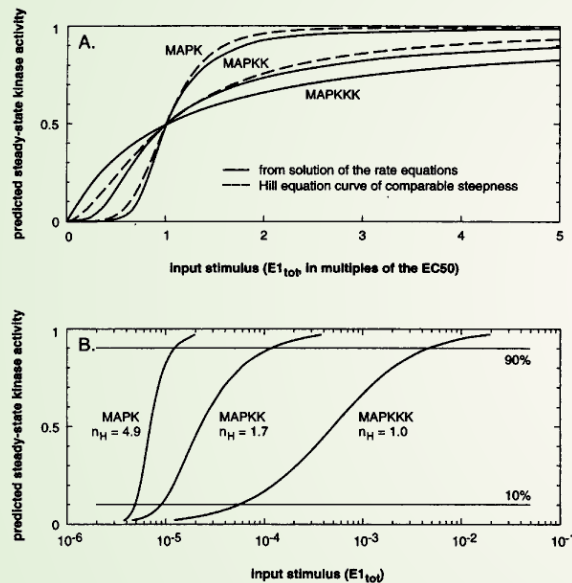
$$d[\text{NAD}]/dt = -d[\text{NADH}]/dt \quad (19)$$

# Simulation Experiments



# Simulation Experiments

Curation tab of BioModel #9

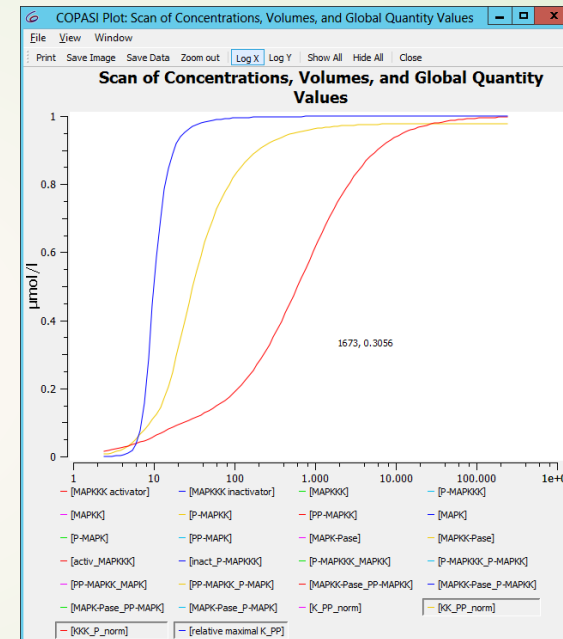
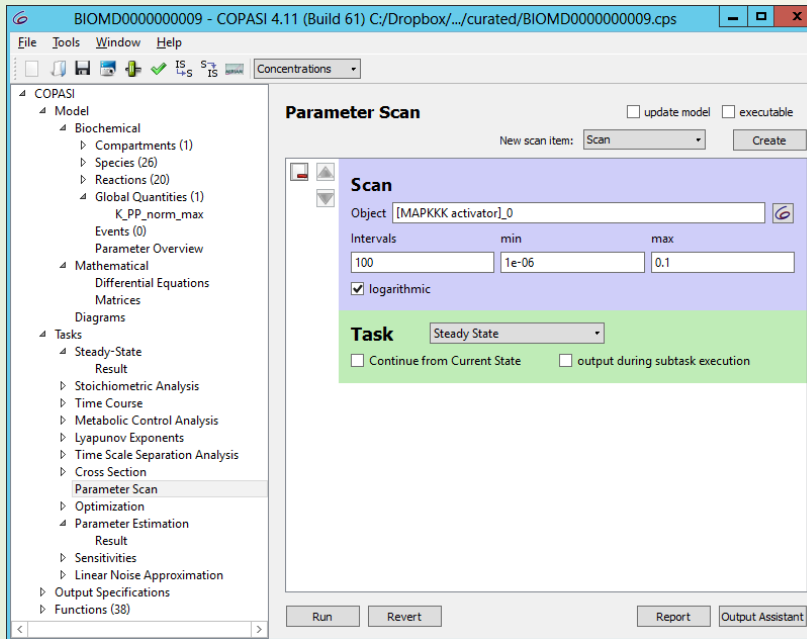


**Curator's comment:** (updated: 15 Jul 2013 13:25:23 BST)

Figure 2B of the reference publication has been reproduced using Copasi 4.10 (Build 55). A logarithmic parameter scan over a range of "MAPKKK activator (Ras)" values with simultaneous calculation of the steady state was performed.



# Simulation Experiments



**Curator's comment:** (updated: 15 Jul 2013 13:25:23 BST)

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Simulation Experiment  
Description Markup Language



# SED-ML: Repeatable simulation experiments



Model

# SED-ML: Repeatable simulation experiments



Simulation

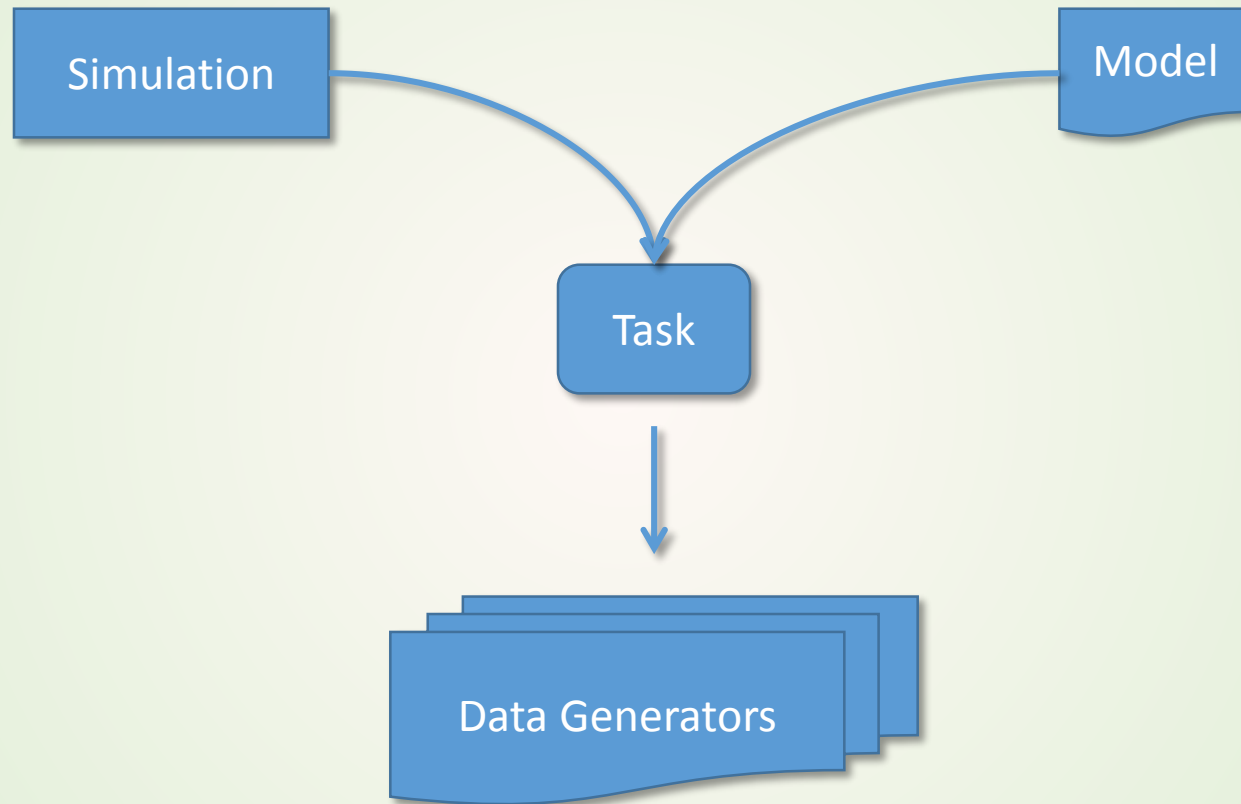
The diagram consists of two blue rectangular boxes with a slight drop shadow. The box on the left is labeled 'Simulation' and the box on the right is labeled 'Model'. The 'Model' box has a wavy bottom edge. They are positioned horizontally, with the 'Simulation' box on the left and the 'Model' box on the right, separated by a significant gap.

Model

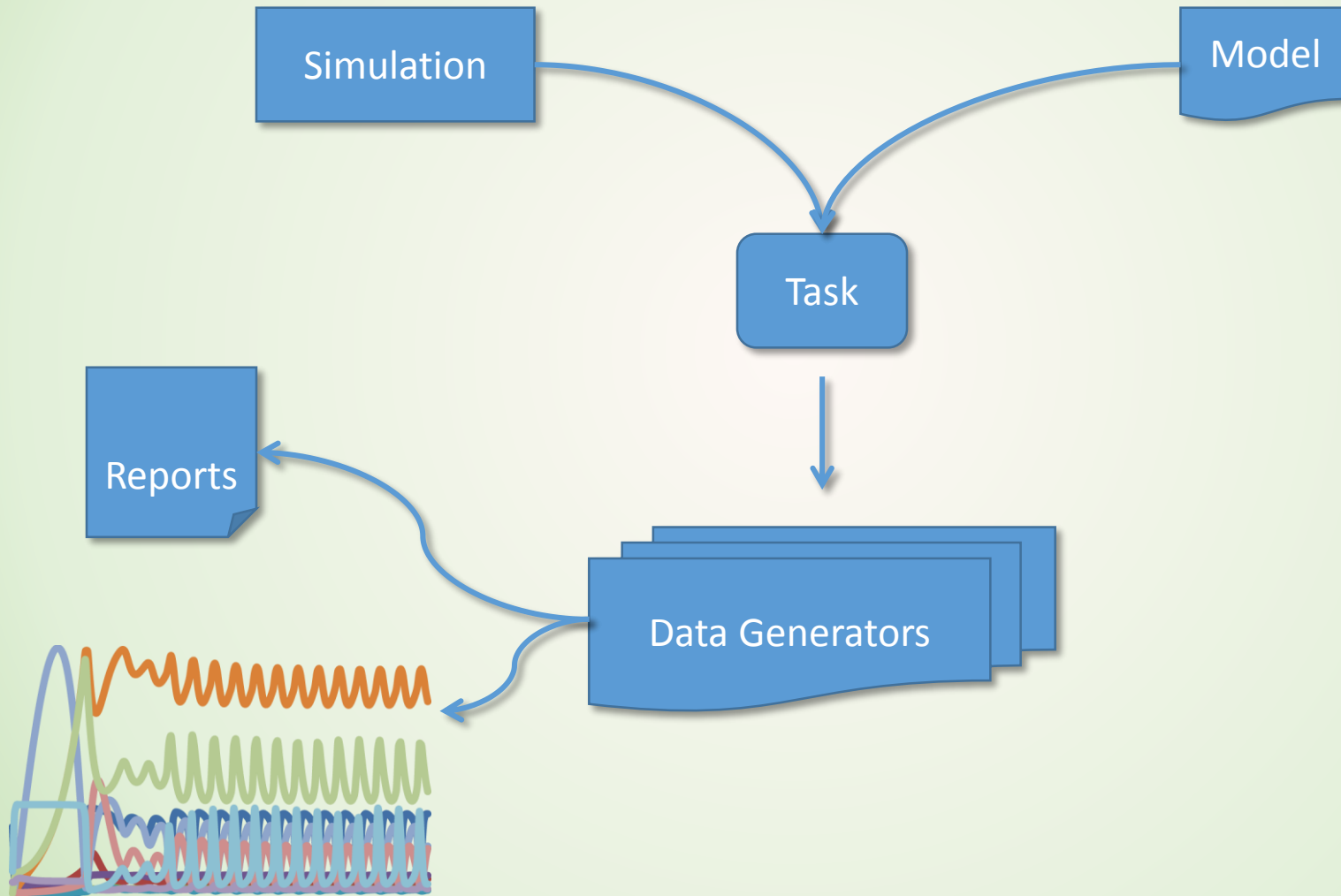
# SED-ML: Repeatable simulation experiments



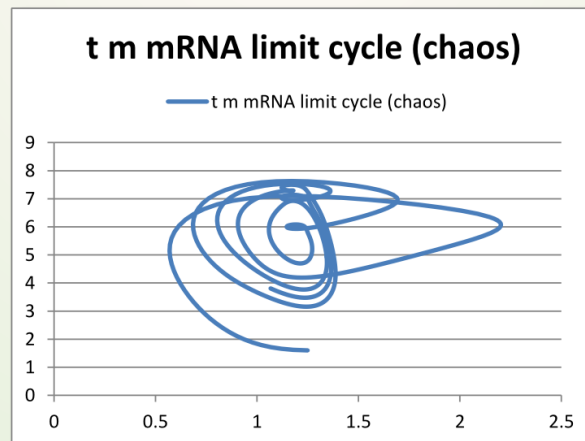
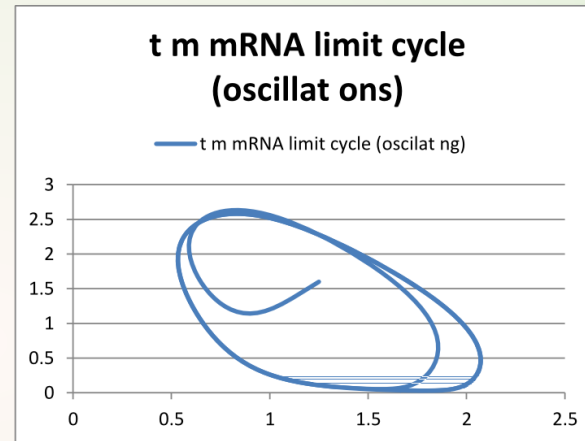
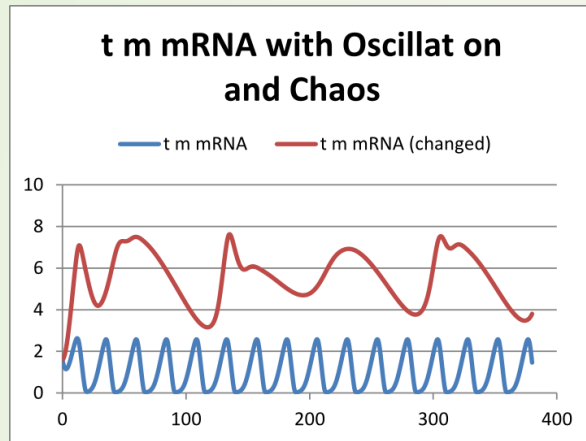
# SED-ML: Repeatable simulation experiments



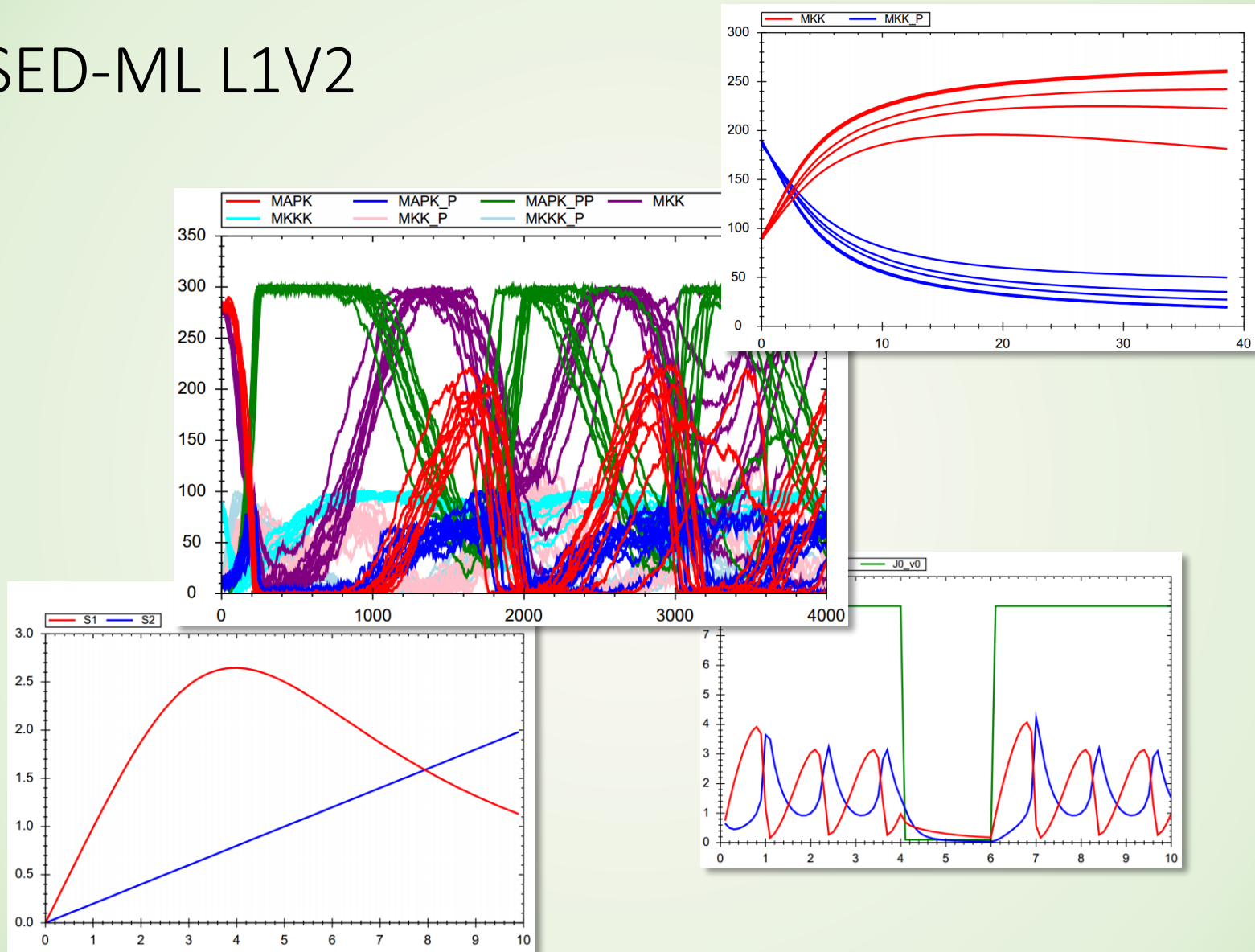
# SED-ML: Repeatable simulation experiments



# SED-ML Level 1 Version 1



# SED-ML L1V2





# Software Support - Libraries

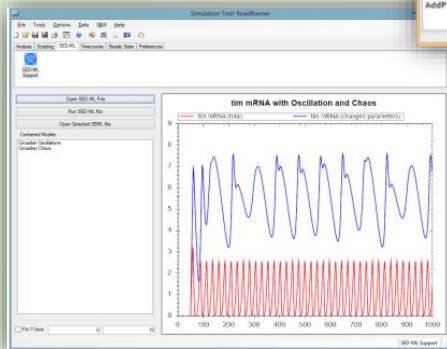
- libSedML: *.NET*; BSD License  
<http://libsedml.sourceforge.net>
- libSEDML: *C/C++ with bindings for .NET, Java, Perl, Python, R, Ruby*; BSD License, <https://github.com/fbergmann/libsedml>
- jlibsedml: *Java*; MIT License  
<http://sourceforge.net/projects/jlibsedml/>
- clibsedml,: *C*; BSD License  
<http://sourceforge.net/projects/clibsedml>

# Software Support

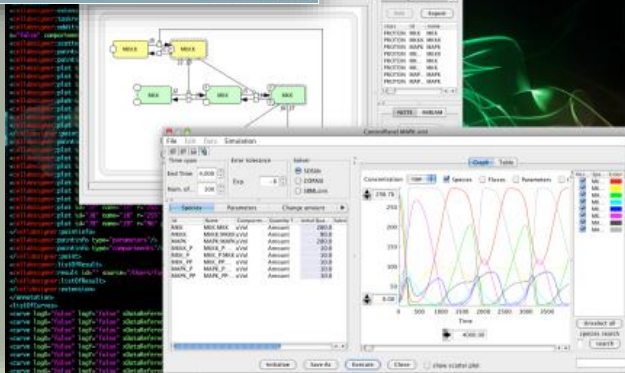
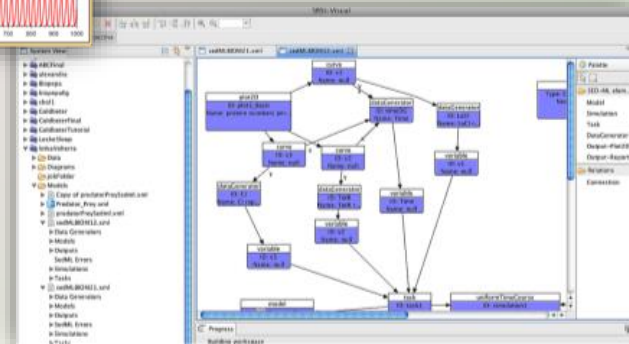
## SED-ML Script Editor

```
SED-ML Script Editor
File Edit View Help
AddTimeCourseSimulation('simulation1', 'KISAO:0000019', 0, 50, 1000, 1000)
AddModel('model1', 'urn:miriam:biomodels.db:BIOPD0000000021', 'urn:sedml:language:sbml')
AddModel('model2', 'model1', 'urn:sedml:language:sbml')
AddChange('model2', '/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter
[sid="v_0"]/@value', '0.28')
AddChange('model2', '/sbml:sbml/sbml:model/sbml:listOfParameters/sbml:parameter
[sid="v_0"]/@value', '4.8')
AddTask('task1', 'simulation1', 'model1')
AddTask('task2', 'simulation1', 'model2')
AddColumn('time', [['var_time_0', 'task1', 'time']])
AddColumn('time1', [['v1', 'task1', 'ME']])
AddColumn('time2', [['v2', 'task2', 'ME']])
AddPlot('plots', 'time mRNA with Oscillation and Chaos'
```

SBW



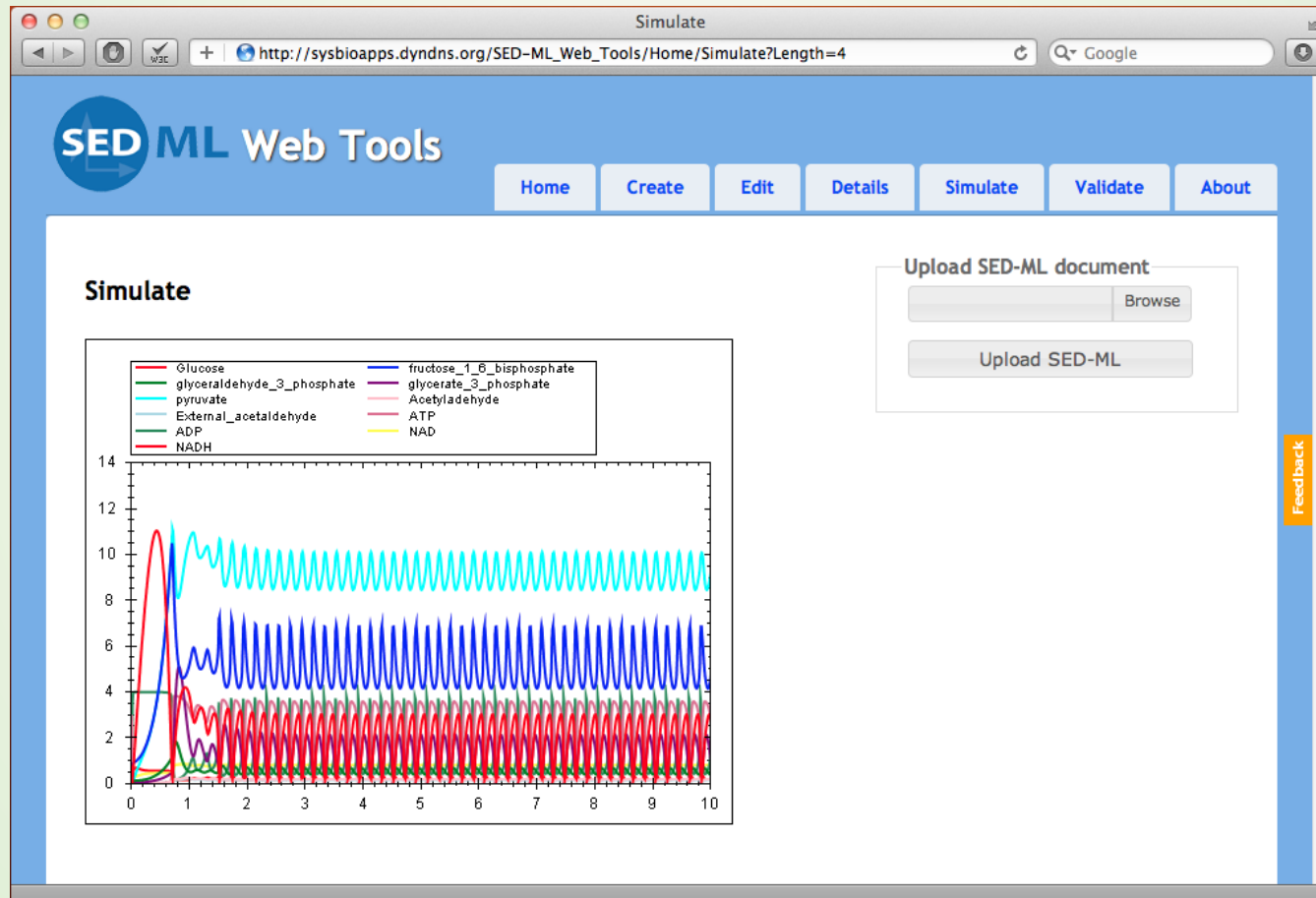
SBSI SED-ED



CellDesigner

→●→ PySCeS  
Python Simulator for Cellular Systems

# SED-ML Web Tools



# SED-ML Future

Experimental Data

File

all\_experiments\_TNfa\_100000.txt  
mRNA\_data\_100000.txt

Experiment

Experiment\_6  
Experiment\_7  
Experiment\_8  
Experiment\_10

Experiment: Experiment\_6 First Row: 41 Last Row: 49

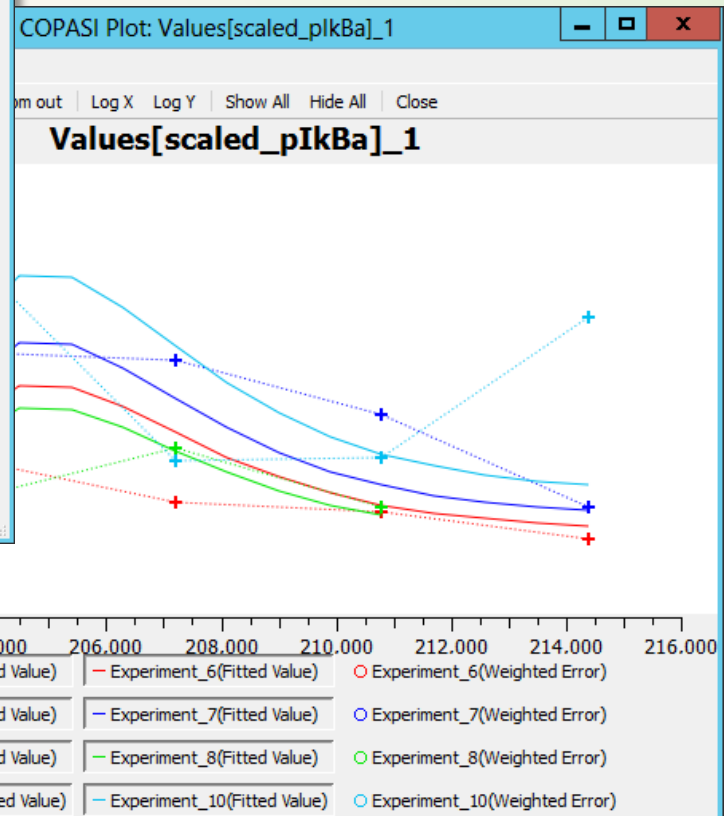
Copy Settings ☐ from previous ☒ to next

Experiment Type ☐ Steady State ☒ Time Course Header: 1 ☒

Weight Method: Mean Square Separator:  ☒ <tab>

	Column Name	Type	Model Object	Weight
1	time	Time		
2	p65	ignored		
3	pp65	dependent	Values[scaled_pp65]	(0.939848)
4	IkBα	dependent	Values[scaled_IkBα]	(0.530059)
5	plkBα	dependent	Values[scaled_plkBα]	(1)
6	A20	ignored		
7	YAP	ignored		
8	pYAP	ignored		

OK Revert Cancel



# SED-ML Future

Wednesday AM

Experimental Data

File

all\_experiments\_TNfa\_100000.txt  
mRNA\_data\_100000.txt

Experiment

Experiment\_6  
Experiment\_7  
Experiment\_8  
Experiment\_10

Experiment: Experiment\_6 First Row: 41 Last Row: 49

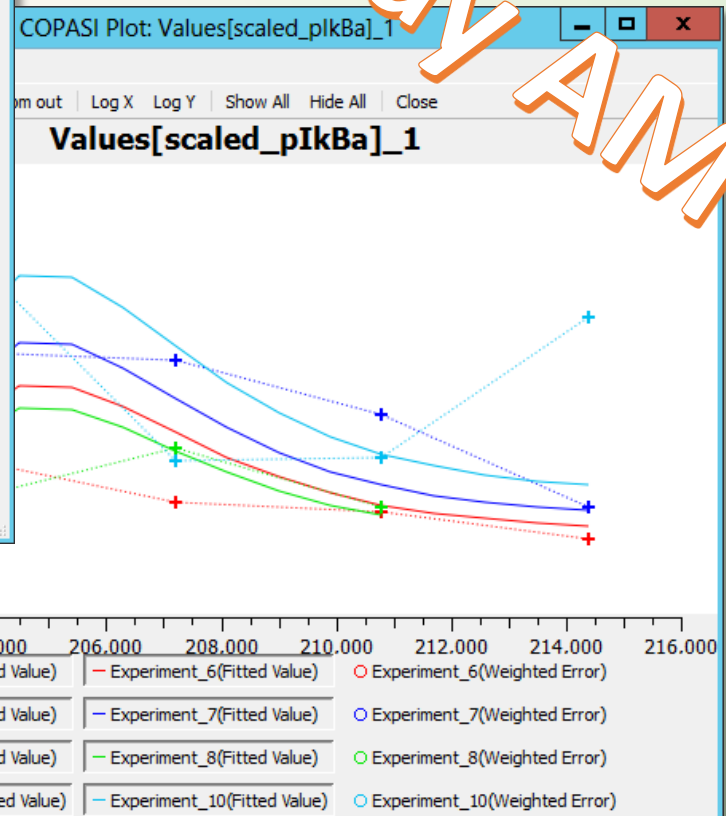
Copy Settings ☐ from previous ☒ to next

Experiment Type ☐ Steady State ☒ Time Course Header: 1 ☒

Weight Method: Mean Square Separator:  ☒ <tab>

Column Name	Type	Model Object	Weight
1 time	Time		
2 p65	ignored		
3 pp65	dependent	Values[scaled_pp65]	(0.939848)
4 IkBa	dependent	Values[scaled_IkBa]	(0.530059)
5 plkB	dependent	Values[scaled_plkB]	(1)
6 A20	ignored		
7 YAP	ignored		
8 pYAP	ignored		

OK Revert Cancel



# Acknowledgements

- SED-ML Editors: Frank T. Bergmann, Dagmar Waltemath, Jonathan Cooper, David Nickerson, Nicolas Le Novère, Andrew Miller, Richard Adams
- BioModels Support Team
- SED-ML Community