Towards truly integrated modelling in Systems Biology
Developing the Software and Standards

Brett G. Olivier[1,3], Maciej Swat[4], Katy J. Wolstencroft[2], Jacky L. Snoep[2,5], Joost Boele[1], Timo Maarleveld[1,3]

[1] Systems Bioinformatics, VU University Amsterdam, Amsterdam, The Netherlands
[2] Molecular Cell Physiology, VU University Amsterdam, Amsterdam, The Netherlands
[3] Life Sciences, Centrum Wiskunde & Informatica (CWI), Amsterdam, The Netherlands
[4] EMBL European Bioinformatics Institute, Hinxton, Cambridge, United Kingdom
[5] Triple-J Group, Stellenbosch University, Stellenbosch, South Africa

b.g.olivier@vu.nl

NETHERLANDS INSTITUTE FOR SYSTEMS BIOLOGY

➢ A core principle of Systems Biology is an iterative, process that cycles between theory, modelling and experiment.
➢ This requires the integration of new and existing software using community driven standards and application interoperability
➢ Here we present a selection of web-based and standalone modelling and data-management solutions that implement standards e.g. the *Systems Biology Markup Language* (SBML), *SBML Flux Balance Constraints* (SBML-FBC) and *Systems Biology Graphical Notation* (SBGN).
➢ The future challenge is to develop the standards and frameworks that allows the seamless integration of these and future tools.

JWS Online

Web-based Systems Biology curated database of kinetic models simulation tool
➢ Includes simulation, steady-state, structural and metabolic control analysis
➢ SBGN pathway representation with SED-ML support included with OneStop

jjj.biochem.sun.ac.za
jjj.bio.vu.nl
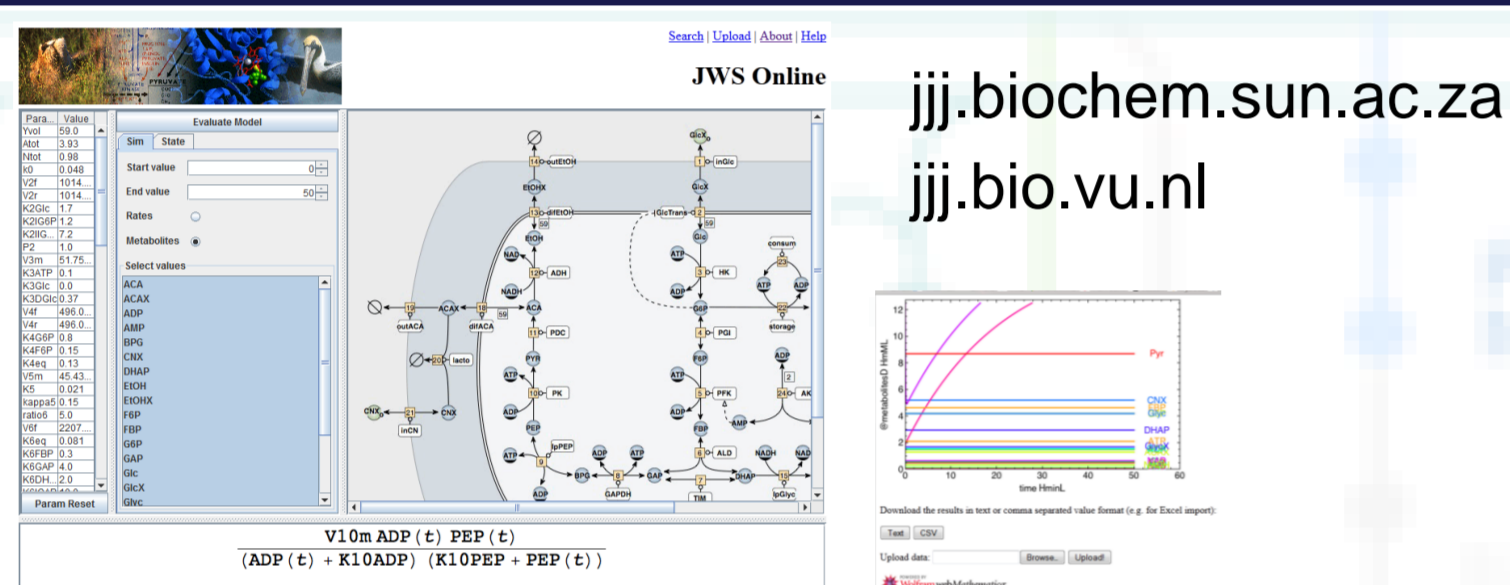
Olivier B.G. and Snoep J.L., *Web-based kinetic modelling using JWS Online*, Bioinformatics (2004) 20, 2143-2144

FAME

Web-based genome-scale modeling and visualisation environment
➢ Model construction, analysis and visualization
➢ Supports SBML and SBML-FBC models
➢ Open source: PHP/Python based

f-a-m-e.org
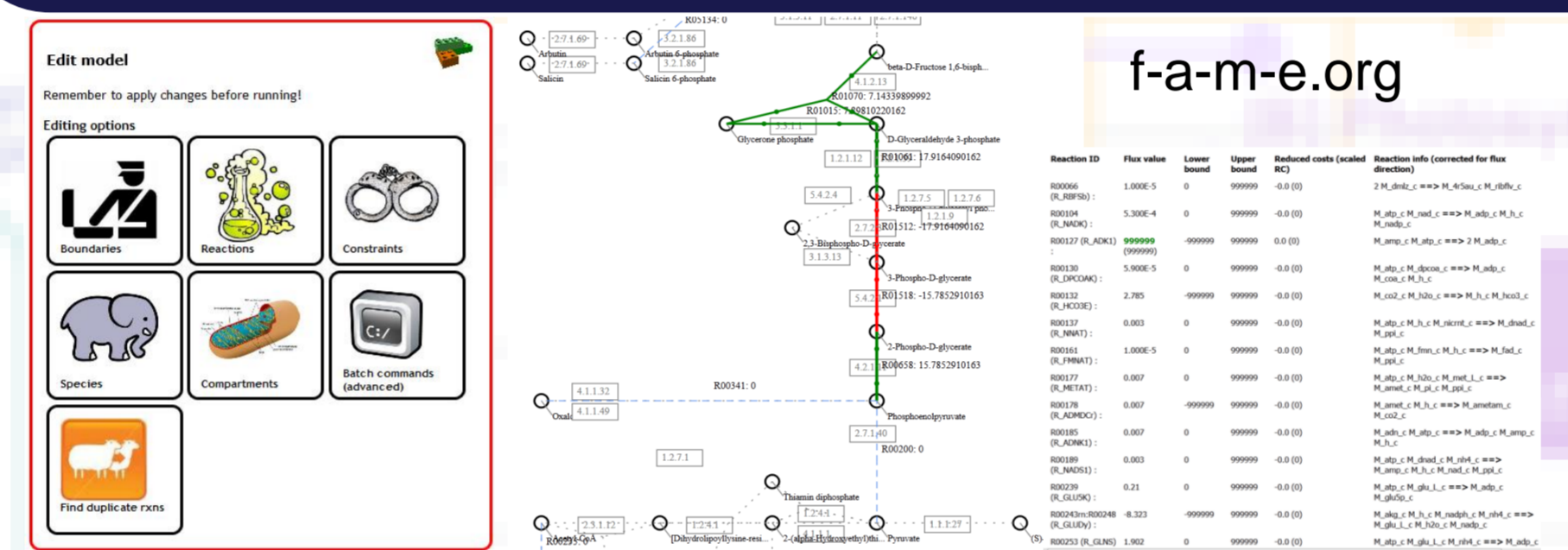
Boele J, Olivier BG, Teusink B., *FAME: the Flux Analysis and Modeling Environment*, BMC Systems Biology (2012) 6, 8

SBPKPD

Web-based platform for Systems Biology driven Pharmacokinetics and Pharmacodynamics
➢ Contains published and peer-reviewed models and user libraries for fitting physiological data
➢ Implemented in R and GWT

www.sbpkpd.org
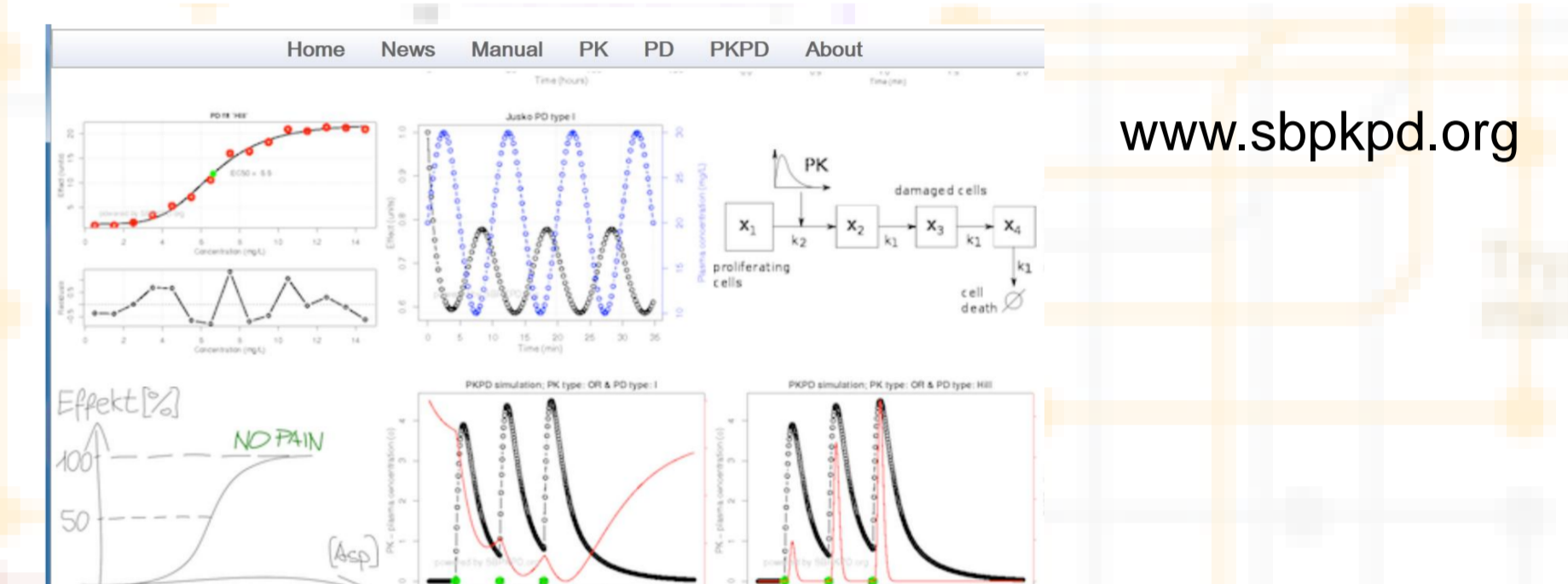
Swat, M. et al., *What it takes to understand and cure a living system* Interface Focus. (2011) 1, 16–23.

PySCeS

Interactive, flexible, extendable research tool for the numerical analysis of cellular systems
➢ Includes simulation, steady-state, bifurcation structural and metabolic control analysis
➢ Supports SBML, provides a Python based, scriptable, open source, modelling platform

pysces.sourceforge.net
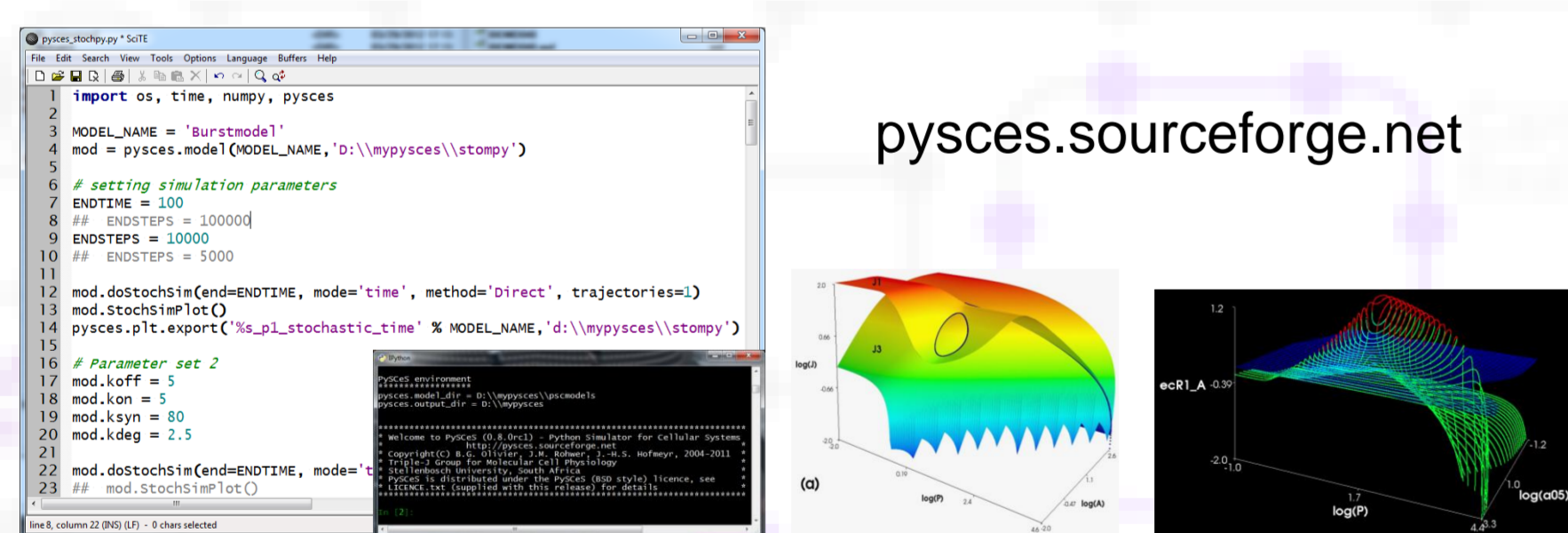
Olivier, B.G., Rohwer J.M. and Hofmeyr J.-H. S. *Modelling Cellular Systems with PySCeS*, Bioinformatics (2005) 21, 560-561

Biological models
SBML
www.sbml.org

Constraint based models
SBML-FBC
www.sbml.org

Systems Bioinformatics
Molecular Cell Physiology
vrije Universiteit amsterdam

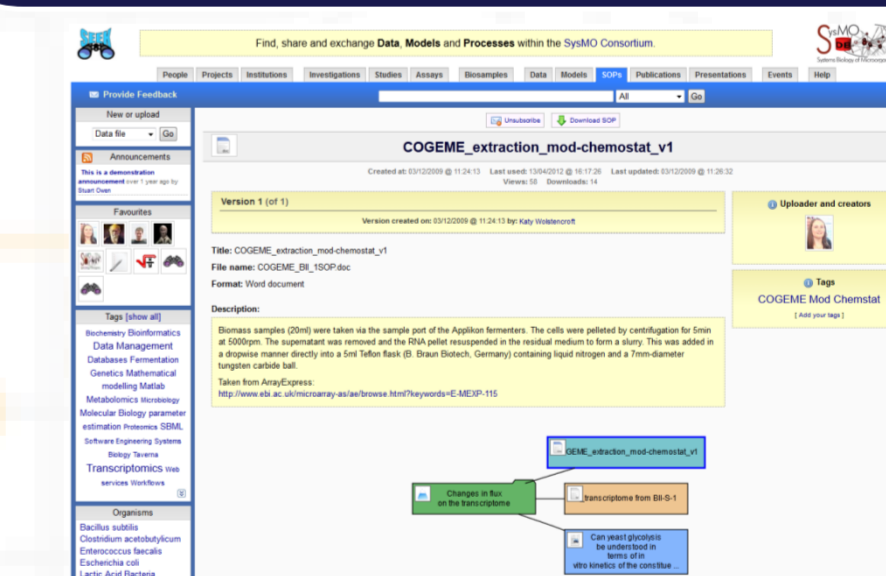**Graphical Notation**
SBGN
www.sbgn.org

Simulation experiments
SED-ML
sed-ml.org

SEEK

Web-based SB data and model management
➢ Integrated platform for data, protocol management and annotation
➢ Open source: part of the SySMO-DB project
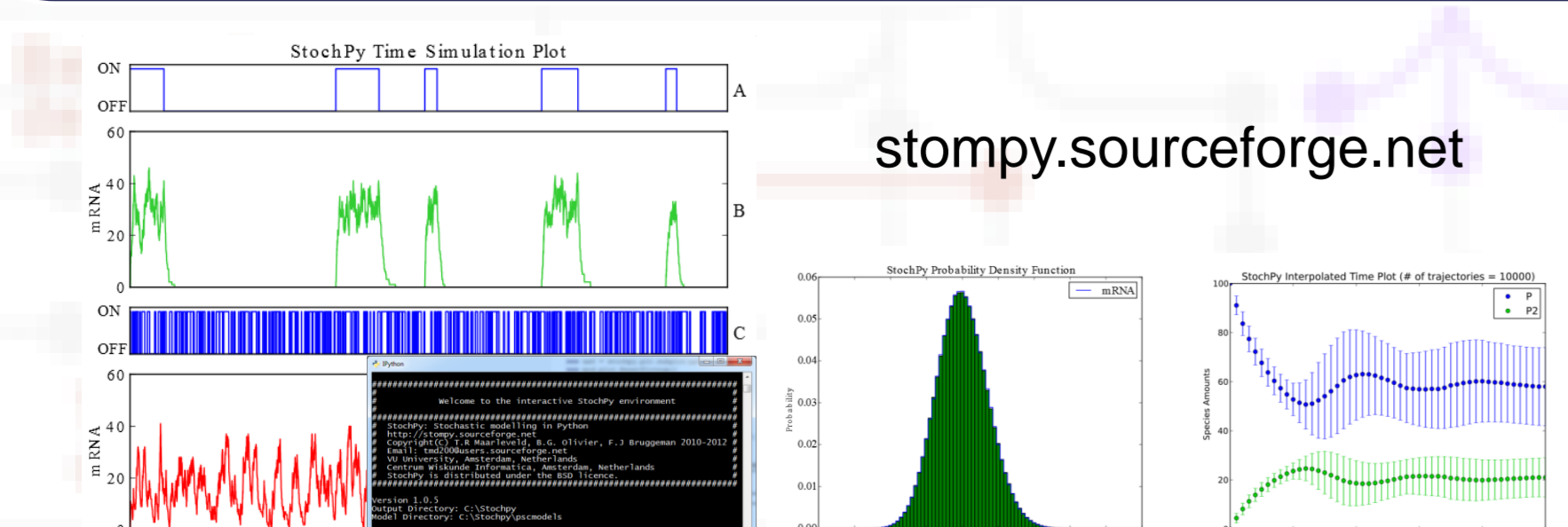➢ Includes JWS Online OneStop module

www.sysmo-db.org/seek

StochPy

Interactive flexible package, for the stochastic simulation of biochemical systems
➢ Includes various SSA's and statistical analyses
➢ Supports SBML and interfaces links to other software e.g. CAIN, StochKit and PySCeS
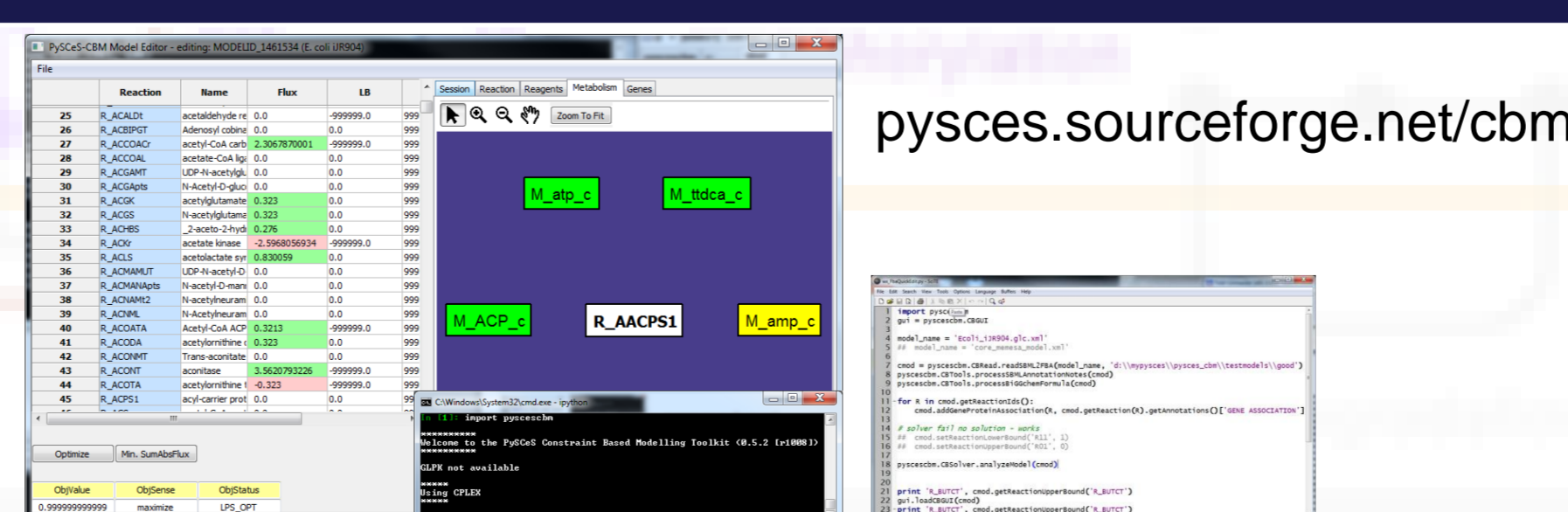➢ Open source Python implementation

stompy.sourceforge.net

PySCeS-CBM

Open source, flexible workbench for constraint based modelling of genome scale models
➢ Includes flux balance and variability analysis, gene deletions and minimal distance methods
➢ Has interactive, scripted and graphical user interfaces and support the SBML-FBC standard
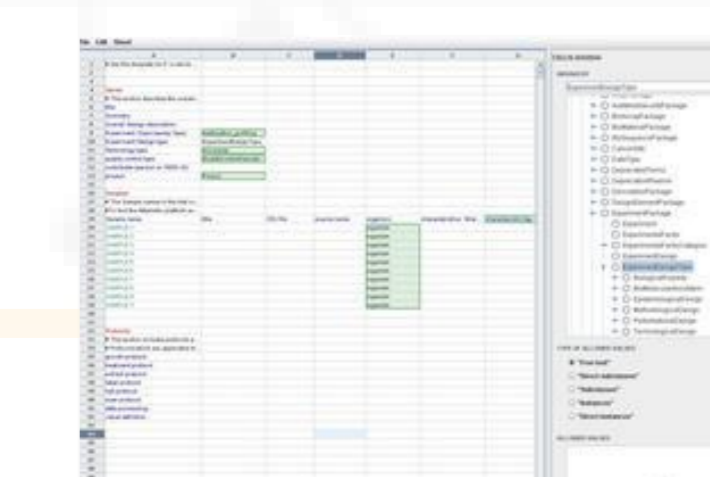
pysces.sourceforge.net/cbm

RightField

Embed semantics directly into spreadsheet templates
➢ Enables simple, standards-compliant data annotation
➢ Open source spreadsheet add-in

www.sysmo-db.org/rightfield

K.Wolstencroft, et al., *RightField: Embedding ontology annotation in spreadsheets*. Bioinformatics (2011), May 2011.

vrije Universiteit amsterdam

NWO
Netherlands Organisation for Scientific Research

CWI
Centrum Wiskunde & Informatica