

COPASI – a complex pathway simulator

Stefan Hoops¹, Sven Sahle^{2,*}, Ralph Gauges², Jürgen Pahle⁵, Natalia Simus², Ursula Kummer^{2,5}, Pedro Mendes^{1,3,4}

¹ Virginia Bioinformatics Institute, Blacksburg, VA

² Department for Modeling of biological Processes, University of Heidelberg, Germany

³ School of Computer Science, Oxford Road, Manchester, UK

⁴ Manchester Centre for Integrative Systems Biology, Manchester Interdisciplinary Biocentre, UK

⁵ EML Research gGmbH, Heidelberg, Germany

* Email: sven.sahle@bioquant.uni-heidelberg.de

COPASI is a platform-independent, user-friendly software tool that allows easy access to powerful numerical methods for simulation and analysis of biochemical reaction networks. We will give an overview of its features and highlights some new developments.

General features

COPASI is freely available for academic users. It runs on all major operating systems (Linux, Mac OSX, Windows, and Solaris). Two versions are provided: one with an easy to use graphical user interface that allows editing the model, running calculations, and viewing the results (see screen shots). The other version is a command line tool that can be used for batch processing or for interfacing with other software tools.

New features

Variable compartment volumes and arbitrary mathematical expressions for metabolite concentrations

In older versions of COPASI the volume of each compartment was considered to be constant. Now a variable compartment volume can be specified, either as a differential equation or as an algebraic assignment. This allows great flexibility for the modeler. The compartment volume can change over time in a predefined way, or it can be calculated from other variables, e.g. the production of some metabolite.

The concentrations of the metabolites can now also be specified in a more flexible way. Usually the simulator determines the changes of metabolite concentrations from the reactions the metabolite participates in. Now the modeler can also provide an explicit differential equation or an algebraic expression for the concentration of a metabolite.

Model „debugging“ features

COPASI can perform a sophisticated analysis of the reactions and kinetic functions in a model to find some common modeling problems. As an example, COPASI can identify rate laws that are used for an irreversible reaction but which are not zero if one of the substrates is not present. Such rate laws could lead to negative concentrations in the course of a simulation.

New optimization / parameter fitting features

COPASI's long list of optimization algorithms has been expanded with a Particle Swarm Algorithm. This algorithm was inspired by a flock of birds looking for food. Each particle performs a random walk attracted by its own best location as well as that of its neighbors.

Handling reversible reactions in stochastic simulation

One of the key features of COPASI is that the user can transparently switch between a deterministic and a stochastic simulation framework, using the same model. However, stochastic simulation is only possible if all reactions in the model are irreversible. COPASI features an algorithm that can automatically split a reversible reaction into two irreversible reactions.

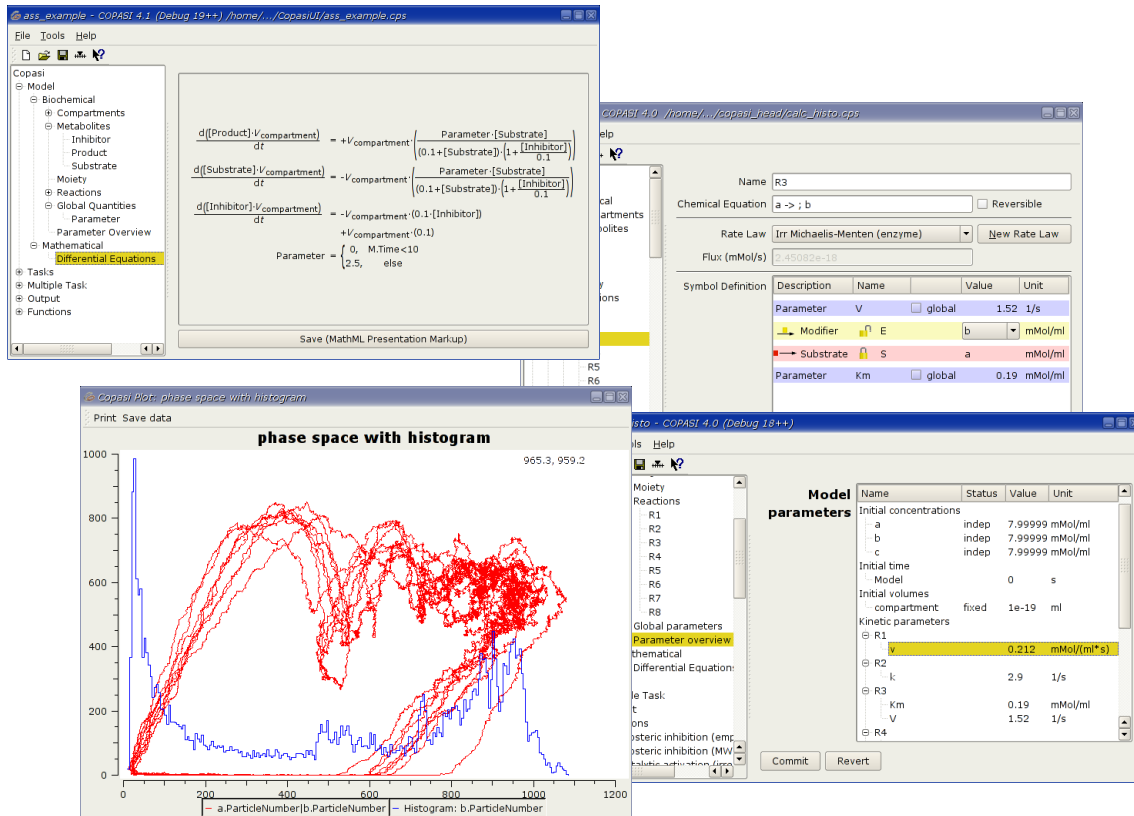


Figure: Some COPASI screen shots (clockwise from upper left): The display of the differential equations of a model. A time-dependent assignment for a parameter is given – the view for a single reaction – the overview of all parameters of a model – a plot containing an overlay of a phase space plot and a histogram of a stochastic simulation run