

Recent Developments in SBML

Michael Hucka, Ph.D.

*Department of Computing and Mathematical Sciences
California Institute of Technology
Pasadena, CA, USA*

Email: mhucka@caltech.edu

Twitter: [@mhucka](https://twitter.com/mhucka)

COMBINE 2014, Los Angeles, August 2014

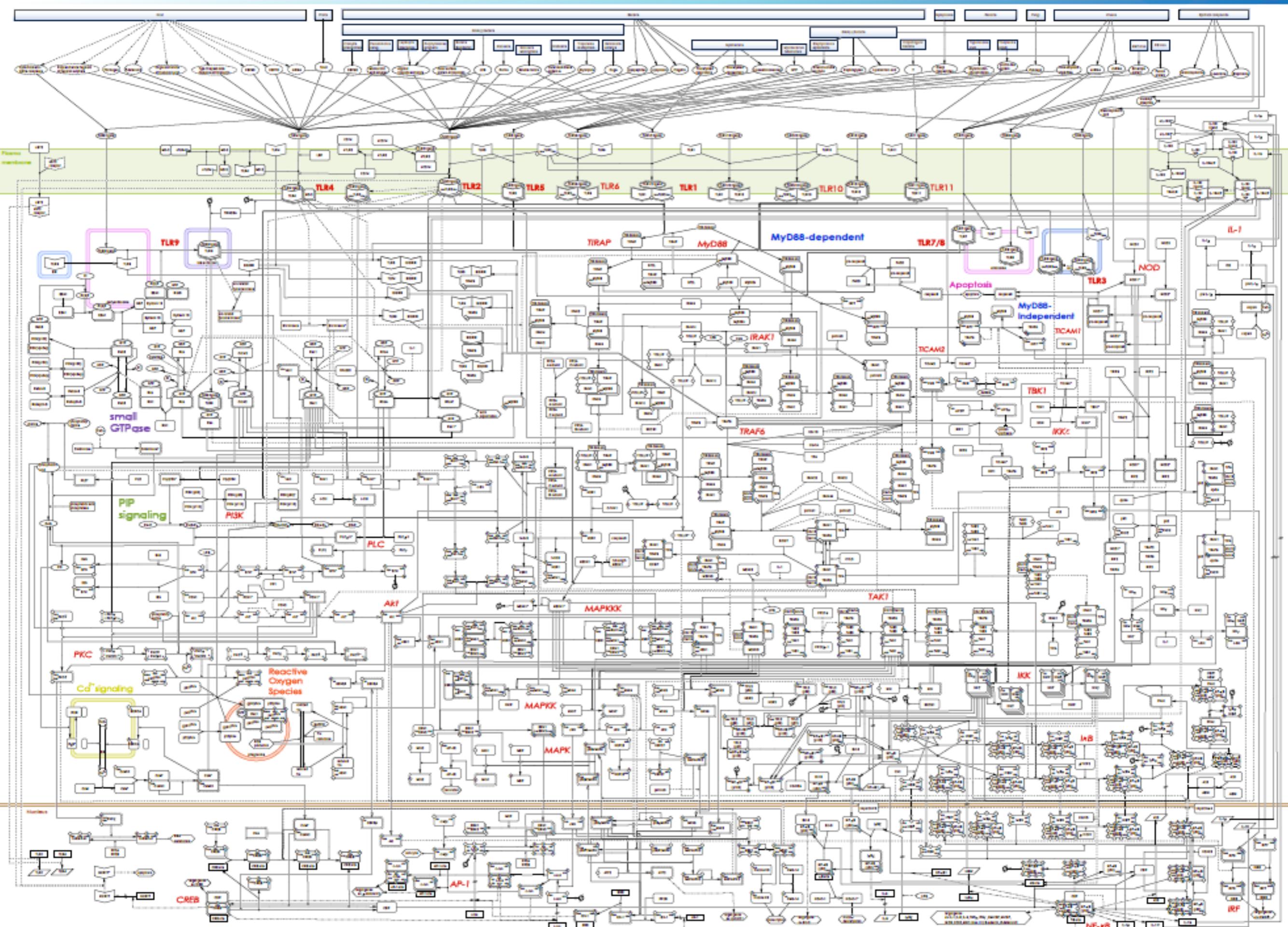
What is SBML for, and why would anyone care?

A comprehensive map of Toll-like receptor signaling

(TIRMAP v1.0) Kanae Oda (1, 2), Hiroaki Kitano (1, 2, 3)

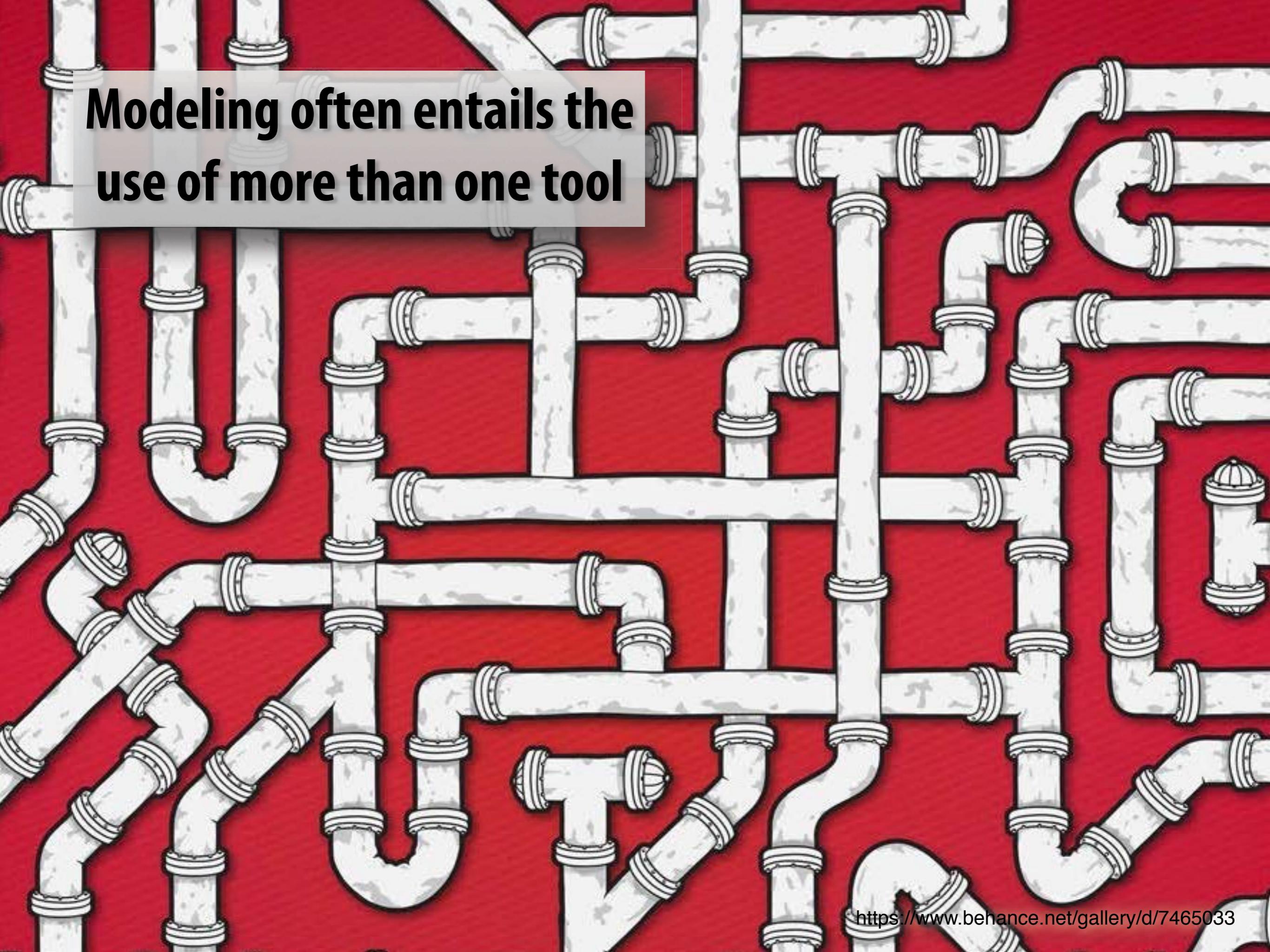
(1) The Systems Biology Institute, Tokyo, Japan; (2) Department of Fundamental Science and Technology, Asia University, Tokyo, Japan; (3) Key Computer Science Laboratories, Inc., Tokyo, Japan

The Systems Biology Institute, Tokyo, Japan
<http://www.systems-biology.org>



| | | | | |
|----------------------------|--------------------------|----------------------------|----------------------|---------------------------|
| ABC-SysBio | CellNetAnalyzer | Karyote* | PaVESy | SBW: Auto Layout |
| acs1Xtreme | CellNOpt | KEGGconverter | PAYAO | sbw: javasim |
| ALC | Cellware | KEGGtranslator | PET | sbw: stochastic simulator |
| AMIGO | CLEML | Kineticon | PhysioLab Modeler | SCIpath |
| Antimony | CL-SBML | Kinsolver | PINT | SED-ML Web Tools |
| APMonitor | COBRA | libAnnotationSBML | PK-Sim / MoBi | semanticSBML |
| Arcadia | CompuCell3D | libRoadRunner | PNK | SensSB |
| Asmparts | ConsensusPathDB | libSBML | PottersWheel | SGMP |
| Athena | COPASI | libSBMLSim | PRISM | Sigmoid* |
| AutoSBW | CRdata | libStruct | ProcessDB | SIGNALIGN |
| AVIS | CycSim | MASS Toolbox | ProMoT | SignalLink |
| BALSA | CySBML | MatCont | PROTON | SigPath |
| BASIS | Cytoscape | MathSBML | pybrn | SigTran |
| BetaWB | Cyto-Sim | Medicel | PyDSTool | SIMBA |
| Bifurcation Discovery Tool | DBSolve | MEMOSys | PySB | SimBiology |
| BiGG | DEDDiscover | MesoRD | PySCeS | Simpathica |
| BiNoM | Dizzy | Meta-All | RANGE | SimPheny* |
| BiNoM Cytoscape Plugin | DOTcvpSB | Metaboflux | RAVEN | Simulate3D |
| Bio Sketch Pad | E-CELL | MetaCrop | Reactome | Simulation Core Library |
| BioBayes | eCellJ | MetaFluxNet | ReMatch | Simulation Tool |
| BIOCHAM | EPE | Metannogen | RMBNToolbox | SimWiz |
| BioCharon | ESS | Metatool | roadRunner | SloppyCell |
| BioCyc | Facile | MetExplore | RSBML | SmartCell |
| BioGRID | FAME | MetNetMaker | SABIO-RK | Snoopy |
| Biological Networks | FASIMU | MIRIAM Resources | Saint | SOSlib |
| BioMet Toolbox | FBASBW | MMT2 | SBFC | SPDBS |
| BioModels Database | FERN | modelMaGe | SBML Harvester | SRS |
| BioModels Importer | FluxBalance | ModeRator | SBML Layout | STEPS |
| BioNessie | Fluxor | Modesto | SBML Reaction Finder | StochKit |
| BioNetGen | Genetdes | Moleculizer | SBML Translators | StochPy |
| BioPARKIN | Genetic Network Analyzer | MonaLisa | SBML2APM | StochSim |
| BioPathwise | Gepasi | Monod | SBML2BioPax | STOCKS |
| BioPAX2SBML | Gillespie2 | MOOSE | SBML2LaTeX | SurreyFBA |
| BioRica | GINsim | MuVal (Multi-valued logic) | SBML2NEURON | SyBIL |
| BioSens | GNAT | Narrator | SBML2Octave | SYCAMORE |
| BioSPICE Dashboard | GNU MCSim | nemo | SBML2SMW | SynBioSS |
| BioSpreadsheet | GRENDEL | NetBuilder' | SBML2TikZ | Systrip |
| BioSyS | HSMB | NetPath | SBML2XPP | TERANODE Suite |
| BioTapestry | HybridSBML | NetPro | SBMLEditor | The Cell Collective |
| BioUML | iBioSim | Odefy | SBML-PET-MPI | Tide |
| BoolNet | IBRENA | Omix | SBMLR | TinkerCell |
| braincirc | Insilico Discovery | ONDEX | SBML-SAT | Trelis |
| BRENDA | insilicoIDE | optflux | SBML-shorthand | UTKornTools |
| BSTLab | iPathways | Oscill8 | SBMLSim | VANTED |
| ByoDyn | JACOBIAN | PANTHER Pathway | SBMLSqueezer | Vcell |
| CADLIVE | Jacobian Viewer | PathArt | sbmltidy | WebCell |
| Cain | Jarnac | Pathway Access | SBMLToolbox | WinSCAMP |
| CARMEN | JarnacLite | Pathway Analyser | SBMM assistant | Wolfram SystemModeler |
| Cell Illustrator | JDesigner | Pathway Builder | SBO | xCellerator |
| CellDesigner | JigCell | Pathway Solver | SBSI | Xholon |
| Cellerator | JSBML | PATIKAweb | PTI | XPPAUT |
| CellMC | JSim | SBW | SBW | |
| CellML2SBML | JWS Online | | | |

Many software tools for
modeling available today



Modeling often entails the
use of more than one tool



**Often need flexible,
intermediate connections**

The BioModels Database homepage features a header with the EMBL-EBI logo and a search bar. Below the header, there are links for Databases, Tools, Research, Training, Industry, and About Us. A main content area titled "BioModels Database - A Database of Annotated Published Models" contains a brief description of the database's purpose and a "BioModels" logo. To the right, there is a sidebar with links for BioModels Home, Models, Submit, Support, and About BioModels.

The COPASI 4.8 software interface shows a central panel with the COPASI logo and version information ("Version 4.8 (Build 35)"). On the left, a navigation tree lists categories like Model, Biochemical, Tasks, and Mathematical Diagrams. At the bottom, a note states "The use of this software indicates the acceptance of the attached license." with a "View License" link.

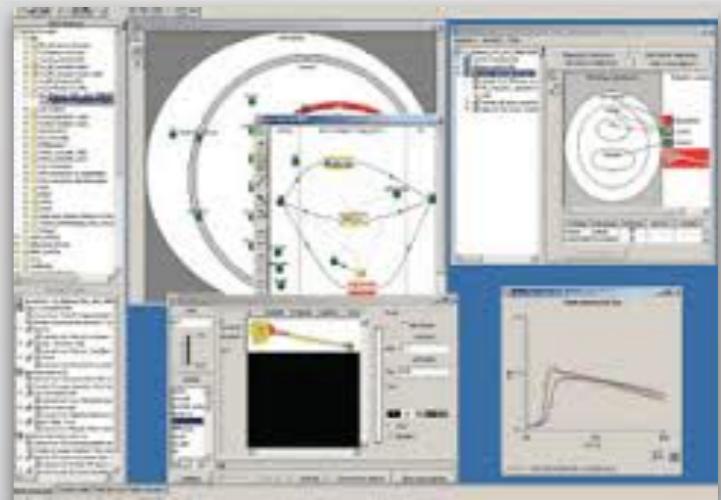
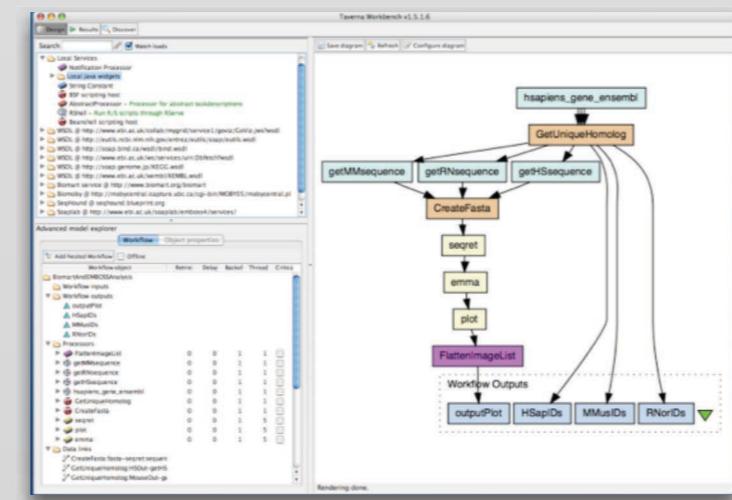
The CellDesigner software interface displays a complex biological pathway diagram with various compartments, species, and interactions. The left side shows a hierarchical tree of models and components. The main workspace is filled with a detailed diagram of a metabolic or signaling pathway.

The Janac 3.0 software interface includes a code editor showing a Janus-Monod glycolysis model, a reaction graph, and a time-series plot for metabolite concentrations over time. The plot shows oscillatory behavior for several metabolites. A legend identifies the metabolites by color.



The SBML Grid Editor software interface shows a grid-based schematic editor for creating and modifying SBML models. A grid of boxes contains labels like "C1 lambda", "C2 lambda", etc., with some cells highlighted in blue. A sidebar on the right provides options for "Edit Grid Size", "Zoom", "Un-Zoom", "Pan", and "Model".

The SABIO Biochemical Reaction Kinetics database homepage features a search bar and links for Home, Search, Web Services, News, Documentation, and Help. A welcome message highlights that SABIO-RE is a curated database of biochemical reactions with their kinetic rate equations and experimental conditions. The background features a blue and white abstract design.



Why not simply distribute a model in the original format?

Why not simply distribute a model in the original format?

Yes, do that – vital for good science

- Others can try to run model, understand it, verify it, reuse it, etc.
- Opinion: should **always do this**

Why not simply distribute a model in the original format?

Yes, do that – vital for good science

- Others can try to run model, understand it, verify it, reuse it, etc.
- Opinion: should **always do this**

But it's still **not ideal** for communication of scientific results

- **Biological semantics** usually **not encoded**
- **Not everyone can run** the same software
- **Not everyone wants** to use the same software
- What if they want to use a **different conceptual framework?**
- How will people **relate the model to other work?**

What *is* SBML?

The raw SBML (as XML)

```
<listOfSpecies>
    <species compartment="cytosol" id="ES" initialAmount="0"      name="ES"/>
    <species compartment="cytosol" id="P"  initialAmount="0"      name="P"/>
    <species compartment="cytosol" id="S"  initialAmount="1e-20"   name="S"/>
    <species compartment="cytosol" id="E"  initialAmount="5e-21"   name="E"/>
</listOfSpecies>
<listOfReactions>
    <reaction id="veq">
        <listOfReactants>
            <speciesReference species="E"/>
            <speciesReference species="S"/>
        </listOfReactants>
        <listOfProducts>
            <speciesReference species="ES"/>
        </listOfProducts>
        <kineticLaw>
            <math xmlns="http://www.w3.org/1998/Math/MathML">
                <apply>
                    <times/>
                    <ci>cytosol</ci>
                    <apply>
                        <minus/>
                        <apply>
                            <times/>
                            <ci>kon</ci>
                            <ci>E</ci>
                            <ci>S</ci>
                        </apply>
                        <apply>
                            <times/>
                            <ci>koff</ci>
                            <ci>ES</ci>
                        </apply>
                    </apply>
                </math>
            </kineticLaw>
        </reaction>
    </listOfReactions>

```

The raw SBML (as XML)

```
<listOfSpecies>
    <species compartment="cytosol" id="ES" initialAmount="0"      name="ES"/>
    <species compartment="cytosol" id="P"  initialAmount="0"      name="P"/>
    <species compartment="cytosol" id="S"  initialAmount="1e-20"   name="S"/>
    <species compartment="cytosol" id="E"  initialAmount="5e-21"   name="E"/>
</listOfSpecies>
<listOfReactions>
    <reaction id="veq">
        <listOfReactants>
            <speciesReference species="E"/>
            <speciesReference species="S"/>
        </listOfReactants>
        <listOfProducts>
            <speciesReference species="ES"/>
        </listOfProducts>
        <kineticLaw>
            <math xmlns="http://www.w3.org/1998/Math/MathML">
                <apply>
                    <times/>
                    <ci>cytosol</ci>
                    <apply>
                        <minus/>
                        <apply>
                            <times/>
                            <ci>kon</ci>
                            <ci>E</ci>
                            <ci>S</ci>
                        </apply>
                        <apply>
                            <times/>
                            <ci>koff</ci>
                            <ci>ES</ci>
                        </apply>
                    </apply>
                </apply>
            </math>
        </kineticLaw>
    </reaction>
</listOfReactions>
```

Don't work with it directly! Let software do it.

SBML = Systems Biology Markup Language

Format for representing models of biological processes

- Data structures + principles + serialization to XML
- (Mostly) Declarative, not procedural—not a scripting language

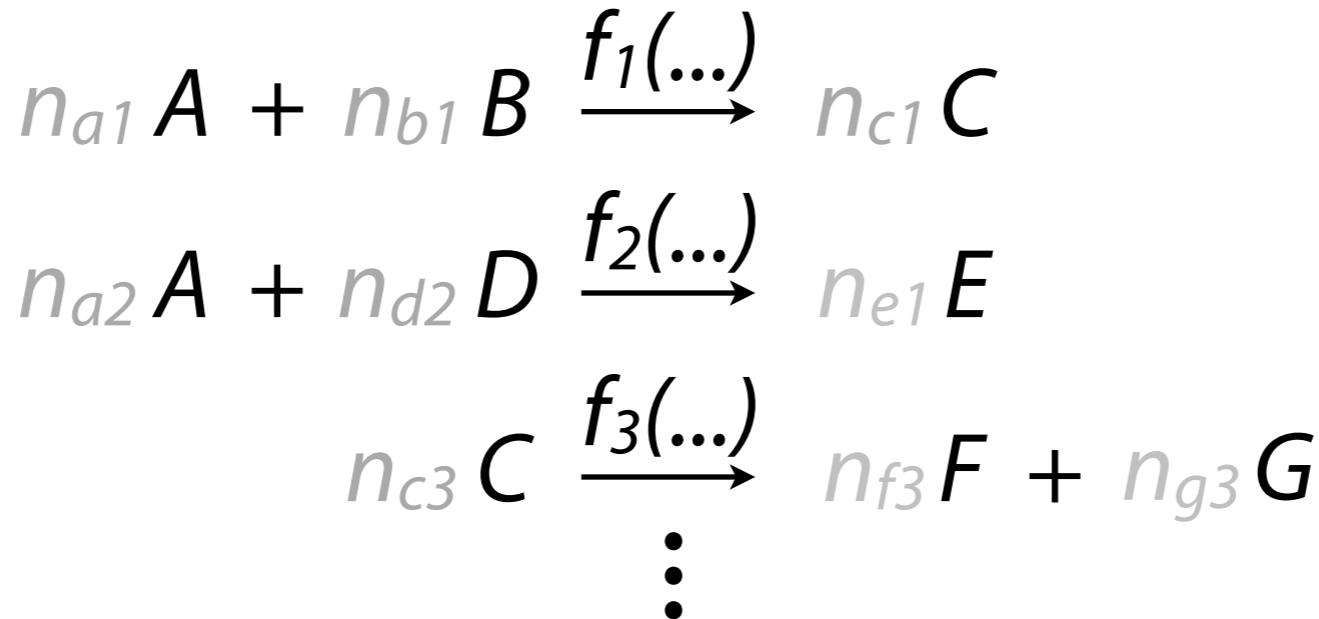
(Mostly) **neutral** with respect to modeling framework

- E.g., ODE, stochastic systems, etc.

For **software** to read/write, **not humans**

The process is central

- Literally called “**reaction**” (not necessarily biochemical)
- Participants are pools of entities of the same kind (“**species**”)



- Species are located in containers (“**compartments**”)

Models can further include:

- Other constants & variables
- Discontinuous **events**
- Unit definitions
- **Annotations**
- Other, explicit math

Core SBML concepts are fairly simple

Example of model type

Typical ODE models (e.g., cell differentiation)

Conductance-based models (e.g., Hodgkin-Huxley)

*Typically do not use SBML “reaction” construct,
but instead use “rate rules” construct*

Neural models (e.g., spiking neurons)

Typically use “events” for discontinuous changes

Pharmacokinetic/dynamics models

“Species” are not required to be biochemical entities

Infectious diseases

Example model

BioModels Database model
#BIOMD0000000451

BioModels Database model
#BIOMD0000000020

BioModels Database model
#BIOMD0000000127

BioModels Database model
#BIOMD0000000234

BioModels Database model
#MODEL1008060001

List originally by Nicolas Le Novére

Core SBML constructs support many types of models

Accepted by dozens of journals *

100's of software tools available today

- Libraries: **libSBML, JSBML**
- 260+ listed in SBML Software Guide †

1000's of models available

- ... in public databases, e.g., BioModels Database, Reactome
- ... as supplementary data to papers
- ... in private repositories

The screenshot shows the homepage of SBML.org. At the top, there is a navigation bar with links for News, Documents, Downloads, Forums, Facilities, Community, Events, About, and a search bar. The main content area features three sections: 'For the curious', 'For modelers', and 'For software developers'. Each section includes a brief description and a call to action. Below these sections is a note about staying updated with news and community efforts. At the bottom, there are social media links for Google+, Facebook, and Twitter, along with a SourceForge link.

http://sbml.org

* http://sbml.org/Documents/Publications_known_to_accept_submissions_in_SBML_format

† http://sbml.org/SBML_Software_Guide

Many examples of SBML and software resources are available

What resources are available for software developers?

SBML specification documents

Documents/Specifications – SBML.caltech.edu

sbml.org/Documents/Specifications

Reader

SBML Level 3

At this time, only *Version 1 Core* of SBML Level 3 has been released. Definitions of packages to go with Version 1 Core are expected in the very near future. When the specifications become available, they will be listed below. For now, you can find information about the ongoing activities in the [community wiki](#).

SBML Level 3 Version 1 Core

The most recent release of SBML Level 3 Version 1 Core is **Release 1**.

The Systems Biology Markup Language (SBML): Language Specification for Level 3 Version 1 Core

Authors: Michael Hucka, Frank Bergmann, Stefan Hoops, Sarah Keating, Sven Sahle, James Schaff, Lucian Smith, and Darren Wilkinson

This is the final Release 1 specification of 6 Oct. 2010.

The document link refers to the file on SourceForge.net. If you have any problems accessing the PDF file from there, a backup copy of the document is also available [locally from this server](#).

Specification →

Errata →

Submit issue →

Schemas →



Issues with the specification are tracked on the *issue tracker* whose link is indicated above. Accepted issues are periodically collected and listed on the *Errata* page indicated above. Once a general consensus emerges that the known errata warrant a new release of the SBML specification, a new *Release* is made.

SBML Level 3 Packages

Each individual SBML Level 3 package effort has its own separate status page. Please follow the relevant links in the table below to find out more about a given package, including any draft specifications that may be available. This list is in

API libraries

The screenshot shows a web browser window with the title "Downloads – SBML.org". The address bar displays "sbml.org/Downloads". The main content area features the SBML.org logo and the heading "The Systems Biology Markup Language". Below this is a navigation menu with links for News, Documents, Downloads (which is highlighted in blue), Forums, Facilities, Community, Events, and About. There are also social media icons for Twitter, RSS, and Google+.

Parent pages: [SBML.org](#)

Downloads

Software by the SBML Team and the BioModels.net Team

The SBML Project helps develop a variety of software packages for working with SBML. (Many more third-party packages also support SBML—visit the [SBML Software Guide](#) to find out more about them!)



LibSBML

A free, open-source [API](#) library for working with SBML content. It supports many programming languages and operating systems.



JSBML

A free, open-source, pure-Java library for working with SBML. It emulates libSBML's API, with more Java idioms and without native object code.



SBMLToolbox

A free, open-source package for working with SBML in [MATLAB](#). It provides functions for reading, writing, manipulating, and simulating SBML models.



SBML Converters

The [BioModels Database](#) team provides several converters between SBML and other formats.



SBMLEditor

A graphical editor for SBML models written in Java. It provides a visual interface for creating and editing SBML models.



SBML Test Suite

A conformance testing suite for assessing compliance of SBML models against the SBML specification.

API libraries

Downloads – SBML.org

sbml.org/Downloads

Reader Word Google Site Search

News Documents **Downloads** Forums Facilities Community Events About

Parent pages: SBML.org

Go to “Downloads”

Downloads

Software by the SBML Team and the BioModels.net Team

The SBML Project helps develop a variety of software packages for working with SBML. (Many more third-party packages also support SBML—visit the [SBML Software Guide](#) to find out more about them!)

LibSBML
A free, open-source API library for working with SBML content. It supports many programming languages and operating systems.

SBMLToolbox
A free, open-source package for working with SBML in MATLAB. It provides functions for reading, writing, manipulating, and simulating SBML models.

JSBML
A free, open-source, pure-Java library for working with SBML. It emulates libSBML's API, with more Java idioms and without native object code.

SBML Converters
The BioModels Database team provides several converters between SBML and other formats.

SBMLEditor
A graphical editor for SBML models.

SBML Test Suite
A performance testing suite for assessing

API libraries

Downloads – SBML.org

sbml.org/Downloads

Reader

News Documents Downloads Forums Facilities Community Events About

Google Site Search

Parent pages: SBML.org

Downloads

libSBML JSBML

Software by the SBML Team and the BioModels.net Team

The SBML Project helps develop a variety of software packages for working with SBML. (Many more third-party packages also support SBML—visit the [SBML Software Guide](#) to find out more about them!)

LibSBML

A free, open-source [API](#) library for working with SBML content. It supports many programming languages and operating systems.

JSBML

A free, open-source, pure-Java library for working with SBML. It emulates libSBML's API, with more Java idioms and without native object code.

SBMLToolbox

A free, open-source package for working with SBML in [MATLAB](#). It provides functions for reading, writing, manipulating, and simulating SBML models.

SBML Converters

The [BioModels Database](#) team provides several converters between SBML and other formats.

SBMLEditor

A graphical editor (written in Java) for SBML models.

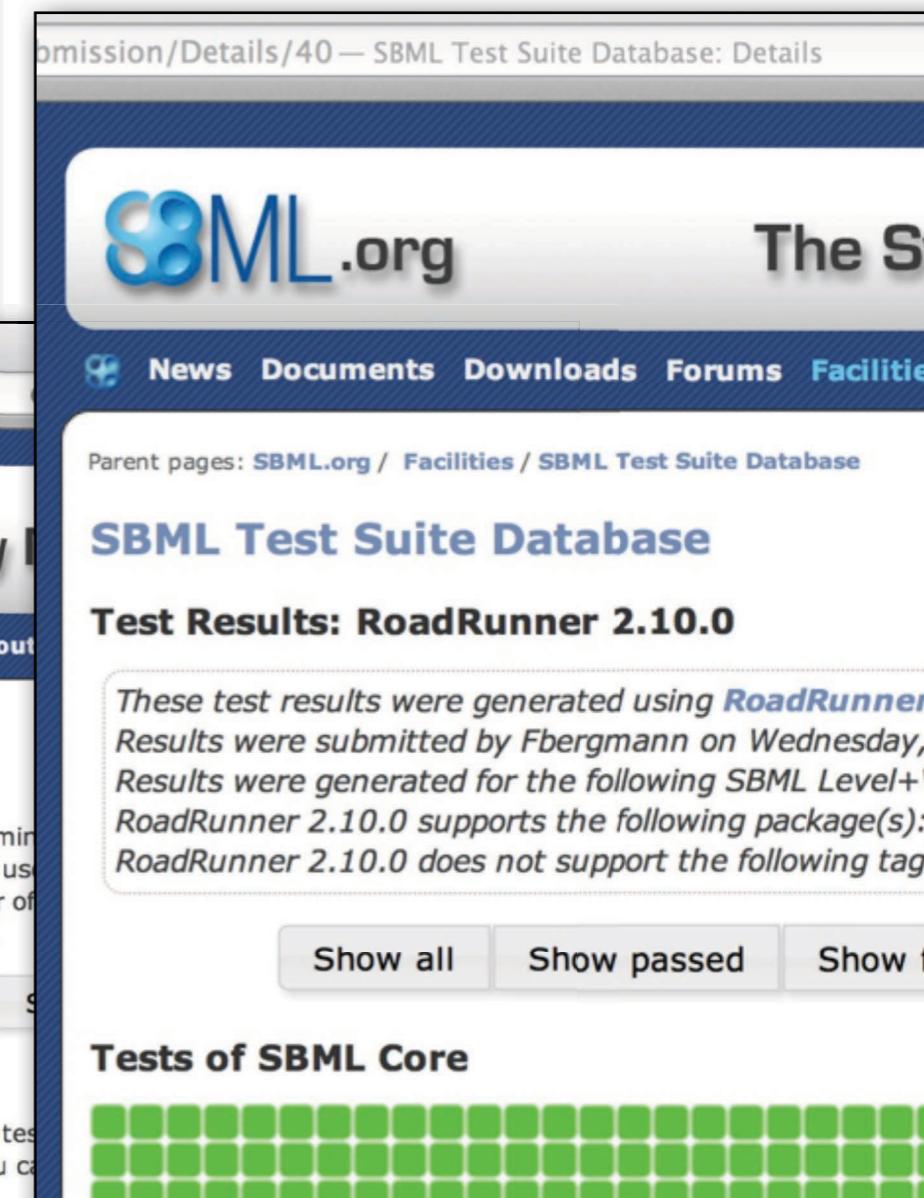
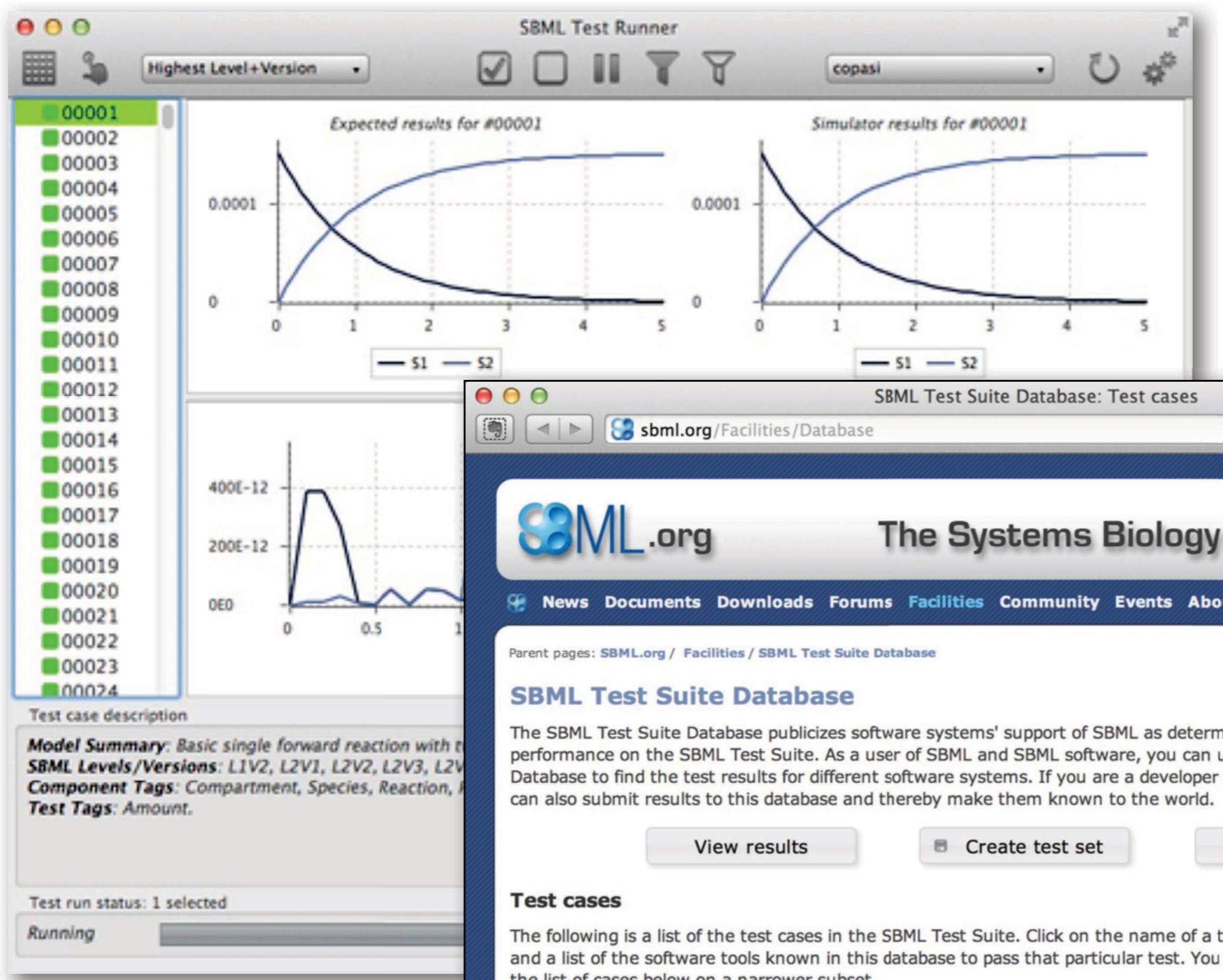
SBML Test Suite

A performance testing suite for assessing

SBML Test Suite – http://sbml.org/Facilities/SBML_Test_Suite

Suite of **test cases** (1200) + **test runners** (both standalone app & online)

Database of test results on sbml.org



Online SBML Validator – <http://sbml.org/Facilities/Validator>

The screenshot shows a web browser window for the "Online SBML Validator" at sbml.org/Facilities/Validator/. The page has a blue header with the SBML.org logo and the text "The Systems Biology Markup Language". A navigation bar below the header includes links for News, Documents, Downloads, Forums, Facilities, Community, Events, About, and a search bar for Google Site Search. The main content area contains a brief description of the validator's purpose, instructions for uploading SBML content, and validation options. On the right, there is a sidebar for retrieving previously-scheduled validation results and a "Sign in or Register" link.

Parent pages: [SBML.org](#) / [Facilities](#) / [Online SBML Validator](#)

This system can test the syntax and internal consistency of an SBML file. Passing this validator doesn't guarantee a file is 100% correct SBML, but it's the best automated assessment available.

Use the form below to upload your SBML content. You can also access this service via a [network API](#). By using any part of this service or website, you agree to be bound by the terms of the [privacy notice](#).

Sign in or Register with this service.

You can retrieve the result of a previously-scheduled validation run by entering its key here:

(E.g., `7bf66904-7d67-49bb-9127-bee77a8f96ba`)

Upload File **Submit URL** **Paste SBML**

Browse **Clear Queue**

Select an SBML file located on your computer. The file can be uncompressed, or compressed using [zip](#), [gzip](#) or [bzip2](#).

Validate now **Schedule for Validation**

Validation options:

- Check consistency of measurement units associated with quantities ([SBML L2V4 rules 105nn](#))
- Check correctness and consistency of identifiers used for model entities ([SBML L2V4 rules 103nn](#))
- Check syntax of MathML mathematical expressions ([SBML L2V4 rules 102nn](#))
- Check validity of [SBO identifiers](#) (if any) used in the model ([SBML L2V4 rules 107nn](#))
- Perform static analysis of whether the model is **overdetermined**
- Perform additional checks for recommended good [modeling practices](#)

Online SBML Validator – <http://sbml.org/Facilities/Validator>

A screenshot of a web browser displaying the "Online SBML Validator" page from sbml.org. The page features the SBML.org logo and navigation links for News, Documents, Downloads, Forums, Facilities, Community, Events, and About. A red speech bubble with the text "Find it here" points to the "Facilities" link in the top navigation bar. Below the navigation, a section titled "Parent pages: SBML.org / Facilities / Online SBML Validator" contains text about the validator's purpose and usage. It includes a "Sign in or Register" link, a field for entering a validation key, and a "Submit" button. At the bottom, there are sections for file upload ("Upload File", "Submit URL", "Paste SBML", "Browse", "Clear Queue"), validation options ("Validate now", "Schedule for Validation"), and a "Validation options" section with several checkboxes.

Find it here

The Systems Biology Markup Language

News Documents Downloads Forums **Facilities** Community Events About

Parent pages: SBML.org / Facilities / Online SBML Validator

This system can test the syntax and internal consistency of an SBML file. Passing this validator doesn't guarantee a file is 100% correct SBML, but it's the best automated assessment available.

Use the form below to upload your SBML content. You can also access this service via a [network API](#). By using any part of this service or website, you agree to be bound by the terms of the [privacy notice](#).

Sign in or Register with this service.

You can retrieve the result of a previously-scheduled validation run by entering its key here:

(E.g., 7bf66904-7d67-49bb-9127-bee77a8f96ba)

Upload File **Submit URL** **Paste SBML**

Browse **Clear Queue**

Select an SBML file located on your computer. The file can be uncompressed, or compressed using [zip](#), [gzip](#) or [bzip2](#).

Validate now **Schedule for Validation**

Validation options:

- Check consistency of measurement units associated with quantities ([SBML L2V4 rules 105nn](#))
- Check correctness and consistency of identifiers used for model entities ([SBML L2V4 rules 103nn](#))
- Check syntax of MathML mathematical expressions ([SBML L2V4 rules 102nn](#))
- Check validity of [SBO identifiers](#) (if any) used in the model ([SBML L2V4 rules 107nn](#))
- Perform static analysis of whether the model is **overdetermined**
- Perform additional checks for recommended good [modeling practices](#)

Online SBML Validator – <http://sbml.org/Facilities/Validator>

The screenshot shows a web browser window for the "Online SBML Validator" at sbml.org/Facilities/Validator/. The page has a blue header with the SBML.org logo and the text "The Systems Biology Markup Language". A navigation bar below the header includes links for News, Documents, Downloads, Forums, Facilities, Community, Events, About, and a search bar for Google Site Search. The main content area contains a brief description of the validator's purpose, instructions for uploading SBML content, and validation options. On the right, there is a sidebar for retrieving previously-scheduled validation results and a "Sign in or Register" link.

Parent pages: [SBML.org](#) / [Facilities](#) / [Online SBML Validator](#)

This system can test the syntax and internal consistency of an SBML file. Passing this validator doesn't guarantee a file is 100% correct SBML, but it's the best automated assessment available.

Use the form below to upload your SBML content. You can also access this service via a [network API](#). By using any part of this service or website, you agree to be bound by the terms of the [privacy notice](#).

Sign in or Register with this service.

You can retrieve the result of a previously-scheduled validation run by entering its key here:

(E.g., `7bf66904-7d67-49bb-9127-bee77a8f96ba`)

Upload File **Submit URL** **Paste SBML**

Browse **Clear Queue**

Select an SBML file located on your computer. The file can be uncompressed, or compressed using [zip](#), [gzip](#) or [bzip2](#).

Validate now **Schedule for Validation**

Validation options:

- Check consistency of measurement units associated with quantities ([SBML L2V4 rules 105nn](#))
- Check correctness and consistency of identifiers used for model entities ([SBML L2V4 rules 103nn](#))
- Check syntax of MathML mathematical expressions ([SBML L2V4 rules 102nn](#))
- Check validity of [SBO identifiers](#) (if any) used in the model ([SBML L2V4 rules 107nn](#))
- Perform static analysis of whether the model is **overdetermined**
- Perform additional checks for recommended good [modeling practices](#)

SBML Software Guide – http://sbml.org/SBML_Software_Guide

The screenshot shows the SBML Software Guide page. At the top, there's a navigation bar with links for News, Documents, Downloads, Forums, Facilities, Community, Events, About, and a Google Site Search bar. Below the header, it says "Parent pages: SBML.org". The main content area has a title "The Systems Biology Markup Language" and a sub-section "SBML Software Guide". It states: "The following pages describe SBML-compatible software packages known to us. We offer different ways of viewing the information, all drawn from the same underlying data collected from the systems' developers via our [software survey](#). The *Matrix* provides a table listing all known software and a variety of their features; the *Summary* provides general descriptions of most of the software; and the *Showcase* provides a sequential slideshow of a subset of the software." A message below says "Number of software packages listed in the matrix today: 263." There are three main links: "Go to the SBML Software Matrix", "Go to the SBML Software Summary", and "Go to the SBML Software Showcase". The "Software Matrix" link shows a small screenshot of a table with many columns and rows. The "Software Summary" link shows a small screenshot of a list of software packages. The "Software Showcase" link shows a small screenshot of a graph with multiple curves. Below these links, a message says "Please [tell us about additions and updates](#)". Under "Historical trend", there's a bar chart showing the total number of known SBML-compatible software packages each year from 2001 to 2013. The y-axis ranges from 0 to 300. The chart shows a steady increase over time, starting near zero in 2001 and reaching approximately 263 by 2013. At the bottom, there's a section titled "SBML conformance testing" which describes the SBML Test Suite and its database.

| Year | Number of Packages |
|------|--------------------|
| 2001 | ~10 |
| 2002 | ~20 |
| 2003 | ~30 |
| 2004 | ~40 |
| 2005 | ~80 |
| 2006 | ~100 |
| 2007 | ~110 |
| 2008 | ~140 |
| 2009 | ~170 |
| 2010 | ~190 |
| 2011 | ~220 |
| 2012 | ~240 |
| 2013 | 263 |

Go to the SBML Test Suite Database

Information about known
SBML compatible software

New questionnaire – please
fill it out if you're a developer!

New version of the guide is
coming!

SBML Software Guide – http://sbml.org/SBML_Software_Guide

SBML Software Survey

<https://docs.google.com/forms/d/16FIRYvsG8FDOFxNmmuqLRk0yvwkYYVMxE...>

SBML Software Survey

What is your email address?
Providing an email address will enable us to send you the URL for updating your software entry in the future, and it will also enable us to contact you if we have any questions. Your email address will not be put in the SBML Software Guide.

What is the software's short title, without version number?
Examples from existing software: "COPASI", "Virtual Cell", "JDesigner", "BioModels Database", "SBML2LaTeX".

Does your software have alternative names?
If you renamed your software and it used to be called something else, please let us know the previous name(s). Also, if the software has both a standalone form and a plug-in for another system, the variants are probably not sufficiently distinct from the main or core system to be considered separate software tools in their own right. In that case, we would want to have a single entry for the software, but we need to know how to recognize the different forms. Please list the alternative names here, separated by commas. Examples: "CopasiWeb", "CopasiWS".

What is the URL for the home page for your software?
This should be to a page that describes the software. (Note: this should NOT be a link to download the software; it should be the address of a human-readable, general page of information.)

What is the version number your software at this time?
This is often a series of numbers, such as "1.1", "3.1.1", or similar.

What was the date of your release of that version of your software?
Since you may not be filling out this form at the time the release was actually made, it is necessary to ask for this information separately.

yyyy-mm-dd

Please give a concise summary of your software.
What is its main purpose? What does it do? What kind of problems is it designed to address? Why might other users be interested in it? Please make sure to mention if it's an add-on package to another system (e.g., a plug-in for MATLAB). Please keep the length under 1024 characters.

about known
ole software
naire – please
re a developer!
of the guide is

SBML Software Guide – http://sbml.org/SBML_Software_Guide

The screenshot shows the SBML Software Guide page. At the top, there's a navigation bar with links for News, Documents, Downloads, Forums, Facilities, Community, Events, About, and a Google Site Search bar. Below the header, it says "Parent pages: SBML.org". The main content area has a title "The Systems Biology Markup Language" and a sub-section "SBML Software Guide". It states: "The following pages describe SBML-compatible software packages known to us. We offer different ways of viewing the information, all drawn from the same underlying data collected from the systems' developers via our [software survey](#). The *Matrix* provides a table listing all known software and a variety of their features; the *Summary* provides general descriptions of most of the software; and the *Showcase* provides a sequential slideshow of a subset of the software." A message below says "Number of software packages listed in the matrix today: 263." There are three main links: "Go to the SBML Software Matrix", "Go to the SBML Software Summary", and "Go to the SBML Software Showcase". The "Software Matrix" link shows a small screenshot of a table with many columns and rows. The "Software Summary" link shows a small screenshot of a list of software packages. The "Software Showcase" link shows a small screenshot of a graph with multiple curves. Below these links, a message says "Please tell us about additions and updates." Under "Historical trend", it says: "The following graph shows the total number of known SBML-compatible software packages each year, as counted by the SBML Team. The counts shown are for approximately the middle of each year." A bar chart shows the growth of software packages over time:

| Year | Count |
|------|-------|
| 2001 | ~10 |
| 2002 | ~20 |
| 2003 | ~30 |
| 2004 | ~50 |
| 2005 | ~80 |
| 2006 | ~100 |
| 2007 | ~110 |
| 2008 | ~140 |
| 2009 | ~170 |
| 2010 | ~190 |
| 2011 | ~220 |
| 2012 | ~240 |
| 2013 | ~260 |

SBML conformance testing
The [SBML Test Suite](#) provides an operational means of testing SBML support in software simulation and analysis systems. Software authors can choose to make the test results for their software public in the [SBML Test Suite Database](#), where you can inspect them.

[Go to the SBML Test Suite Database](#)

Information about known SBML compatible software

New questionnaire – please fill it out if you're a developer!

New version of the guide is coming!

SBML Software Guide – http://sbml.org/SBML_Software_Guide

The screenshot shows the SBML Software Guide page. At the top, there's a navigation bar with links for News, Documents, Downloads, Forums, Facilities, Community, Events, About, and a Google Site Search. Below the navigation is a header with the SBML.org logo and the text "The Systems Biology Markup Language". A sub-header "SBML Software Guide" is present. The main content area contains several sections: "Number of software packages in the matrix today: 263.", a link to "Go to the SBML Software Matrix" (with a red speech bubble pointing to it), a link to "Go to the SBML Software Showcase" (with a red oval around it), and a button labeled "Please tell us about additions and updates." A red circle highlights the "Please tell us about additions and updates." button. Below this is a section titled "Historical trend" featuring a bar chart showing the growth of known SBML-compatible software packages from 2001 to 2013. The final section is "SBML conformance testing" with a link to "Go to the SBML Test Suite Database".

Information about known
SBML compatible software

New questionnaire – please
fill it out if you're a developer!

New version of the guide is
coming!

What has been happening with SBML lately?

**Level 3 packages add constructs
on top of SBML Level 3 Core**



| Level 3 package | What it enables | Status |
|--------------------------------|---|---------------|
| Hierarchical model composition | Models containing submodels | ✓ |
| Flux balance constraints | Constraint-based models | ✓ |
| Qualitative models | Petri net models, Boolean models | ✓ |
| Graph layout | Diagrams of models | ✓ |
| Multicomponent/state species | Entities w/ structure; also rule-based models | draft |
| Spatial | Nonhomogeneous spatial models | draft |
| Graph rendering | Diagrams of models | draft |
| Groups | Arbitrary grouping of components | draft |
| Arrays & sets | Arrays or sets of entities | draft |
| Dynamic structures | Creation & destruction of components | draft |
| Distributions | Numerical values as statistical distributions | in dev |
| Annotations | Richer annotation syntax | |

| Level 3 package | What it enables | Status |
|--------------------------------|---|---------|
| Hierarchical model composition | Models containing submodels | ✓ |
| Flux balance constraints | Constraint-based models | ✓ |
| Qualitative models | Petri net models, Boolean models | ✓ |
| Graph layout | Diagrams of models | ✓ |
| Multicomponent/state species | Entities w/ structure; also rule-based | Updated |
| Spatial | Nonhomogeneous spatial models | Updated |
| Graph rendering | Diagrams of models | draft |
| Groups | Arbitrary grouping of components | draft |
| Arrays & sets | Arrays or sets of entities | Updated |
| Dynamic structures | Creation & destruction of components | New |
| Distributions | Numerical values as statistical distributions | in dev |
| Annotations | Richer annotation syntax | |

Community-based development process

Defines process for

- **Proposing** changes and additions to SBML and SBML packages
- **Developing** specifications
- **Voting**
- **The roles** of editors

**Small changes forthcoming
in package requirements and
procedures**

The screenshot shows a web browser window displaying the SBML.org website. The title bar reads "Documents/SBML Development Process - SBML.caltech.edu". The main content area features the SBML.org logo and the text "The Systems Biology Markup Language". Below this is a navigation menu with links to News, Documents, Downloads, Forums, Facilities, Community, Events, About, and social media icons. A search bar labeled "Google Site Search" is also present. The main article is titled "SBML Development Process" and discusses the evolution of the process from an informal, participative approach to a formal, systematic one. It mentions the formation of the SBML Team and Editors, and the adoption of a more formal organization. The article is dated mid-2008. To the right of the main content is a sidebar with a list of links for translations, goals, community organization, development procedures, and guidelines. At the bottom of the sidebar, there is a section for "Translations".

Translations of this page to other languages are available – please see the bottom of this page.

Contents [hide]

1 Goals and Motivations for SBML
2 Goals of the SBML Development Process
3 SBML Community Organization
 3.1 The SBML Forum
 3.1.1 Requirements for membership
 3.1.2 Conduct of meetings
 3.2 The SBML Editors
 3.2.1 Responsibilities of SBML Editors
 3.2.2 Terms for SBML Editors
 3.2.3 Election process for SBML Editors
 3.2.4 Selection of the Chair of the SBML Editors
 3.3 The SBML Team
 3.4 The SBML Scientific Advisory Board
4 SBML Development Procedures and Guidelines
 4.1 General Procedures and Guidelines
 4.1.1 Public participation
 4.1.2 Communication and transparency
 4.1.3 Achieving consensus
 4.2 Language Development Process
 4.2.1 SBML Levels, Versions, and Releases
 4.2.2 Process for SBML Level 2
 4.2.3 Process for SBML Level 3
5 Translations

Goals and Motivations for SBML

The ultimate goal of the Systems Biology Markup Language (SBML) is to serve as a declarative representation language for computational models in biology. More precisely, the goal of SBML is to serve as a software lingua franca supporting the encoding of models such that those models can be exchanged and interpreted unambiguously by different software systems. SBML is not intended to encode the details of algorithms used to instantiate the models, nor the procedures used to process and analyze the models. Further, SBML is not linked to any specific software system.

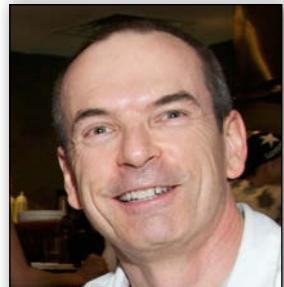
A past quote from a member of the SBML community summarizes the motivations nicely:

If Systems Biology is to succeed, one needs such a lingua franca. Not to exchange details on the use of Euler versus Runge-Kutta [...] but to exchange basic information on the structure of the models: the reactions, the species, the parameters [...]. One of the biggest problems of "Theoretical Biology" was the failure of two of Popper's criteria for science: reproducibility and falsification. I have reviewed papers in the field for quite a few years now, and there is one commonality. You can't really evaluate them. You have to completely trust what is written by the authors. SBML could change that. It could permit better evaluation of modeling, and bring the whole field to a new level of confidence and consideration by other scientists in life sciences.

SBML Editors



Frank Bergmann

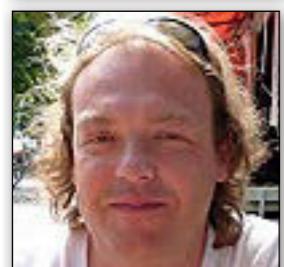


Michael Hucka

(chair)



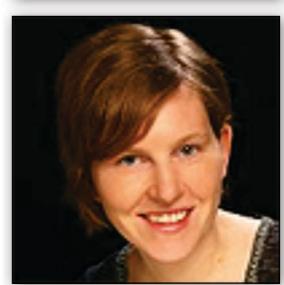
Nicolas Le Novère



Brett Olivier



Sven Sahle



Dagmar Waltemath

Current

Past

Stefan Hoops

Sarah Keating

Chris Myers

James Schaff

Lucian Smith

Darren Wilkinson

Google Summer of Code 2014

Open Bioinformatics Foundation (OBF) as mentoring organization



Victor Kofia

Redesign the implementation of the JSBML math class ASTNode



Ibrahim Vazirabad

Create a CellDesigner plugin for JSBML that will convert between the layout format used by CellDesigner and SBML Level 3 layout



Leandro Watanabe

Implement support in JSBML for the SBML Level 3 Arrays package

Acknowledgments

Mike Hucka, Sarah Keating, Frank Bergmann, Lucian Smith,

SBML & Andrew Finney, Herbert Sauro, Hamid Bolouri, Ben Bornstein, Maria

JSBML Team: Schilstra, Jo Matthews, Bruce Shapiro, Linda Taddeo, Akira Funahashi,
Akiya Juraku, Ben Kovitz, Nicolas Rodriguez, Andreas Dräger, Alex Thomas

Mike Hucka, Frank Bergmann, Sarah Keating, Nicolas Le Novère, Chris Myers,

SBML Editors: Lucian Smith, Stefan Hoops, Sven Sahle, James Schaff, Dagmar Waltemath,
Darren Wilkinson, Brett Olivier

GoSC students: Victor Kofia, Ibrahim Vazirabad, Leandro Watanabe

*And a huge thanks to everyone in the SBML and COMBINE communities
for massive contributions to SBML development and continuing support*



National Institute of General Medical Sciences (USA)

Google Summer of Code

European Molecular Biology Laboratory (EMBL)

Drug Disease Model Resources (EU-EFPIA Innovative Medicine Initiate)

JST ERATO Kitano Symbiotic Systems Project (Japan) (to 2003)

JST ERATO-SORST Program (Japan)

ELIXIR (UK)

Beckman Institute, Caltech (USA)

Keio University (Japan)

International Joint Research Program of NEDO (Japan)

Japanese Ministry of Agriculture

Japanese Ministry of Educ., Culture, Sports, Science and Tech.

BBSRC (UK)

National Science Foundation (USA)

DARPA IPTO Bio-SPICE Bio-Computation Program (USA)

Air Force Office of Scientific Research (USA)

STRI, University of Hertfordshire (UK)

Molecular Sciences Institute (USA)

SBML funding sources over the past 14 years