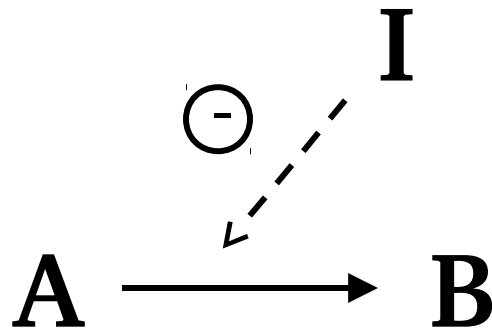


# An introduction to modeling and simulation with COPASI

**Pedro Mendes**

<http://www.comp-sys-bio.org>

# Reactions and kinetic functions



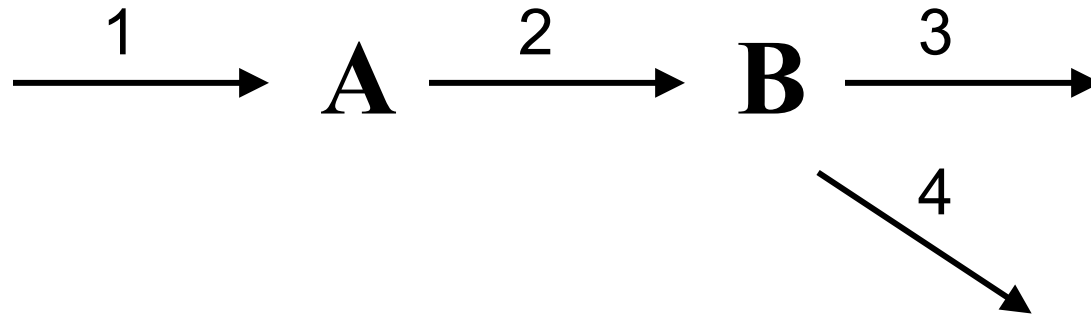
$$v = f(A, B, I; V, K_{ms}, K_{mp}, K_i)$$

$$v = \frac{\frac{A}{K_{ms}} \cdot V}{1 + \frac{A}{K_{ms}} + \frac{B}{K_{mp}} + \frac{I}{K_i}}$$

The rate of each reaction is a function of:

- concentration of the substrates
- concentration of the products
- concentration of the modifiers
- a set of constants

# Species concentrations are represented by ODEs

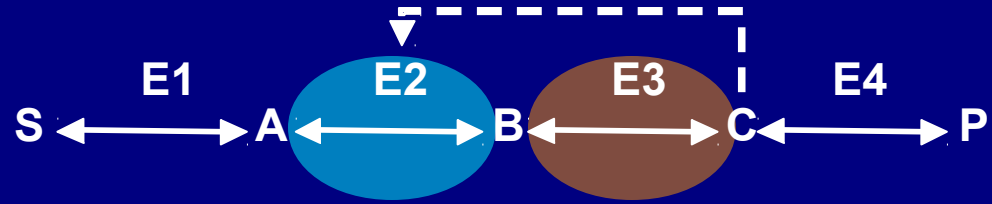


$$\frac{dA}{dt} = v_1 - v_2$$

$$\frac{dB}{dt} = v_2 - v_3 - v_4$$

The rate of change of a species concentration is the algebraic sum of the rates producing it and the ones consuming it

# An example

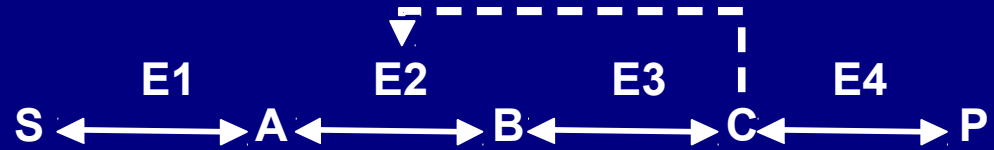


$$\mathcal{E}_A = \frac{V_1^f \frac{S}{K_{1S}} - V_1^r \frac{A}{K_{1A}}}{1 + \frac{S}{K_{1S}} + \frac{A}{K_{1A}}} - \frac{\left( V_2^f \frac{A}{K_{2A}} \right) \left( 1 - \frac{B}{S \cdot K_{2eq}} \right) \left( \frac{A}{K_{2A}} + \frac{B}{K_{2B}} \right)^{h-1}}{\left( \frac{A}{K_{2A}} + \frac{B}{K_{2B}} \right)^h + \frac{1 + \left( \frac{C}{K_{2C}} \right)^h}{1 + \alpha \left( \frac{C}{K_{2C}} \right)^h}}$$

$$\mathcal{E}_B = \frac{\left( V_2^f \frac{A}{K_{2A}} \right) \left( 1 - \frac{B}{S \cdot K_{2eq}} \right) \left( \frac{A}{K_{2A}} + \frac{B}{K_{2B}} \right)^{h-1}}{\left( \frac{A}{K_{2A}} + \frac{B}{K_{2B}} \right)^h + \frac{1 + \left( \frac{C}{K_{2C}} \right)^h}{1 + \alpha \left( \frac{C}{K_{2C}} \right)^h}} - \frac{V_3^f \frac{B}{K_{3B}} - V_3^r \frac{C}{K_{3C}}}{1 + \frac{B}{K_{3B}} + \frac{C}{K_{3C}}}$$

$$\mathcal{E}_C = \frac{V_3^f \frac{B}{K_{3B}} - V_3^r \frac{C}{K_{3C}}}{1 + \frac{B}{K_{3B}} + \frac{C}{K_{3C}}} - \frac{V_4^f \frac{C}{K_{4C}} - V_4^r \frac{P}{K_{4P}}}{1 + \frac{C}{K_{4C}} + \frac{P}{K_{4P}}}$$

# An example



$$\begin{bmatrix} \mathcal{F}_A \\ \mathcal{F}_B \\ \mathcal{F}_C \end{bmatrix} = \begin{bmatrix} 1 & -1 & 0 & 0 \\ 0 & 1 & -1 & 0 \\ 0 & 0 & 1 & -1 \end{bmatrix}$$

$$\begin{bmatrix} \frac{V_1^f \frac{S}{K_{1S}} - V_1^r \frac{A}{K_{1A}}}{1 + \frac{S}{K_{1S}} + \frac{A}{K_{1A}}} \\ \frac{\left( V_2^f \frac{A}{K_{2A}} \right) \left( 1 - \frac{B}{S \cdot K_{2eq}} \right) \left( \frac{A}{K_{2A}} + \frac{B}{K_{2B}} \right)^{h-1}}{\left( \frac{A}{K_{2A}} + \frac{B}{K_{2B}} \right)^h + \frac{1 + \left( \frac{C}{K_{2C}} \right)^h}{1 + \alpha \left( \frac{C}{K_{2C}} \right)^h}} \\ \frac{V_3^f \frac{B}{K_{3B}} - V_3^r \frac{C}{K_{3C}}}{1 + \frac{B}{K_{3B}} + \frac{C}{K_{3C}}} \\ \frac{V_4^f \frac{C}{K_{4C}} - V_4^r \frac{P}{K_{4P}}}{1 + \frac{C}{K_{4C}} + \frac{P}{K_{4P}}} \end{bmatrix}$$

$$\mathcal{F} = \mathbf{N} \cdot \mathbf{v}(\mathbf{x}, \mathbf{k})$$

# COPASI simulation methods

**COPASI allows simulations based on:**

- ODEs
  - Built directly from reaction kinetics
  - Arbitrary ODEs
  - Compartment volumes can be variables (ODE)
- Stochastic kinetics based on Gillespie's SSA
- Models can have:
  - Algebraic assignments
  - Discrete events

# Parameters and variables

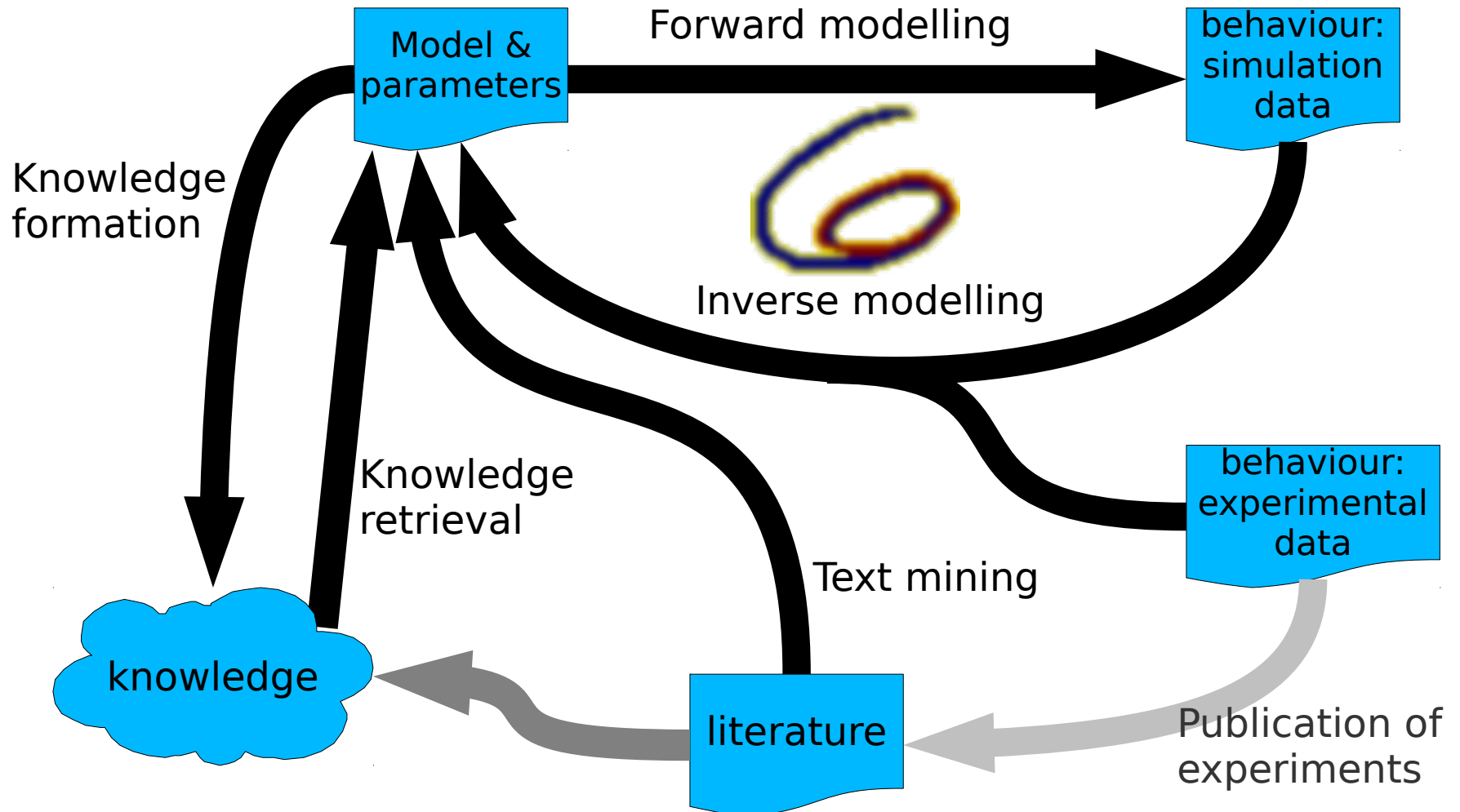
- **Parameters** are items that are independent of the system, *i.e.* are set by outside agents (*causes*).
- **Variables** are items of the system whose values are determined exclusively by the parameters (*effects*).
- **State** of the system is the set of all variables.
- One set of parameters determines unambiguously the variables.
- One set of variables can be caused by many parameter sets.

# The central modelling question

- Given a model of a system: **how do the parameters affect the state of the system?**
- Answers explain:
  - which parameters have highest effect on desired outcomes (eg drug design)
  - what properties of the model are more fragile or robust
  - which parameters need accurate estimates (experimental design)



# Modelling cycle



*Systems biology*

## COPASI—a COmplex PATHway Simulator

Stefan Hoops<sup>1,†</sup>, Sven Sahle<sup>2,†</sup>, Ralph Gauges<sup>2</sup>, Christine Lee<sup>1</sup>, Jürgen Pahle<sup>2</sup>, Natalia Simus<sup>2</sup>, Mudita Singhal<sup>1</sup>, Liang Xu<sup>1</sup>, Pedro Mendes<sup>1,\*</sup> and Ursula Kummer<sup>2</sup>

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Advance Access publication October 10, 2006

Associate Editor: Jonathan Wren

### ABSTRACT

**Motivation:** Simulation and modeling is becoming a standard approach to understand complex biochemical processes. Therefore, there is a big need for software tools that allow access to diverse simulation and modeling methods as well as support for the usage of these methods.

**Results:** Here, we present COPASI, a platform-independent and user-friendly biochemical simulator that offers several unique features. We discuss numerical issues with these features; in particular, the criteria to switch between stochastic and deterministic simulation methods, hybrid deterministic–stochastic methods, and the importance of random num-

and flux analysis (Klamt *et al.*, 2003). However, some tools contain whole suites of functionalities, e.g. simulation, flux and control analysis (Tomita *et al.*, 1999; Sauro *et al.*, 2003; Meng *et al.*, 2004).

In order to improve the compatibility of these tools, markup languages such as SBML (Hucka *et al.*, 2003) and CellML (Lloyd *et al.*, 2004) were created to allow model exchange. Many tools are now able to read and write models in these file formats.

Here we present a new program—COPASI (Complex Pathway Simulator)—which combines all of the above standards and some unique methods for the simulation and analysis of biochemical




# Frequent releases...

## COPASI 4.8 (Build 35) Released

By: Stefan Hoops on: Tue 20 of Dec., 2011 17:21 GMT (3836 Reads)



The COPASI team announces the immediate availability of the stable release COPASI 4.8 (Build 35).



[Read More](#) (1251 bytes)   

## New Language Bindings for COPASI 4.7 (Build 34)

By: gauges on: Sat 13 of Aug., 2011 12:24 GMT (2128 Reads)



New versions of the COPASI language bindings based on the latest COPASI 4.7 (Build 34) have been released.




[Read More](#) (678 bytes)   

## COPASI 4.7 (Build 34) Released

By: Stefan Hoops on: Thu 14 of July, 2011 01:57 GMT (3203 Reads)



The COPASI team announces the immediate availability of the stable release COPASI 4.7 (Build 34).

[Read More](#) (2218 bytes)   

# Documentation and support

Several sources available at [www.copasi.org](http://www.copasi.org):

- User manual
- FAQ
- User forum
- Issue tracker
- Technical documentation:
  - File format specification (including schema)
  - Documentation of API

**Quick Edit a Wiki Page**
  

**Search**
 in:  
 ▾ 
**Latest Versions**
**Stable:**

COPASI 4.8 (Build 35)

**Development:**

 COPASI 4.6.33  
 (development)

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 Logged in as: [mendes](#)
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Switch User

 User:  ?

**User Settings**

 To change your password email or other personal information please click [here](#).

**Menu**
[Home](#)  
[Search](#)

# User Support Forum

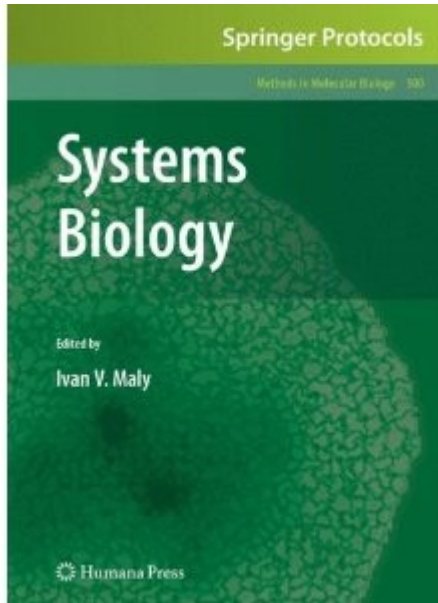
We have limited posting to this forum to registered users to prevent spamming. However, the registration is open to everyone. If you need any help regarding COPASI we kindly ask you to [register](#).

[Forums](#) > [User Support Forum](#)
[New Topic](#) [Forum List](#) [Edit Forum](#) [Manage Reported Messages \(1\)](#)


**Moderator Actions**

Type	Title	Replies	Reads	Last Post	Author								
<input type="checkbox"/>	Running several simulations with different parameter values	1	8463	Tue 04 of Dec., 2012 17:00 GMT <i>Re: Running several simulations with different parameter values</i> by <a href="#">shoops</a>	<a href="#">tschirmer</a>								
<input type="checkbox"/>	reaction without species???	9	28118	Tue 11 of Dec., 2012 14:54 GMT <i>Re: Re: reaction without species???</i> by <a href="#">shoops</a>	<a href="#">Max</a>								
<input type="checkbox"/>	global fitting of model to experimental data acquired at varying conditions	9	23989	Tue 27 of Nov., 2012 00:39 GMT <i>Re: global fitting of model to experimental data acquired at varying conditions</i> by <a href="#">Holmes</a>	<a href="#">tschirmer</a>								
<input type="checkbox"/>	What does "An equilibrium steady state (zero flux)" mean?	2	3269	Sat 24 of Nov., 2012 01:27 GMT <i>Re: What does "An equilibrium steady state (zero flux)" mean?</i> by <a href="#">Holmes</a>	<a href="#">Holmes</a>								
<input type="checkbox"/>	overlay of curves from different runs	3	4535	Sat 24 of Nov., 2012 11:46 GMT <i>Re: overlay of curves from different runs</i> by <a href="#">tschirmer</a>	<a href="#">tschirmer</a>								
<input type="checkbox"/>	Stochastic simulations not working	3	5747	Mon 26 of Nov., 2012 02:36 GMT <i>Re: Stochastic simulations not working</i> by <a href="#">bp</a>	<a href="#">bp</a>								
<input type="checkbox"/>	time dependent reaction rates for stochastic simulation	3	9925	Mon 26 of Nov., 2012 10:31 GMT <i>Re: time dependent reaction rates for stochastic simulation</i> by <a href="#">sven</a>	<a href="#">anezupanic</a>								
<input type="checkbox"/>	Modeling lysis-lysogeny decision circuit in Lambda phage	1	11783	Mon 26 of Nov., 2012 15:48 GMT <i>Re: Modeling lysis-lysogeny decision circuit in Lambda phage</i> by <a href="#">shoops</a>	<a href="#">shawon</a>								
<input type="checkbox"/>	Modeling Protein degradation	1	8039	Tue 13 of Nov., 2012 12:52 GMT <i>Re: Modeling Protein degradation</i> by <a href="#">shoops</a>	<a href="#">zoltuz</a>								
<input type="checkbox"/>	Residence time	2	9718	Mon 26 of Nov., 2012 10:40 GMT	<a href="#">Aman</a>								

 Reported Messages:1  
 Queued Messages:0



Mendes, P, Hoops, S, Sahle, S, Gauges, R, Dada, J, Kummer, U (2009) Computational Modeling of Biochemical Networks Using COPASI. *Methods Mol. Biol.* 500, 17-59.

## Chapter 2

### **Computational Modeling of Biochemical Networks Using COPASI**

**Pedro Mendes, Stefan Hoops, Sven Sahle, Ralph Gauges, Joseph Dada, and Ursula Kummer**

#### **Summary**

Computational modeling and simulation of biochemical networks is at the core of systems biology and this includes many types of analyses that can aid understanding of how these systems work. COPASI is a generic software package for modeling and simulation of biochemical networks which provides many of these analyses in convenient ways that do not require the user to program or to have deep knowledge of the numerical algorithms. Here we provide a description of how these modeling techniques can be applied to biochemical models using COPASI. The focus is both on practical aspects of software usage as well as on the utility of these analyses in aiding biological understanding. Practical examples are described for steady-state and time-course simulations, stoichiometric analyses, parameter scanning, sensitivity analysis (including metabolic control analysis), global optimization, parameter estimation, and stochastic simulation. The examples used are all published models that are available in the BioModels database in SBML format.



# Systems Biology Markup Language

- Exchange medium for systems biology models, based on XML (used by >100 programs)
- Specifies models based on the biology, not on the maths
- Software interpret the models and translate them into mathematical/computational representations
- Allows ODEs, assignment rules, and events

<http://www.sbml.org>

# Model Definition

Olsen2003\_peroxidase - COPASI 4.4 (Build 26) /usr/.../examples/Olsen2003\_peroxid

File Tools Help

Concentrations

Copasi

- Model
  - Biochemical
    - Compartments
    - Species
    - Reactions
    - Global Quantities
    - Parameter Overview
  - Mathematical
  - Tasks
  - Multiple Task
  - Output
  - Functions

	Status	Name	Equation	Rate Law
1		v1	$\text{NADH} + \text{O}_2 = \text{H}_2\text{O}_2 + \text{NAD}$	function_4_v1
2		v2	$\text{per3} + \text{H}_2\text{O}_2 = \text{col}$	function_4_v2
3		v3	$\text{ArH} + \text{col} = \text{Ar} + \text{coll}$	function_4_v3
4		v4	$\text{coll} + \text{ArH} = \text{per3} + \text{Ar}$	function_4_v4
5		v5	$\text{NADrad} + \text{O}_2 = \text{NAD} + \text{super}$	function_4_v5
6		v6	$\text{per3} + \text{super} = \text{coll}$	function_4_v6
7		v7	$2 * \text{super} = \text{H}_2\text{O}_2 + \text{O}_2$	function_4_v7
8		v8	$\text{NADrad} + \text{coll} = \text{NAD} + \text{col}$	function_4_v8
9		v9	$2 * \text{NADrad} = \text{NAD}_2$	function_4_v9
10		v10	$\text{per3} + \text{NADrad} = \text{per2} + \text{NAD}$	function_4_v10
11		v11	$\text{per2} + \text{O}_2 = \text{coll}$	function_4_v11
12		v12	$\text{NADHres} = \text{NADH}$	function_4_v12
13		v131	$\text{O}_2\text{g} = \text{O}_2$	function_4_v131
14		v132	$\text{O}_2 = \text{O}_2\text{g}$	function_4_v132
15		v14	$\text{NADH} + \text{Ar} = \text{NADrad} + \text{ArH}$	function_4_v14
16				

Commit Revert Clear Delete/Undelete New



# Model Definition

**COPASI 4.4 (Build 26) - Main Window**

Status	Name	Equation	Rate Law
1	v1	NADH + O2 = H2O2 + NAD	function_4_v1
2	v2	per3 + H2O2 = col	function_4_v2
3	v3	ArH + c	
4	v4	coll + A	
5	v5	NADrad	
6	v6	per3 +	
7	v7	2 * supe	
8	v8	NADrad	
9	v9	2 * NAD	
10	v10	per3 + f	
11	v11	per2 + c	
12	v12	NADHre	
13	v131	O2g = O	
14	v132	O2 = O	
15	v14	NADH +	
16			

**COPASI 4.4 (Build 26) - Functions Dialog**

Function Name: Bi Bi (very simple)

Formula:  $V/K*(A*B-P*Q)/(K+A+B+P+Q)$

Function Type:  reversible  irreversible  General

Name	Description	Unit
V	Parameter	mmol/(ml*s) or mmol/s
A	Substrate	mmol/ml
B	Substrate	mmol/ml
P	Product	mmol/ml
Q	Product	mmol/ml
K	Parameter	mmol/ml

Application restrictions:  
 Only reversible reactions  
 Exactly 2 substrates  
 Exactly 2 products

# Stoichiometric analyses

BIOMD0000000070 - COPASI 4.4 (Build 26) /home/.../curated/BIOMD0000000070.cps

File Tools Help

Concentrations

Copasi

- Model
  - Biochemical
  - Mathematical
- Tasks
  - Steady-State
  - Stoichiometry
    - Elementary Modes
    - Mass Conservation
    - Result**
  - Time Course
  - Metabolic Control Anal
  - Lyapunov Exponents

### Moieties Result

save data

Moieties (7)	Stoichiometry	Link Matrix	Reduced Stoichiometry
	Dependent Species	Total Amount	Expression
1	Protein2 bound NADPH	1.6862e+19	"Protein2 bound NADPH" + NADPH + NADP - Protein1 + "Protein2 bound NADP"
2	ATP	1.20443e+21	ATP + MgATP + ADP + MgAMP + AMP + MgADP
3	MgGri23P2	1.6862e+21	MgGri23P2 + MgATP + Mg + MgAMP + MgADP
4	Protein2	-2.40886e+18	Protein2 - NADPH - NADP + Protein1
5	Protein1 bound NADPH	1.44531e+19	"Protein1 bound NADPH" + Protein1 + "Protein1 bound NADP"
6	NAD	3.9445e+19	NAD + NADH
7	Oxidized Glutathione	9.37768e+20	"Oxidized Glutathione" + 0.5 * "Reduced Glutathione"

# Stoichiometric analyses

The screenshot shows the COPASI 4.4 interface with two windows open for stoichiometric analysis.

**Moieties Result Window:**

- Title: BIOMD0000000070 - COPASI 4.4 (Build 26) /home/.../curated/BIOMD0000000070.cps
- Menu: File Tools Help
- Dropdown: Concentrations
- Buttons: save data

**Elementary Flux Modes Window:**

- Title: BIOMD0000000070 - COPASI 4.4 (Build 26) /home/.../curated/BIOMD0000000070.cps
- Menu: File Tools Help
- Dropdown: Concentrations
- Checkbox:  executable
- Flux Modes: 105

Reversibility	Reaction Name	Reaction Equation
Reversible	-1 * Glucose transport	"Glucose outside" = "Glucose in"
Reversible	-1 * Hexokinase	"Glucose in" + MgATP = "Glucose 6-phosphate" + MgADP
Reversible	-3 * Phosphoglycerate kinase	"3-Phosphoglycerate" + MgADP + H <sub>2</sub> O = "3-Phosphoglycerate" + MgADP + H <sub>2</sub> O
Reversible	3 * Bisphosphoglycerate mutase	"1,3-Bisphosphoglycerate" = "3-Phosphoglycerate" + H <sub>2</sub> O
Reversible	3 * Bisphosphoglycerate phosphatase	"2,3-Bisphosphoglycerate" = "3-Phosphoglycerate" + Pi
Reversible	-2 * Lactate dehydrogenase_2	"Pyruvate" + NADPH = "Lactate" + NADP
Reversible	-1 * Adenylate kinase	MgATP + AMP = ADP + MgADP
Reversible	-1 * Glucose 6-phosphate dehydrogenase	"Glucose 6-phosphate" + NADP = "6-Phosphogluconate" + NADP + H <sub>2</sub> O
Reversible	-1 * Phosphogluconate dehydrogenase	"6-Phosphogluconate" + NADP = "2-Keto-3-deoxy-6-phosphogluconate" + NADP + H <sub>2</sub> O
Reversible	-1 * Ribose phosphate isomerase	"Ribulose 5-phosphate" = "Ribose 5-phosphate" + H <sub>2</sub> O
Reversible	-1 * Phosphoribosylpyrophosphate synthetase	MgATP + "Ribose 5-phosphate" = "Phosphoribosylpyrophosphate" + MgADP
Reversible	-3 * Phosphate exchange	"Phosphate external" = "Phosphate internal" + H <sub>2</sub> O
Reversible	2 * Lactate exchange	"External Lactate" = "Lactate internal" + H <sub>2</sub> O
Reversible	-2 * Pyruvate exchange	"External Pyruvate" = "Pyruvate internal" + H <sub>2</sub> O
Reversible	1 * MgADP dissociation	MgADP = Mg + ADP
Reversible	-1 * MgAMP dissociation	MgAMP = Mg + AMP
Reversible	-1 * Glucose transport	"Glucose outside" = "Glucose in"
Reversible	-1 * Hexokinase	"Glucose in" + MgATP = "Glucose 6-phosphate" + MgADP
Reversible	2 * Glucosephosphate isomerase	"Glucose 6-phosphate" = "Fructose 6-phosphate" + H <sub>2</sub> O

Buttons at the bottom: Run, Revert, Report, Output Assistant

# Deterministic time course simulations

The screenshot shows the COPASI 4.4 (Build 26) interface. The window title is "BIOMD0000000098 - COPASI 4.4 (Build 26) /home/.../curated/BIOMD0000000098". The menu bar includes "File", "Tools", and "Help". The toolbar contains icons for file operations and simulation controls. The left sidebar shows a tree view of the model structure, with "Time Course" selected under the "Tasks" category. The main panel displays the "Time Course" configuration options:

- Time Course** (checkbox)  update model  executable
- Duration:
- Interval Size:  Intervals:
- Start Output Time:   delayed
- Save Result in Memory
- Method:
- Method Parameter table:

Method Parameter	Value
Integrate Reduced Model	0
Relative Tolerance	1e-06
Absolute Tolerance	1e-12
Adams Max Order	12
BDF Max Order	5
Max Internal Steps	10000

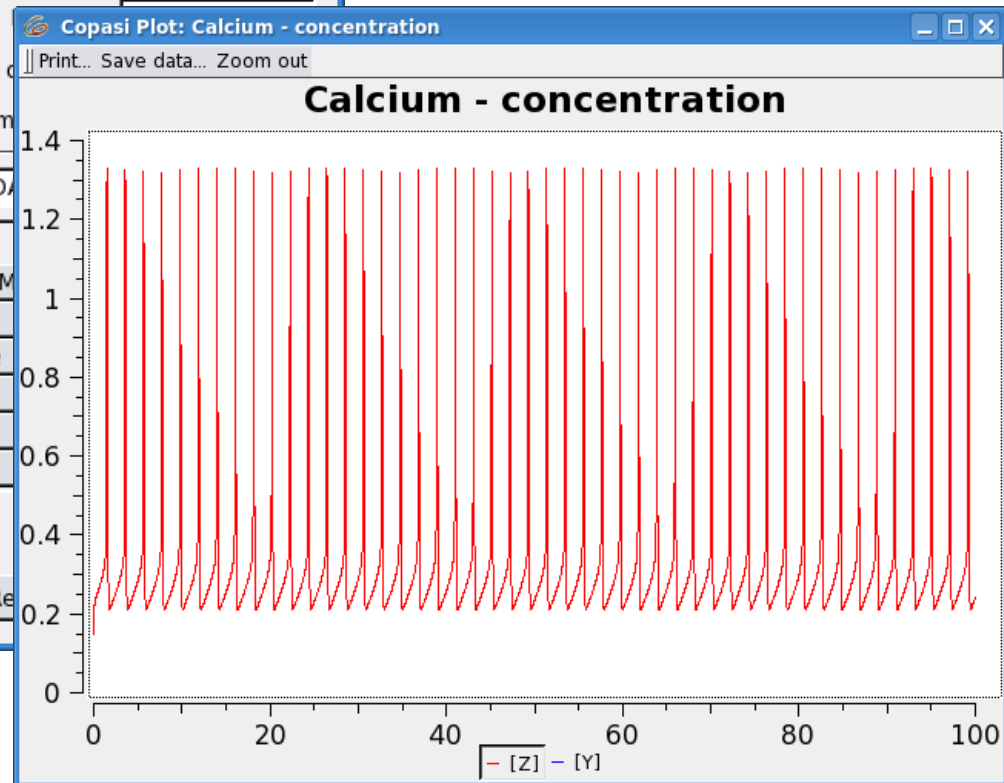
At the bottom of the panel are four buttons: "Run", "Revert", "Report", and "Output Assistant".

# Deterministic time course simulations

The screenshot shows the COPASI 4.4 (Build 26) interface. The main window title is "BIOMD0000000098 - COPASI 4.4 (Build 26) /home/.../curated/BIOMD0000000098". The menu bar includes "File", "Tools", and "Help". The toolbar contains icons for file operations and simulation controls. The left sidebar shows a tree view with "Copasi" as the root, containing "Model", "Tasks", "Output", and "Plots". Under "Tasks", "Time Course" is selected. The "Time Course" panel is active, showing the following settings:

- Duration: 100
- Interval Size: 0.01
- Start Output Time: 0
- Method: Deterministic (LSODA)
- Method Parameter: A list of parameters including "Integrate Reduced M", "Relative Tolerance", "Absolute Tolerance", "Adams Max Order", "BDF Max Order", and "Max Internal Steps".

Buttons for "Run" and "Revert" are visible at the bottom of the panel.



# Hybrid ODE-discrete event

- System of ODEs is associated with events
- An event (conditional state transition) consist of:
  - a trigger (Boolean expression)
  - at least one assignment
  - a delay (optional)
- When trigger expression changes from FALSE to TRUE, the event triggers and causes the assignments. If there is a delay, the trigger will only be that time after the trigger

# Stochastic time course simulations

BIOMD0000000098 - COPASI 4.4 (Build 26) /home/.../curated/BIOMD0000000098

File Tools Help

Concentrations

Copasi

- Model
- Tasks
  - Steady-State
  - Stoichiometry
  - Time Course**
  - Metabolic Control Anal
  - Lyapunov Exponents
- Multiple Task
- Output
  - Plots
    - Calcium - concentra
  - Reports
- Functions

**Time Course**  update model  executable

Duration

Interval Size  Intervals

Start Output Time   delayed

Save Result in Memory

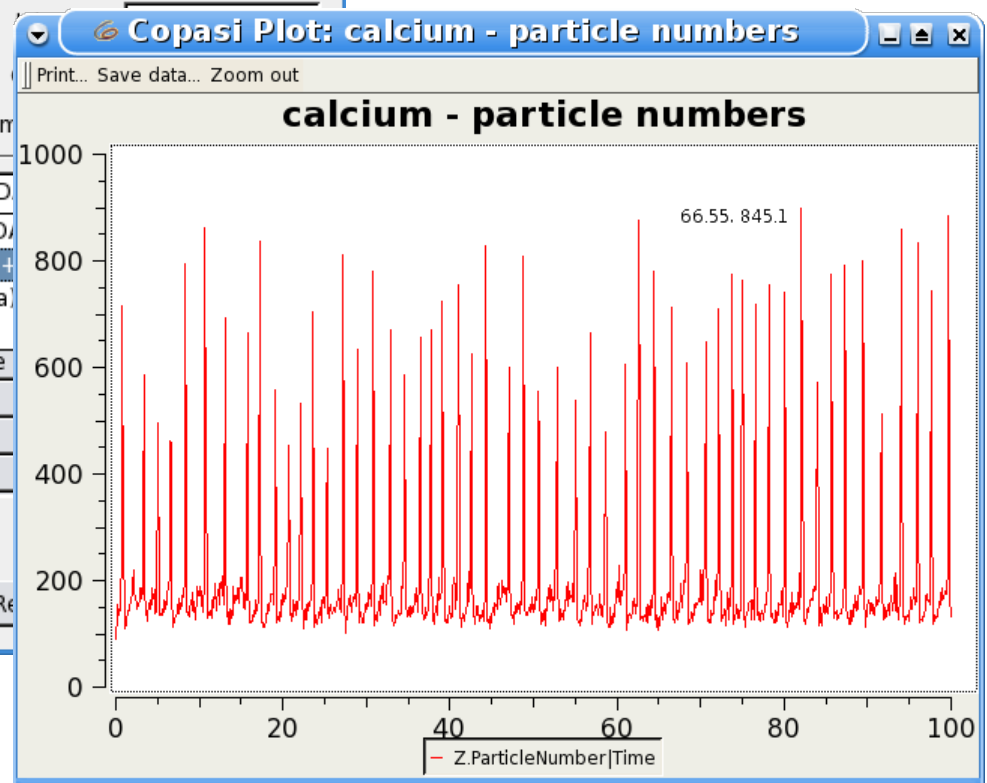
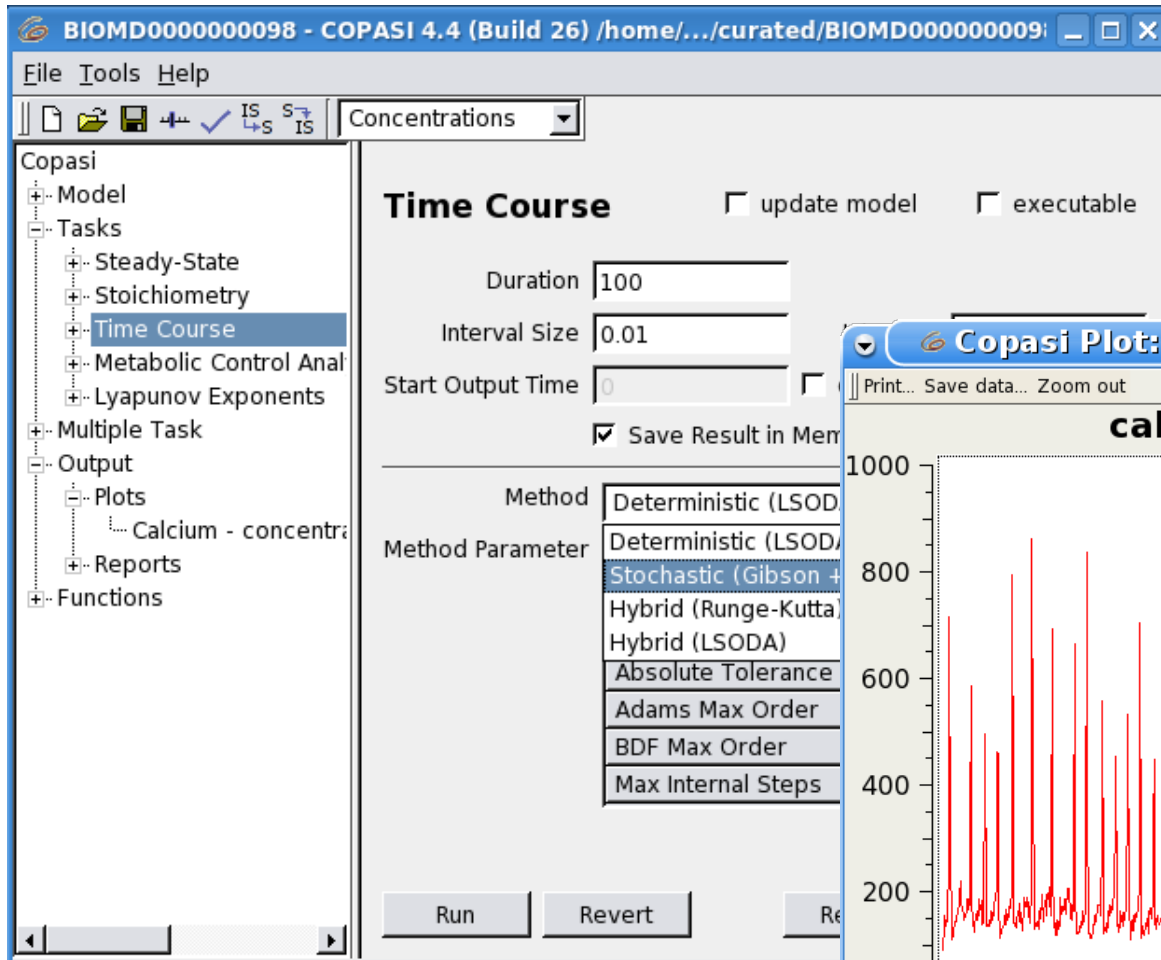
Method

Method Parameter

Deterministic (LSODA)	
Stochastic (Gibson + Bruck)	
Hybrid (Runge-Kutta)	
Hybrid (LSODA)	
Absolute Tolerance	1e-12
Adams Max Order	12
BDF Max Order	5
Max Internal Steps	10000

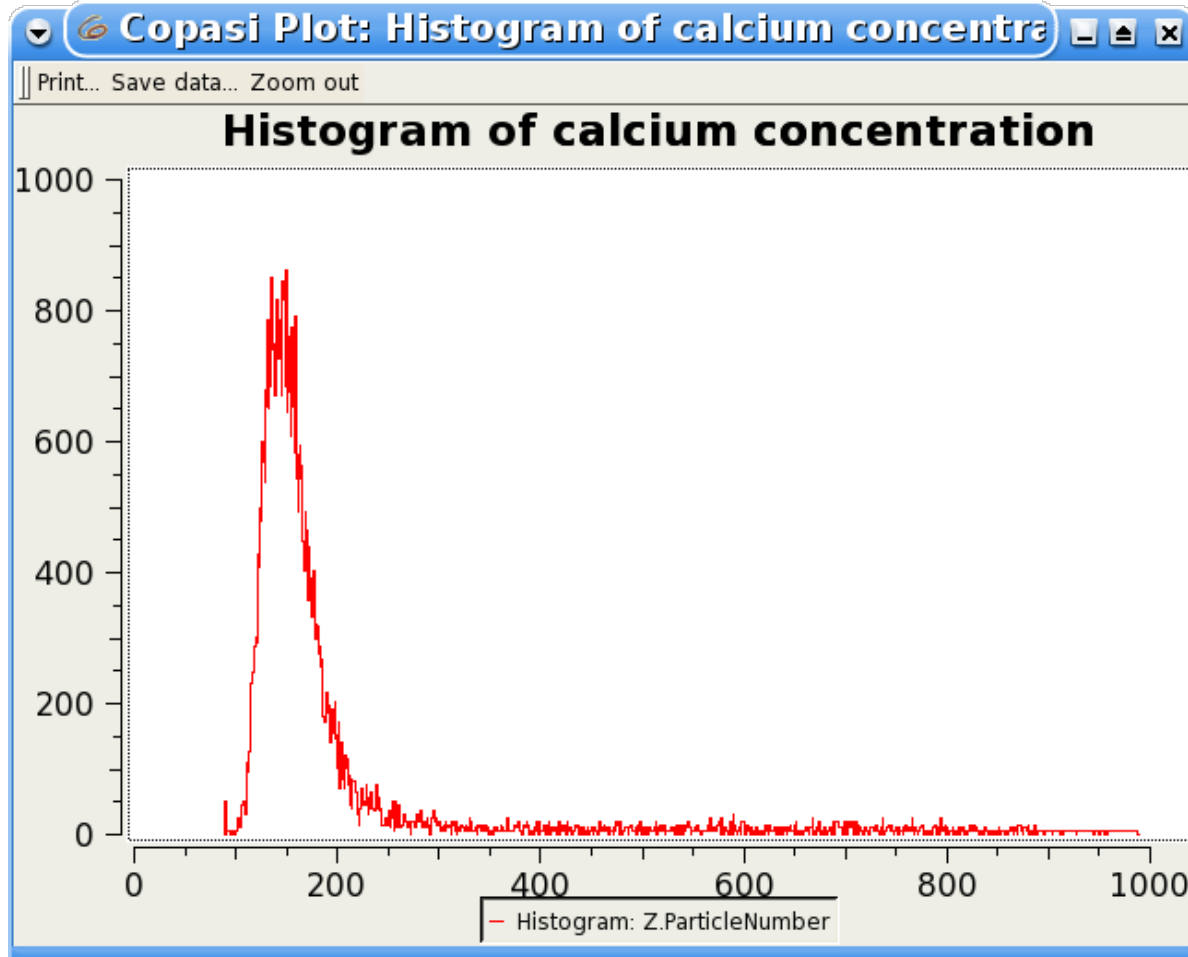
Run Revert Report Output Assistant

# Stochastic time course simulations





# Histograms



# Automatic conversion to irreversible reactions

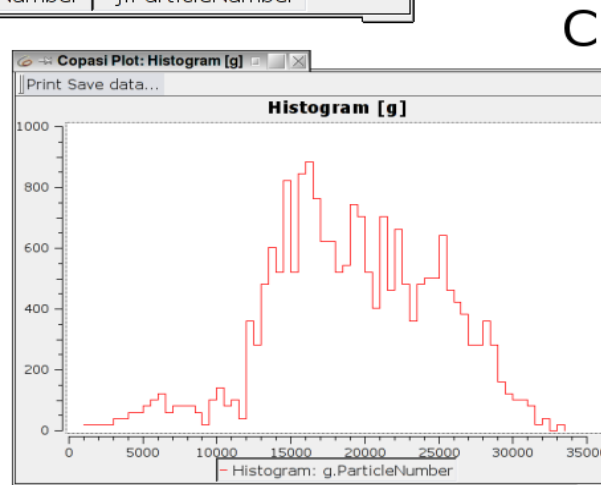
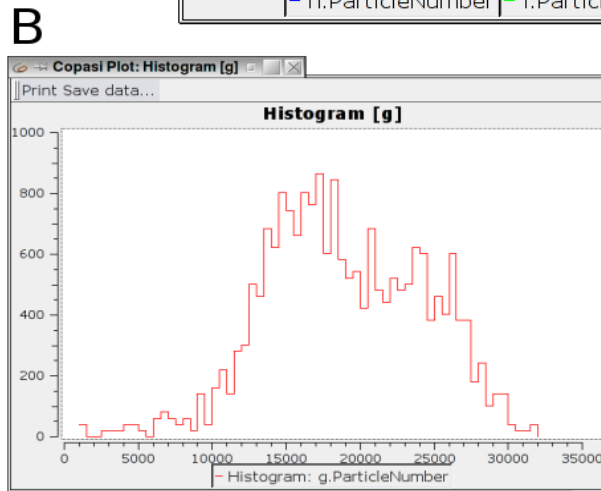
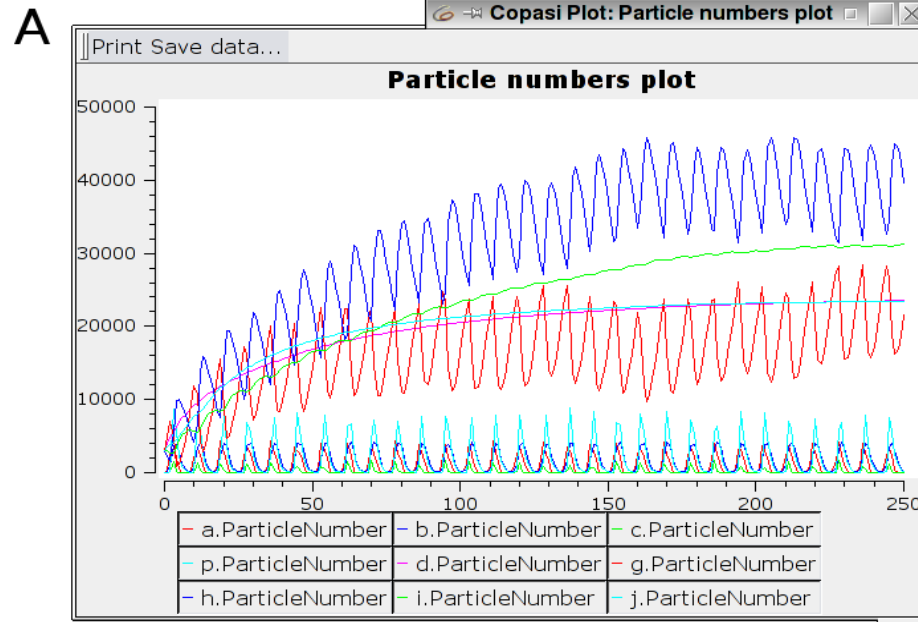
The screenshot shows the COPASI 4.3 (Build 25) interface. The title bar reads "BIOMD0000000098 - COPASI 4.3 (Build 25) /home/.../bookc". The "Tools" menu is open, and the "Convert to irreversible" option is highlighted with a red circle. Other menu items include "Object Browser", "Show...", "Check model", "Apply initial state", "Update initial state from current state", and "Preferences...".

The main window displays a table of reactions with the following columns: Name, Equation, and Rate Law.

Name	Equation	Rate Law
flux	-> Z	function_4_Ca influx
dependent Ca influx	-> Z	function_4_InsP3 dependent Ca influ
driven Ca pumping into store	Z -> Y	function_4_ATP driven Ca pumping
driven pumping into cytosol	Y -> Z	function_4_ATP driven pumping into
leak	Y -> Z	function_4_Ca leak
Ca efflux	Z ->	Mass action (irreversible)

At the bottom of the window, there are buttons for "Commit", "Revert", "Clear", "Delete/Undelete", and "New".

# Hybrid ODE-stochastic



# Parameter scanning & sampling

BIOMD0000000068 - COPASI 4.4 (Build 26) /home/.../curated/BIOMD0000000068.cps

File Tools Help

Concentrations

Copasi

- Model
  - Biochemical
    - Compartments
    - Species
      - "Inorganic phosphate"
      - Cystathionine
      - Cysteine
      - Homoserine
      - Phosphohomoserine
      - Threonine
    - Reactions
      - Cystathionine gamma-synt
      - Phosphohomoserine syntl
      - Threonine Synthase
    - Global Quantities
    - Parameter Overview
  - Mathematical
- Tasks
  - Multiple Task
    - Parameter Scan**
    - Optimization
    - Parameter Estimation
    - Sensitivities
  - Output
    - Plots
      - AdoMet effect on Fluxes
    - Reports
  - Functions

**Parameter Scan**  update model  executable

New scan item: Parameter Scan ... Create!

Scan	Parameter	Intervals	min	max	logarithmic scan
1	[Cysteine]_0	5	0.3	300	<input checked="" type="checkbox"/>
2	(Threonine Synthase).AdoMet	50	0	100	<input type="checkbox"/>

**Task** Steady-State

always use initial conditions  output from subtask

Run Revert Report Output Assistant

# Parameter scanning & sampling

BIOMD0000000068 - COPASI 4.4 (Build 26) /home/.../curated/BIOMD0000000068.cps

File Tools Help

Concentrations

Copasi

- Model
  - Biochemical
    - Compartments
    - Species
      - "Inorganic phosphate"
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      - Homoserine
      - Phosphohomoserine
      - Threonine
    - Reactions
      - Cystathionine gamma-synt
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  - Output
    - Plots
      - AdoMet effect on Fluxes
    - Reports
  - Functions

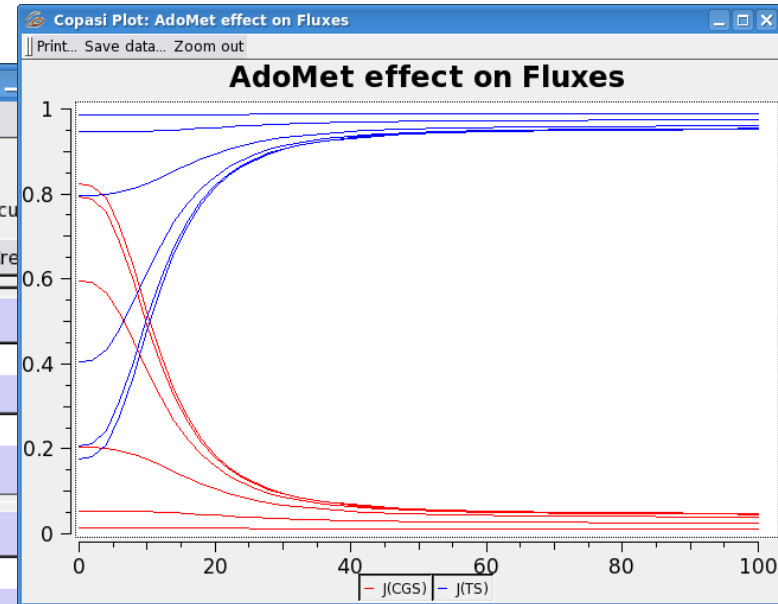
**Parameter Scan**  update model  execu

New scan item: Parameter Scan ... Cre

Scan	Parameter	Intervals	min	max	logarithmic scan
1	[Cysteine]_0	5	0.3	300	<input checked="" type="checkbox"/>
2	(Threonine Synthase).AdoMet	50	0	100	<input type="checkbox"/>

**Task** Steady-State  always use initial conditions  output from subtask

Run Revert Report Output Assistant



# Parameter scanning & sampling

BIOMD0000000068 - COPASI 4.4 (Build 26) /home/.../curated/BIOMD0000000068.cps

File Tools Help

Concentrations

Copasi

- Model
  - Biochemical
    - Compartments
    - Species
      - "Inorganic phosphate"
      - Cystathionine
      - Cysteine
      - Homoserine
      - Phosphohomoserine
      - Threonine
    - Reactions
      - Cystathionine gamma-synt
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    - Global Quantities
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  - Tasks
    - Multiple Task
      - Parameter Scan
      - Optimization
      - Parameter Estimation
      - Sensitivities
    - Output
      - Plots
        - AdoMet effect on Fluxes
      - Reports
    - Functions

**Parameter Scan**  update model  execu

New scan item: Parameter Scan ... Cre

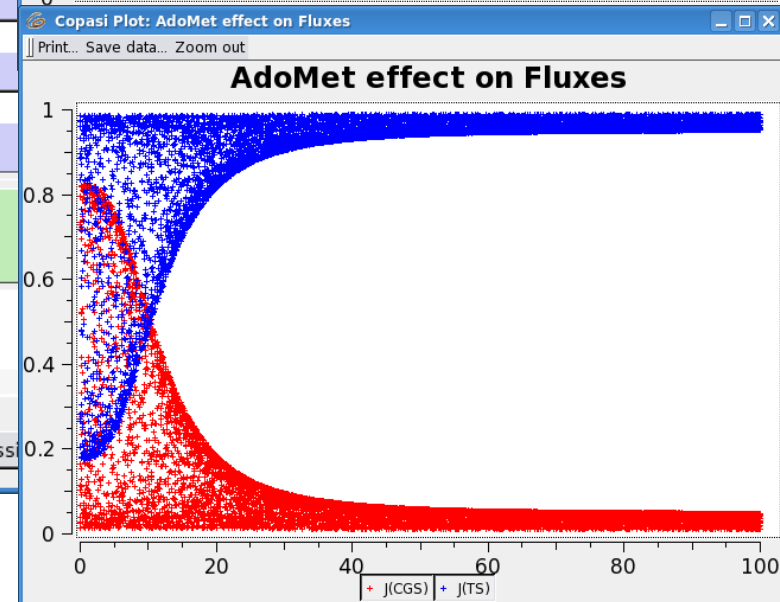
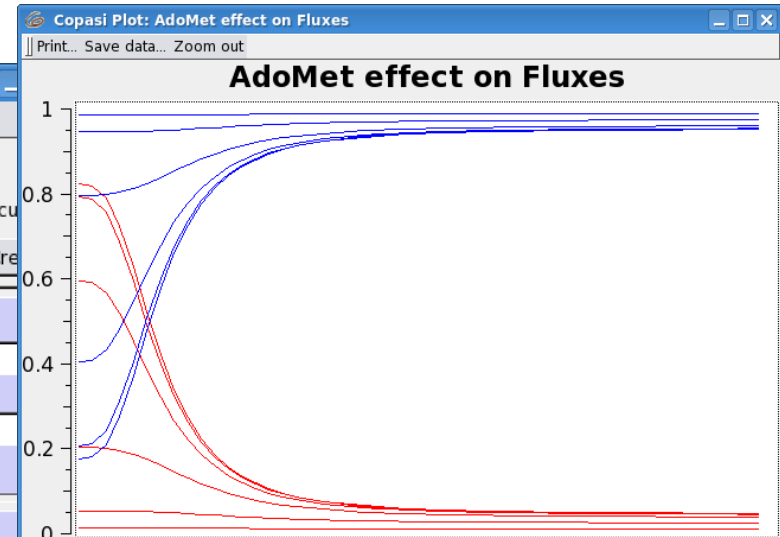
Scan	Parameter
<input type="checkbox"/>	[Cysteine]_0
Intervals	min max
5	0.3 300
<input checked="" type="checkbox"/> logarithmic scan	

Scan	Parameter
<input type="checkbox"/>	(Threonine Synthase).AdoMet
Intervals	min max
50	0 100
<input type="checkbox"/> logarithmic scan	

**Task** Steady-State

always use initial conditions  output from subtask

Run Revert Report Output Ass



# Sensitivity analysis (MCA)

BIOMD0000000023 - COPASI 4.4 (Build 26) /Users/.../Documents/BIOMD0000000023.cps

Concentrations

Steady State found. All coefficients available. scaled

Elasticities Flux Control Coefficients Concentration Control Coefficients

Rows: Reactions (reduced system)  
Columns: Species (reduced system)

	HexP	Fru	Suc	Glc	Suc6P
(v1)	0	-0.609497	0	0	0
(v2)	0	0	0	-0.536628	0
(v3)	-0.00773174	-0.00925229	0	0.0192642	0
(v4)	-0.00773181	0.990748	0	-0.980736	0
(v5)	0	-0.769302	0	0	0
(v6)	1.26013	0	0	0	-0.00447428
(v7)	0	0	0	0	0.954415
(v8)	0.610067	0.406732	-0.434553	0	0
(v9)	0	-0.569948	0.78062	-0.667482	0
(v10)	0.53809	0	0	0	0
(v11)	0	0	0.905688	0	0

# Sensitivity analysis (general)

BIOMD0000000023 - COPASI 4.4 (Build 26) /Users/.../Documents/BIOMD0000000023.cps

Concentrations

Copasi

- ▶ Model
- ▼ Tasks
  - ▶ Steady-State
  - ▶ Stoichiometry
  - ▶ Time Course
  - ▼ Metabolic Control Analysis
    - Result
  - ▶ Lyapunov Exponents
- ▼ Multiple Task
  - Parameter Scan
  - ▶ Optimization
  - ▶ Parameter Estimation
  - ▼ Sensitivities (selected)
    - Result
- ▶ Output
- ▶ Functions

**Sensitivities**  update model  executable

Subtask Method: Steady State

Function: Concentration Fluxes of Reactions  
[Please Choose Object.] --->

Variable: All Parameter Values  
[Please Choose Object.] --->

Second Variable: Not Set  
[Please Choose Object.] --->

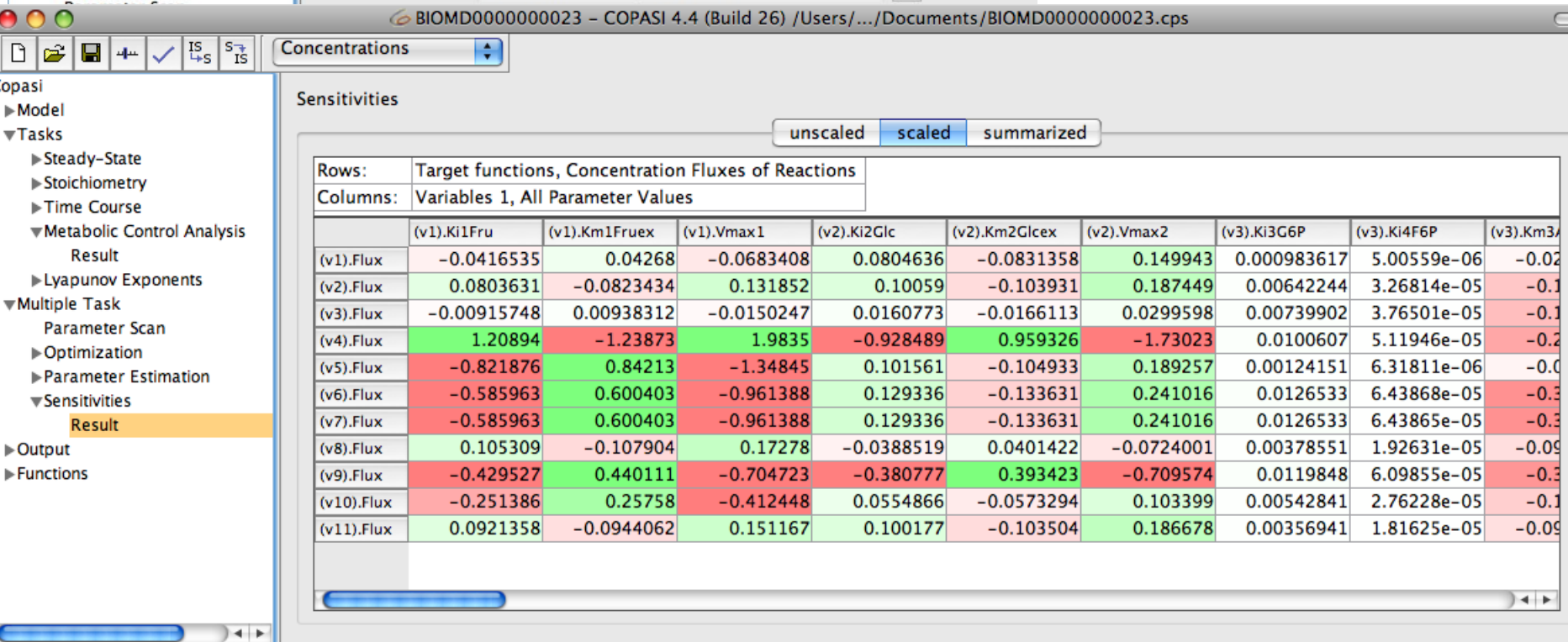
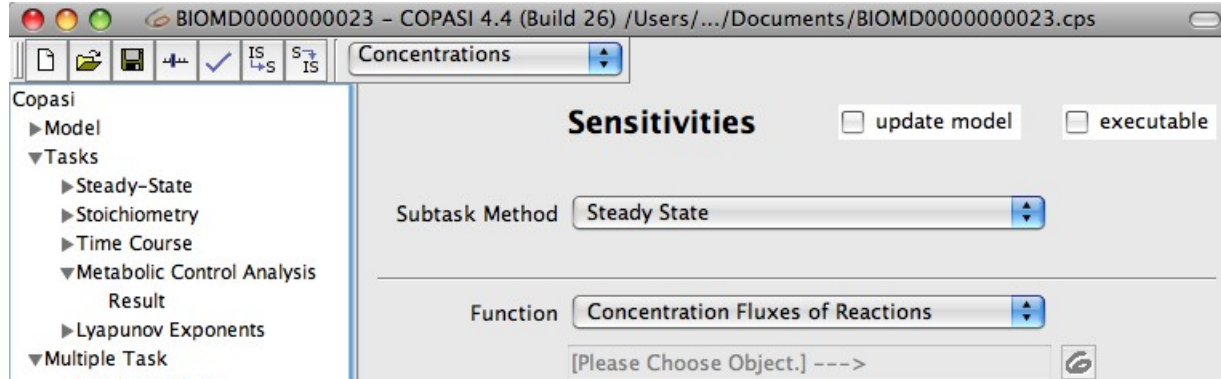
Method Parameter

	Value
Delta factor	1e-06
Delta minimum	1e-12

Run Revert Report Output Assistant



# Sensitivity analysis (general)



# Global optimisation

BIOMD000000023 - COPASI 4.4 (Build 26) /home/.../curated/BIOMD000000023.cps

File Tools Help

Concentrations

Copasi

- Model
  - Biochemical
    - Compartments
    - Species
    - Reactions
    - Global Quantities
    - Parameter Overview
  - Mathematical
- Tasks
  - Steady-State
  - Stoichiometry
  - Time Course
  - Metabolic Control Analysis
  - Lyapunov Exponents
- Multiple Task
  - Parameter Scan
  - Optimization
  - Result
- Parameter Estimation
- Sensitivities
- Output
  - Plots
    - progress of optimizat
  - Reports
- Functions

**Optimization**  update model  executable

Expression `<(v9).Flux>/<(v11).Flux>`

Experiment Type  Steady State  Time Course

Parameters (5) Constraints (2)

ID	Constraint	Start Value
1	$0.143 \leq (v1).Vmax1 \leq 1.43$	0.286
2	$0.143 \leq (v2).Vmax2 \leq 1.43$	0.286
3	$0.0985 \leq (v3).Vmax3 \leq 0.985$	0.197
4	$0.0985 \leq (v4).Vmax4 \leq 0.985$	0.197
5	$0.082 \leq (v5).Vmax5 \leq 0.82$	0.164

Object: (v1).Vmax1

Lower Bound  - Infinity: 0.143

Upper Bound  + Infinity: 1.43

Start Value: 0.286

Method: Particle Swarm

Method Parameter	Value
Iteration Limit	50
<b>Swarm Size</b>	50
Std. Deviation	1e-06
Random Number Generator	1

Run Revert Report Output Assistant

File Tools Help



- Copasi
  - + Model
  - + Tasks
    - Multiple Task
      - ... Parameter Scan
      - + Optimization
      - + **Parameter Estimation**
      - + Sensitivities
  - + Output
  - + Functions

## Parameter Estimation

update model     executable

Experimental Data    Cross Validation Data

Parameters (41)    Constraints (0)

1	1e-6 < (R1).Ka < 1; Start Value = 0.0494349
2	1e-6 < (R1).Kb < 1; Start Value = 0.0091214
3	1 < (R1).Keq < 10; Start Value = 1.41073
4	1e-6 < (R1).Kq < 1; Start Value = 0.0115745
5	1e-6 < (R1).Kp < 1; Start Value = 0.00429233
6	1e-6 < (R2).k1 < 0.001; Start Value = 3.25306e-05
7	1e-5 < (R1).Vf < 0.1; Start Value = 0.000422036
8	1.55e-2 < [NADP]_0; {Experiment_0} < 6.20e-2; Start Value = 0.0155
9	1.55e-2 < [NADP]_0; {Experiment_1} < 6.20e-2; Start Value = 0.0155

Object	(R1).Ka		
Lower Bound	<input type="checkbox"/> - Infinity	1e-6	
Upper Bound	<input type="checkbox"/> + Infinity	1	
Start Value		0.0494349	
Affected Experiments	<input checked="" type="checkbox"/> all		
Affected Cross Validations	<input checked="" type="checkbox"/> all		

Duplicate for each Experiment

Method **Hooke & Jeeves**

Method Parameter	Value
Iteration Limit	5000
Tolerance	1e-12
Rho	0.2

Run

Revert

Report

Output Assistant



- Copasi
  - Model
  - Tasks
    - Multiple Task
      - Parameter Scan
      - Optimization
      - Parameter Estimation**
      - Sensitivities
  - Output
  - Functions

## Parameter Estimation

update model     executable

Experimental Data    Cross Validation Data

Parameters (41)    Constraints (0)

1	1e-6 < (R1).Ka < 1; Start Value = 0.0494349
2	1e-6 < (R1).Kb < 1; Start Value = 0.0091214
3	1 < (R1).Keq < 10; Start Value = 1.41073
4	1e-6 < (R1).Kq < 1; Start Value = 0.0115745
5	1e-6 < (R1).Ks < 1; Start Value = 0.0091214
6	1e-6 < (R1).Kt < 1; Start Value = 0.0091214
7	1e-5 < (R1).Kv < 1; Start Value = 0.0091214
8	1.55e-2 < (R1).Kw < 1; Start Value = 0.0091214
9	1.55e-2 < (R1).Kx < 1; Start Value = 0.0091214

- Object
- Lower Bound
- Upper Bound
- Start Value
- Affected Experiment
- Affected Cross Validation

- Method
- Method Parameter

### Experimental Data

File: Experiment

MAPKdata.txt    Experiment

Name: Experiment    First Row: 1    Last Row: 11

Copy settings below  from previous     to next

Experiment Type:  Steady State     Time Course    Header: 1

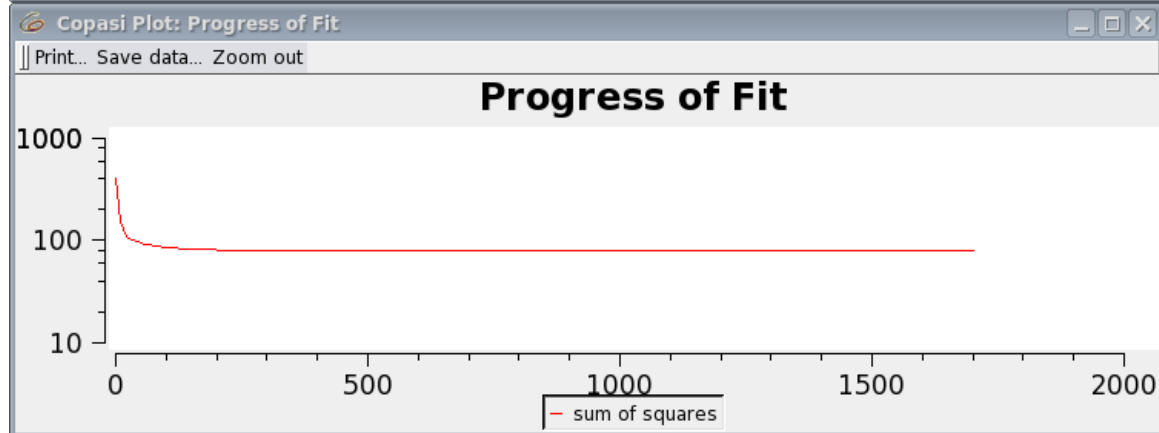
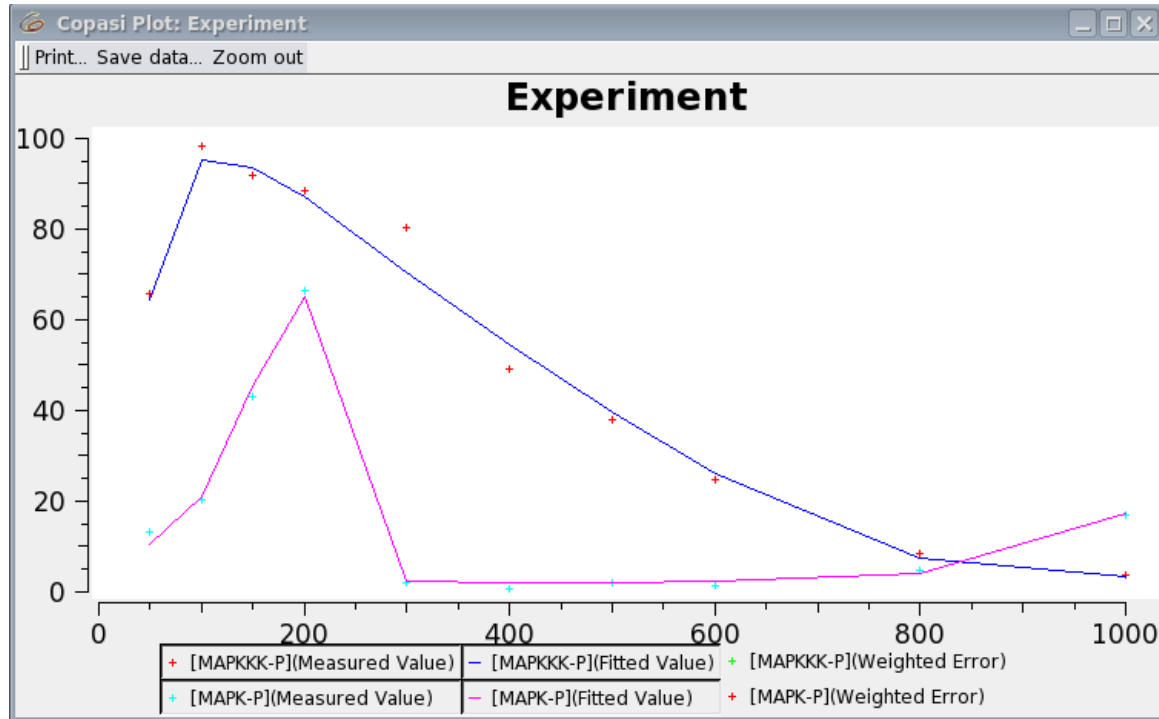
Weight Method: Mean Square    Separator: <tab>

	Column Name	Type	Model Object	Weight
1	time	Time		
2	MAPKKK-P	dependent	[MAPKKK-P]	(0.417105)
3	MAPK-P	dependent	[MAPK-P]	(1)

OK    Revert    Cancel

Run

# Parameter estimation



# Command line version

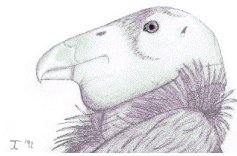
- **CopasiSE**

All model relevant information is contained in .cps file (COPASIML, an XML schema)

Usage: CopasiSE [options] [file]

<code>--configdir string</code>	The configuration directory for copasi. The default is .copasi in the home directory.
<code>--configfile string</code>	The configuration file for copasi. The default is copasi in the ConfigDir.
<code>--exportBerkeleyMadonna string</code>	The Berkeley Madonna file to export.
<code>--exportC string</code>	The C code file to export.
<code>--home string</code>	Your home directory.
<code>--license</code>	Display the license.
<code>--verbose</code>	Enable output of messages during runtime to <code>std::error</code> .
<code>-c, --copasidir string</code>	The COPASI installation directory.
<code>-e, --exportSBML string</code>	The SBML file to export.
<code>-i, --importSBML string</code>	A SBML file to import.
<code>-s, --save string</code>	The file the model is saved to after work.
<code>-t, --tmp string</code>	The temp directory used for autosave.

# Condor-COPASI high-throughput computing



Condor-COPASI Web Frontend - Stochastic Simulation - Mozilla Firefox

File Edit View History Bookmarks Tools Help

Condor-COPASI Web Frontend - Stochas... X +

## Condor-COPASI

Welcome **mendes** | Administration | Logout

Home >> Tasks >> Stochastic Simulation >>

- Home
- My Account
- Tasks
  - Sensitivity Optimization
  - Stochastic Simulation
  - Scan in Parallel
  - Optimization Repeat
  - Parameter Estimation Repeat
  - Optimization Repeat (Different Algorithms)
- Help

### Stochastic Simulation

Select the COPASI model to submit. Before submitting, ensure the model has been correctly configured:

- Time Course task:**
  - The Time Course should be set up as if a single run were to take place on the local machine
  - An appropriate stochastic method must be selected

Condor-COPASI will automatically generate an appropriate report; no report needs to be set for the Time Course task.

**Please note - it is very important that the COPASI file is saved using a supported version of COPASI. At present, only Build 33 (version 4.6.33) and Build 34 (version 4.6.34) are supported.**

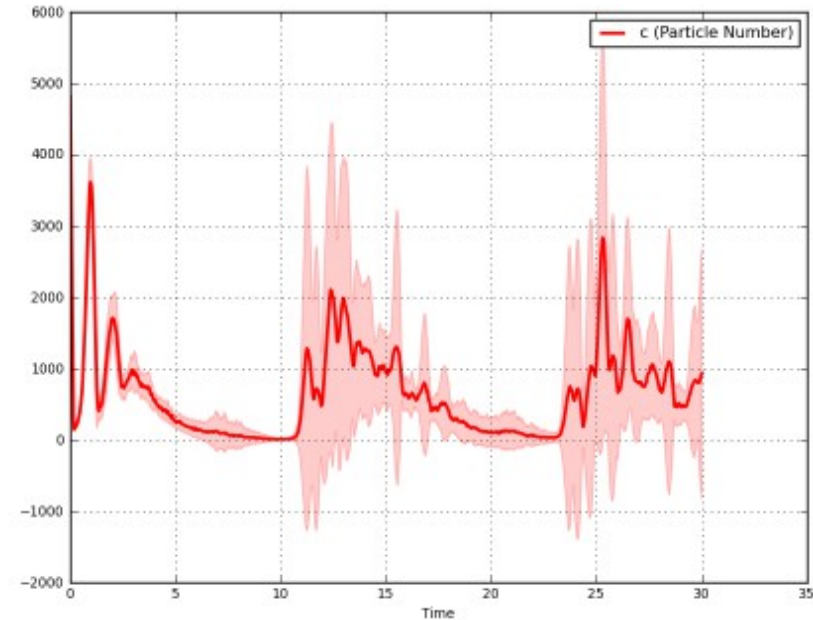
Model file:  Browse...

Job Name:   
For your reference, enter a name for this job

**Skip load balancing step:** Select this to skip the automatic load balancing step, and make the run time of each parallel job as short as possible. **Use with caution! This has the potential to overload the Condor system with huge numbers of parallel jobs.** Not applicable for some job types - see documentation for further details.

Repeats:   
The number of repeats to perform

Submit



Compare Global Sensitivity Job Output

