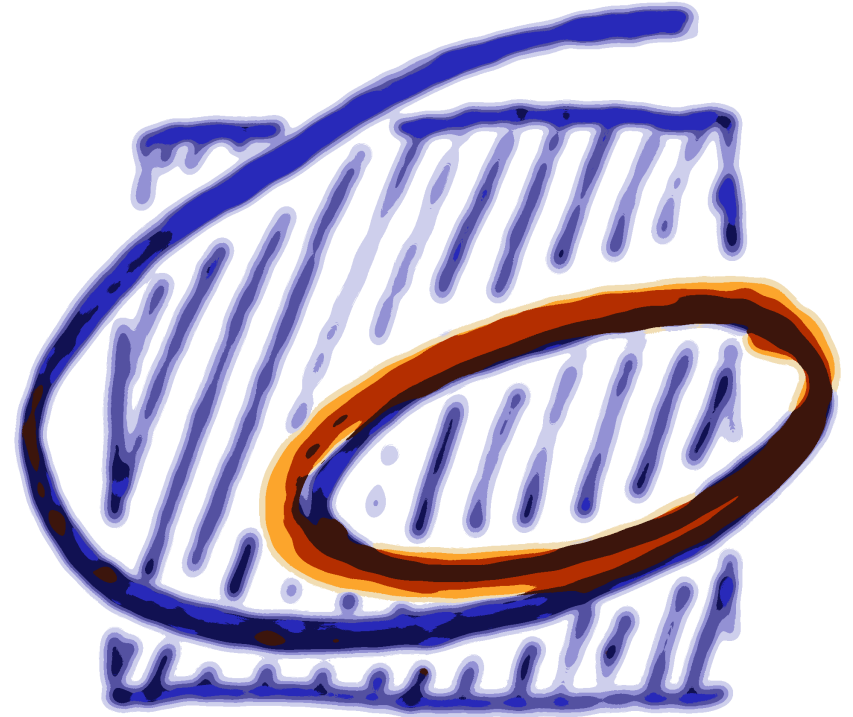


COPASI

Complex Pathway Simulator



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COS Heidelberg / BIOQUANT
Abt. Modellierung biologischer Prozesse



General info about COPASI

COPASI is a software tool for editing, simulating, and analyzing quantitative models of biochemical reaction networks.

COPASI is available for all major platforms (**Linux, Windows, OS X**), easy to install

COPASI is free software.

General info (continued)

COPASI is a joint project of the groups of Ursula Kummer (Heidelberg) and Pedro Mendes (Blacksburg, VA and Manchester)

COPASI is designed to be robust and user friendly, intended for general use not only by experts

Download from [**www.copasi.org**](http://www.copasi.org)

Checking models

COPASI can identify some common sources of problems with biochemical models.

Example: A reaction is marked as irreversible but its rate is not zero when a substrate is missing.

This is done by symbolic analysis of the kinetic functions.

SBML support

SBML is an XML file format to exchange biochemical models between different tools.

www.sbml.org

COPASI implements a large subset of the SBML specification. SBML compliance is well tested. The COPASI team is actively involved in the development of SBML



MIRIAM annotations

Editing and display of annotations is supported.

The screenshot displays the COPASI 4.7 (Build 34) application window. The title bar indicates the file path: BIOMD0000000061 - COPASI 4.7 (Build 34) /Users/.../curated/BIOMD0000000061.cps. The interface is divided into a left sidebar and a main right pane.

Left Sidebar: A tree view under 'COPASI' shows the hierarchy: Model > Biochemical > Compartments (2) > Species (25). The species 'Cytosolic glucose' is selected and highlighted in orange.

Main Pane: The 'Concentrations' tab is active. It contains several sections for editing annotations:

- Created at:** A date and time selector set to '04.09.11 11:38'.
- Authors:** A table with columns: #, Family Name, Given Name, Email, and Organization.
- References:** A table with columns: #, Resource, ID, and Description. It includes a '-- select --' option.
- Description:** A table with columns: #, Relationship, Resource, and ID. It lists two references: '1 is ChEBI CHEBI:17234' and '2 is KEGG Compound C00293', followed by a '-- select --' option.
- Modified at:** A table with columns: # and Date and Time Modified.

At the bottom of the main pane, there are 'Delete' and 'Delete All' buttons.

different mathematical interpretations of a model

A key feature is the ability to switch transparently between a deterministic and a stochastic model interpretation

- Deterministic: ODEs are automatically generated and solved using LSODA
- Stochastic: Reaction rates are converted to reaction probabilities. Exact simulation with Gibson/Bruck or hybrid simulation

Steady State analysis

- Robust algorithm to find steady states
- Stability analysis (eigenvalues of jacobian)
- Metabolic control analysis / MCA
(control coefficients)

Structural analysis

- Identification of conservation relations

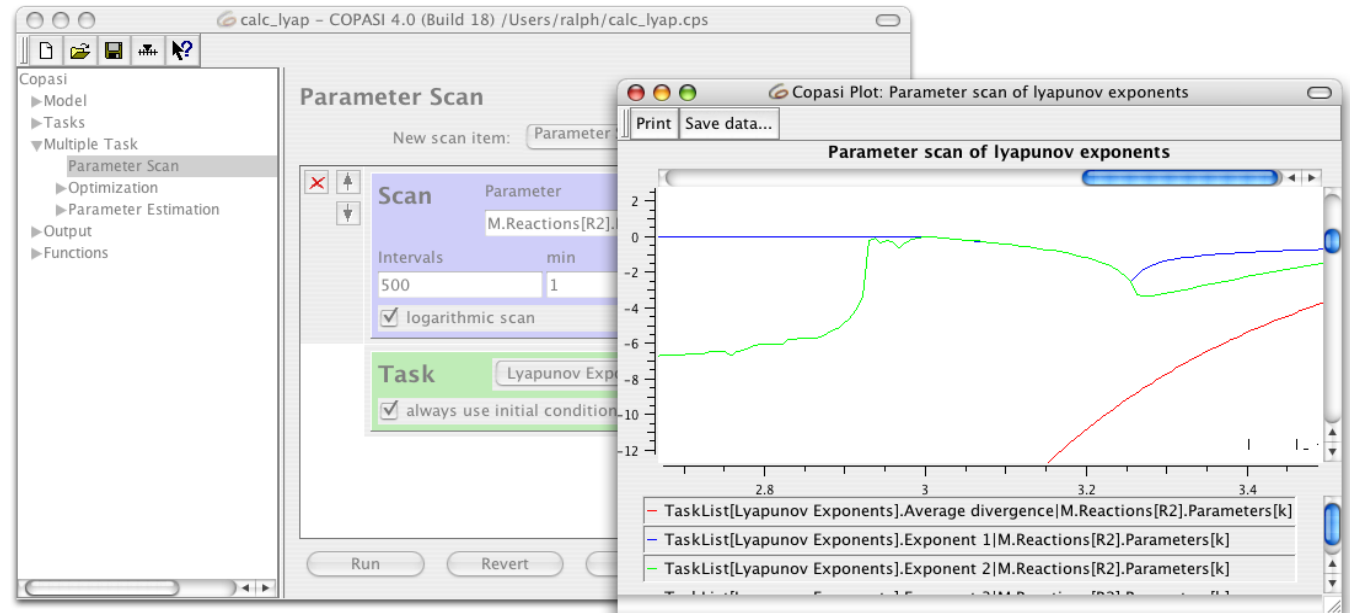


Very efficient and exact algorithm (Householder method)

- Elementary flux modes

Other analysis features

- Lyapunov exponents
- Parameter scan / sampling
- General sensitivities (first and second order)
- Optimization
- Parameter fitting
- Time scale analysis



The COPASI Team

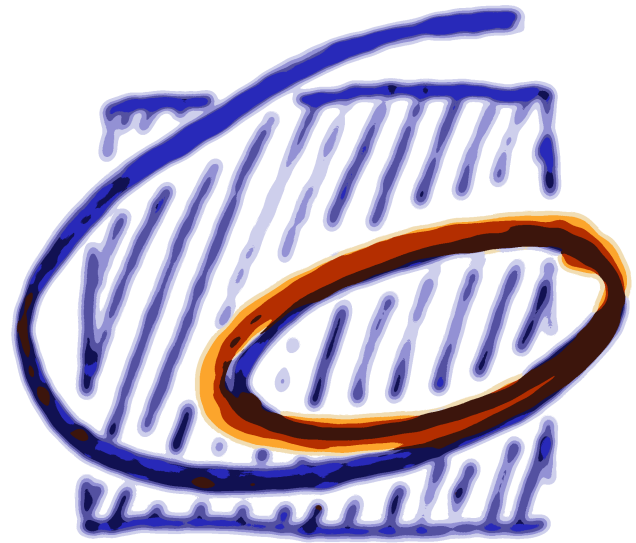
Blacksburg: Stefan Hoops

Manchester: Pedro Mendes, Joseph Dada

Heidelberg: Ralph Gauges, Ursula Kummer, Natalia Simus,
Sven Sahle, Irina Surovtsova

For support: **User forum at www.copasi.org**

We would like to thank the Klaus Tschira Foundation, the BMBF
and the NIH for funding.



The model in COPASI

Screenshots

sm10 - COPASI 4.4.28 (Debug) /Users/.../GAsmallestrangemin/sm10.cps

Concentrations

	Status	Name	Equation	Rate Law	Flux (mol/min)
1		vgp	$P + Gly = G1P$; amp	function_4_vgp	0.00020513
2		vpglm	$G1P = G6P$	function_4_vpglm	0.00020513
3		vpgi	$G6P = F6P$	function_4_vpgi	0.00020513
4		vpfk	$atp + F6P = adp + FDP$; amp	function_4_vpfk	0.00020513
5		vald	$FDP = DHAP + GAP$	function_4_vald	0.00020513
6		vtpi	$GAP = DHAP$	function_4_vtpi	0.00020513
7		vgapdh	$P + GAP + NAD = NADH + DPG$	function_4_vgapdh	0.00041026
8		vpgk	$adp + DPG = atp + P3G$	function_4_vpgk	0.00041026
9		vpgm	$P3G = P2G$	function_4_vpgm	0.00041026
10		ven	$P2G = PEP$	function_4_ven	0.00041026
11		vpk	$adp + PEP = atp + PYR$	function_4_vpk	0.00041026
12		vldh	$NADH + PYR = LAC + NAD$	function_4_vldh	0.00041026
13		vck	$atp + Cr = adp + PCr$	function_4_vck	0
14		vadk	$atp + amp = 2 * adp$	function_4_vadk	.72451e-21
15		vatpase	$atp \rightarrow adp + P$	Mass action (irreversible)	.000615389
16		vfout	$LAC \rightarrow LACo$	Mass action (irreversible)	0.00041026
17					

Commit Revert Clear Delete/Undelete New

Example (continued)

A reaction in COPASI

sm10 - COPASI 4.4.28 (Debug) /Users/.../GAsmallestrangemin/sm10.cps

Concentrations

Reaction Annotation RDF Browser

Name:

Chemical Equation:

☒ Reversible ☐ Multi Compartment

Rate Law:

Flux (mol/min):

Symbol Definition

Description	Name	Value	Unit
→ Substrate	F6P	<input type="text" value="F6P"/>	mol/l
→ Product	FDP	<input type="text" value="FDP"/>	mol/l
Parameter	KpfkadpT_4	<input type="checkbox"/> global	0.00271 mol/l
Parameter	Kpfkadp_4	<input type="checkbox"/> global	0.00271 mol/l
Parameter	Kpfkamp_4	<input type="checkbox"/> global	6e-05 mol/l
Parameter	KpfkatpT_4	<input type="checkbox"/> global	0.00025 mol/l
Parameter	Kpfkatp_4	<input type="checkbox"/> global	8e-05 mol/l
Parameter	Kpfkf6pT_4	<input type="checkbox"/> global	0.02 mol/l

ODEs generated from the reaction network

Example (continued)

The screenshot shows the COPASI 4.4.28 (Debug) interface. The main window displays the 'Differential Equations' section, showing the mathematical model for the reaction network. The equations are presented in a structured format, with the left side showing the derivative of the species concentration over time, and the right side showing the sum of production and consumption rates.

Equation 1 (Top):

$$\frac{d([DHAP] \cdot V_{uVol})}{dt} = + V_{uVol} \cdot \left[\frac{V_{fald_5_vald} \cdot [FDP]}{K_{aldfdp_5_vald}} - \frac{V_{fald_5_vald} \cdot K_{aldgap_5_vald} \cdot K_{alddhap_5_vald} \cdot [DHAP] \cdot [GAP]}{K_{aldfdp_5_vald} \cdot 9.5e-05 \cdot K_{aldgap_5_vald} \cdot K_{alddhap_5_vald}} \right]$$

Equation 2 (Bottom):

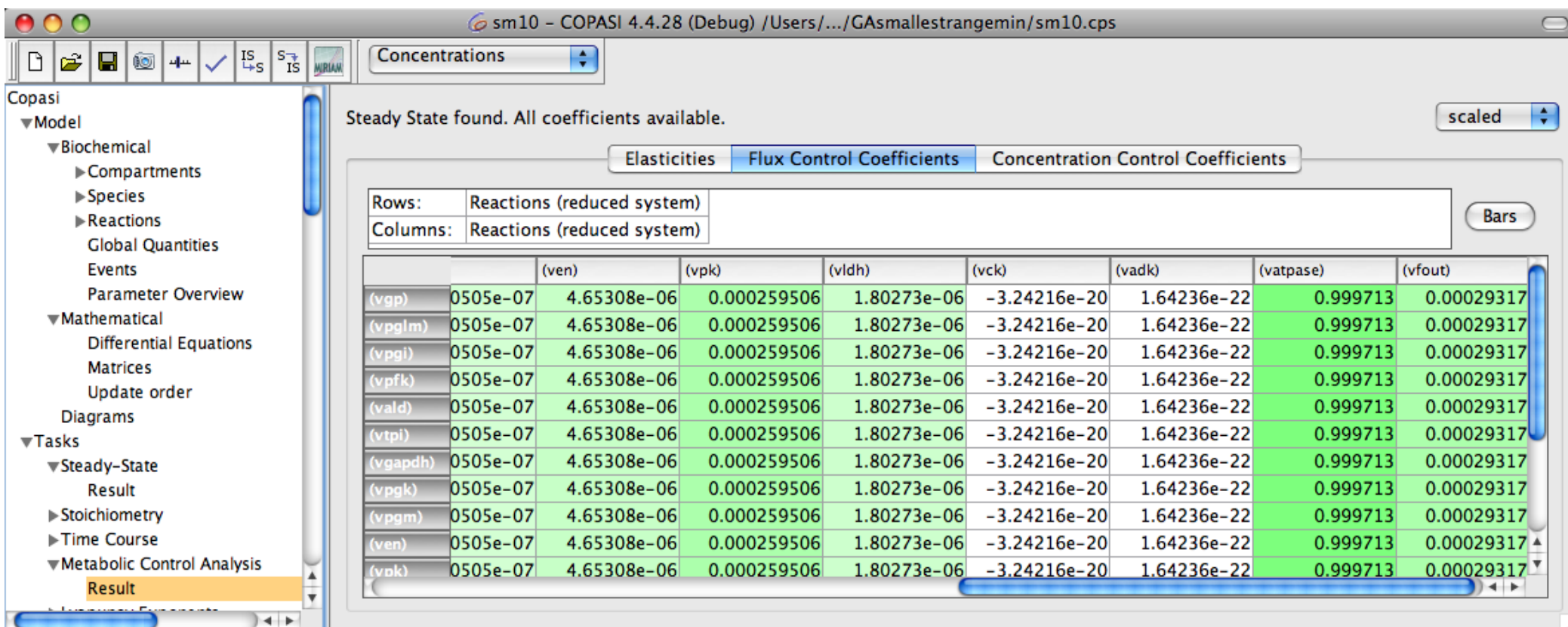
$$\frac{d([GAP] \cdot V_{uVol})}{dt} = + V_{uVol} \cdot \left[\frac{V_{ftpi_6_vtpi} \cdot K_{tpidhap_6_vtpi} \cdot [DHAP]}{K_{tpigap_6_vtpi} \cdot 19.2 \cdot K_{tpidhap_6_vtpi}} - \frac{V_{fald_5_vald} \cdot K_{aldgap_5_vald} \cdot K_{alddhap_5_vald} \cdot [DHAP] \cdot [GAP]}{K_{aldfdp_5_vald} \cdot 9.5e-05 \cdot K_{aldgap_5_vald} \cdot K_{alddhap_5_vald}} \right]$$

The interface includes a sidebar on the left with a tree view of the model structure, including compartments, species, reactions, and various analysis tasks. The bottom of the window features controls for 'local parameters' (display name) and 'functions' (expand only kinetic functions), along with a 'Save Formula to Disk' button.

MCA results

Example (continued)

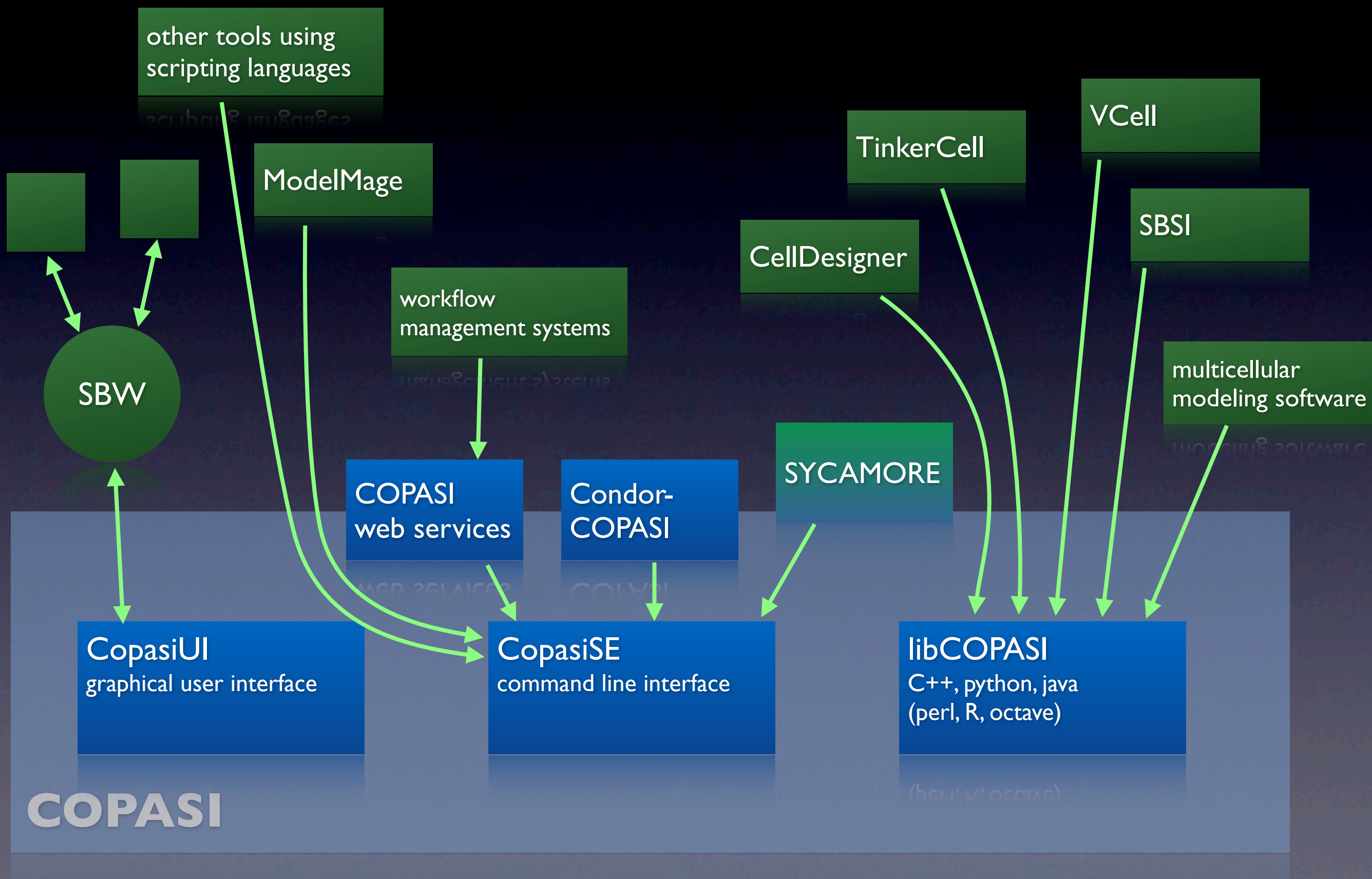
- For the given parameters the steady state is almost completely controlled by the ATPase.





COPASI

Integration with
other community software



SBW integration

- The GUI version of COPASI has support for the Systems Biology Workbench
- for details about SBW -> Frank Bergmann

Scripting with the COPASI command line interface

- Ideal workflow:
SED-ML -> COPASI -> SBRML
- current workflow:
COPASI-ML -> COPASI -> Text file
- example: ModelMage
(<http://sysbio.molgen.mpg.de/modelmage/>)



- **Condor-COPASI** (<http://code.google.com/p/condor-copasi/>)
Implemented by Ed Kent in Manchester
 - Web frontend for distributed calculations using COPASI
- **COPASI Webservices**
Implemented by Joseph Dada

In both cases we provide the implementation,
not the actual service

Both are based on CopasiSE

COPASI language bindings

- COPASI's functionality is available as a library that can be used from a number of programming languages
- C++, python, and java are well supported, perl, R, octave are in progress
- useful documentation is provided
- typically it is released for every stable version of COPASI version
- ask Ralph Gauges for details

Examples



VCeCell - The Virtual Cell

CellDesigner.org