CySBML: a Cytoscape Plugin For SBML.

König M.[1], Dräger A.[2], Holzhütter HG.[1]
[1] *Institute of Biochemistry, University Medicine Charité, Berlin Germany, matthias.koenig@charite.de*
[2] *Center for Bioinformatics Tuebingen (ZBIT), University of Tuebingen, Tübingen, Germany*

A major national initiative on Systems Biology of the Liver funded by the German Federal Ministry of Education and Research

Summary
CySBML [1] is a Cytoscape plugin [2] for SBML [3] based on JSBML [4] an open-source Java™ library for SBML.

Main Features
- Supports all versions and levels of SBML
- Handles models in SBML and the SBML Qualitative model format
- Supports the SBML Layout extension
- Access to annotation information (MIRIAM & SBO) and the semantic layer within the network context
- Integration of annotation information with additional web and database resources
- Includes validator for SBML models
- Provides navigation menu based on SBML structure
- Access to SBML models via BioModels web services
- Seemless integration with Cytoscape core and other Cytoscape tools like CyFluxViz [5]

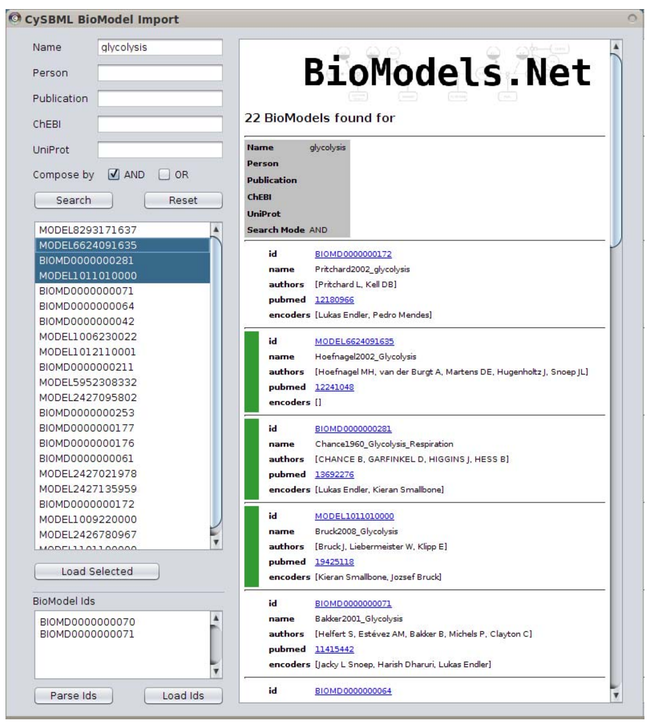
Availability and implementation
Freely available for noncommercial purposes via the Cytoscape App Store or for download at http://sourceforge.net/projects/cysbml/.

Supplementary Information
Tutorial, usage guide, installation instructions and additional figures are available for download at www.charite.de/sysbio/people/koenig/software/cysbml/

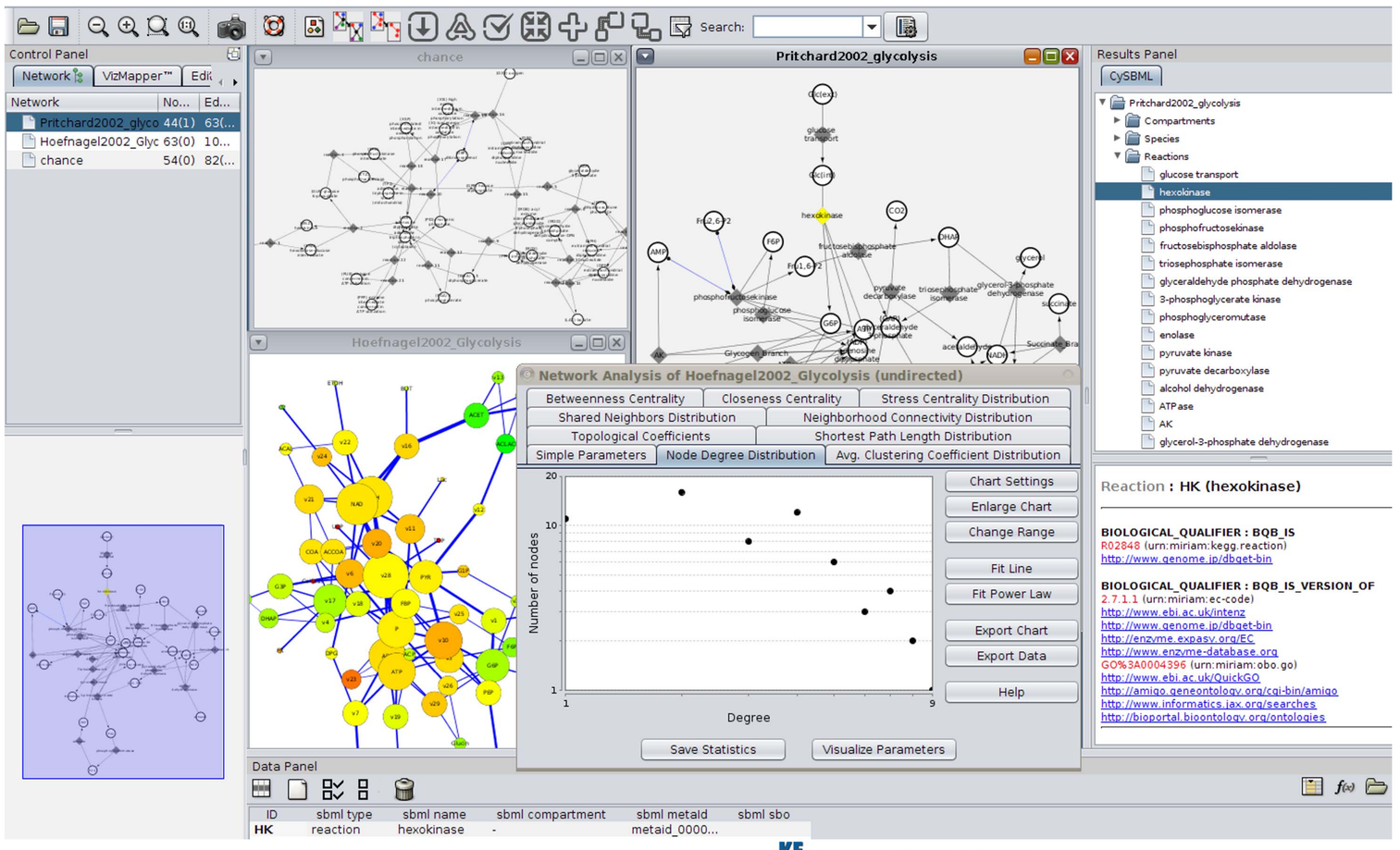
Contact
cysbml-team@lists.sourceforge.net

Funding
This work was supported by the BMBF, Germany within the Virtual Liver Network [grants 0315756 & 0315741].

Publications
[1] *CySBML: a Cytoscape plugin for SBML*
König M., Dräger A. and Holzhütter HG. (2012), Bioinformatics. 2012 Jul 5
[2] *Cytoscape: a software environment for integrated models of biomolecular interaction networks*
Shannon, P., et al. (2003), Genome Res, 13, 2498–250
[3] *The systems biology markup language (SBML): a medium for representation and exchange of biochemical network models*
Hucka, M., et al. (2003), Bioinformatics, 19, 524–531.
[4] *JSBML: a flexible Java library for working with SBML,*
Dräger, A., et al. (2011), Bioinformatics, 27, 2167–2168
[5] *FluxViz - Cytoscape Plug-in for Vizualisation of Flux Distributions in Networks*
König M. and Holzhütter HG. (2010), Genome Informatics 2010, Vol.24, p.96-10

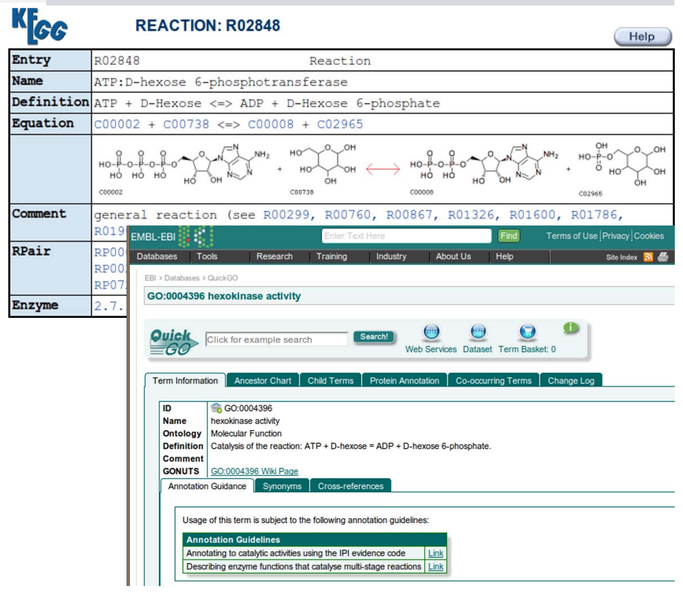


[^] BioModel Import
- Search models by name person, publication, ChEBI or UniProt & Import selected models via Web Services



[^] Usage example
•Multiple glycolysis SBML models (Pritchard2002, Hoefnagel2002, Chance1960) are loaded from BioModels via web service import based on search by name (see BioModel import)
•Topological network parameters of the Hoefnagel2002 model are analysed with NetworkAnalyser
- Node degree distribution shown
- Some of the topological parameters are mapped onto the SBML network (node degree → node size, neighborhood connectivness → node color, edge betweenness → edge width)

•Additional web resources from KEGG and EBI are loaded based on the annotation information for the hexokinase reaction in the Pritchard2002 network

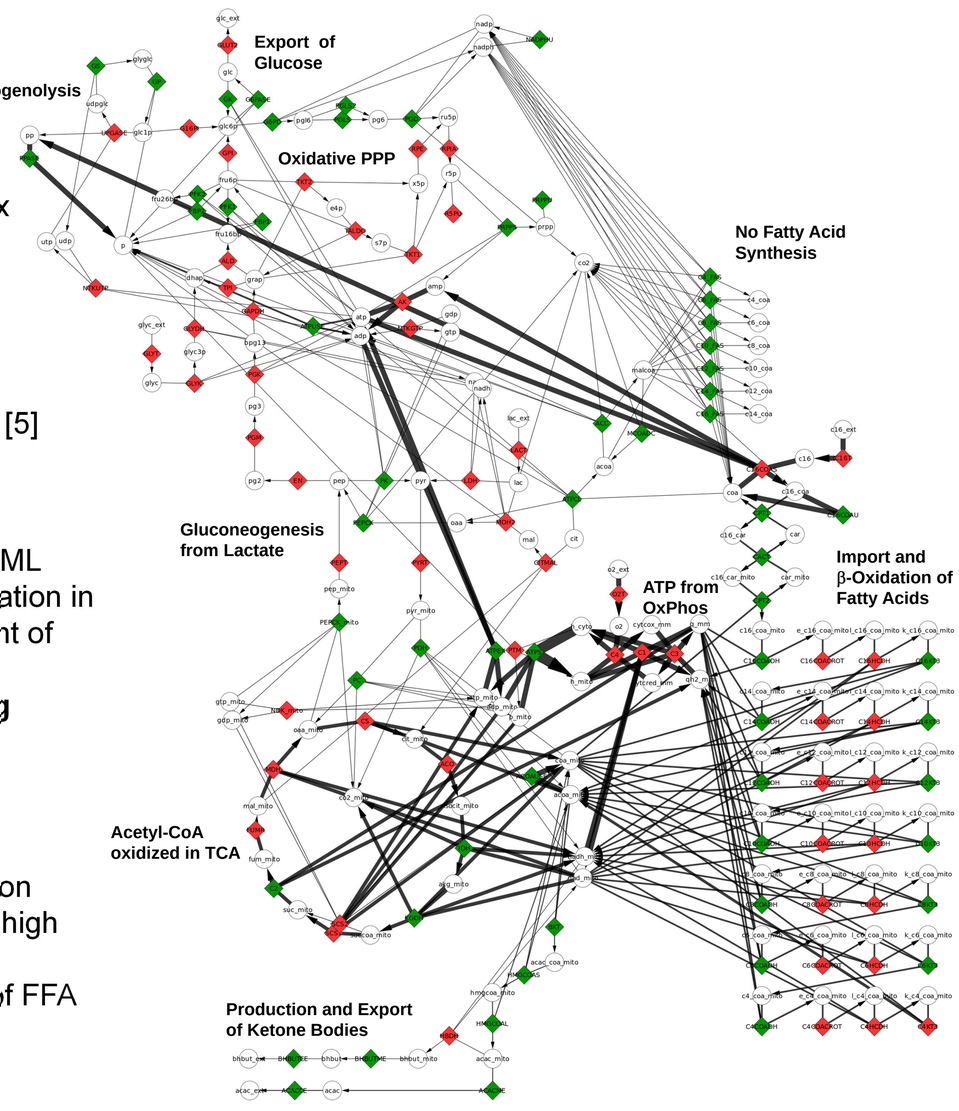


Integration with other Tools
- CySBML integrates seamlessly with other plugins by making SBML information as CyAttributes accessible.
- A wide range of tools works out of the box with CySBML providing additional functionality for SBML models like
  - analysis of topological parameters (NetworkAnalyzer see example)
  - search of network motifs (NetMatch)
  - visualization of fluxes with CyFluxViz [5]

[>] CySBML & CyFluxViz
Visualization of Flux Distributions
Human Hepatocyte model loaded with CySBML and flux distribution from kinetic model simulation in Matlab imported with CyFluxViz [5] (end point of simulation used for visualization)

Simulation Condition: The Liver in Fasting
low blood glucose: 3.5mM
high blood FFA: 3mM

Results
- Gluconeogenesis from lactate
- Glycogenolysis supports glucose production
- Synthesis & export of ketone bodies from high acetyl-CoA
- ATP synthesis via OxPhos & β-oxidation of FFA
- No Fatty Acid Synthesis (FAS) due to low malonyl-CoA & high FFA
- NADPH synthesis via PPP
- β-oxidation results in high amounts of NADH, FADH2 (QH2) & acetyl-CoA



Federal Ministry of Education and Research