Harmonizing Standardization Processes for Model and Data Exchange in Systems Biology

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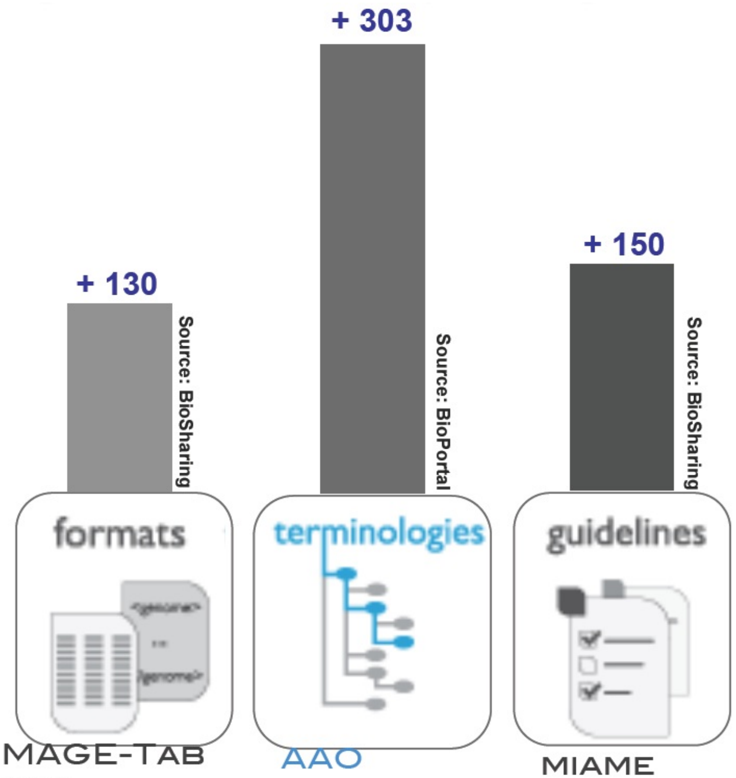
De-facto Standards in Biology & Biotechnology

biosharing

http://biosharing.org/



MAGE-TAB
GCDML
SRAXML
SOFT
CML
FASTA
DICOM
GELML
SBRML
MITAB
MZML
ISA-TAB SEDML...

AAO
CHEBI
OBI VO
PATO ENVO
MOD
TEDDY
XAO
BTO
DO PRO IDO...

MIAME
MIAPA
MIRIAM
MIX MIQAS
REMARK
MIGEN
MIAPE MIQE
CIMR CONSORT
MIASE MISFISHIE....

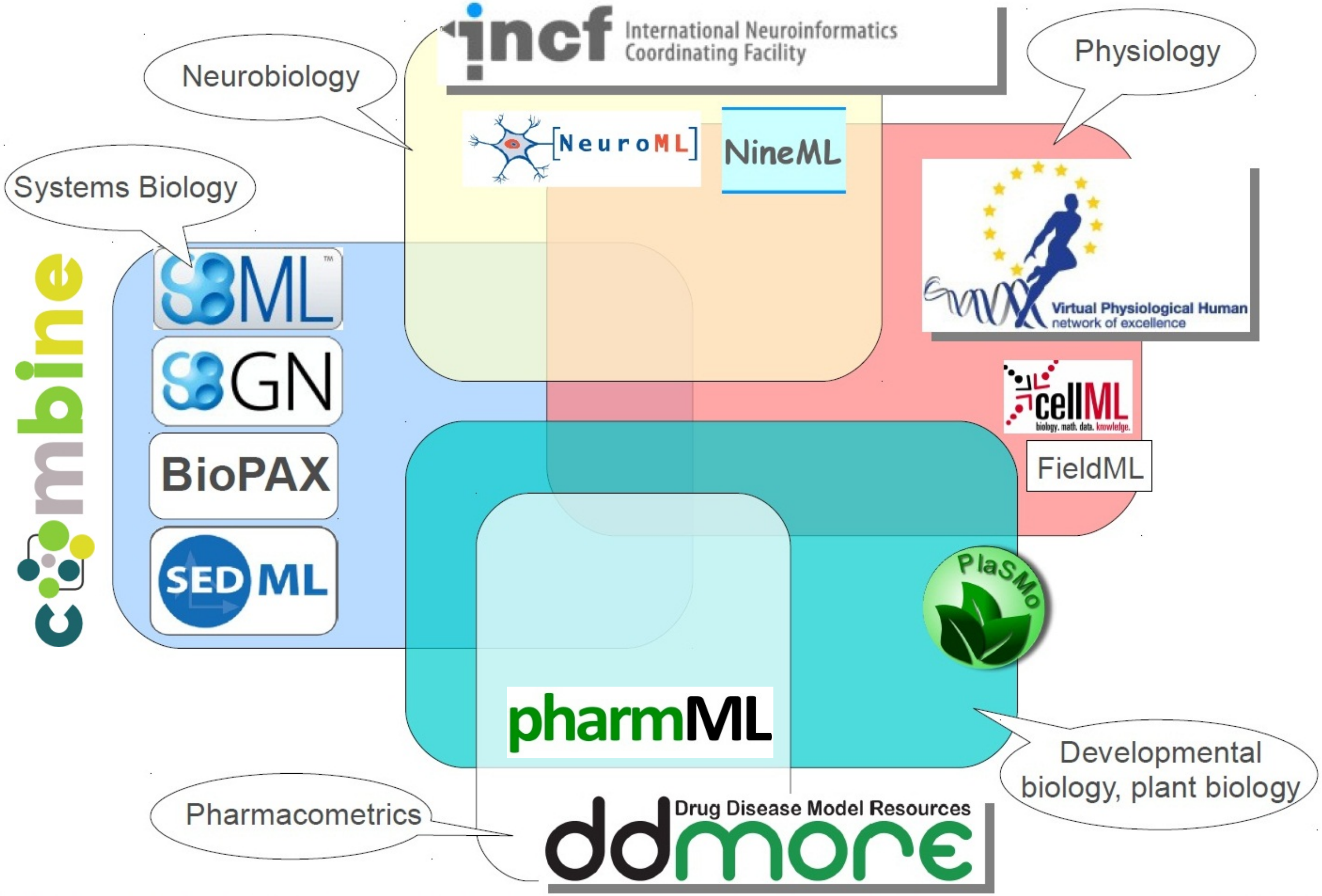
Databases, annotation, curation tools implementing standards

combine

Source: Susanna-Assunta Sansone (University of Oxford, UK)

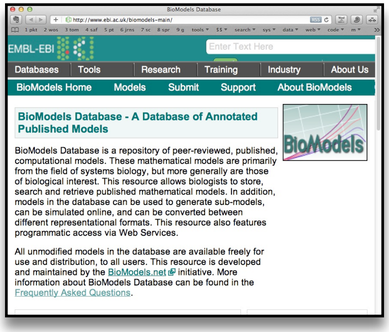
NORMSYS HITS

Community Modelling Standards in Different Fields



Source: Nicolas Le Novère (Babraham Institute, Cambridge, UK)

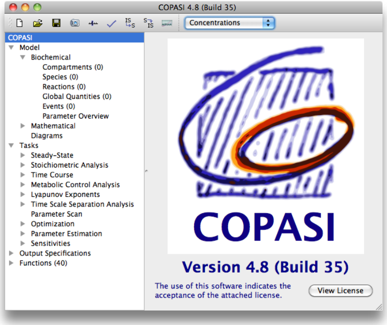
Modelers often need to use more than one software tool



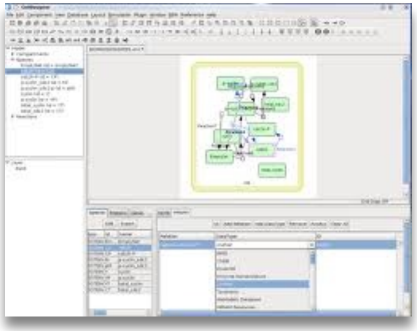
BioModels Database - A Database of Annotated Published Models

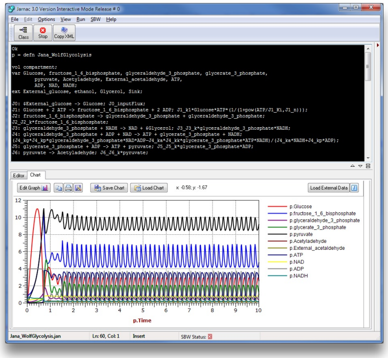
BioModels Database is a repository of peer-reviewed, published, computational models. These mathematical models are primarily from the field of systems biology, but more generally are those of biological interest. This resource allows biologists to store, search and retrieve published mathematical models. In addition, models in the database can be used to generate sub-models, can be simulated online, and can be converted between different representational formats. This resource also features programmatic access via Web Services.

All unmodified models in the database are available freely for use and distribution, to all users. This resource is developed and maintained by the BioModels.net initiative. More information about BioModels Database can be found in the Frequently Asked Questions.



The use of this software indicates the acceptance of the attached license.

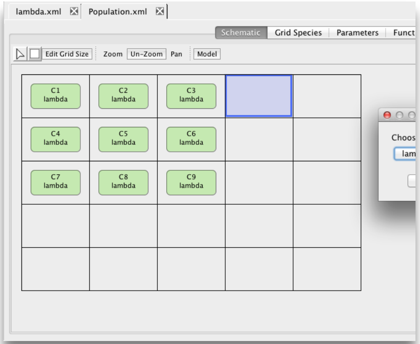


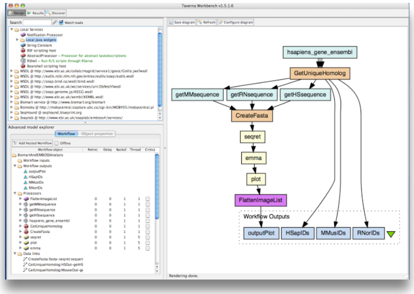


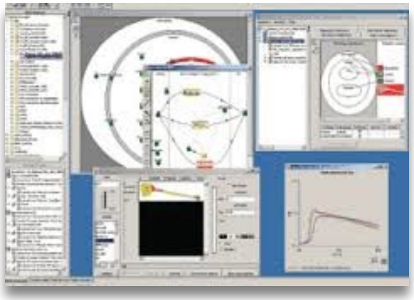
```
Ok
p = defn Jana_WolfGlycolysis

vol compartment;
var Glucose, fructose_1_6_bisphosphate, glyceraldehyde_3_phosphate, glycerate_3_phosphate,
        pyruvate, Acetyladehyde, External_acetaldehyde, ATP,
        ADP, NAD, NADH;
ext External_glucose, ethanol, Glycerol, Sink;

J0: $External_glucose -> Glucose; J0_inputFlux;
J1: Glucose + 2 ATP -> fructose_1_6_bisphosphate + 2 ADP; J1_k1*Glucose*ATP*(1/(1+pow(ATP/J1_Ki,J1_n)));
J2: fructose_1_6_bisphosphate -> glyceraldehyde_3_phosphate + glyceraldehyde_3_phosphate;
J2_J2_k*fructose_1_6_bisphosphate;
J3: glyceraldehyde_3_phosphate + NADH -> NAD + $Glycerol; J3_J3_k*glyceraldehyde_3_phosphate*NADH;
J4: glyceraldehyde_3_phosphate + ADP + NAD -> ATP + glycerate_3_phosphate + NADH;
(J4_kg*J4_kp*glyceraldehyde_3_phosphate*NAD*ADP-J4_ka*J4_kk*glycerate_3_phosphate*ATP*NADH)/(J4_ka*NADH+J4_kp*ADP);
J5: glycerate_3_phosphate + ADP -> ATP + pyruvate; J5_J5_k*glycerate_3_phosphate*ADP;
J6: pyruvate -> Acetyladehyde; J6_J6_k*pyruvate;
```







SBML = format for exchanging biological process models between software systems

Model Exchange: Systems Biology Markup Language

```
<sbrk:sabiork xmlns:sbrk="http://sabiork.h-its.org">
<sbrk:modifierType>Modifier-Catalyst</sbrk:modifierType>
</sbrk:sabiork>                  <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#" xmlns:bqbiol="http://biomodels.net/biology-qualifiers
xmlns:bqmodel="http://biomodels.net/model-qualifiers/">
            <rdf:Description rdf:about="#META_ENZ_140280_Cell">
              <bqbiol:is>
                <rdf:Bag>
                  <rdf:li rdf:resource="http://identifiers.org/uniprot/P05062"/>
                </rdf:Bag>
              </bqbiol:is>
            </rdf:Description>
          </rdf:RDF>
        </annotation>
</species>
    </listOfSpecies>
    <listOfReactions>
      <reaction id="REAC_0" metaid="META_REAC_0" reversible="true" fast="false">
        <annotation>
          <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#" xmlns:bqbiol="http://biomodels.net/biology-qualifiers/" xmlns:bqmodel="http:
qualifiers/">
            <rdf:Description rdf:about="#META_REAC_0">
              <bqbiol:isVersionOf>
                <rdf:Bag>
                  <rdf:li rdf:resource="http://identifiers.org/ec-code/4.1.2.13"/>
                </rdf:Bag>
              </bqbiol:isVersionOf>
              <bqbiol:is>
                <rdf:Bag>
                  <rdf:li rdf:resource="http://identifiers.org/kegg.reaction/R01068"/>
                </rdf:Bag>
              </bqbiol:is>
              <bqbiol:hasTaxon>
                <rdf:Bag>
                  <rdf:li rdf:resource="http://identifiers.org/taxonomy/9606"/>
                </rdf:Bag>
              </bqbiol:hasTaxon>
              <bqbiol:is>
                <rdf:Bag>
                  <rdf:li rdf:resource="http://identifiers.org/sabiork.reaction/1338"/>
                </rdf:Bag>
              </bqbiol:is>
            </rdf:Description>
          </rdf:RDF>
        </annotation>
        <listOfReactants>
          <speciesReference constant="true" species="SPC_1465_Cell" sboTerm="SBO:0000015" stoichiometry="1"/>
        </listOfReactants>
```

Format for **representing** computational models of biological processes

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

Neutral with respect to modeling framework

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

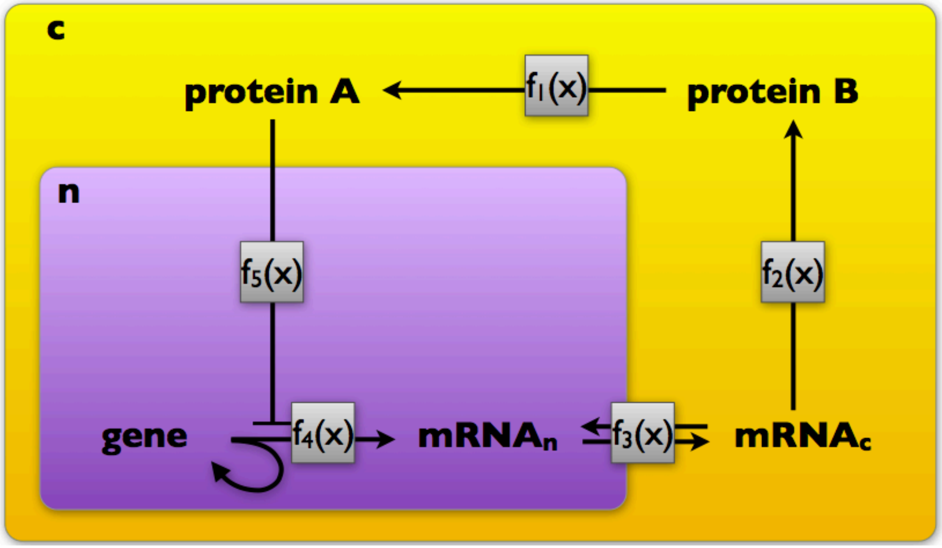
Important: **software** reads/writes SBML, **not humans**

Hucka M, Finney A, Sauro HM, *et al.*: **The systems biology markup language (SBML): a medium for representation and exchange of biochemical network models**. Bioinformatics (2003) 19(4): 524-531

http://sbml.org

Model Exchange: Systems Biology Markup Language

- A typical SBML model is composed of a number of **species** (i.e. proteins, genes, chemical compounds, etc.) and **reactions** that transform these species.
- Biological entities and context are defined mainly via (RDF) **annotations**.



http://sbml.org

- Supported by **more than 280 tools**, enabling researchers to create, annotate, simulate, store, exchange and visualize models.
- Models can be archived in the **BioModels database** and/or **JWS Online**.
- SBML also has parameters, functions, unit definitions, initial assignments, rules for continuous relationships, events for discontinuous state changes, and constraints to indicate when a simulation should terminate.

SBML Level 3 *packages* layer additional constructs over **SBML Level 3 Core**

<u>Packages:</u> Flux balance constraints models, Qualitative models, Hierarchical model composition, Graph layout, Distributions, Spatial, and more → visit **SBML.org**

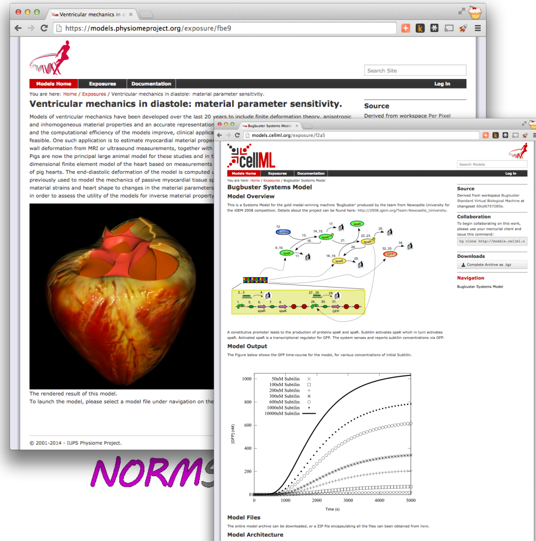
AUCKLAND BIOENGINEERING INSTITUTE
THE UNIVERSITY OF AUCKLAND
NEW ZEALAND

cellML

http://cellml.org/

- Modular framework for encoding mathematical models:
  - differential algebraic equations using MathML
  - math is the primary data, biological context, provenance, etc., provided through annotations using RDF
- Units ensuring unambiguous conversion of numerical values
- Hierarchies of modules enable mathematical abstraction
- Hierarchical modules can be imported → reuse
- Free and open repository: http://models.physiomeproject.org/ supporting versioned model reuse, archiving, collaboration…

combine



You are here: Home / Exposures / Ventricular mechanics in diastole: material parameter sensitivity.

Ventricular mechanics in diastole: material parameter sensitivity.

Models of ventricular mechanics have been developed over the last 20 years to include finite deformation theory, anisotropic and inhomogeneous material properties and an accurate representation and the computational efficiency of the models improve, clinical applica feasible. One such application is to estimate myocardial material proper wall deformation from MRI or ultrasound measurements, together with Pigs are now the principal large animal model for these studies and in t dimensional finite element model of the heart based on measurements of pig hearts. The end-diastolic deformation of the model is computed u previously used to model the mechanics of passive myocardial tissue sp material strains and heart shape to changes in the material parameters in order to assess the utility of the models for inverse material property

The rendered result of this model.
To launch the model, please select a model file under navigation on the

Source
Derived from workspace Per Pixel

© 2001-2014 - IUPS Physiome Project.

You are here: Home / Exposures / Bugbuster Systems Model

Bugbuster Systems Model

Model Overview

This is a Systems Model for the gold medal-winning machine 'Bugbuster' produced by the team from Newcastle University for the iGEM 2008 competition. Details about the project can be found here: http://2008.igem.org/Team:Newcastle_University.

A constitutive promoter leads to the production of proteins spaK and spaR. Subtilin activates spaK which in turn activates spaR. Activated spaR is a transcriptional regulator for GFP. The system senses and reports subtilin concentrations via GFP.

Model Output

The Figure below shows the GFP time-course for the model, for various concentrations of initial Subtilin.

Model Files

The entire model archive can be downloaded, or a ZIP file encapsulating all the files can been obtained from here.

Model Architecture

Source
Derived from workspace Bugbuster Standard Virtual Biological Machine at changeset 60cd6757285e.

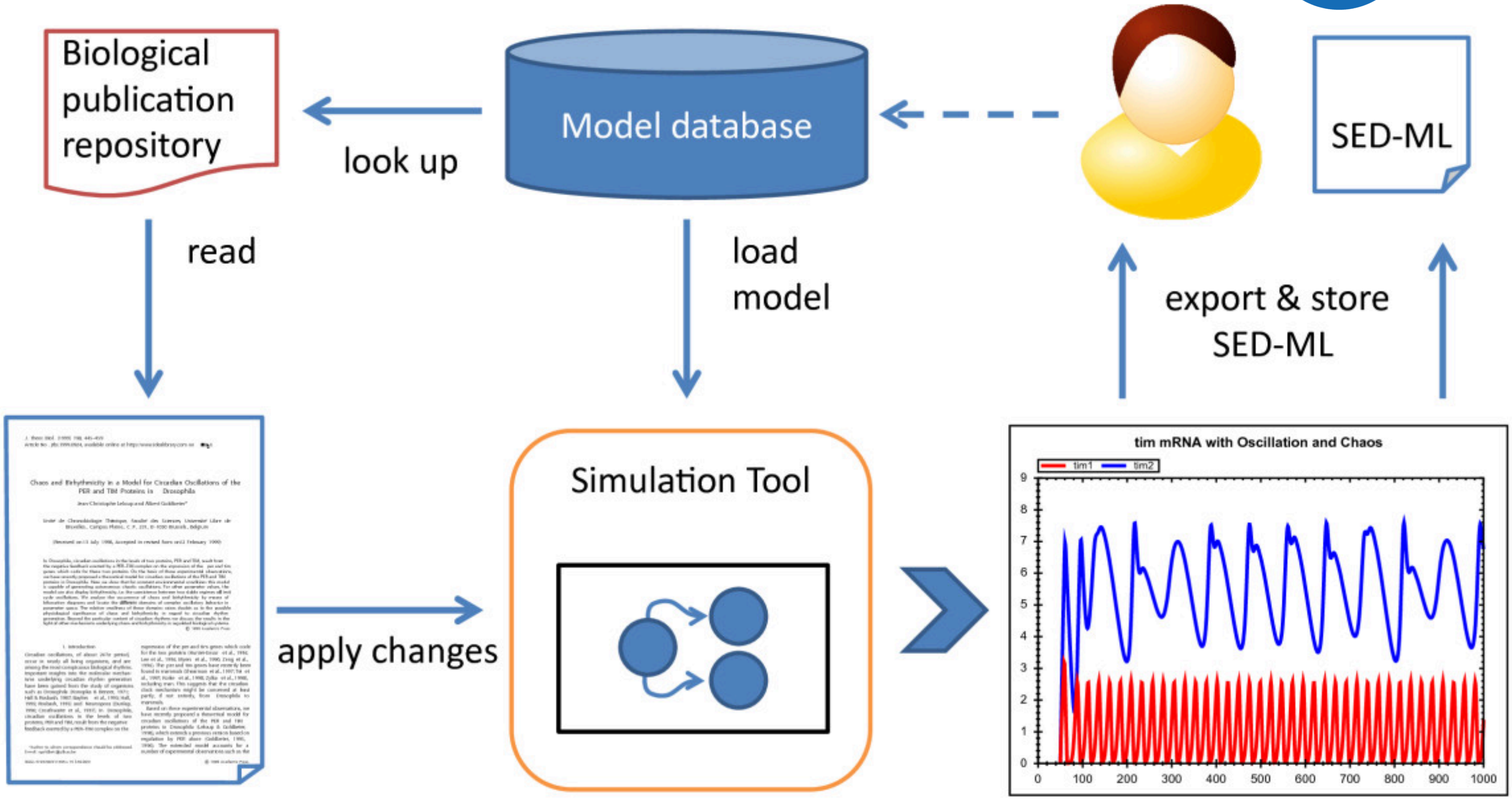
Collaboration
To begin collaborating on this work, please use your mercurial client and issue this command:

```
hg clone http://models.cellml.o
```

Downloads

Navigation
Bugbuster Systems Model

Simulation Experiment Description Markup Language: SED-ML



Biological publication repository

look up

Model database

SED-ML

read

load model

export & store SED-ML

apply changes

Simulation Tool

Waltemath D, Adams R, Bergmann FT, Hucka M, Kolpakov F, Miller AK, Moraru II, Nickerson D, Sahle S, Snoep JL, Le Novère N: **Reproducible computational biology experiments with SED-ML--the Simulation Experiment Description Markup Language.** BMC Systems Biology (2011) 5: 198. doi: 10.1186/1752-0509-5-198.

http://www.sbgn.org

SBGN Systems Biology Graphical Notation

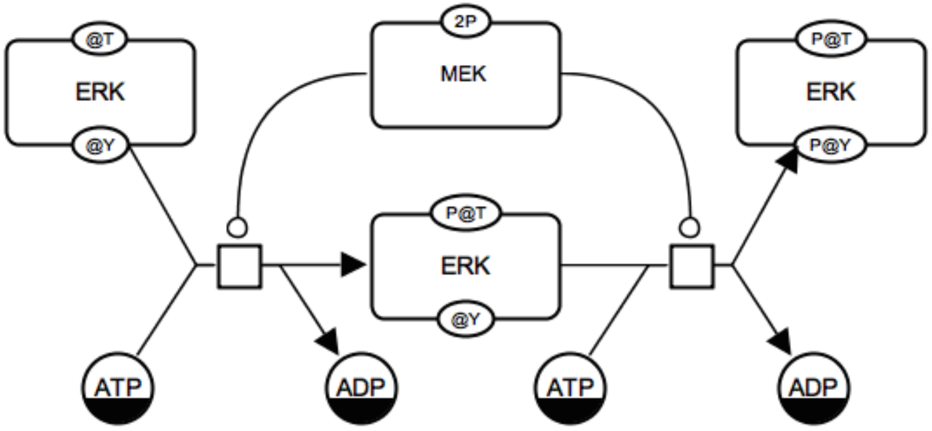
What is SBGN?

- A way to unambiguously describe biochemical and cellular events in graphs
- A graphical representation of quantitative models and biochemical pathways, at different levels of granularity
- Can be translated into executable models, can graphically represent models (e.g. SBML, BioPAX), but can also exists independently
- Three languages
  - Process Descriptions → one state = one glyph
  - Entity Relationships → one entity = one glyph
  - Activity Flow → conceptual level

http://www.sbgn.org

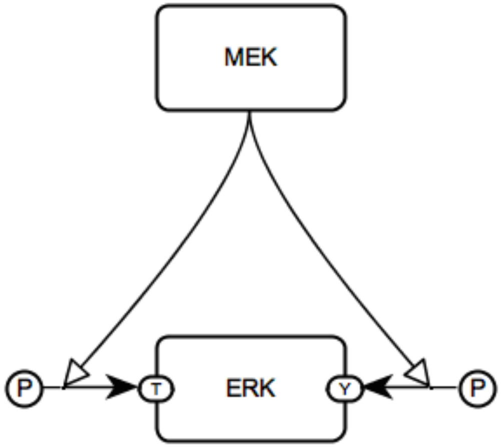
Systems Biology Graphical Notation: SBGN

Process Description maps



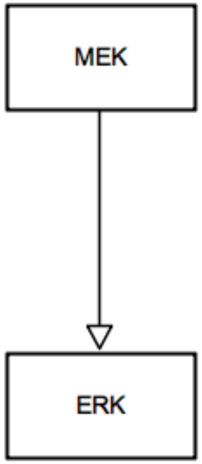
- Unambiguous
- Mechanistic
- Sequential
- Combinatorial explosion

Entity Relationships maps



- Unambiguous
- Mechanistic
- Non-Sequential

Activity Flow maps



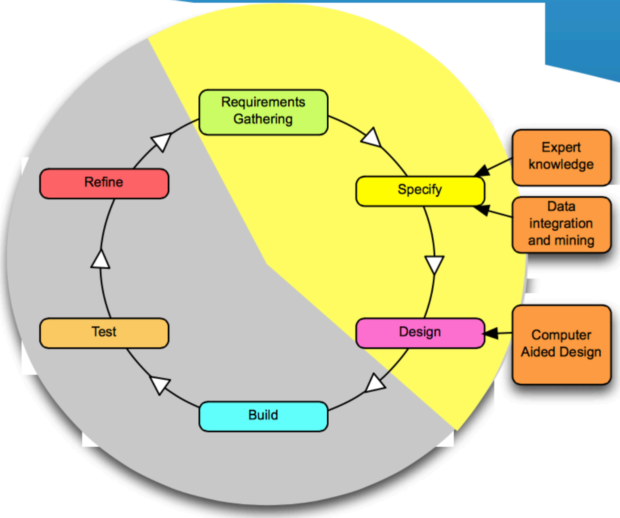
- Ambiguous
- Conceptual
- Sequential

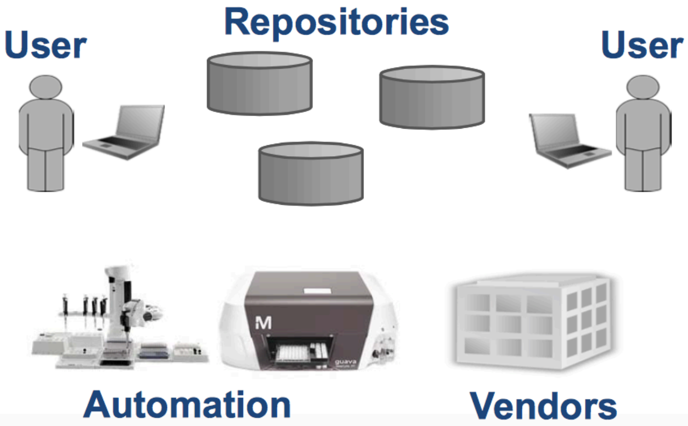
Le Novère N, Hucka M, Mi H, Moodie S, Schreiber F, Sorokin A, Demir E, Wegner K, Aladjem MI, Wimalaratne SM, Bergman FT, Gauges R, Ghazal P, Kawaji H, Li L, Matsuoka Y, Villéger A, Boyd SE, Calzone L, *et al.*
The Systems Biology Graphical Notation. Nature Biotechnology 27(8):735-41 (2009)

http://www.sbgn.org

What is SBOL – why is it needed?

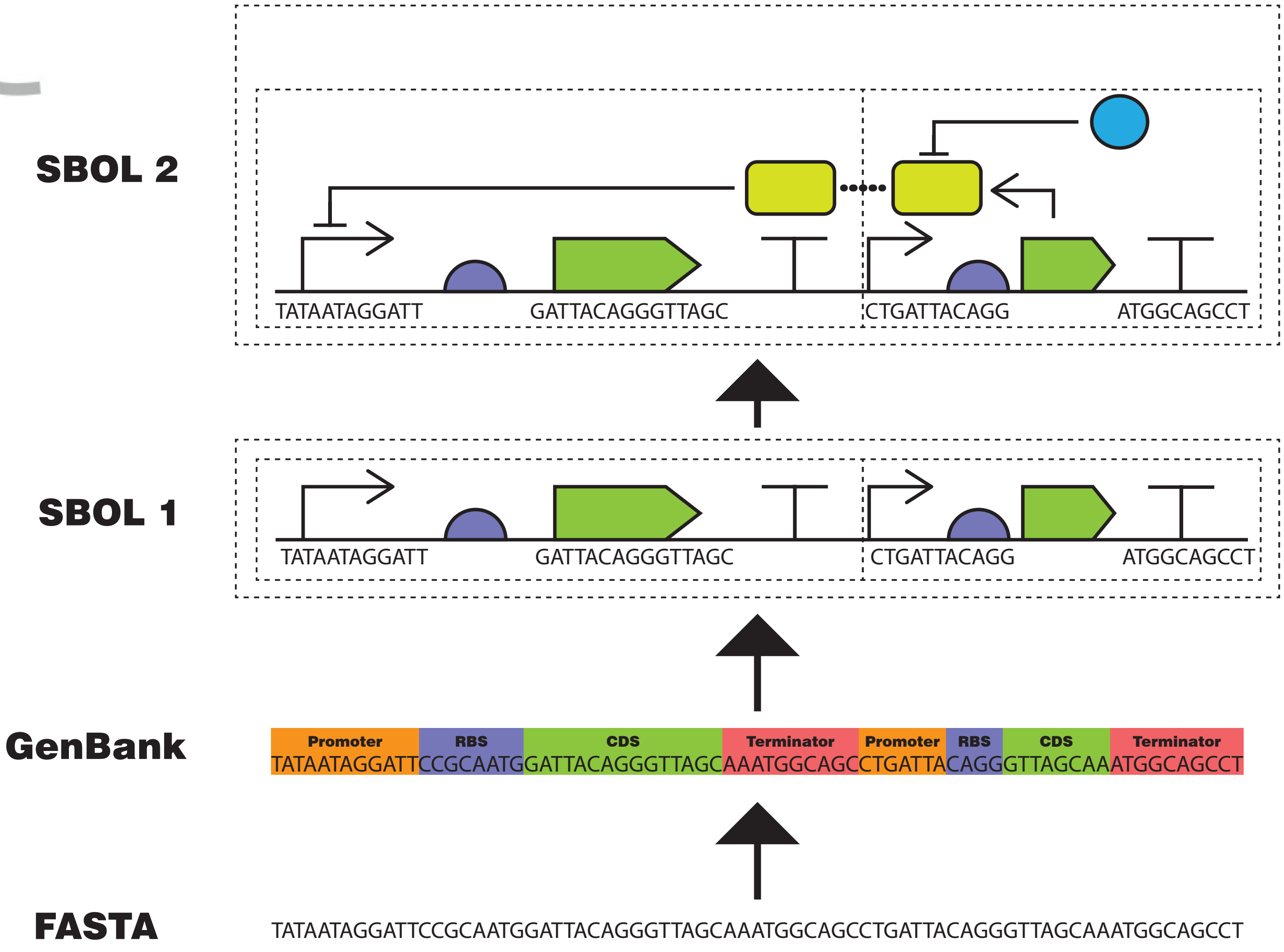
- Synthetic Biology is engineering biology
- Requires movement of data & information
  - Between people, software & machines
  - Across geographic and political boundaries
- Standards needed to ensure interoperability
- SBOL - a standard way to represent information about synthetic biology designs





Michal Galdzicki, Kevin P. Clancy, Ernst Oberortner, Matthew Pocock, Jacqueline Quinn, Cesar A. Rodriguez, Nicholas Roehner, Mandy L. Wilson, *et al.:* **The Synthetic Biology Open Language (SBOL) provides a community standard for communicating designs in synthetic biology**. Nature Biotechnology 32, 545-550 (2014)

http://sbolstandard.org



SBOL 2

TATAATAGGATT GATTACAGGGTTAGC CTGATTACAGG ATGGCAGCCT

SBOL 1

TATAATAGGATT GATTACAGGGTTAGC CTGATTACAGG ATGGCAGCCT

GenBank

Promoter	RBS	CDS	Terminator	Promoter	RBS	CDS	Terminator
TATAATAGGATT	CCGCAATG	GATTACAGGGTTAGC	AAATGGCAGC	CTGATTA	CAGG	GTTAGCAA	ATGGCAGCCT

FASTA

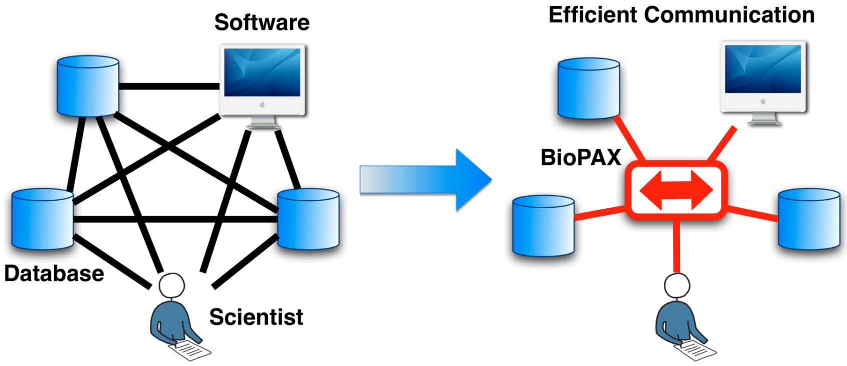
TATAATAGGATTCCGCAATGGATTACAGGGTTAGCAAATGGCAGCCTGATTACAGGGTTAGCAAATGGCAGCCT

Michal Galdzicki, Kevin P. Clancy, Ernst Oberortner, Matthew Pocock, Jacqueline Quinn, Cesar A. Rodriguez, Nicholas Roehner, Mandy L. Wilson, *et al.*: **The Synthetic Biology Open Language (SBOL) provides a community standard for communicating designs in synthetic biology**. Nature Biotechnology 32, 545-550 (2014)

http://sbolstandard.org

Biological Pathway Exchange Format: BioPax

- To represent biological interactions and pathways
  - Pathways: collections of interactions that biologists have found useful to group together for organizational, historic, biophysical or other reasons
  - Types
    - Metabolic pathways
    - Signaling pathways
    - Protein-protein, molecular interactions
    - Gene regulatory pathways
- Encourage a community-wide effort to distribute pathway data in standard format (over 500 databases listed on pathguide.org)



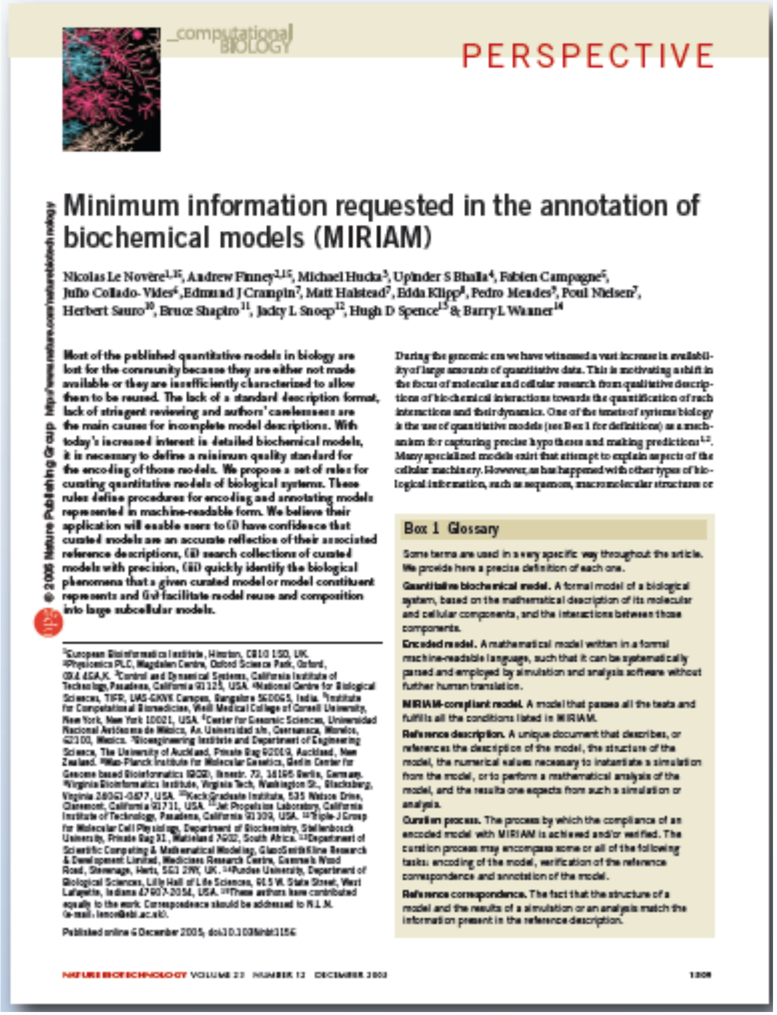
http://www.biopax.org

Reporting Guidlines: e.g. Models

Minimum **I**nformation **R**equested **I**n the **A**nnotation of biochemical **M**odels

Reporting guidelines (Checklists) for the annotation and curation of quantitative biochemical models

www.ebi.ac.uk/miriam



Minimum information requested in the annotation of biochemical models (MIRIAM)

Nicolas Le Novère[1,15], Andrew Finney[2,15], Michael Hucka[3], Upinder S Bhalla[4], Fabien Campagne[5], Julio Collado-Vides[6], Edmund J Crampin[7], Matt Halstead[7], Edda Klipp[8], Pedro Mendes[9], Poul Nielsen[7], Herbert Sauro[10], Bruce Shapiro[11], Jacky L Snoep[12], Hugh D Spence[13] & Barry L Wanner[14]

Most of the published quantitative models in biology are lost for the community because they are either not made available or they are insufficiently characterized to allow them to be reused. The lack of a standard description format, lack of stringent reviewing and authors' carelessness are the main causes for incomplete model descriptions. With today's increased interest in detailed biochemical models, it is necessary to define a minimum quality standard for the encoding of those models. We propose a set of rules for curating quantitative models of biological systems. These rules define procedures for encoding and annotating models represented in machine-readable form. We believe their application will enable users to (i) have confidence that curated models are an accurate reflection of their associated reference descriptions, (ii) search collections of curated models with precision, (iii) quickly identify the biological phenomena that a given curated model or model constituent represents and (iv) facilitate model reuse and composition into large subcellular models.

During the genomic era we have witnessed a vast increase in availability of large amounts of quantitative data. This is motivating a shift in the focus of molecular and cellular research from qualitative descriptions of biochemical interactions towards the quantification of such interactions and their dynamics. One of the tenets of systems biology is the use of quantitative models (see Box 1 for definitions) as a mechanism for capturing precise hypotheses and making predictions[1,2]. Many specialized models exist that attempt to explain aspects of the cellular machinery. However, as has happened with other types of biological information, such as sequences, macromolecular structures or

Box 1 Glossary

Some terms are used in a very specific way throughout the article. We provide here a precise definition of each one.

Quantitative biochemical model. A formal model of a biological system, based on the mathematical description of its molecular and cellular components, and the interactions between those components.

Encoded model. A mathematical model written in a formal machine-readable language, such that it can be systematically parsed and employed by simulation and analysis software without further human translation.

MIRIAM-compliant model. A model that passes all the tests and fulfills all the conditions listed in MIRIAM.

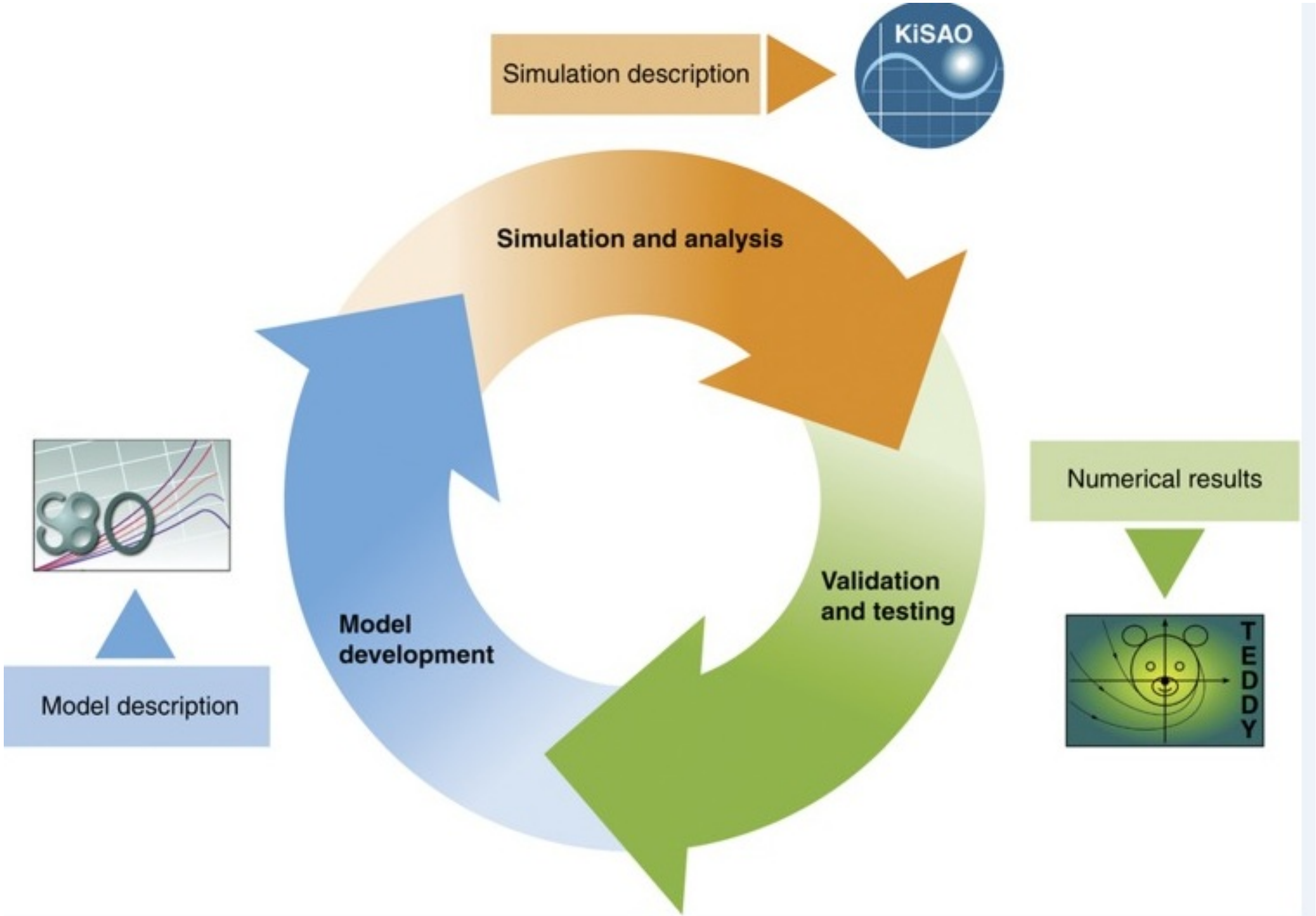
Reference description. A unique document that describes, or references the description of the model, the structure of the model, the numerical values necessary to instantiate a simulation from the model, or to perform a mathematical analysis of the model, and the results one expects from such a simulation or analysis.

Curation process. The process by which the compliance of an encoded model with MIRIAM is achieved and/or verified. The curation process may encompass some or all of the following tasks: encoding of the model, verification of the reference correspondence and annotation of the model.

Reference correspondence. The fact that the structure of a model and the results of a simulation or an analysis match the information present in the reference description.

Nature Biotech. 23(12), Dec. 2005

Terminologies, Ontologies and Controlled Vocabulary



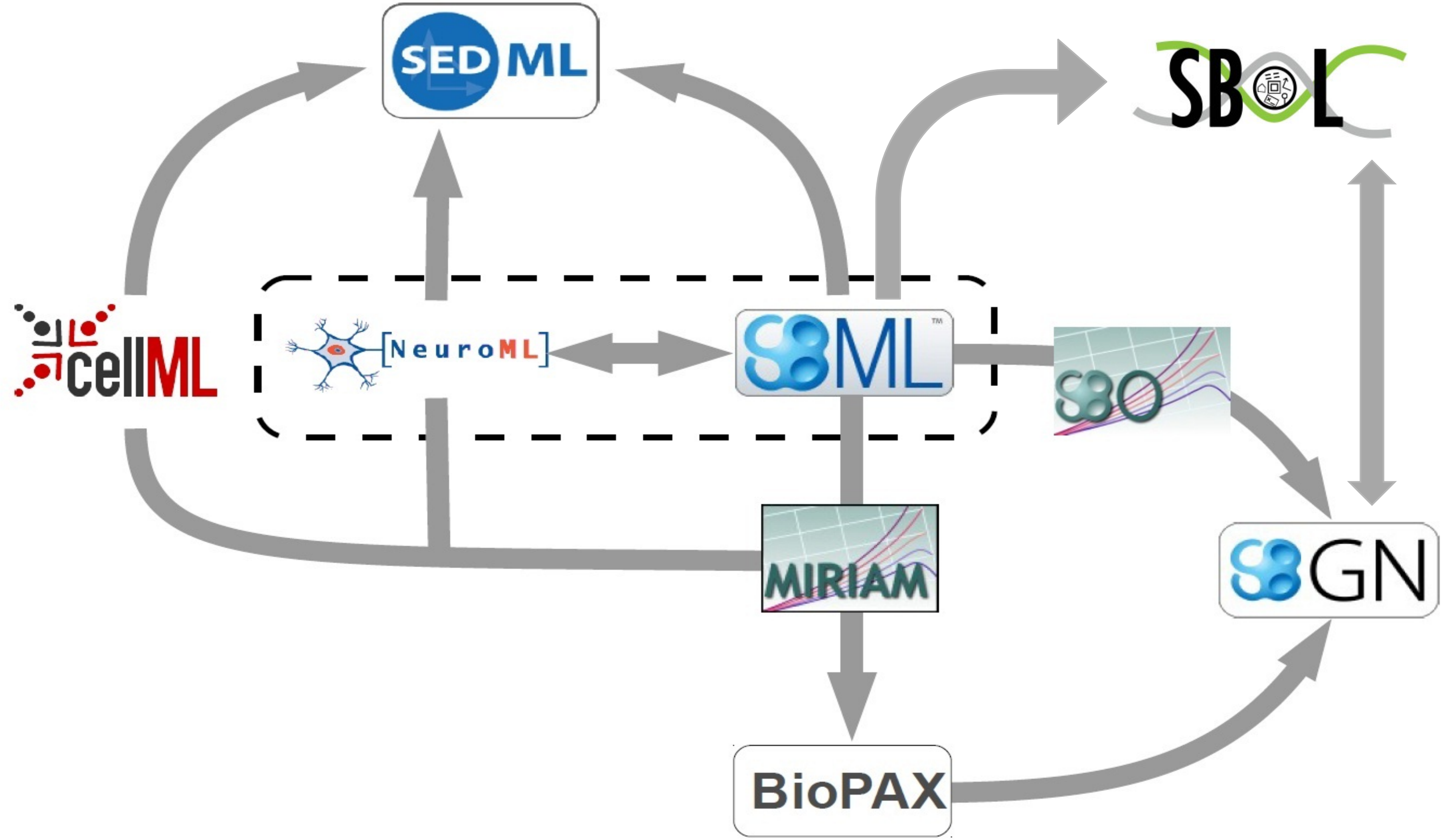
Courtot M, Juty N, Knüpfer C, Waltemath D, Zhukova A, Dräger A, Dumontier M, Finney A, Golebiewski M, Hastings J, Hoops S, Keating S, Kell DB, Kerrien S, Lawson J, Lister A, Lu J, Machne R, Mendes P, Pocock M, Rodriguez N, Villeger A, Wilkinson DJ, Wimalaratne S, Laibe C, Hucka M, Le Novère N: **Controlled vocabularies and semantics in systems biology.** Mol Syst Biol. 2011 Oct 25;7:543

Community Modelling Standards in Systems Biology

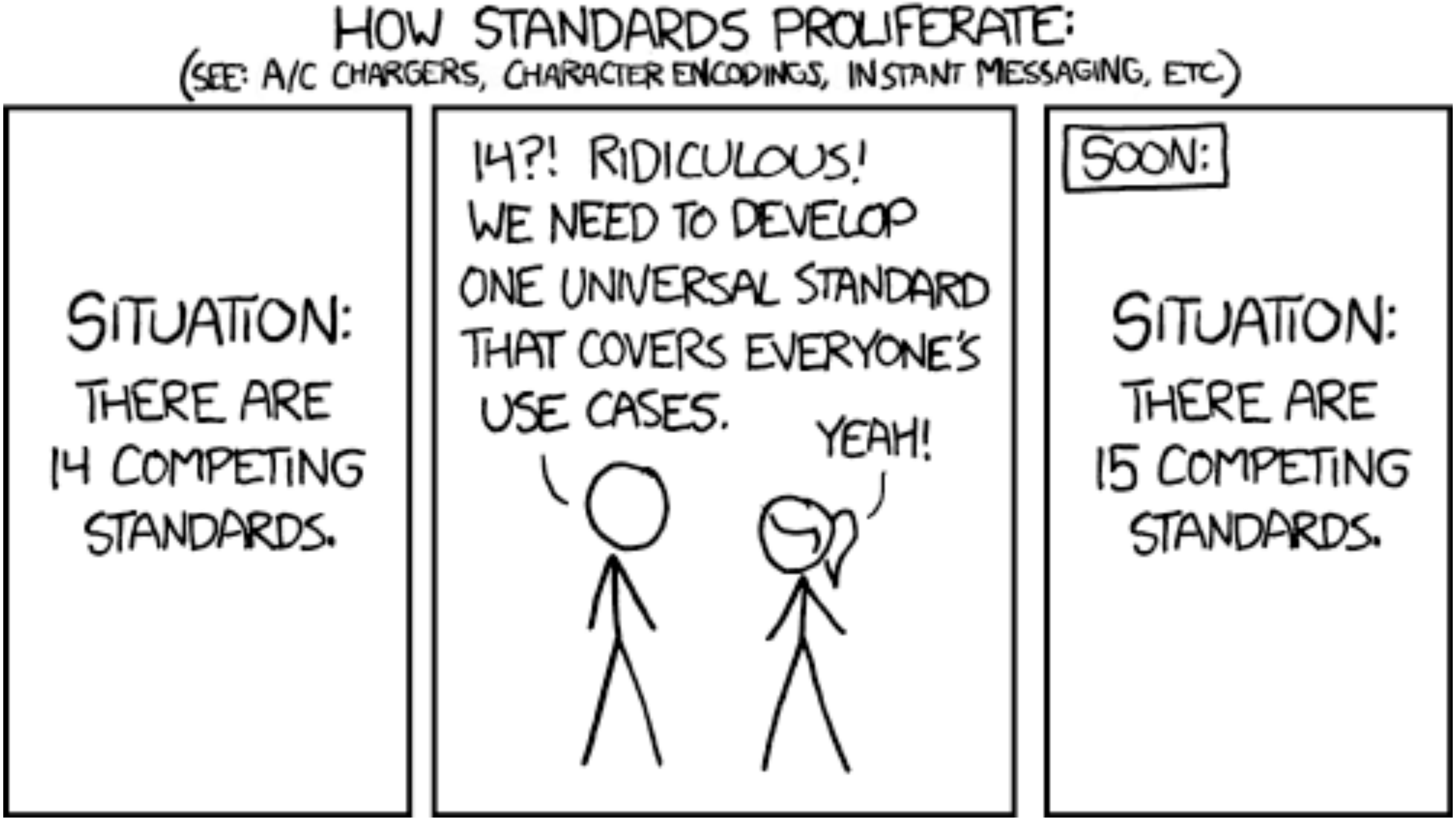
	Model descriptions	Simulations and analysis	results
Minimal requirements	MIRIAM	MIASE	
Data-models	SBML™ SBGN cellML biology. math. data. knowledge.	SED ML	NuML
Terminologies	SBO	KISAO	TEDDY

Source: Nicolas Le Novère (Babraham Institute, Cambridge, UK)

Interfacing and Interoperability of Modelling Standards



So many standards...



Coordination of Standard Development in Systems Biology

the combine
computational modeling in biology network

http://co.mbine.org/

The "WorldWide Web consortium" of modelling in biology

Interoperable Standards
For modelling in biology

Hucka M, Nickerson DP, Bader GD, Bergmann FT, Cooper J, Demir E, Garny A, Golebiewski M, Myers CJ, Schreiber F, Waltemath D, Le Novère N:
Promoting Coordinated Development of Community-Based Information Standards for Modeling in Biology: The COMBINE Initiative
Front Bioeng Biotechnol. (2015) 3:19. doi: 10.3389/fbioe.2015.00019

combine de.NBI GERMAN NETWORK FOR BIOINFORMATICS INFRASTRUCTURE NORMSYS HITS

combine

Tasks and Actions:

- Computational Modeling in Biology Network
- Concerted meetings of standards:
  HARMONY & COMBINE
- Training in application of standards (COMBINE tutorials)
- Coordinate standards development
- Develop common procedures & tools
- Provide a recognized voice

combine

de.NBI
GERMAN NETWORK FOR BIOINFORMATICS INFRASTRUCTURE

NORMSYS

HITS

Overview of the COMBINE standards

Core Standards

Standards for Knowledge Representation

BioPAX

SBOL

Standards for Visual Representation

SBGN

SBOL VISUAL

Standards for Models and their Analyses

SBML

CellML

NeuroML

SED-ML

Associated Standards

Used by core standards

Projects

Infrastructure

BioModels.net qualifiers

Controlled Vocabularies

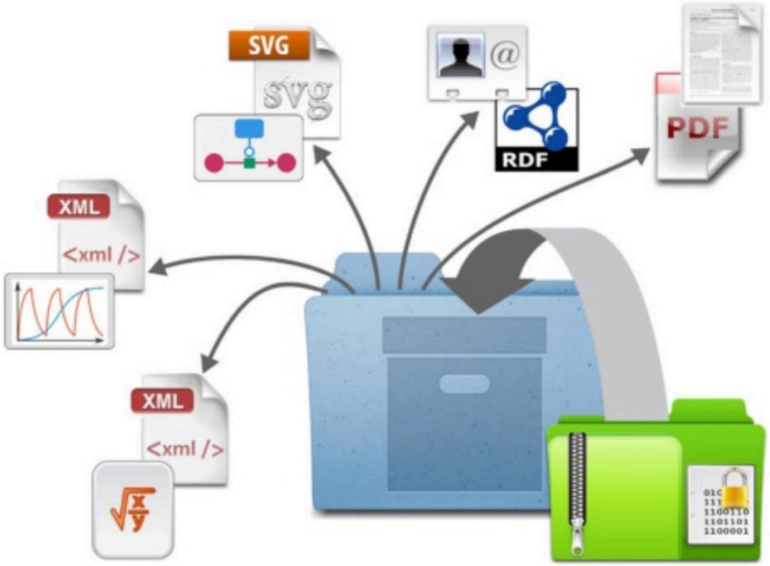
SBO

KiSAO

adapted from:
Schreiber F, Bader GD, Gleeson P, Golebiewski M, Hucka M, Le Novère N, Myers C, Nickerson D, Sommer B, Walthemath D:
Specifications of Standards in Systems and Synthetic Biology: Status and Developments in 2016
J Integr Bioinform. (2016) 13:289. doi: 10.2390/biecoll-jib-2016-289

combine de.NBI GERMAN NETWORK FOR BIOINFORMATICS INFRASTRUCTURE NORMSYS HITS

Bundle All Information About Your Model in One File



COMBINE Archive format = single file that supports exchange of all information necessary for any modeling and simulation experiment

- Not SBML-specific at all
- Not programming-language specific
- Not domain specific

OMEX = file format for COMBINE Archive

- ZIP file containing manifest file (in XML form) + other files
- Use of ZIP leverages many existing programming libraries

http://co.mbine.org/documents/archive

Enabling technologies

2003
libSBML

2005
MIRIAM, SBO, BioModels qualifiers
2006
PaxTools

2007
MIASE, KiSAO

2011
Identifiers.org

September 2014
COMBINE Archive

Representation formats

March 2001
SBML Level 1

August 2001
CellML 1.0, NeuroML

June 2003
SBML Level 2

July 2004
BioPAX Level 1

December 2005
BioPAX Level 2

August 2008
SBGN PD L1

September 2009
SBGN ER L1, SBGN AF L1

March 2010
SED-ML Level 1

July 2010
BioPAX Level 3

October 2010
SBML Level 3

October 2011
SBOL v1

March 2013
SBOLvisual v1

July 2015
SBOL v2

1999

Influential meetings

April 1999
NATO workshop, proposing to create
a language to encode metabolic models

April 2000
Start of SBML at the
1st “ERATO Kitano” workshop,

August 2002
Start of BioPAX project at the
4st Biopathway consortium meeting

July 2003
1st SBML hackathon

October 2005
Start of SBGN project at
the BioPAX face 2 face meeting

2006
Decision to create a language for synth biol designs
January 2008
Okinawa superhackathon
SBGN, BioPAX, SBO, MIRIAM

April 2008
1st SBOL meeting

April 2009
Waiheke combined meeting
CellML, SBGN, BioPAX, SBO, MIASE

2010

Creation of COMBINE

October 2010
1st COMBINE forum
April 2011
1st HARMONY hackathon

Myers, Bader, Gleeson, Golebiewski, Hucka, Le Novère, Nickerson, Schreiber, and Waltemath: ‚A Brief History of COMBINE‘, *in press*

COMBINE Coordination Board

Gary D. Bader
(University of Toronto, Canada)
BioPAX Delegate

Mike Hucka
(Caltech, Pasadena, USA)
SBML Delegate

Chris Myers
(University of Utah, USA)
SBOL Delegate

David Nickerson
(University of Auckland, NZ)
CellML Delegate

Falk Schreiber
(Monash University Melbourne, AUS)
SBGN Delegate

Dagmar Waltemath
(University of Rostock, Germany)
SED-ML Delegate

Padraig Gleeson
(University College London, UK)
NeuroML Delegate

Martin Golebiewski
(HITS gGmbH, Germany)

Nicolas Le Novère
(Babraham Institute, UK)

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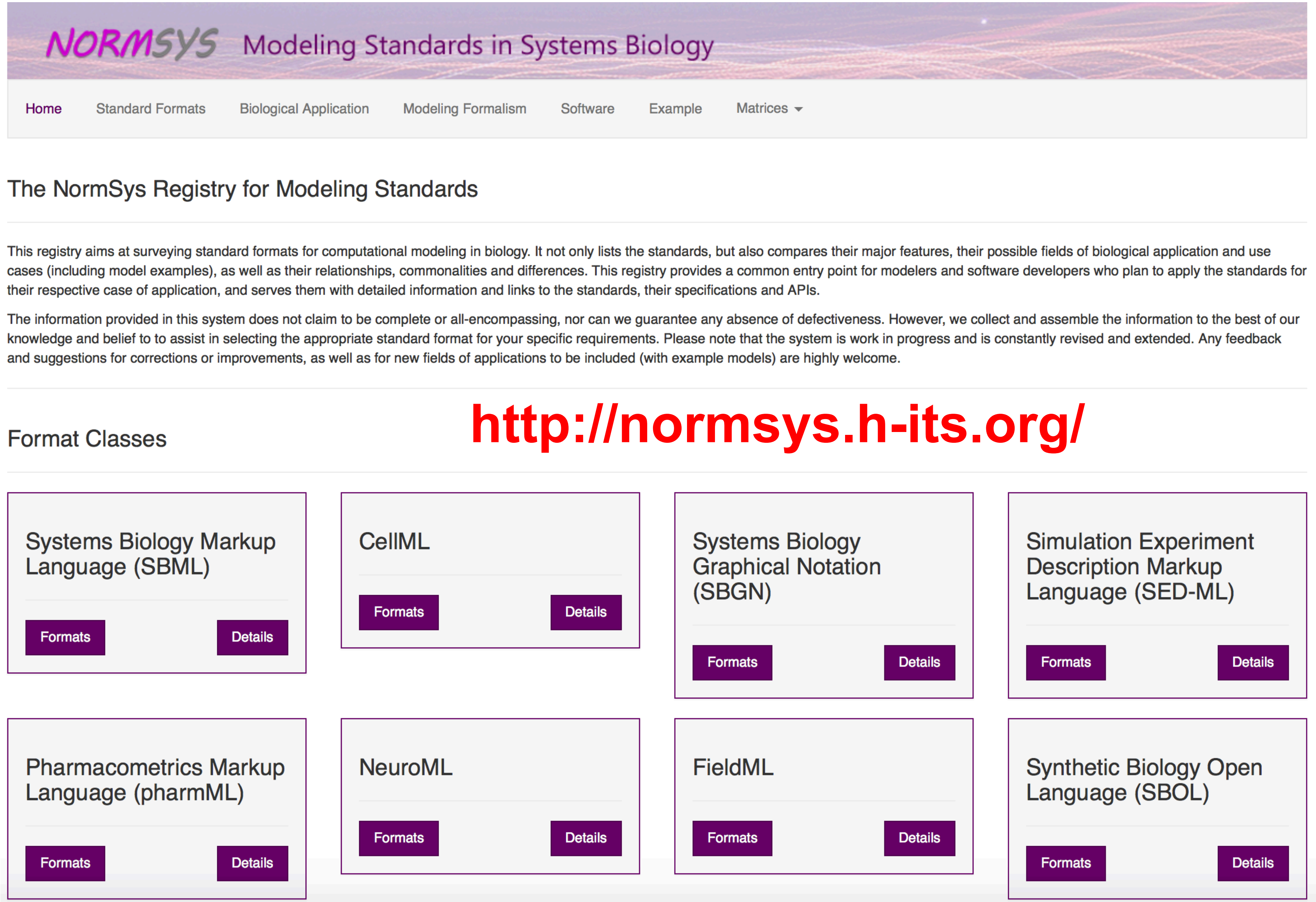

The NormSys Registry for Modeling Standards

This registry aims at surveying standard formats for computational modeling in biology. It not only lists the standards, but also compares their major features, their possible fields of biological application and use cases (including model examples), as well as their relationships, commonalities and differences. This registry provides a common entry point for modelers and software developers who plan to apply the standards for their respective case of application, and serves them with detailed information and links to the standards, their specifications and APIs.

The information provided in this system does not claim to be complete or all-encompassing, nor can we guarantee any absence of defectiveness. However, we collect and assemble the information to the best of our knowledge and belief to to assist in selecting the appropriate standard format for your specific requirements. Please note that the system is work in progress and is constantly revised and extended. Any feedback and suggestions for corrections or improvements, as well as for new fields of applications to be included (with example models) are highly welcome.

Format Classes

http://normsys.h-its.org/

- Systems Biology Markup Language (SBML)
- CellML
- Systems Biology Graphical Notation (SBGN)
- Simulation Experiment Description Markup Language (SED-ML)
- Pharmacometrics Markup Language (pharmML)
- NeuroML
- FieldML
- Synthetic Biology Open Language (SBOL)

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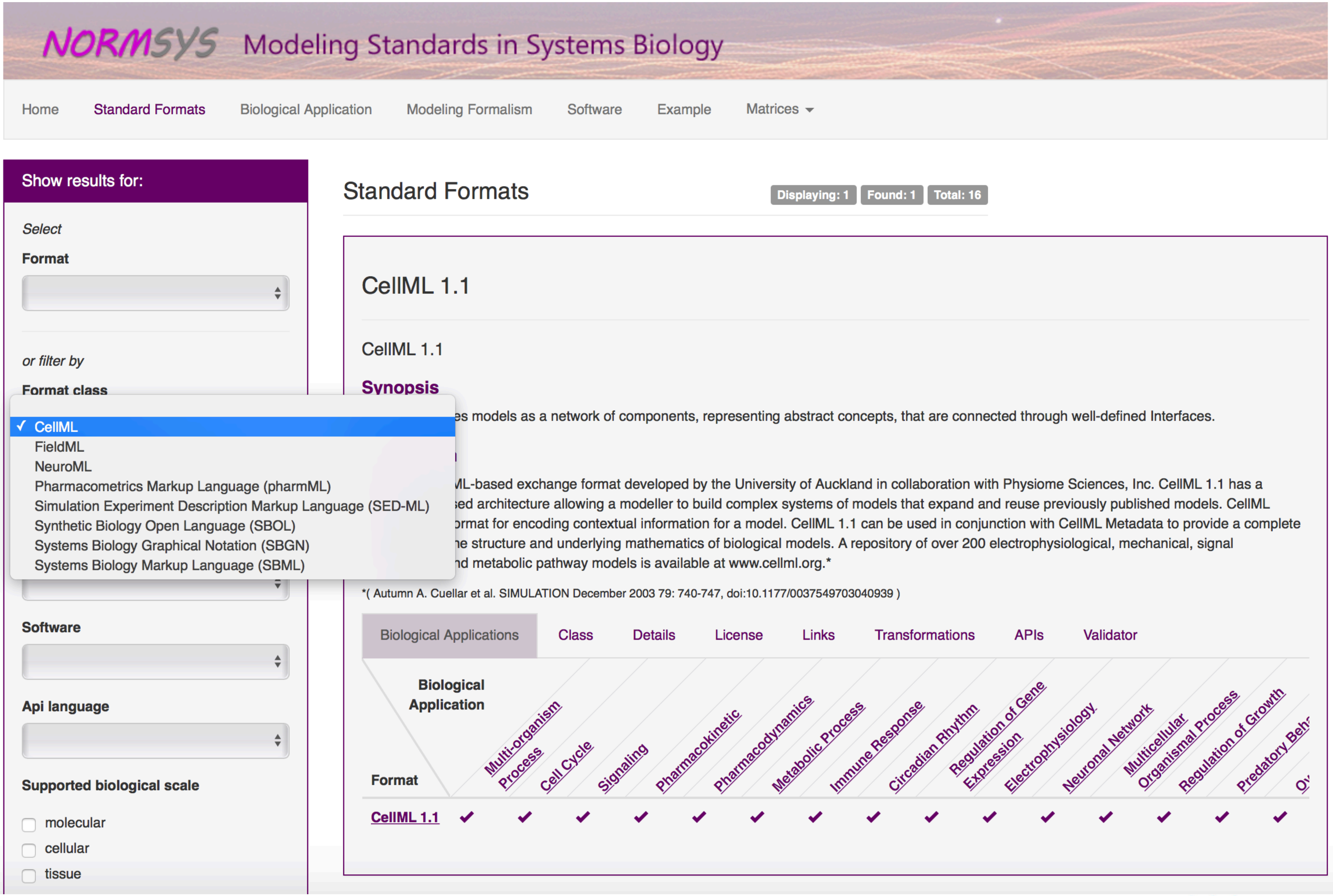


Standard Formats

CellML 1.1

CellML 1.1

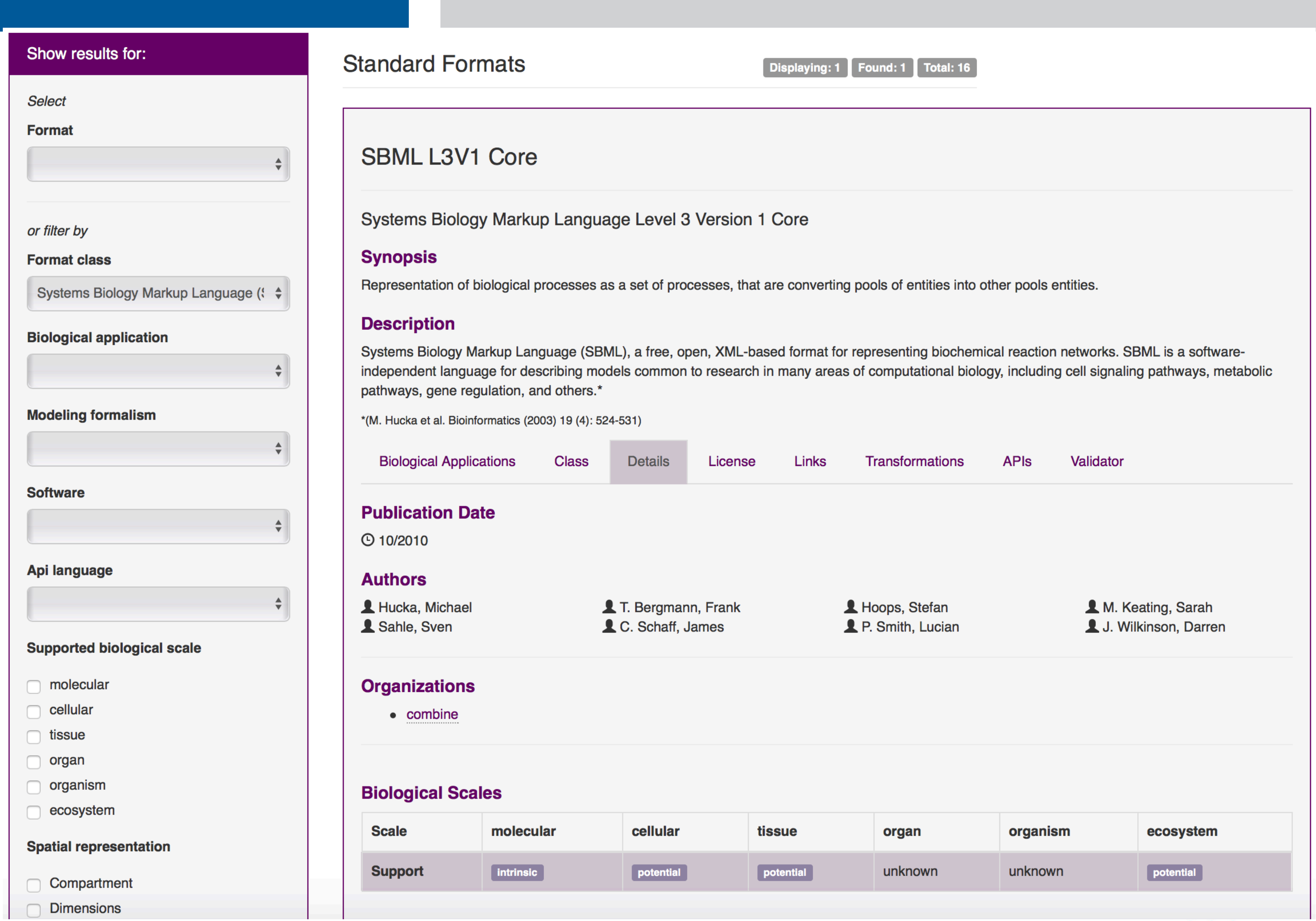
Synopsis

es models as a network of components, representing abstract concepts, that are connected through well-defined Interfaces.

ML-based exchange format developed by the University of Auckland in collaboration with Physiome Sciences, Inc. CellML 1.1 has a
sed architecture allowing a modeller to build complex systems of models that expand and reuse previously published models. CellML
ormat for encoding contextual information for a model. CellML 1.1 can be used in conjunction with CellML Metadata to provide a complete
ne structure and underlying mathematics of biological models. A repository of over 200 electrophysiological, mechanical, signal
nd metabolic pathway models is available at www.cellml.org.*

*(Autumn A. Cuellar et al. SIMULATION December 2003 79: 740-747, doi:10.1177/0037549703040939)

Biological Application / Format	Multi-organism Process	Cell Cycle	Signaling	Pharmacokinetic	Pharmacodynamics	Metabolic Process	Immune Response	Circadian Rhythm	Regulation of Gene Expression	Electrophysiology	Neuronal Network	Multicellular Organismal Process	Regulation of Growth	Predatory Beh	Ov
CellML 1.1	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓



Supported biological scale

☐ molecular
☐ cellular
☐ tissue
☐ organ
☐ organism
☐ ecosystem

Spatial representation

☐ Compartment
☐ Dimensions

Standard Formats

SBML L3V1 Core

Systems Biology Markup Language Level 3 Version 1 Core

Synopsis

Representation of biological processes as a set of processes, that are converting pools of entities into other pools entities.

Description

Systems Biology Markup Language (SBML), a free, open, XML-based format for representing biochemical reaction networks. SBML is a software-independent language for describing models common to research in many areas of computational biology, including cell signaling pathways, metabolic pathways, gene regulation, and others.*

*(M. Hucka et al. Bioinformatics (2003) 19 (4): 524-531)

Publication Date

10/2010

Authors

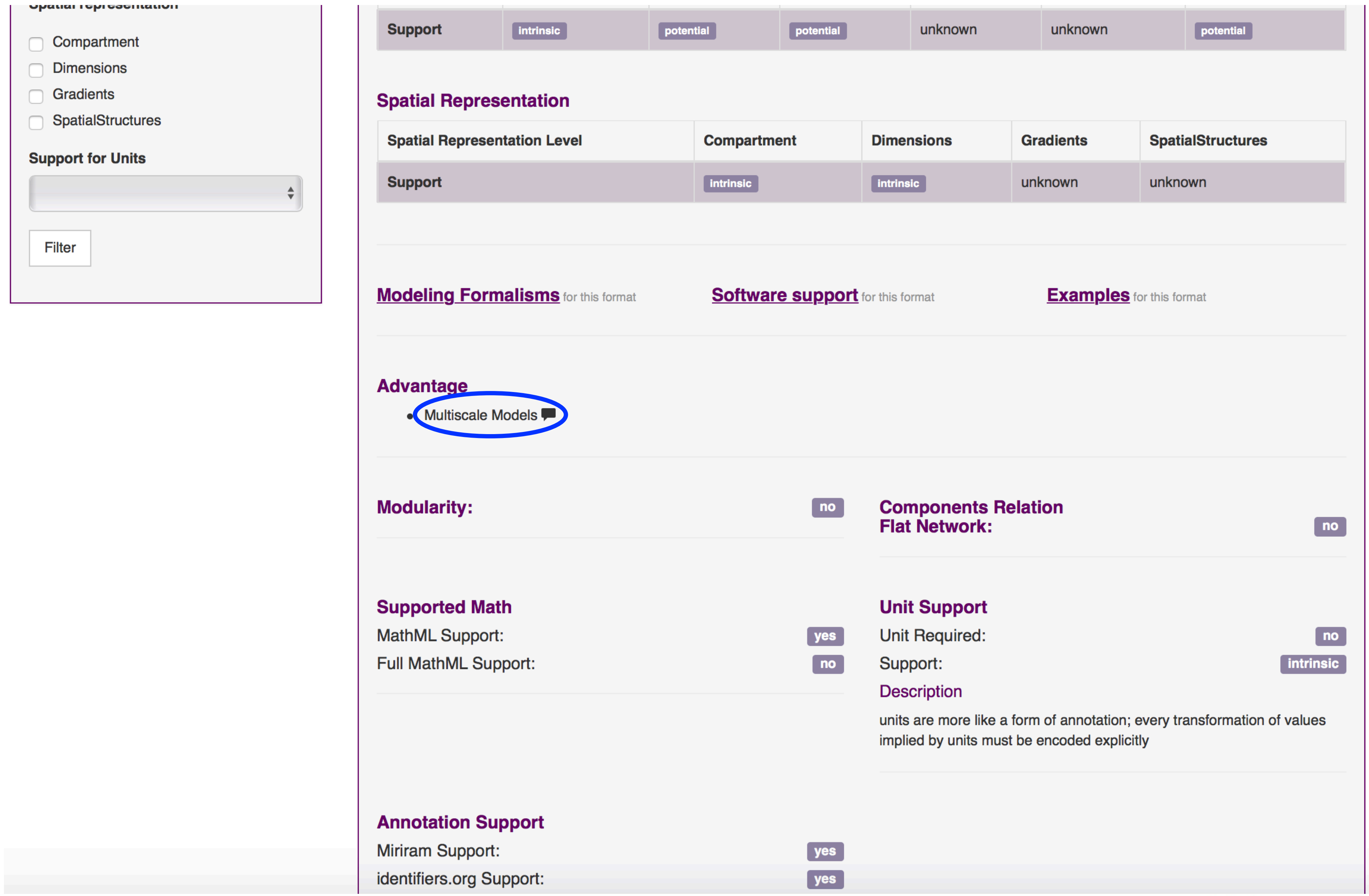
Hucka, Michael	T. Bergmann, Frank	Hoops, Stefan	M. Keating, Sarah
Sahle, Sven	C. Schaff, James	P. Smith, Lucian	J. Wilkinson, Darren

Organizations

- combine

Biological Scales

Scale	molecular	cellular	tissue	organ	organism	ecosystem
Support	intrinsic	potential	potential	unknown	unknown	potential



Spatial representation

- ☐ Compartment
- ☐ Dimensions
- ☐ Gradients
- ☐ SpatialStructures

Support for Units

Support	intrinsic	potential	potential	unknown	unknown	potential

Spatial Representation

Spatial Representation Level	Compartment	Dimensions	Gradients	SpatialStructures
Support	intrinsic	intrinsic	unknown	unknown

Modeling Formalisms for this format **Software support** for this format **Examples** for this format

Advantage

- Multiscale Models

Modularity: no

Components Relation Flat Network: no

Supported Math

MathML Support: yes

Full MathML Support: no

Unit Support

Unit Required: no

Support: intrinsic

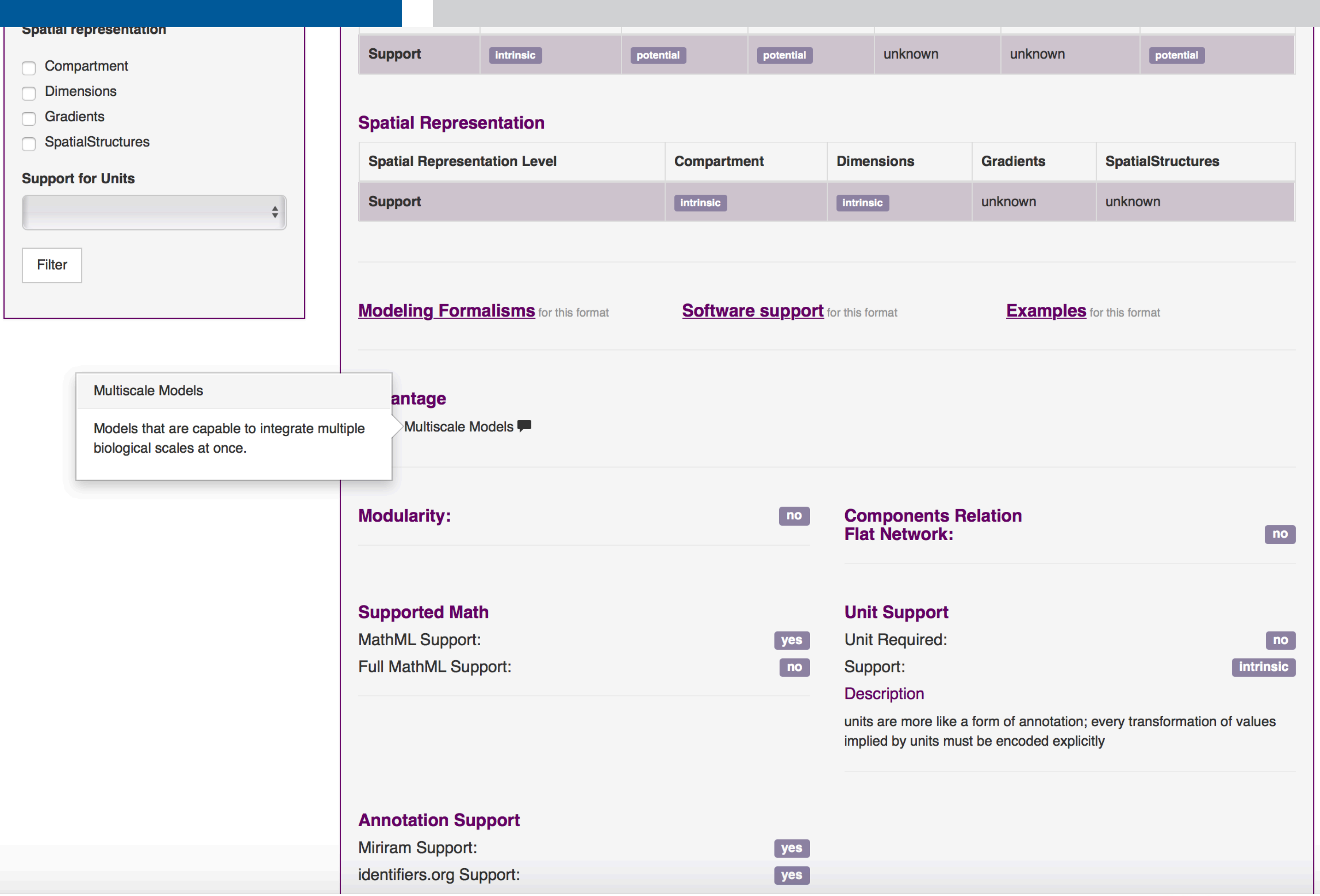
Description

units are more like a form of annotation; every transformation of values implied by units must be encoded explicitly

Annotation Support

Miriam Support: yes

identifiers.org Support: yes



Spatial representation

☐ Compartment
☐ Dimensions
☐ Gradients
☐ SpatialStructures

Support for Units

Support	intrinsic	potential	potential	unknown	unknown	potential

Spatial Representation

Spatial Representation Level	Compartment	Dimensions	Gradients	SpatialStructures
Support	intrinsic	intrinsic	unknown	unknown

Modeling Formalisms for this format **Software support** for this format **Examples** for this format

Multiscale Models

Models that are capable to integrate multiple biological scales at once.

antage

Multiscale Models

Modularity: no

Components Relation Flat Network: no

Supported Math

MathML Support:	yes
Full MathML Support:	no

Unit Support

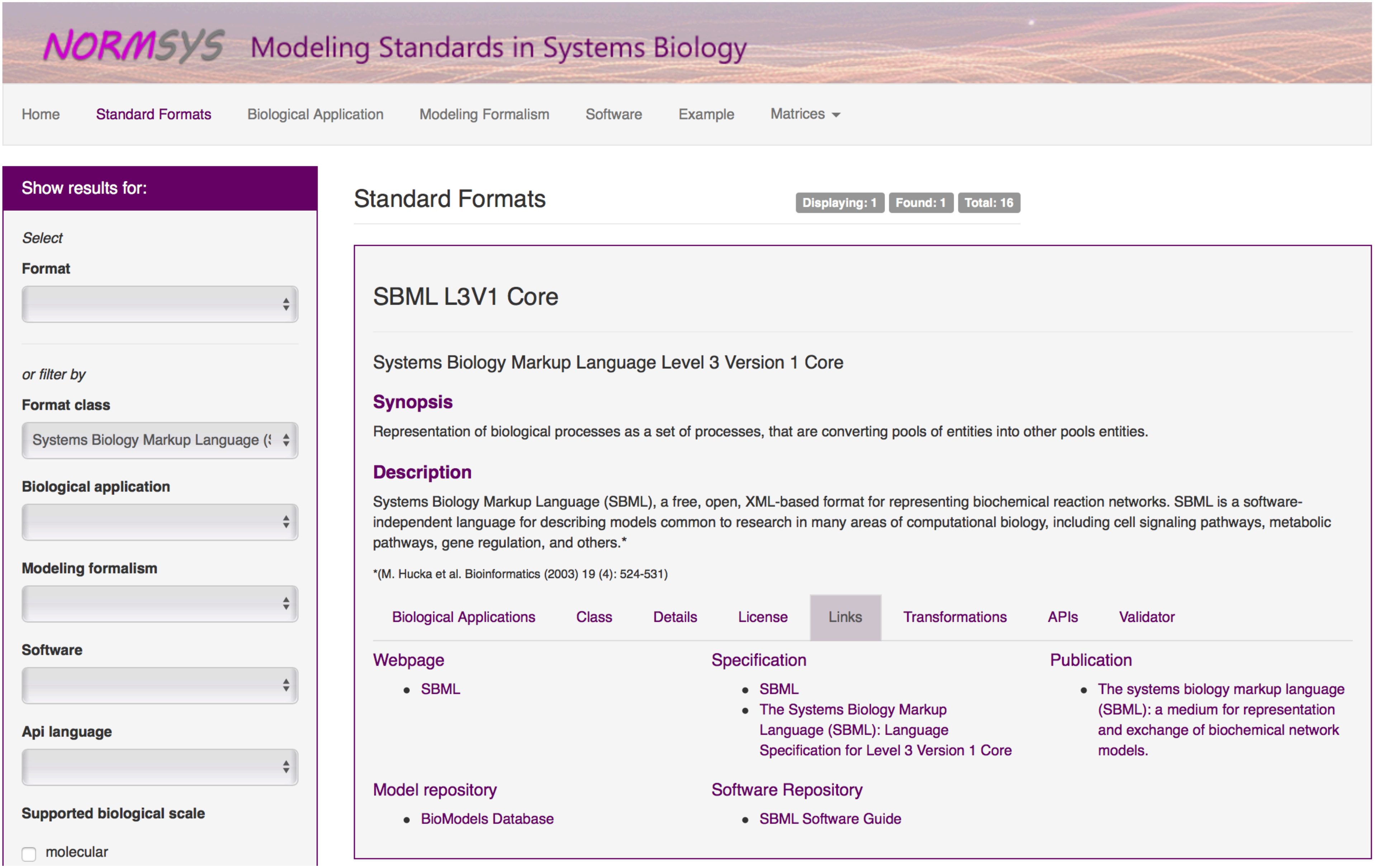
Unit Required:	no
Support:	intrinsic

Description

units are more like a form of annotation; every transformation of values implied by units must be encoded explicitly

Annotation Support

Miriram Support:	yes
identifiers.org Support:	yes



Show results for:

Select

Format

or filter by

Format class

Systems Biology Markup Language (

Biological application

Modeling formalism

Software

Api language

Supported biological scale

☐ molecular

Standard Formats

Displaying: 1 Found: 1 Total: 16

SBML L3V1 Core

Systems Biology Markup Language Level 3 Version 1 Core

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*(M. Hucka et al. Bioinformatics (2003) 19 (4): 524-531)

Webpage

- SBML

Specification

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

Publication

- The systems biology markup language (SBML): a medium for representation and exchange of biochemical network models.

Model repository

- BioModels Database

Software Repository

- SBML Software Guide

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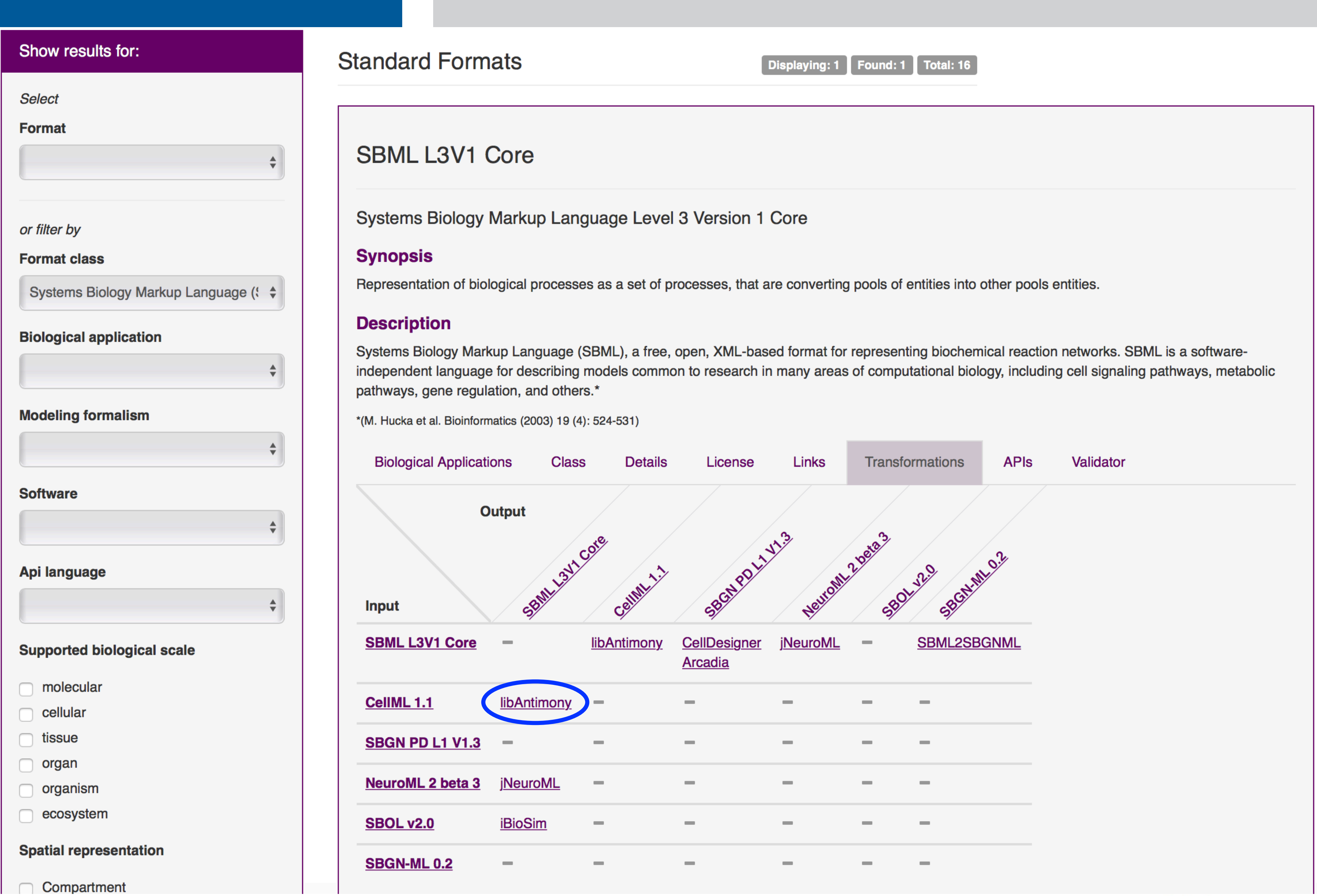

Show results for:

Select

Format

or filter by

Format class

Systems Biology Markup Language (

Biological application

Modeling formalism

Software

Api language

Supported biological scale

☐ molecular
☐ cellular
☐ tissue
☐ organ
☐ organism
☐ ecosystem

Spatial representation

☐ Compartment

Standard Formats

Displaying: 1 Found: 1 Total: 16

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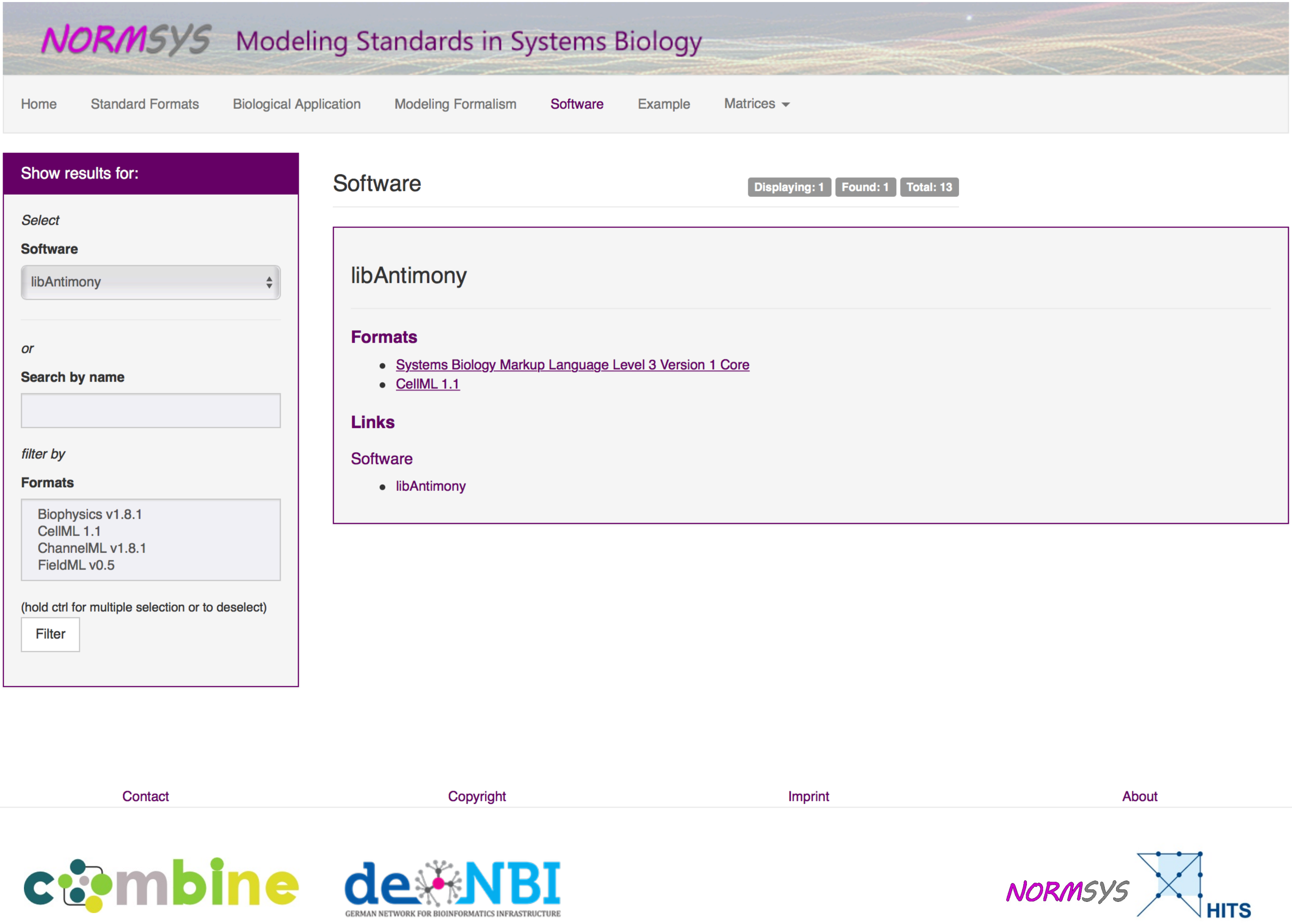
*(M. Hucka et al. Bioinformatics (2003) 19 (4): 524-531)

Input \ Output	SBML L3V1 Core	CellML 1.1	SBGN PD L1 V1.3	NeuroML 2 beta 3	SBOL v2.0	SBGN-ML 0.2
SBML L3V1 Core	–	libAntimony	CellDesigner Arcadia	jNeuroML	–	SBML2SBGNML
CellML 1.1	libAntimony	–	–	–	–	–
SBGN PD L1 V1.3	–	–	–	–	–	–
NeuroML 2 beta 3	jNeuroML	–	–	–	–	–
SBOL v2.0	iBioSim	–	–	–	–	–
SBGN-ML 0.2	–	–	–	–	–	–



Show results for:

Select

Software

libAntimony

or

Search by name

filter by

Formats

Biophysics v1.8.1
CellML 1.1
ChannelML v1.8.1
FieldML v0.5

(hold ctrl for multiple selection or to deselect)

Software

libAntimony

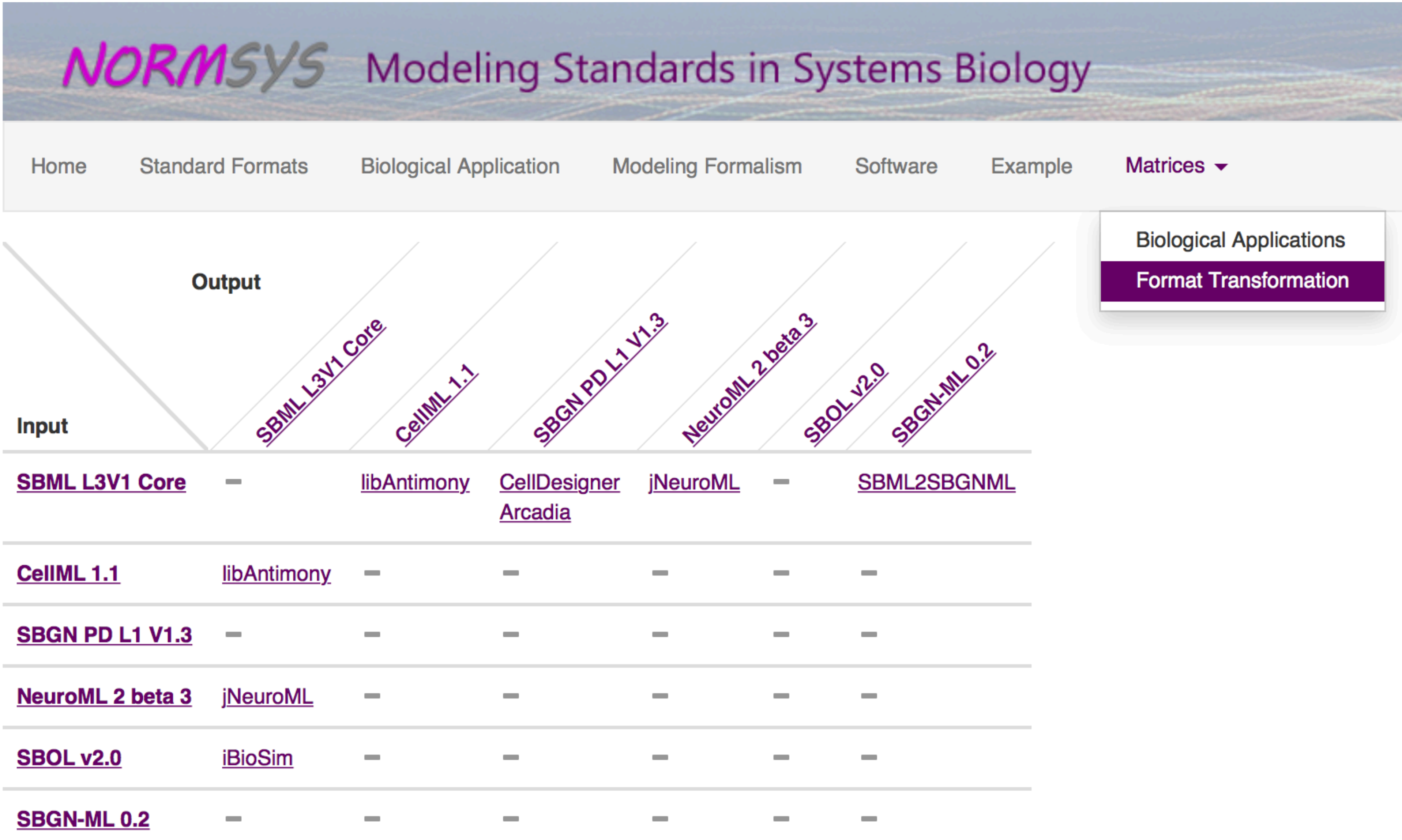
Formats

- Systems Biology Markup Language Level 3 Version 1 Core
- CellML 1.1

Links

Software

- libAntimony



Input \ Output	SBML L3V1 Core	CellML 1.1	SBGN PD L1 V1.3	NeuroML 2 beta 3	SBOL v2.0	SBGN-ML 0.2
SBML L3V1 Core	—	libAntimony	CellDesigner Arcadia	jNeuroML	—	SBML2SBGNML
CellML 1.1	libAntimony	—	—	—	—	—
SBGN PD L1 V1.3	—	—	—	—	—	—
NeuroML 2 beta 3	jNeuroML	—	—	—	—	—
SBOL v2.0	iBioSim	—	—	—	—	—
SBGN-ML 0.2	—	—	—	—	—	—

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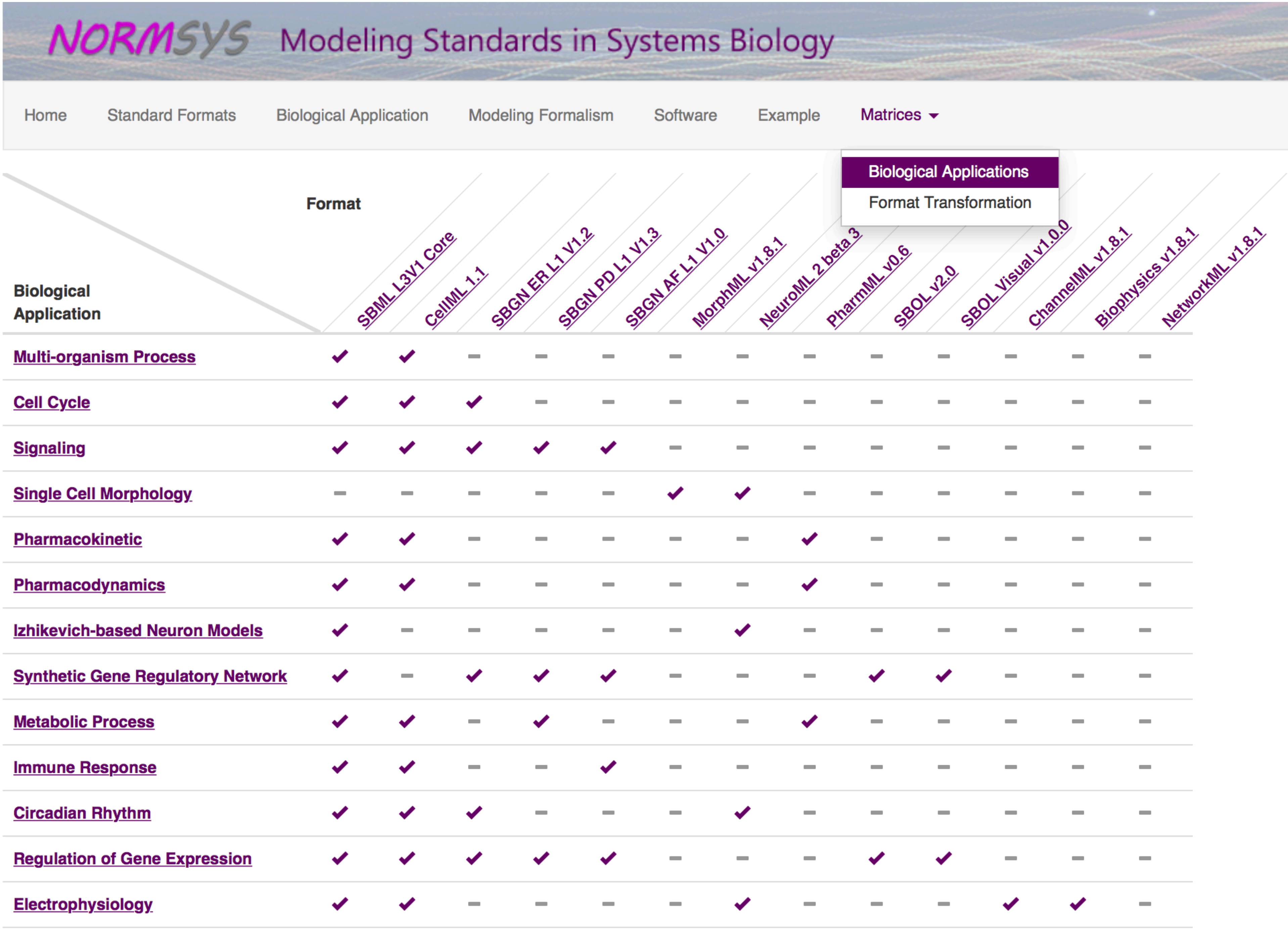
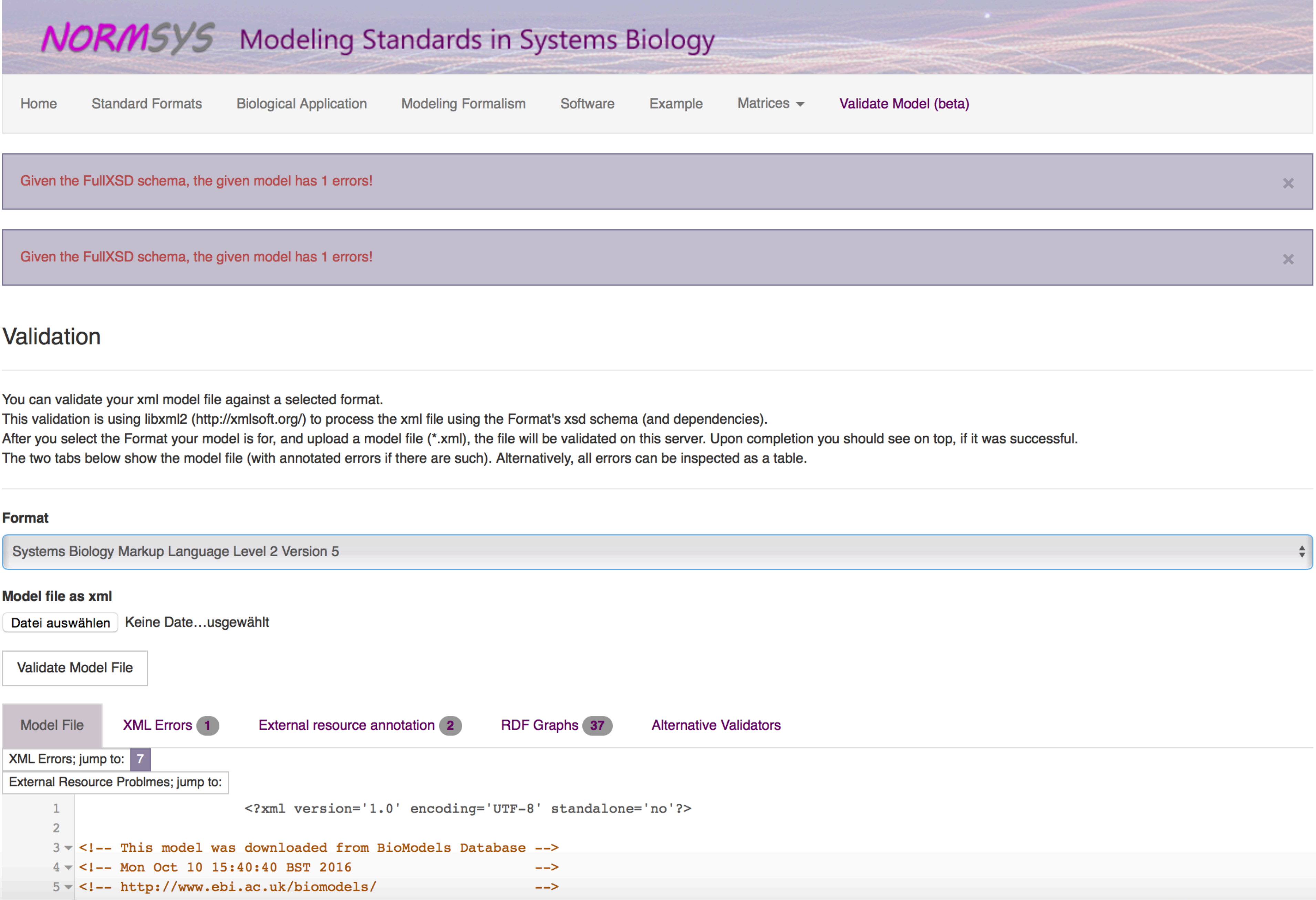


Biological Application \ Format	SBML L3V1 Core	CellML 1.1	SBGN ER L1 V1.2	SBGN PD L1 V1.3	SBGN AF L1 V1.0	MorphML v1.8.1	NeuroML 2 beta 3	PharmML v0.6	SBOL v2.0	SBOL Visual v1.0.0	ChannelML v1.8.1	Biophysics v1.8.1	NetworkML v1.8.1
Multi-organism Process	✓	✓	–	–	–	–	–	–	–	–	–	–	–
Cell Cycle	✓	✓	✓	–	–	–	–	–	–	–	–	–	–
Signaling	✓	✓	✓	✓	✓	–	–	–	–	–	–	–	–
Single Cell Morphology	–	–	–	–	–	✓	✓	–	–	–	–	–	–
Pharmacokinetic	✓	✓	–	–	–	–	–	✓	–	–	–	–	–
Pharmacodynamics	✓	✓	–	–	–	–	–	✓	–	–	–	–	–
Izhikevich-based Neuron Models	✓	–	–	–	–	–	✓	–	–	–	–	–	–
Synthetic Gene Regulatory Network	✓	–	✓	✓	✓	–	–	–	✓	✓	–	–	–
Metabolic Process	✓	✓	–	✓	–	–	–	✓	–	–	–	–	–
Immune Response	✓	✓	–	–	✓	–	–	–	–	–	–	–	–
Circadian Rhythm	✓	✓	✓	–	–	–	✓	–	–	–	–	–	–
Regulation of Gene Expression	✓	✓	✓	✓	✓	–	–	–	✓	✓	–	–	–
Electrophysiology	✓	✓	–	–	–	–	✓	–	–	–	✓	✓	–



Given the FullXSD schema, the given model has 1 errors!

Given the FullXSD schema, the given model has 1 errors!

Validation

You can validate your xml model file against a selected format.
This validation is using libxml2 (http://xmlsoft.org/) to process the xml file using the Format's xsd schema (and dependencies).
After you select the Format your model is for, and upload a model file (*.xml), the file will be validated on this server. Upon completion you should see on top, if it was successful.
The two tabs below show the model file (with annotated errors if there are such). Alternatively, all errors can be inspected as a table.

Format

Systems Biology Markup Language Level 2 Version 5

Model file as xml

```
<?xml version='1.0' encoding='UTF-8' standalone='no'?>

<!-- This model was downloaded from BioModels Database -->
<!-- Mon Oct 10 15:40:40 BST 2016                      -->
<!-- http://www.ebi.ac.uk/biomodels/                   -->
```

https://normsys.h-its.org/validate

NormSys Registry for Modelling Standards

- **Information** resource for community standards
- **Comparison** of their main characteristics and features
- **Classification** by fields of application (with examples)
- **Transformation** options between the standards
- **Bundled links** to corresponding web resources: specifications, websites, publications, repositories, APIs...
- **Faceted browsing** and search by different criteria
- **Validation** of models for several standards
- COMBINE standards and related efforts (for a start)

HITS

Universität Potsdam

LifeGlimmer GmbH

http://normsys.h-its.org/

Supported by:
Federal Ministry for Economic Affairs and Energy

NORMSYS

Heidelberg Institute for Theoretical Studies

HITS

http://normsys.h-its.org/

Concept & project lead: Martin Golebiewski
Design: Jill Zander
Implementation: Nils Wötzel
Content: Martin Golebiewski, Alexander Nikolaew

Collaboration partners:
Susanne Hollmann & Bernd Müller-Röber (University of Potsdam, D)
Babette Regierer (LifeGlimmer GmbH, Berlin, D)

ISO DIN combine

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for Economic Affairs
and Energy

Need for a meta-standard for standards

Example: Great Baltimore fire of 1904

Individual fire hydrants depending on region with 600 variations of hose couplings
→ Need for a standard for general interfaces