

CySBML: a Cytoscape plugin for SBML

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Cytoscape & SBML

- **Cytoscape**

- Open-source platform for complex network analysis and visualization (*Shannon, et al., 2003*)

- **Systems Biology Markup Language (SBML)**



- **Free and open interchange format for computer models of biological processes** (*Hucka, et al., 2003*)
 - Supported by over 230 software tools
 - Representation of **models for a wide range of cell biology** like metabolism, cell signaling and gene regulation
 - **Common standard of interoperability and exchange** to work with diverse tools on building, curation, annotation, simulation, analysis, and visualization of the same model
 - **BioModels** : standard repository of SBML models (*Li, et al., 2010*)

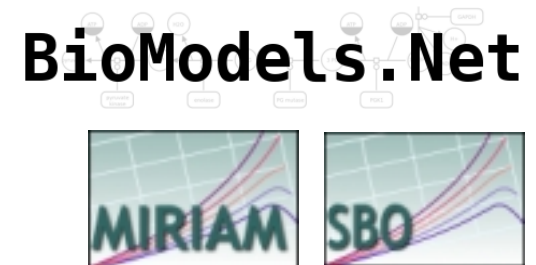
Model Annotation

- **Preserving models without the semantic layer** of information needed for an unambiguous identification and interpretation **of model components is meaningless** (Courtot, et al., 2011).
- SBML is annotated based on
 - MIRIAM (Minimum Information Required for the Annotation of Models) (*Laibe and Le Novère, 2007*)
 - SBO (Systems Biology Ontology) a set of controlled vocabularies in systems biology (*Le Novère, 2006*)



CySBML

- SBML plugin for Cytoscape based on JSBML (*Dräger, et al., 2011*), a free, open-source Java™ library for SBML.
- Supports all versions and levels of SBML
- Handles SBML Models and SBML Qualitative Models
- Supports SBML Layout extension (*Gauges, et al., 2006*)
- Access to BioModels via web services (*Li, et al., 2010*)
- Reads MIRIAM annotations of the SBML elements and provides access to the annotated resources within the network visualization
- Validation of imported SBML files
- Navigation menu based on SBML structure



CySBML Interface

Interplay
FluxViz & NetMatch

CySBML Menu Bar

SBML Navigation Tree

The screenshot displays the CySBML interface with several key components:

- Top Panel:** Cytoscape Desktop (New Session) with a menu bar (File, Edit, View, Select, Layout, Plugins, Help) and a toolbar. A search bar is present.
- Left Panel:** A table listing nodes and their associated reactions. The table has columns for 'Mat...', 'Occurr...', 'Nodes', and 'Image'.

Mat...	Occurr...	Nodes	Image
1	2	AcAld, ADH, Succinate_Bra nch	
2	2	AcAld, PDC, Succinate_Bra nch	
3	2	NADH, G3PDH, Succinate_Bra nch	
- Center Panel:** Network Analysis of path_hsa00450 (undirected). It displays various network statistics:

Betweenness Centrality	Closeness Centrality	Stress Centrality Distribution
Shared Neighbors Distribution	Neighborhood Connectivity Distribution	
Topological Coefficients	Shortest Path Length Distribution	
Simple Parameters	Node Degree Distribution	Avg. Clustering Coefficient Distribution

Clustering coefficient : 0.0
Connected components : 12
Network diameter : 8
Network radius : 1
Network centralization : 0.069
Shortest paths : 3336 (61%)
Characteristic path length : 4.309
Avg. number of neighbors : 2.081

Number of nodes : 74
Network density : 0.029
Network heterogeneity : 0.976
Isolated nodes : 10
Number of self-loops : 0
Multi-edge node pairs : 0
Analysis time (sec) : 0.077
- Right Panel:** SBML Navigation Tree showing a list of SBML files (Se-Methylselenomethionine, Selenomethionyl-tRNA(Met), Protein, Methylselenol, Dimethyl selenide, Methylseleninate, Methylselenocysteine). Below this is the Species: Methylselenol (Methylselenol) section with SBO:0000247 and various biological qualifiers.
- Bottom Left Panel:** CySBML BioModel Import. It includes a search bar with 'glycolysis' entered, a list of 22 BioModels found for 'glycolysis', and a table of results:

Name	glycolysis
id	BIOMD0000000172
name	Pritchard2002_glycolysis
authors	[Pritchard L, Kell DB]
pubmed	12180966
encoders	[Lukas Endler, Pedro Mendes]
- Bottom Center Panel:** Interplay NetworkAnalyzer. It displays a network graph for path_hsa00450, showing nodes and their interactions.
- Bottom Right Panel:** Annotation Area & WebLinks. It shows the chemical structure of Methylselenol (CH3SeH) and various biological qualifiers with links to external resources.

BioModel Import

- SBML BioModels search via
 - identifiers
 - name
 - author
 - publication
 - ChEBI
 - UniProts
- Import multiple models for comparative analysis

The screenshot displays the 'CySBML BioModel Import' web application. The search criteria are set to 'glycolysis'. The interface shows a list of 22 BioModels found. The results are displayed in a table with columns for Name, Person, Publication, ChEBI, and UniProt. The search mode is set to AND.

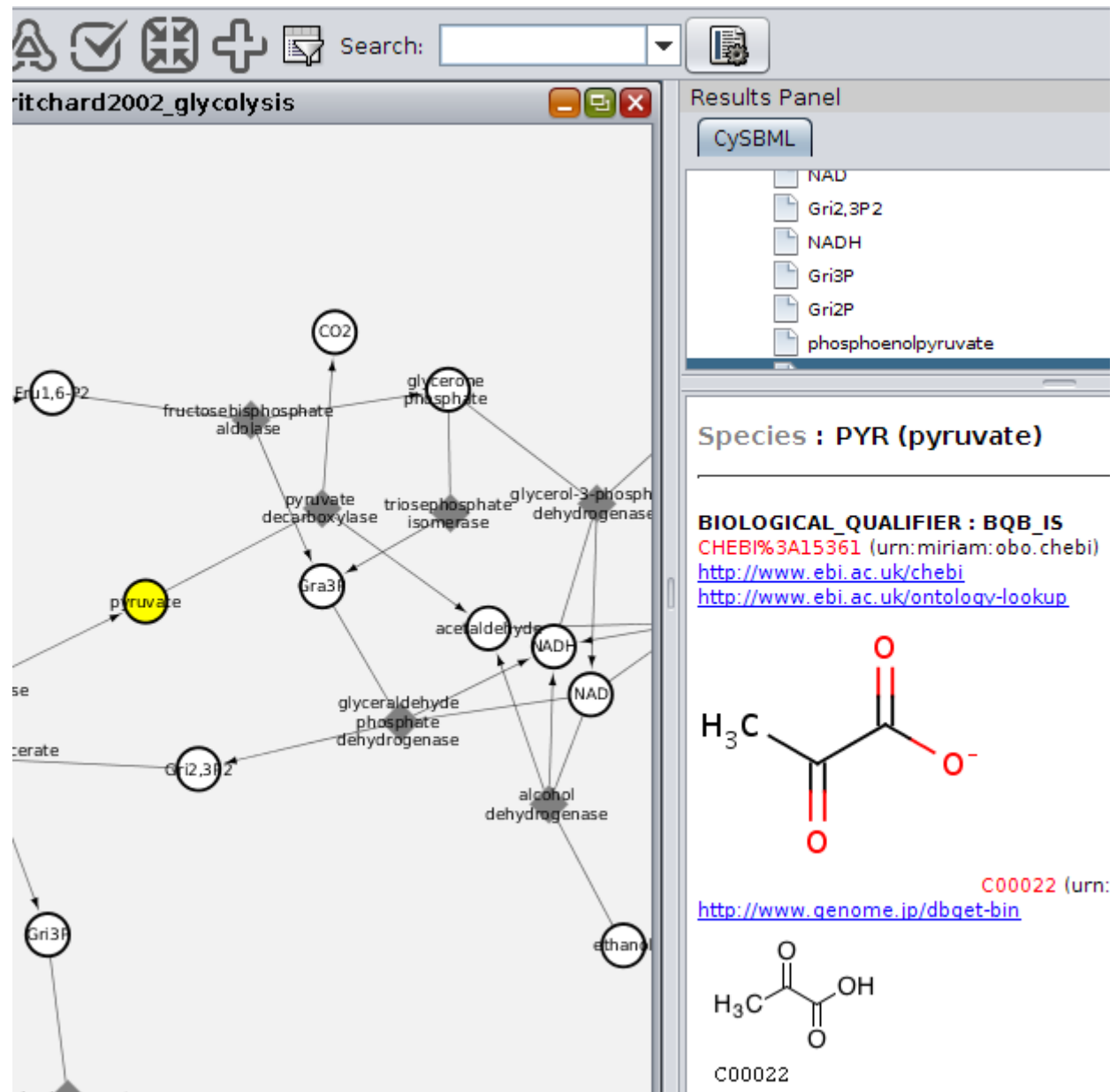
BioModels.Net

22 BioModels found for

Name	glycolysis
id	BIOMD0000000172
name	Pritchard2002_glycolysis
authors	[Pritchard L, Kell DB]
pubmed	12180966
encoders	[Lukas Endler, Pedro Mendes]
id	MODEL6624091635
name	Hoefnagel2002_Glycolysis
authors	[Hoefnagel MH, van der Burgt A, Martens DE, Hugenholtz J, Snoep JL]
pubmed	12241048
encoders	[]
id	BIOMD0000000281
name	Chance1960_Glycolysis_Respiration
authors	[CHANCE B, GARFINKEL D, HIGGINS J, HESS B]
pubmed	13692276
encoders	[Lukas Endler, Kieran Smallbone]
id	MODEL1011010000
name	Bruck2008_Glycolysis
authors	[Bruck], Liebermeister W, Klipp E]
pubmed	19425118
encoders	[Kieran Smallbone, Jozsef Bruck]
id	BIOMD0000000071
name	Bakker2001_Glycolysis
authors	[Helfert S, Estévez AM, Bakker B, Michels P, Clayton C]
pubmed	11415442
encoders	[Jacky L Snoep, Harish Dharuri, Lukas Endler]
id	BIOMD0000000064

CySBML Annotations

- Parsed MIRIAM & SBO annotations
- Access to annotated resources within the network visualization
- WebLinks to online resources and databases
- Integration of information from wide range of sources



SBML Validation

- imported SBML models can be validated
- Validation results can be filtered with respect to the severity of the errors

CySBML Validator : Pritchard2002_glycolysis

Info	0
Warning	106
Error	0
Fatal	0
All	106

E1 Units consistency (Warning)

Message [lang=en_US, messageContent=(LibSBML Check #99505) Missing unit declarations on parameters or literal numbers in expression]

Line: 502 (LibSBML Check #99505) In situations where a mathematical expression contains literal numbers or parameters whose units have not been declared, it is not possible to verify accurately the consistency of the units in the expression. The units of the expression ' $v_{max_1} * (GLCo - GLCi) / K_{glc_1} / (1 + (GLCo + GLCi) / K_{glc_1} + K_{i_1} * GLCo * GLCi / pow(K_{glc_1}, 2))$ ' cannot be fully checked. Unit consistency reported as either no errors or further unit errors related to this object may not be accurate.

E2 Modeling practice (Warning)

Message [lang=en_US, messageContent=(Modeling Practice Guideline #80701) It's best to declare units for every parameter in a model]

Line: 549 (Modeling Practice Guideline #80701) As a principle of best modeling practice, the units of a should be declared rather than be left undefined. Doing so improves the ability of software to check the consistency of units and helps make it easier to detect potential errors in models.

E3 Modeling practice (Warning)

Message [lang=en_US, messageContent=(Modeling Practice Guideline #80701) It's best to declare units for every parameter in a model]

Line: 550 (Modeling Practice Guideline #80701) As a principle of best modeling practice, the units of a should be declared rather than be left undefined. Doing so improves the ability of software to check the consistency of units and helps make it easier to detect potential errors in models.

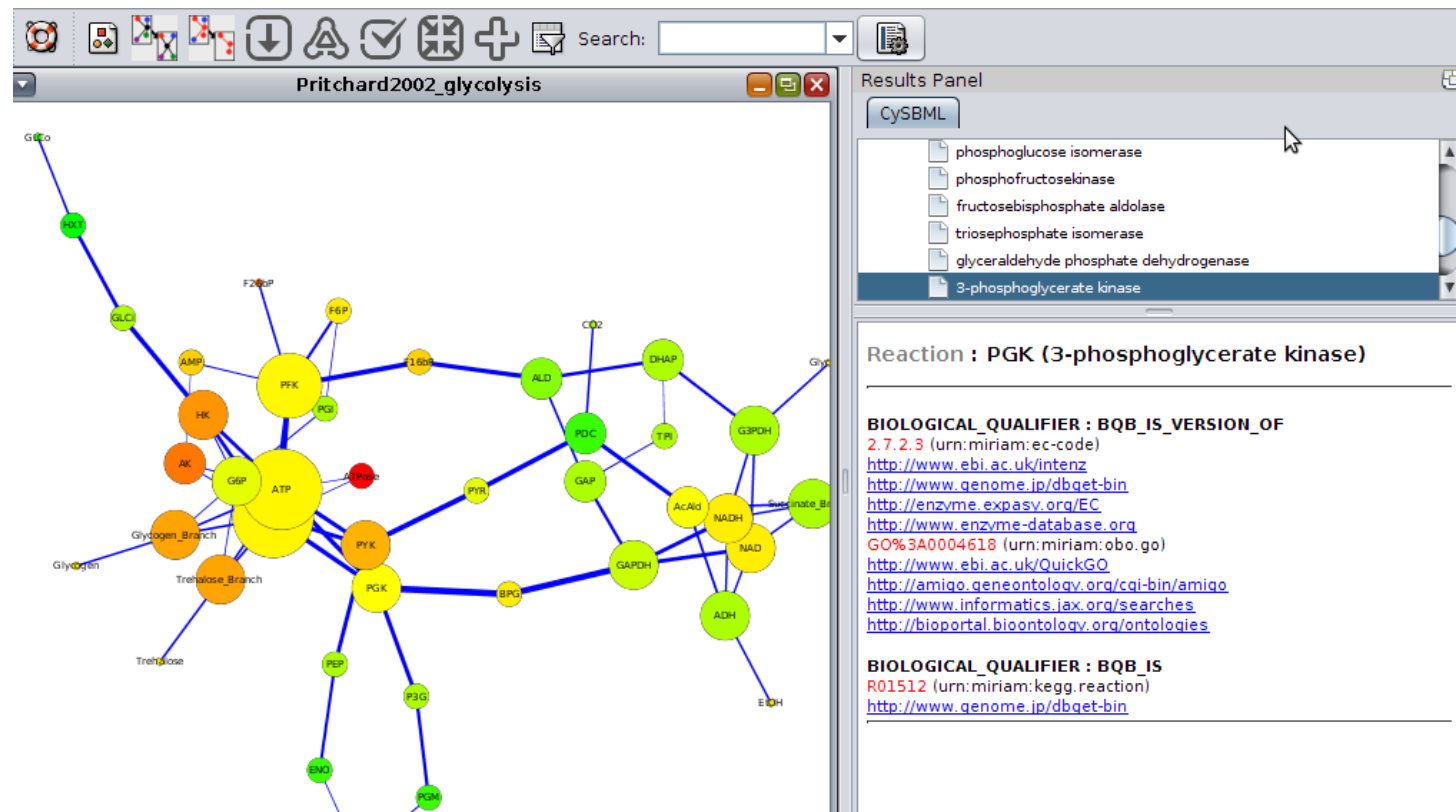
E4 Modeling practice (Warning)

Message [lang=en_US, messageContent=(Modeling Practice Guideline #80701) It's best to declare units for every parameter in a model]

Line: 551 (Modeling Practice Guideline #80701) As a principle of best modeling practice, the units of a should be declared rather than be left undefined. Doing so improves the ability of software to check the consistency of units and helps make it easier to detect potential errors in models.

Integration with other Plugins

- Seamless integration with other plugins NetworkAnalyzer (Assenov, et al., 2008), FluxViz (König and Holzhütter, 2010) or NetMatch (Ferro, et al., 2007)
- SBML information provided as Cytoscape node and edge attributes
- Rich functionality for SBML encoded networks



Availability

- **Availability and implementation:** Freely available for noncommercial purposes via the Cytoscape plugin manager, Cytoscape App Store or for download at <http://sourceforge.net/projects/cysbml/>
- **Contact:** matthias.koenig@charite.de
- **Supplementary information:** Tutorial, usage guide, installation instructions and additional figures are available for download at <http://www.charite.de/sysbio/people/koenig/software/cysbml/>



[Introduction](#)
[Installation](#)
[Usage Guide](#)
[FAQ](#)
[Additional Resources](#)

Documents



Release Information

[14|June|2012]

Release of CySBML-v1.2

New Dialogue and Interface, bug reversibility fixed.

[05|June|2012]

Release of CySBML-v1.1 new BioModel

Import/Search.

Minor Bug fixes.

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- **Sebastian Fröhlich** and **Clemens Wrzodek** (Layout support in JSBML)
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