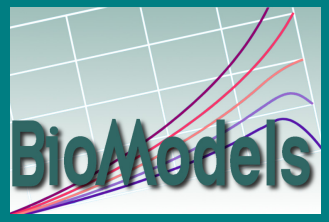
BioModels Database, a public model-sharing resource

The 11th International Conference on Systems Biology (ICSB)
Edinburgh.
10th October 2010.

Lukas Endler and Vijayalakshmi Chelliah



EMBL-EBI

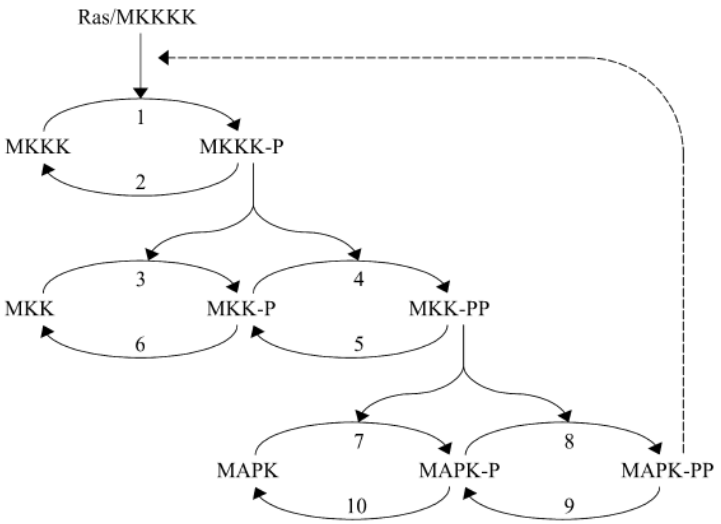


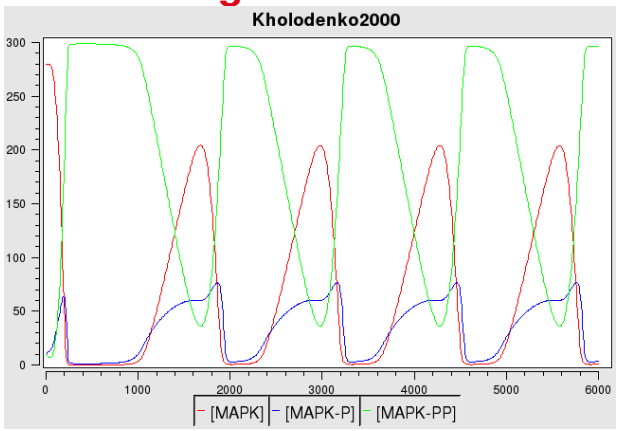
Table 2. Rate equations and parameter values of the MAPK cascade model. Concentrations and the Michaelis constants (K_1–K_{10}) are given in nM. The catalytic rate constants (k_3, k_4, k_7, k_8) and the maximal enzyme rates (V_1, V_2, V_5, V_6, V_9, V_{10}) are expressed in s^{-1} and nM·s^{-1}, respectively.

Reaction number	Rate equation	Parameter values
1	$V_1 \cdot [MKKK]/((1 + ([MAPK\text{-}PP]/K_I)^n) \cdot (K_1 + [MKKK]))$	$V_1 = 2.5$; $n = 1$; $K_I = 9$; $K_1 = 10$;
2	$V_2 \cdot [MKKK\text{-}P]/(K_2 + [MKKK\text{-}P])$	$V_2 = 0.25$; $K_2 = 8$;
3	$k_3 \cdot [MKKK\text{-}P] \cdot [MKK]/(K_3 + [MKK])$	$k_3 = 0.025$; $K_3 = 15$;
4	$k_4 \cdot [MKKK\text{-}P] \cdot [MKK\text{-}P]/(K_4 + [MKK\text{-}P])$	$k_4 = 0.025$; $K_4 = 15$;
5	$V_5 \cdot [MKK\text{-}PP]/(K_5 + [MKK\text{-}PP])$	$V_5 = 0.75$; $K_5 = 15$;
6	$V_6 \cdot [MKK\text{-}P]/(K_6 + [MKK\text{-}P])$	$V_6 = 0.75$; $K_6 = 15$;
7	$k_7 \cdot [MKK\text{-}PP] \cdot [MAPK]/(K_7 + [MAPK])$	$k_7 = 0.025$; $K_7 = 15$;
8	$k_8 \cdot [MKK\text{-}PP] \cdot [MAPK\text{-}P]/(K_8 + [MAPK\text{-}P])$	$k_8 = 0.025$; $K_8 = 15$;
9	$V_9 \cdot [MAPK\text{-}PP]/(K_9 + [MAPK\text{-}PP])$	$V_9 = 0.5$; $K_9 = 15$;
10	$V_{10} \cdot [MAPK\text{-}P]/(K_{10} + [MAPK\text{-}P])$	$V_{10} = 0.5$; $K_{10} = 15$;

Total concentrations: $[MKKK]_{total} = 100$; $[MKK]_{total} = 300$; $[MAPK]_{total} = 300$

output

eg. time course



computer readable format, eg.

SBML

simulation software eg. Copasi

Kholodenko, *Eur J Biochem* (2000) 267: 1583-1588.

Repository of models: motivation & requirement

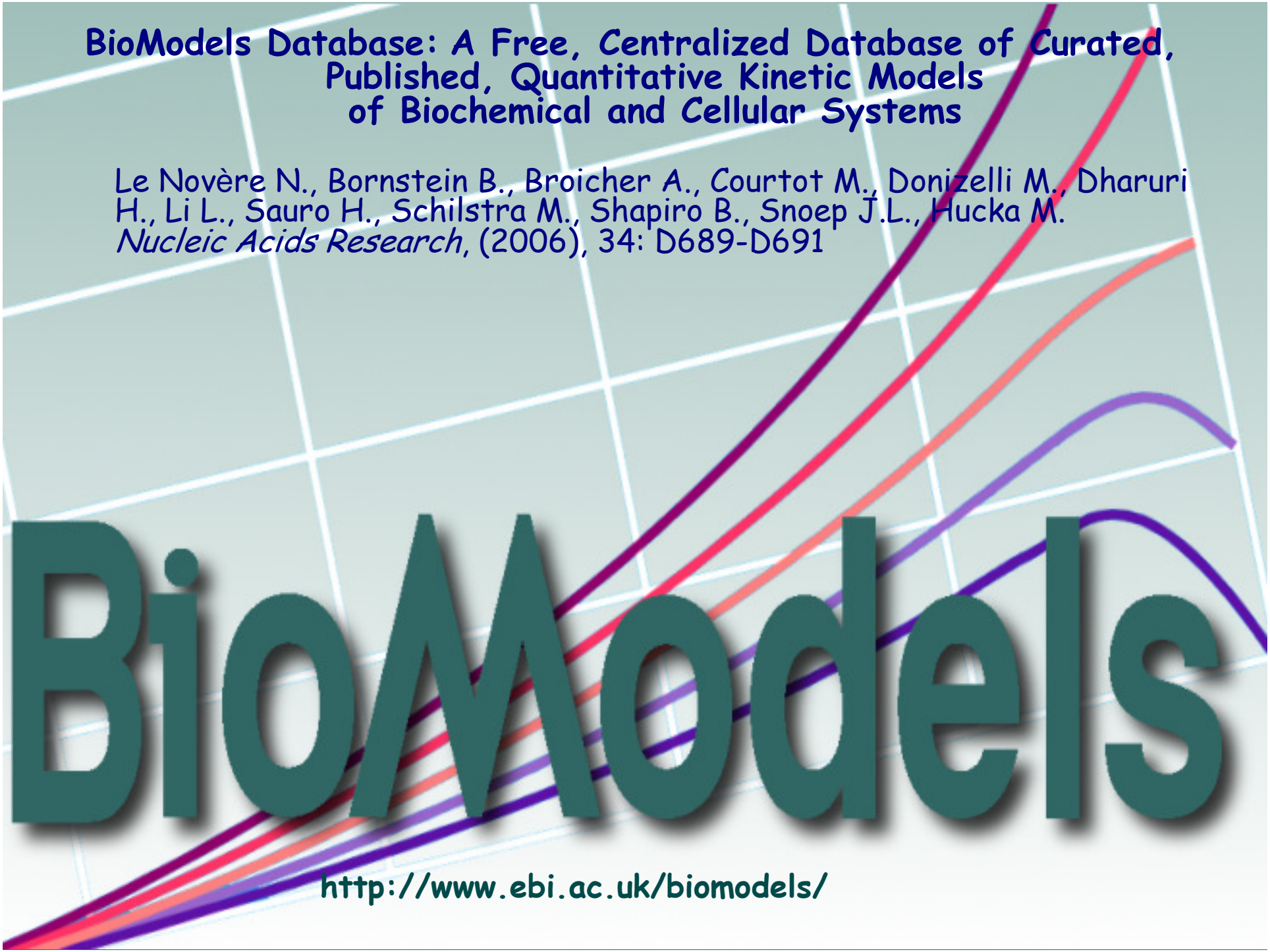
- both number and complexity of quantitative models in biology are increasing rapidly.
- modelers increasingly reuse and combine existing models. It often becomes impractical to reimplement models from literature.

- For easy and efficient use of the already published models, models

  - should be accessible.
  - source and detailed description of each model should be available and linked.
  - the modeller must be able to rely on the accuracy of the models.
  - the models should be available in common formats
    (eg.:SBML (http://www.sbml.org),
    CellML (http://www.cellml.org)
  - should be searchable for different criteria.
  - the structure and the components of the model should be browsable and identifiable.

BioModels Database: A Free, Centralized Database of Curated, Published, Quantitative Kinetic Models of Biochemical and Cellular Systems

Le Novère N., Bornstein B., Broicher A., Courtot M., Donizelli M., Dharuri H., Li L., Sauro H., Schilstra M., Shapiro B., Snoep J.L., Hucka M.
Nucleic Acids Research, (2006), 34: D689-D691

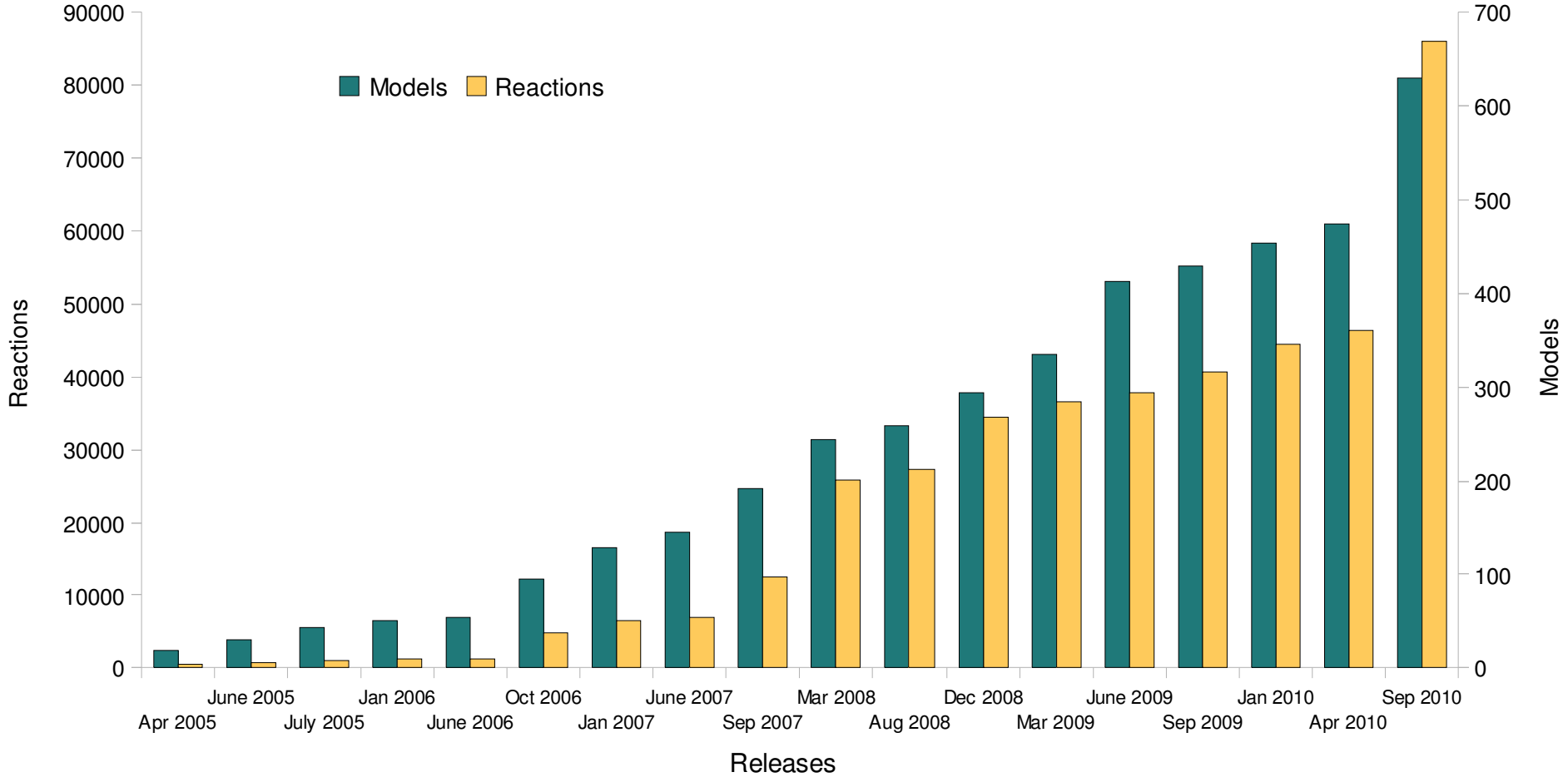


http://www.ebi.ac.uk/biomodels/

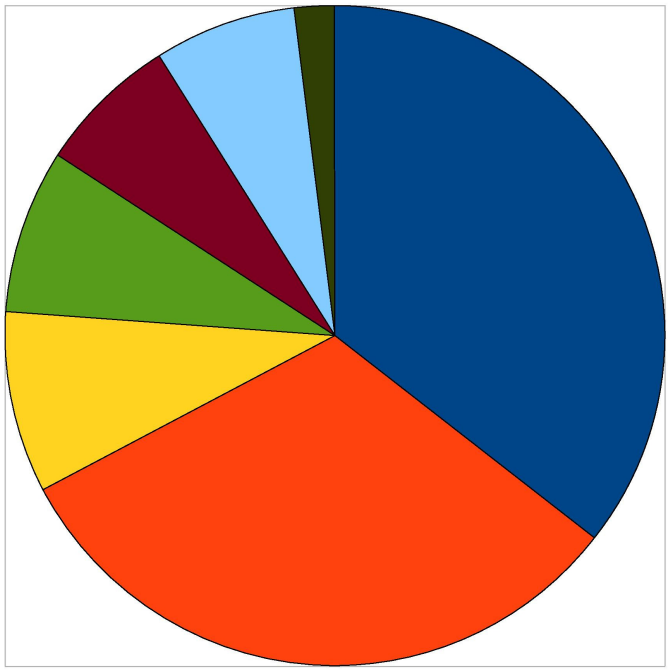
BioModels Database

- first launched on 11th April 2005.
- data resource that allows biologists to store and serve quantitative models of biomedical interest.
- stores only models described in the peer-reviewed scientific literature.
- Models are annotated and linked to relevant data resources, such as publications, databases of compounds and pathways, etc. to improve identification and retrieval.
- Models are accepted in several formats and served in several others.
- Partial/Sub models can be created and downloaded.
- online simulation available.

Database Growth

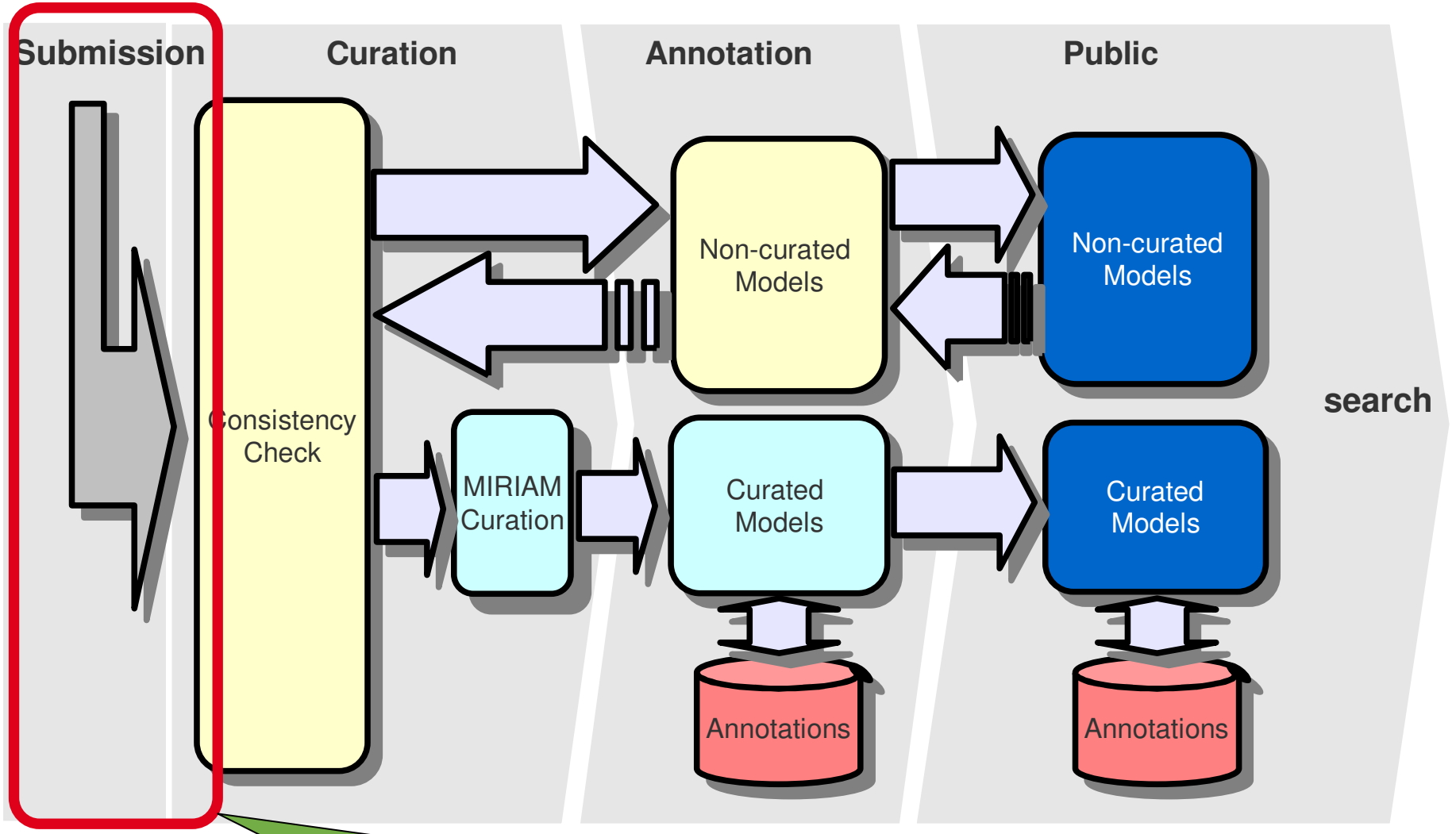


Types of Models in the BioModels Database



- cellular metabolic process (GO:0044237, wo. translation & transcription)
- signal transduction (GO:0007165)
- cell cycle (GO:0007049)
- circadian rhythm (GO:0007623)
- cytosolic calcium ion homeostasis (GO:0051480)
- transmission of nerve impulse (GO:0019226)
- cell differentiation (GO:0030154)

Production pipeline



Where do models come from?

- submitted by curators
  - imported from other repositories (DOQCS, CellML, JWS)
  - reimplemented from literature
  - imported from journals webpages
- from authors before grant application or publication
  - some journals advocate submission to BioModels DB:
  - Molecular Systems Biology
  - PLoS journals
  - BioMedCentral journals
- various people who are interested.

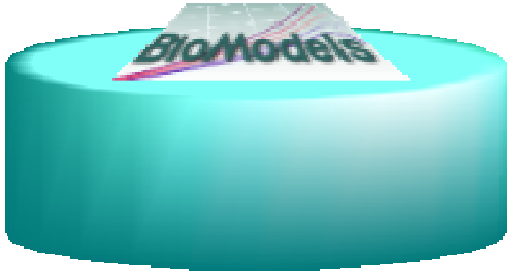
Model Format

Level 1 Version 1
Level 1 Version 2
Level 2 Version 1
Level 2 Version 3
Level 2 Version 4

Level 2 Version 1
Level 2 Version 2
Level 2 Version 3
Level 2 Version 4

Temporarily unavailable

Version 1.1



XPP-Aut

Scilab

Version 1.0
Version 1.1

VCell

BioPAX

Octave

SBML.org

The Systems Biology Markup Language

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Google Site Search...

The **Systems Biology Markup Language** (**SBML**) is a computer-readable format for representing models of biochemical reaction networks in software. It's applicable to models of metabolism, cell-signaling, and many others. SBML has been evolving since mid-2000 thanks to an international community of software developers and users. This website is the portal for the global SBML development effort; here you can find information about all aspects of SBML.

For the curious

What *is* SBML? Read our basic introduction and then perhaps browse the mailing lists to get a sense for what's currently going on in the world of SBML.

For modelers

Are you looking for ready-to-run software that supports SBML? Take a look at the SBML Software Guide, which lists over **160** software packages. Are you instead looking for ready-to-use models? Visit the BioModels Database, where you can find hundreds!

For software developers

you interested in developing SBML support for your software?
d our basic introduction and then the SBML specifications to
lerstand how to use SBML. After that, you may want to look at
BML, an API library supporting many programming languages.

SBML as a modeler or a developer, we invite you to sign up for
ther through our **RSS feed** or one of the mailing lists, and get
mmunity efforts to help keep SBML improving. You can also call
project's support of SBML by displaying the SBML logo.

SBML News

SBML tools list reaches 160
(27 Apr. '09) The number of tools listed in the SBML Software Guide has reached 160!

LibSBML 4.0.0 beta!
(17 Mar.'09) LibSBML is an API library for SBML. Version 4.0.0's API changes make it harder to create invalid SBML.

LibSBML 3.3.2 released!
(3 Mar.'09) LibSBML is an API library for SBML. The new release fixes bugs and a memory leak in 3.3.1.

Older news ...

Community News

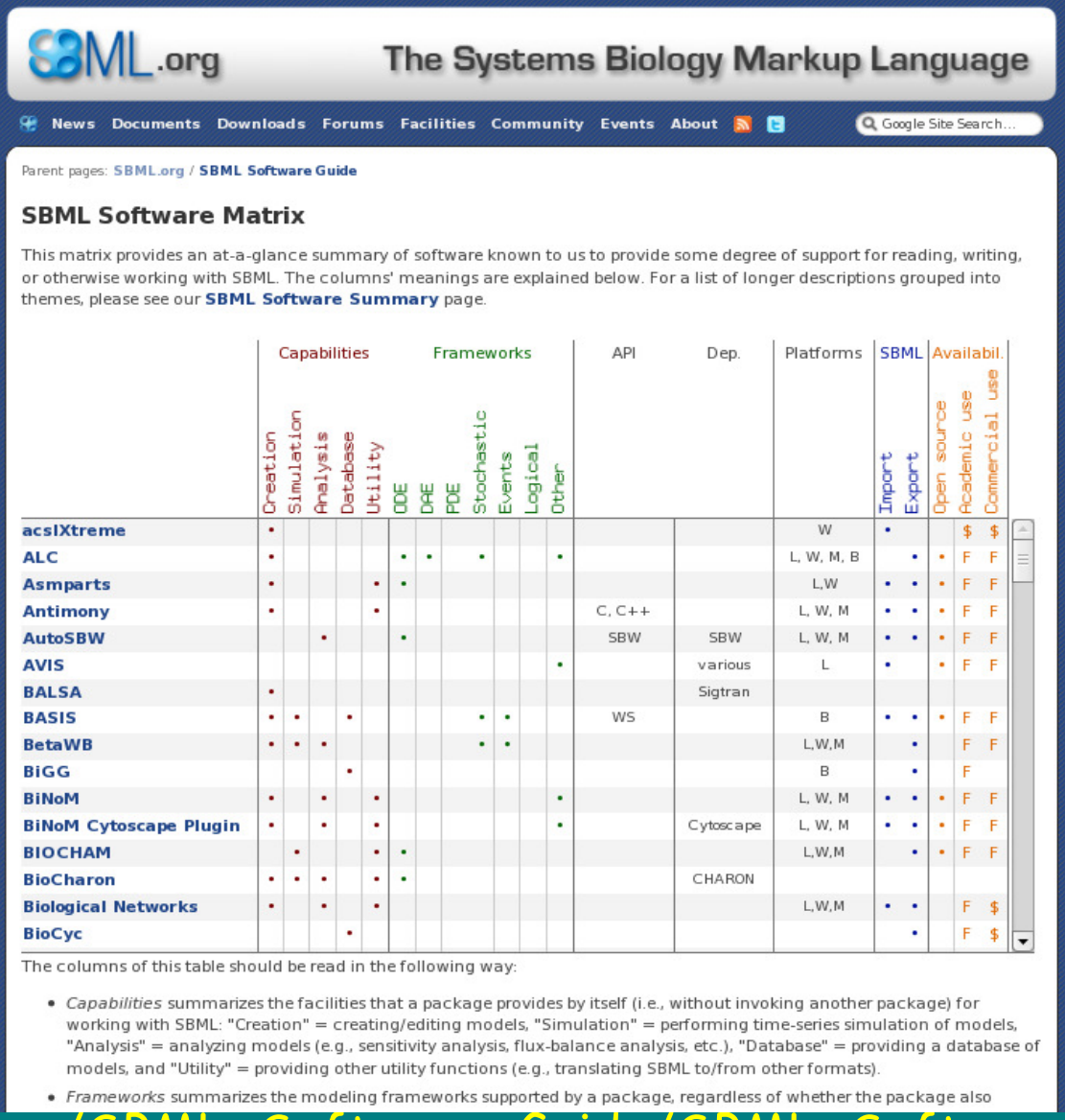
MCSim supports SBML
(25 Apr.'09) **GNU MCSim** lets you design statistical or simulation models and efficiently perform Bayesian inference.

Pathway Tools workshop
(24 Apr.'09) A tutorial & workshop on SRI's Pathway Tools and BioCyc Database Collection will take place in August '09.

Cain 0.12 released
(23 Apr.'09) **Cain** is a stochastic simulator with highly efficient implementations of many methods.

Older news ...

>180tools support SBML



SBML.org — The Systems Biology Markup Language

News Documents Downloads Forums Facilities Community Events About

Google Site Search...

Parent pages: SBML.org / SBML Software Guide

SBML Software Matrix

This matrix provides an at-a-glance summary of software known to us to provide some degree of support for reading, writing, or otherwise working with SBML. The columns' meanings are explained below. For a list of longer descriptions grouped into themes, please see our **SBML Software Summary** page.

	Capabilities					Frameworks							API	Dep.	Platforms	SBML		Availabil.		
	Creation	Simulation	Analysis	Database	Utility	ODE	DAE	PDE	Stochastic	Events	Logical	Other				Import	Export	Open source	Academic use	Commercial use
acslXtreme	•														W	•			$	$
ALC	•					•	•		•			•			L, W, M, B		•	•	F	F
Asmparts	•				•	•									L,W	•	•	•	F	F
Antimony	•				•								C, C++		L, W, M	•	•	•	F	F
AutoSBW			•			•							SBW	SBW	L, W, M	•	•	•	F	F
AVIS												•		various	L	•		•	F	F
BALSA	•													Sigtran						
BASIS	•	•		•					•	•			WS		B	•	•	•	F	F
BetaWB	•	•	•						•	•					L,W,M		•		F	F
BiGG				•											B		•		F	
BiNoM	•		•		•							•			L, W, M	•	•	•	F	F
BiNoM Cytoscape Plugin	•		•		•							•		Cytoscape	L, W, M	•	•	•	F	F
BIOCHAM		•			•	•									L,W,M		•	•	F	F
BioCharon	•	•	•		•	•								CHARON						
Biological Networks	•		•		•										L,W,M	•	•		F	$
BioCyc				•													•		F	$

The columns of this table should be read in the following way:

- *Capabilities* summarizes the facilities that a package provides by itself (i.e., without invoking another package) for working with SBML: "Creation" = creating/editing models, "Simulation" = performing time-series simulation of models, "Analysis" = analyzing models (e.g., sensitivity analysis, flux-balance analysis, etc.), "Database" = providing a database of models, and "Utility" = providing other utility functions (e.g., translating SBML to/from other formats).
- *Frameworks* summarizes the modeling frameworks supported by a package, regardless of whether the package also

http://sbml.org/SBML_Software_Guide/SBML_Software_Matrix

EMBL-EBI

http://www.ebi.ac.uk/biomodels/

EMBL-EBI | EB-eye Search | All Databases | Enter Text Here | Go | Reset | Advanced Search | Give us feedback

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BioModels Home | Models | Submit | Support | About BioModels | Contact us

BioModels Database - A Database of Annotated Published Models

BioModels Database is a data resource that allows biologists to store, search and retrieve published mathematical models of biological interests. Models present in BioModels Database are annotated and linked to relevant data resources, such as publications, databases of compounds and controlled vocabularies.
BioModels Database also allows users to generate sub-models, provides access to online simulation tools and features programmatic access via Web Services.

Search | Go to the model | Advanced search

Browse models

- Curated models (269)
- Browse models using GO
- Non-curated models (361)

Simulate in JWS Online

Submit a model

Main instance at European Bioinformatics Institute http://www.ebi.ac.uk/biomodels/

Mirror at California Institute of Technology http://biomodels.caltech.edu

BioModels AT SourceForge http://sourceforge.net/projects/biomodels/

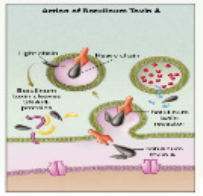
Web Services http://www.ebi.ac.uk/biomodels-main/webservices

Download archived models http://www.ebi.ac.uk/biomodels/models-main/tars/

Model of the month

August, 2010

Botulinum neurotoxin serotype A (BoNT/A) causes flaccid paralysis by a multi-step mechanisim. Two mathematical models that has been developed, to estimate upper limits of the time during which antitoxin and other impermeable inhibitors of BoNT/A can exert an effect, is described here.
Read more...



News

30 September 2010 **Eighteenth Release!**
Download All Models Under SBML Format

29 June 2010 **New BioModels Database publication**
New BioModels Database paper published in *BMC Systems Biology*: BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models.

2nd June 2010 **SBML to VCML converter updated**
The Virtual Cell recently released a new version of the SBML to VCML converter...

EMBL-EBI

Submit - Step 1

You can submit here models to be included in the BioModels Database. The following formats are currently accepted:

- SBML Level 2 Version 3
- SBML Level 2 Version 2
- SBML Level 2 Version 1
- SBML Level 1 Version 2
- SBML Level 1 Version 1
- CellML 1.1
- CellML 1.0

If you wish to submit a model under a different format, please contact us.

The submitted models will not be incorporated into the BioModels Database straightaway, since they have to undergo a curation phase before. During this curation phase, the models will be first converted to the *SBML Level 2 Version 3* format in case they were submitted under a different format, and then tested to verify that they both are consistent and reproduce the results published in the respective reference publication. To actually facilitate this curation phase, prior to submitting a model, please do the following:

- Enter all the relevant information you believe is necessary for the curation (Relation between the model and publication, modifications or clarifications of the model, etc.) either directly into the model file if possible (for example using the *notes* elements if your model is under one of the *SBML* formats), or into the *Curation comment* text field provided by the form in step 3.
- If you created the model, or collaborated to its creation, and you are not an author of the reference publication, add to the *model* element a *dc:creator* annotation containing your data (first and last name, organisation, email), so that your contribution can be acknowledged. Click here to view an example of a *dc:creator* annotation which you can re-use (skip blue part if already present).
- Choose a meaningful value for the attribute *name* of the *model* element. Examples of good model names are *NameAuthorYear_Topic_Method*, *Levchenko2000_MAPK_noScaffold* or *Edelstein1996_EPSP_AChEvent*.
- Check the validity of the model (for example by using this online validator if your model is under one of the *SBML* formats). All the models undergo a primary XML validity check upon submission anyway, and, as mentioned before, a more thorough testing during the curation phase, but an already valid model is of great help nevertheless!

Thanks a lot for your contribution to the BioModels Database!

Please enter the ID of the reference publication associated with the model, and then click *Continue*, if unpublished the ID is optional.

Publication ID: 1831270 (•) **PubMed** (Search Medline) ( ) **DOI** (Resolve a DOI) ( ) **URL** ( ) **Unpublished**

Continue Reset

Submit - Step 2

Below is the summary for the publication with PubMed ID:

1831270

If the publication summary is not what you expected, click *Back* to enter a different PubMed ID.

Otherwise click *Continue* to go on submitting the model to the curation phase.

Click *Cancel* to return to the models submission page.

Proc Natl Acad Sci U S A 1991 Aug;88(16):7328-32.

Modeling the cell division cycle: cdc2 and cyclin interactions.

Tyson JJ.

Department of Biology, Virginia Polytechnic Institute and State University, Blacksburg 24061.

The proteins cdc2 and cyclin form a heterodimer (maturation promoting factor) that controls the major events of the cell cycle. A mathematical model for the interactions of cdc2 and cyclin is constructed. Simulation and analysis of the model show that the control system can operate in three modes: as a steady state with high maturation promoting factor activity, as a spontaneous oscillator, or as an excitable switch. We associate the steady state with metaphase arrest in unfertilized eggs, the spontaneous oscillations with rapid division cycles in early embryos, and the excitable switch with growth-controlled division cycles typical of nonembryonic cells.

Back Continue Cancel

Submit - Step 3

You can submit here models to be included in the BioModels Database. The following formats are currently accepted:

- SBML Level 2 Version 3
- SBML Level 2 Version 2
- SBML Level 2 Version 1
- SBML Level 1 Version 2
- SBML Level 1 Version 1
- CellML 1.1
- CellML 1.0

If you wish to submit a model under a different format, please contact us.

The submitted models will not be incorporated into the BioModels Database straightaway, since they have to undergo a curation phase before. During this curation phase, the models will be first converted to the *SBML Level 2 Version 3* format in case they were submitted under a different format, and then tested to verify that they both are consistent and reproduce the results published in the respective reference publication. To actually facilitate this curation phase, prior to submitting a model, please do the following:

- Enter all the relevant information you believe is necessary for the curation (reference publication, modifications or clarifications of the model, etc.) either directly into the model file if allowed (for example using the *notes* elements if your model is under one of the *SBML* formats), or into the *Curation comment* text field provided by the form below.
- If you created the model, or collaborated to its creation, and you are not an author of the reference publication, add to the *model* element a *dc:creator* annotation containing your data (first and last name, organisation, email), so that your contribution can be acknowledged. Click here to view an example of a *dc:creator* annotation which you can re-use (skip blue part if already present).
- Choose a meaningful value for the attribute *name* of the *model* element. Examples of good model names are *NameAuthorYear_Topic_Method*, *Levchenko2000_MAPK_noScaffold* or *Edelstein1996_EPSP_AChEvent*.
- Check the validity of the model (for example by using this online validator if your model is under one of the *SBML* formats). All the models undergo a primary XML validity check upon submission anyway, and, as mentioned before, a more thorough testing during the curation phase, but an already valid model is of great help nevertheless!
- If the model was not created directly in SBML, or if it requires a specific software to be simulated adequately, please enter in the *Original Model* form a URL pointing to the model in the original repository. Refrain from entering a generic URL to the repository itself.

Please enter your personal details and any comment useful for thecuration step (underlined fields are required), and then click *Submit*.

First name: Vijayalakshmi

Last name: Chelliah

Organisation: EBI-EMBL

Email: viji@ebi.ac.uk

Comment: Cell division cycle xxxxxxx.....

Original model:

Model file: /automount/nas10b_vol-vol1-homes/viji/work_viji/biomodels/model5/cellcycle.xml Browse...

Submit Reset

Submit - Step 4

Dear **Vijayalakshmi**, your request to submit the model contained within the file:

cellcycle.xml

and with name:

Tyson1991_CellCycle_6variable

has been successfully completed.

The model has been assigned the unique ID:

MODEL8232600906

Submit Another Model

model accession ID is unique and perennial and can be used as a reference in publications and for searching and retrieving the model

Subject: BioModels Database - Notification of New Model Submission
From: biomodels-database-mailer@ebi.ac.uk
Date: 09:30
To: viji@ebi.ac.uk

PLEASE DO NOT REPLY TO THIS EMAIL

Dear submitter,

Thank you for submitting the model Tyson1991_CellCycle_6variable, published in

Proc Natl Acad Sci U S A 1991 Aug;88(16):7328-32.
Modeling the cell division cycle: cdc2 and cyclin interactions.
Tyson JJ.

The model is now in the process pipeline with the unique accession MODEL8232600906. This identifier is unique and can be used, for instance in scientific publications or grant applications. Our team of curators will now verify the syntax and the semantic of the model. You will be notified when this is done and the model enters the annotation phase.

We welcome any updates, comments, or other notices about this or any other models. Please feel free to contact us at:

The BioModels Database team
Computational Neurobiology
EMBL-EBI
Wellcome-Trust Genome Campus
Hinxton Cambridge
CB10 1SD
United-Kingdom

E-mail: biomodels-cura AT ebi.ac.uk

Tel: +44 (0)1223 494521
Fax: +44 (0)1223 494468

Thank you,
The BioModels Database Team

BioModels Database is developed in collaboration by the teams of Nicolas Le Novère (EMBL-EBI, United-Kingdom), Michael Hucka (SBML Team, Caltech, USA), Herbert Sauro (Keck Graduate Institute, USA) and Jacky Snoep (JWS Online, Stellenbosch University, ZA), as part of the BioModels.net initiative. BioModels Database development is funded by the European Molecular Biology Laboratory and the National Institute of General Medical Sciences.

Please quote the reference publication associated with the model, when quoting a model present in the BioModels Database.

Cell

Theory

Ligand-Specific c-Fos Expression Emerges from the Spatiotemporal Control of ErbB Network Dynamics

Takashi Nakakuki,[1,7] Marc R. Birtwistle,[2,3,4,7] Yuko Saeki,[1,5] Noriko Yumoto,[1,5] Kaori Ide,[1] Takeshi Nagashima,[1,5] Lutz Brusch,[6] Babatunde A. Ogunnaike,[3] Mariko Okada-Hatakeyama,[1,5,*] and Boris N. Kholodenko[2,4,*]

[1]Computational Systems Biology Research Group, Advanced Computational Sciences Department, RIKEN Advanced Science Institute, 1-7-22 Tsurumi-ku, Yokohama, Kanagawa 230-0045, Japan

[2]Systems Biology Ireland, University College Dublin, Belfield,

[3]University of Delaware, Department of Chemical Engineering

[4]Department of Pathology, Anatomy, and Cell Biology, Thom

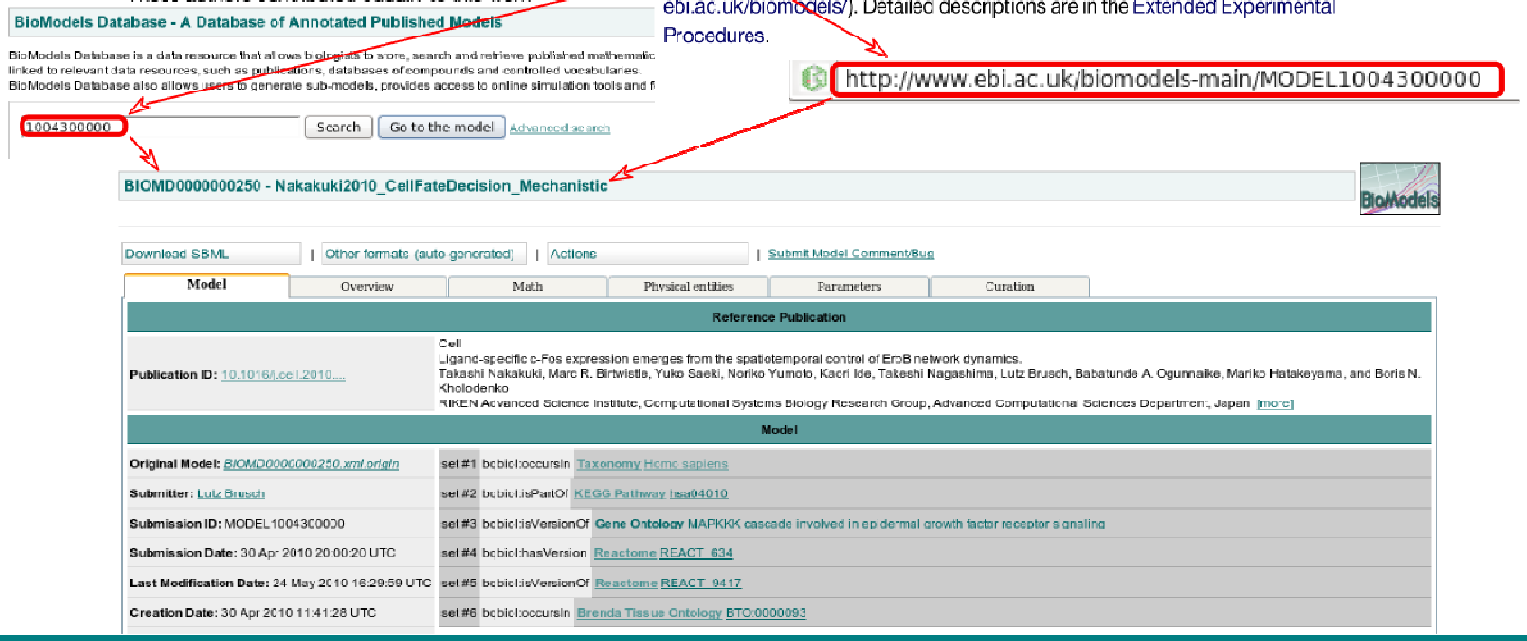
[5]Laboratory for Cellular Systems Modeling, RIKEN Research Japan

[6]Dresden University of Technology, Center for Information Se

[7]These authors contributed equally to this work

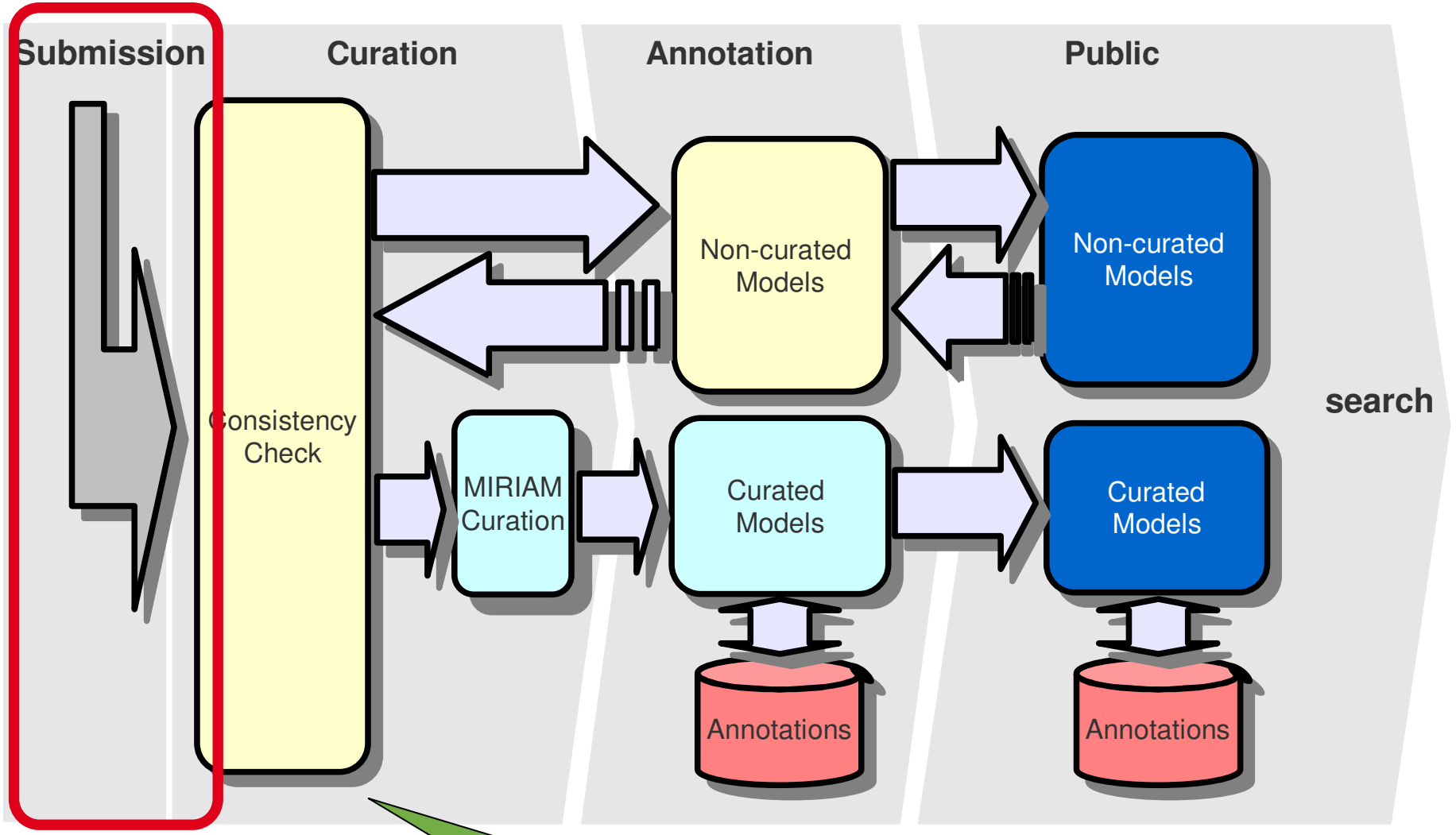
Model Simulation

We describe the biochemical reactions and connectivity of signaling molecules using ordinary differential equations (ODEs) known as chemical kinetic equations. The ODE models were developed and simulated with MATLAB (Mathworks) and are available from the Biomodels database under the IDs 1004300000 (mechanistic model) and 1003170000 (core model) (http://www.ebi.ac.uk/biomodels/). Detailed descriptions are in the Extended Experimental Procedures.

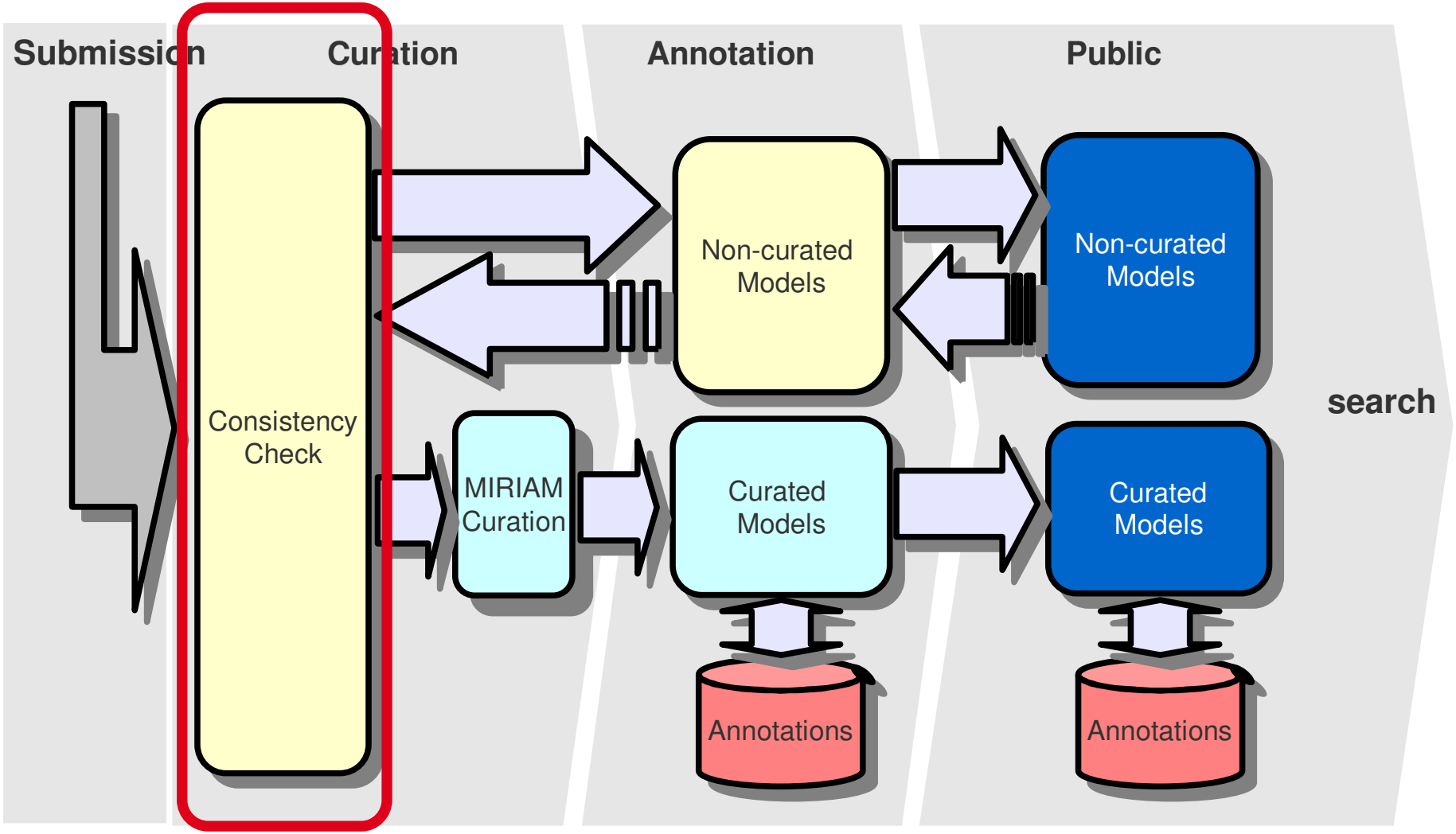


EMBL-EBI

Production pipeline

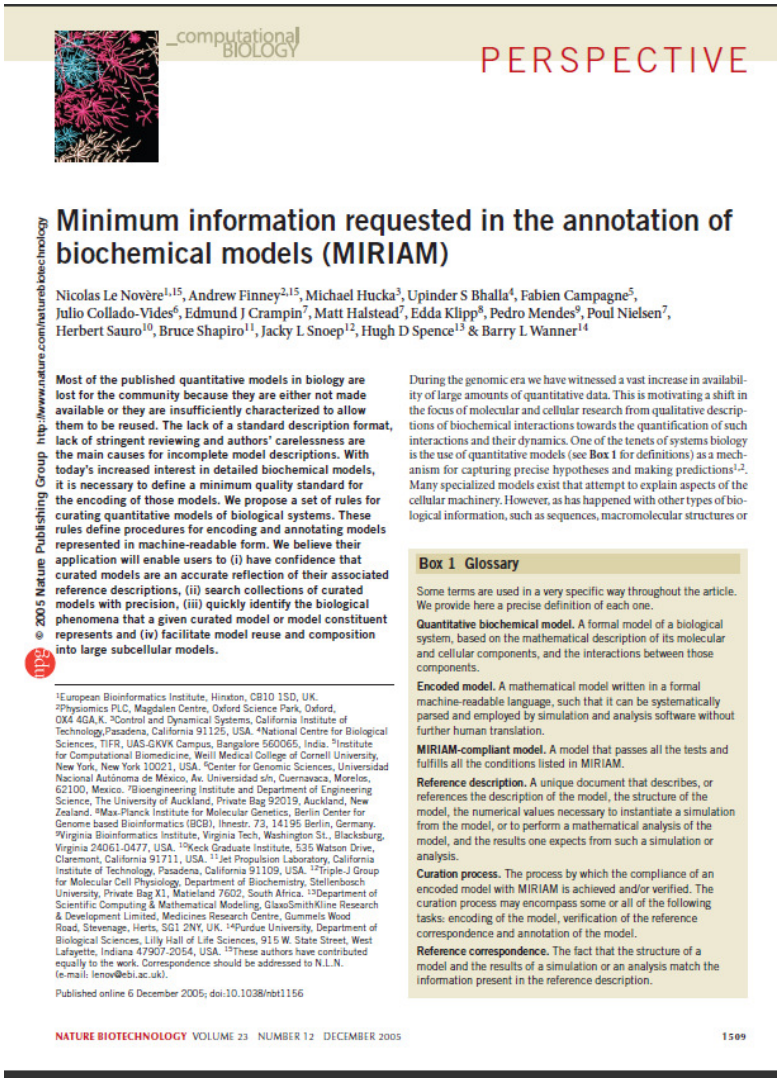


Production pipeline



MIRIAM guidelines

- Reporting guidelines for curation of quantitative models
  - Specifically about encoding & annotating models.
  - Limited for the moment to models that can be numerically evaluated.
- Not specific to SBML; applicable to any structured model format.



computational BIOLOGY

PERSPECTIVE

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.

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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.

MIRIAM compliance

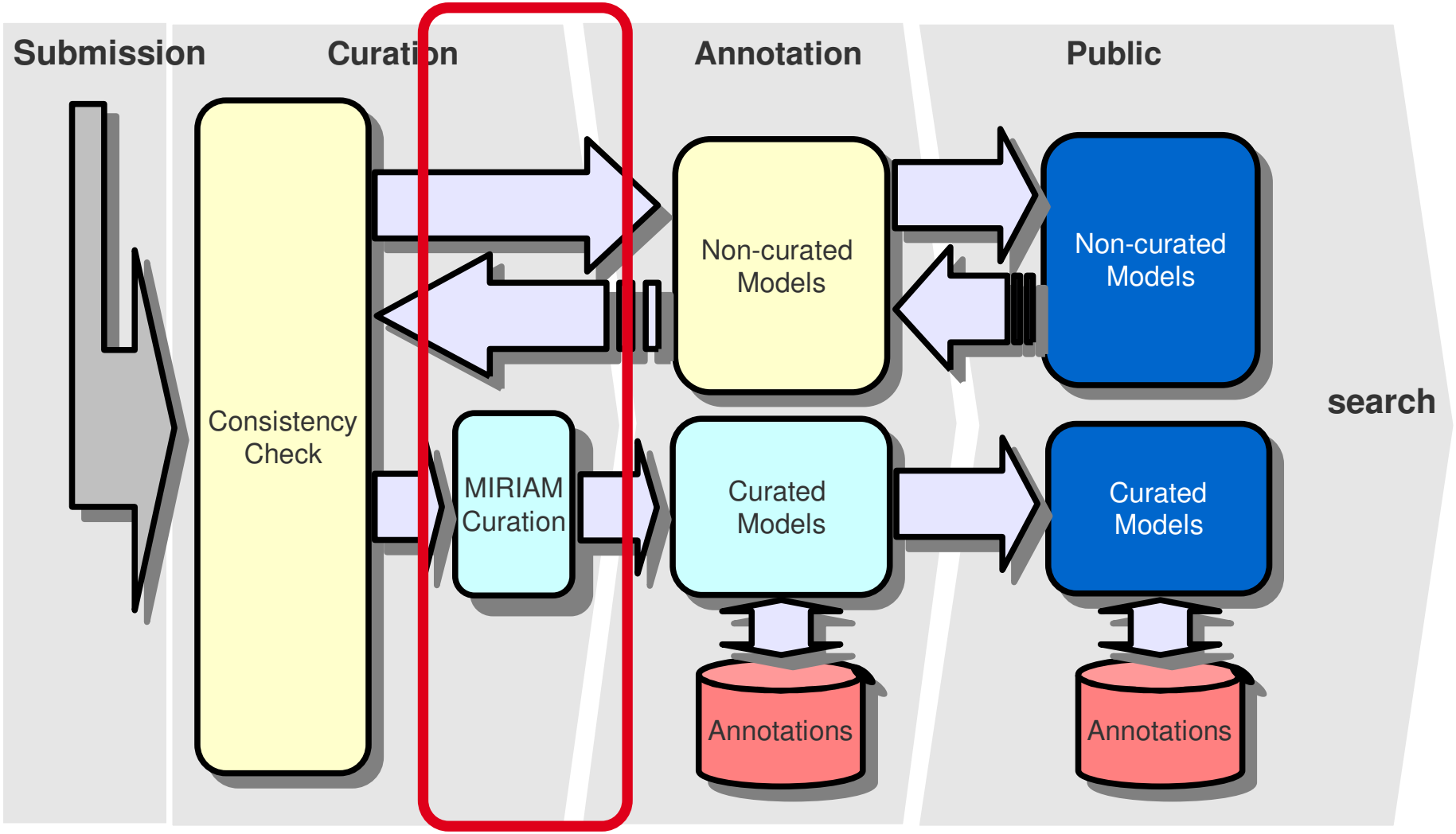
Minimum Information Requested In the Annotation of Models

Le Novère N. et al. *Nature Biotechnology* (2005), 23: 1509-1515

model must :

- be encoded in a standard format (CellML, SBML)
- contain link to a single reference description (peer reviewed for BioMdDB)
- reflect the structure of the biological processes described in the reference paper
- be able to reproduce the results given in the reference paper (all quantitative attributes should be defined)
- contain creator's contact details.

Production pipeline



Curated and Non-curated Models

Curated models – MIRIAM compliance successfully checked

Non-Curated models – valid SBML, not curated or annotated by the curators.

- not MIRIAM compliant
  - can not reproduce results published in the paper.
  - differ in model structure
  - non kinetic models (eg. FBA, stoichiometric maps)
- MIRIAM compliant
  - models contain kinetics that we cannot curate up to now.
  - will be moved into curated branch as soon as possible (model being checked by curators).

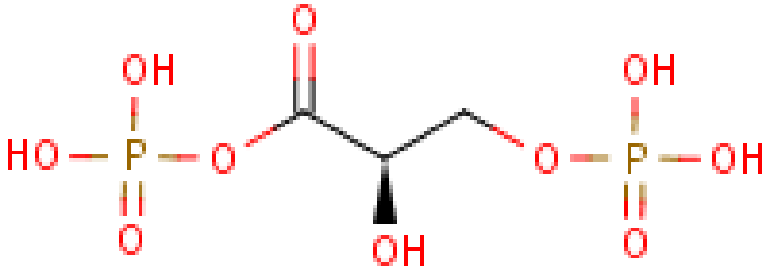
Why are annotations important?

Annotation of model components are essential to:

- unambiguously identify model components
  - improve understanding the structure of the model
  - allow easier comparison of different models
  - ease the integration of models
- allow efficient search strategies
- add a semantic layer to the model
  - improve understanding the biology behind the model
  - allow conversion and reuse of the model
  - ease the integration of model and biological knowledge

Why annotation?

1,3-Bisphosphoglycerate



- Synonyms
  e.g.: Glyceric Acid 1,3 bisphosphate
  3-phospho-D-glyceroyl phosphate
- Identifiers used in models in BioModels Database:
  BPG, BPG13, Gri13P2, DPG, pgp, PGAP ...
- => annotations can help to find models containing BPG
  for example searching using
  KEGG ID (C00236) or CHEBI ID (CHEBI:16001)

MIRIAM Annotations

Each model element is linked to the external data resource. This

- enhances model quality
- is essential for search criteria.

Taxonamy, Gene Ontology, ChEBI, UniPROT, KEGG, Reactome, Enzyme Nomenclature, etc.

MIRIAM Annotations are represented as a triplet which consists of:

- resource (eg. Enzyme Nomenclature)
- identifier (eg. EC 3.1.3.16 = phosphoprotein phosphatase)
- qualifier (eg. *is Version of*)

Resource and identifier together, are in the form of **URI** (*Uniform Resource Identifier*):

urn:miriam:ec-code:3.1.3.16

these are resolved to a **URL** using MIRIAM Resources (http://www.ebi.ac.uk/miriam/)

cdc2k dephosphorylation [cdc2k-P] → [cdc2k];			
Math:	cell × CP × k9 *(Detail)*		
Annotations:	set #1	bqbiol:isVersionOf	**Enzyme Nomenclature** 3.1.3.16 **Gene Ontology** protein amino acid dephosphorylation

BIOMD0000000005 - Tyson1991_CellCycle_6var

SBML formats | Other formats | Actions | Submit Model Comment/Bug

Model | Overview | Math | Physical entities | Parameters | Curation

Reference Publication

Publication ID: 1831270

Proc Natl Acad Sci U S A 1991 Aug;88(16):7328-32.
Modeling the cell division cycle: cdc2 and cyclin interactions.
Tyson JJ.
Department of Biology, Virginia Polytechnic Institute and State University, Blacksburg 24061. [more]

Model

Original Model: *BIOMD0000000005.xml.origin*

Submitter: Nicolas Le Novère

Submission ID: MODEL6614644188

Submission Date: 13 Sep 2005 12:31:08 UTC

Last Modification Date: 10 Aug 2009 14:09:39 UTC

Creation Date: 08 Feb 2005 18:28:27 UTC

Encoders: Bruce Shapiro
Vijayalakshmi Chelliah

	bqbiol:hasVersion	Reactome REACT_152
set #1	bqbiol:isVersionOf	**KEGG Pathway** sce04111 **Gene Ontology** mitotic cell cycle
	bqmodel:is	Taxonomy Fungi/Metazoa group

Notes

This a model from the article:
Modeling the cell division cycle: cdc2 and cyclin interactions.
Tyson JJ *Proc. Natl. Acad. Sci. U.S.A.*1991; 88(16); 7328-32 1831270,
Abstract:
The proteins cdc2 and cyclin form a heterodimer (maturation promoting factor) that controls the major events of the cell cycle. A mathematical model for the interactions of cdc2 and cyclin is constructed. Simulation and analysis of the model show that the control system can operate in three modes: as a steady state with high maturation promoting factor activity, as a spontaneous oscillator, or as an excitable switch. We associate the steady state with metaphase arrest in unfertilized eggs, the spontaneous oscillations with rapid division cycles in early embryos, and the excitable switch with growth-controlled division cycles typical of nonembryonic cells.

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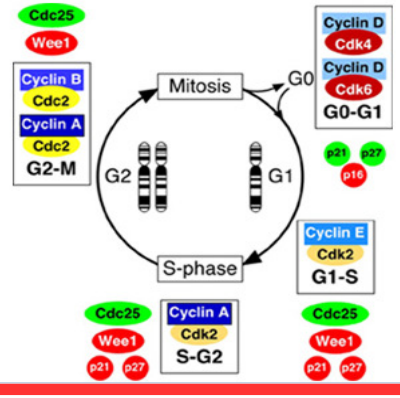
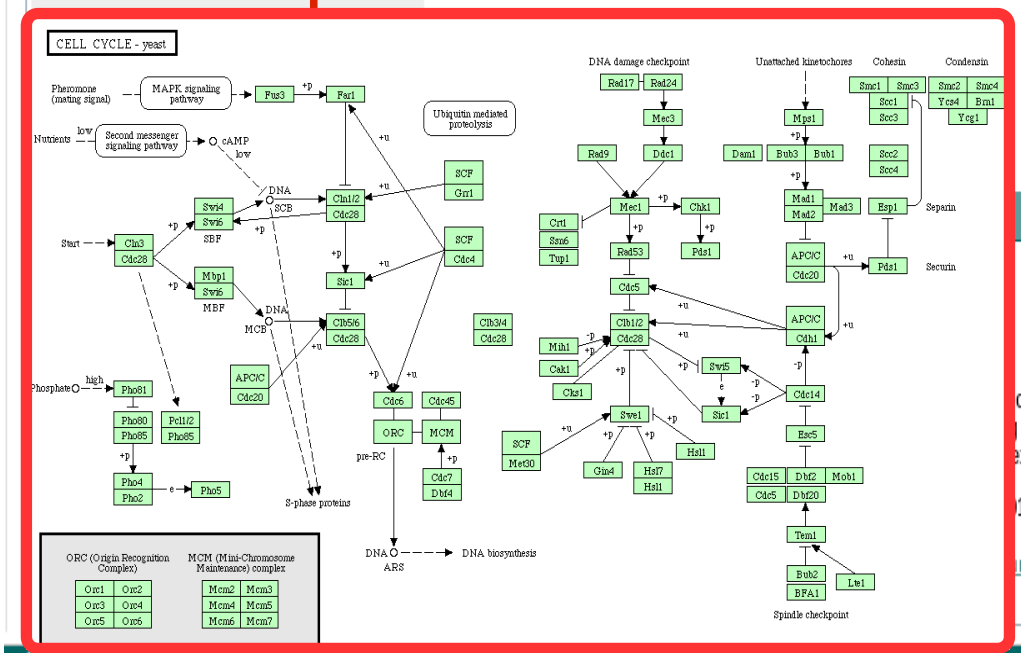
	bqbiol:hasVersion	Reactome REACT_152
set #1	bqbiol:isVersionOf	KEGG Pathway sce04111 Gene Ontology mitotic cell cycle
	bqmodel:is	Taxonomy Fungi/Metazoa group

Cell Cycle, Mitotic

Stable identifier	REACT_152.2
Authored	O'Connell, M, Walworth, N, Bosco, G, 2005-01-01
Reviewed	Manfredi, J

The replication of the genome and the subsequent segregation of chromosomes into daughter cells are controlled by
DNA replication is carried out during a discrete temporal period known as the S (synthesis)-phase, and chromosome
cellular architecture at mitosis. Two gap-phases separate these major cell cycle events: G1 between mitosis and S
development of the human body, cells can exit the cell cycle for a period and enter a quiescent state known as G0,
again, but undergo morphological development to carry out the wide variety of specialized functions of individual tissue
A family of protein serine/threonine kinases known as the cyclin-dependent kinases (CDKs) controls progression throu
the catalytic subunit is dependent on binding to a cyclin partner. The human genome encodes several cyclins and se
order in which they were identified. The oscillation of cyclin abundance is one important mechanism by which these en
at the relevant time and place. Additional regulatory proteins and post-translational modifications ensure that CDK
narrow window of activity.



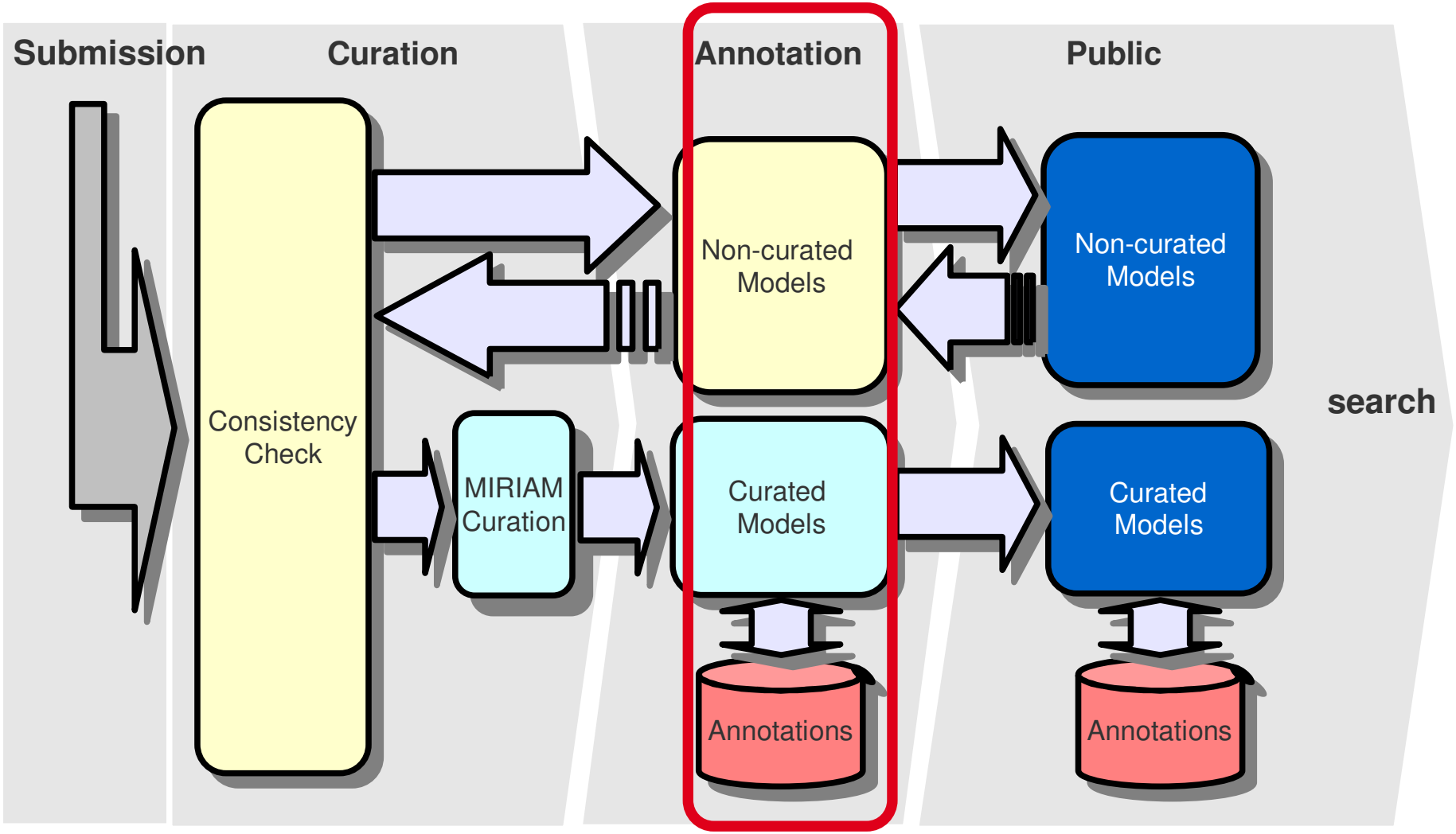


Lineage	Taxonomy identifier	33154
• Eukaryota	Scientific name	Fungi/Metazoa group
	Common name	-
	Other NCBI synonyms	Opisthokonta opisthokonts
	Rank	no rank
	Number of UniProtKB/Swiss-Prot entries	114913
	Number of UniProtKB/TrEMBL entries	1459130

Taxonomy navigation

Up taxonomy tree	Down taxonomy tree
Eukaryota	• Choanoflagellida • Fungi • Fungi/Metazoa incertae sedis • Metazoa

Production pipeline



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BioModels Database is a data resource that allows biologists to store, search and retrieve published mathematical models of biological interests. Models present in BioModels Database are annotated and linked to relevant data resources, such as publications, databases of compounds and controlled vocabularies.
BioModels Database also allows users to generate sub-models, provides access to online simulation tools and features programmatic access via Web Services.

Search | Go to the model | Advanced search

Browse models

- Curated models (269)
- Browse models using GO
- Non-curated models (361)

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Main instance at European Bioinformatics Institute http://www.ebi.ac.uk/biomodels/

Mirror at California Institute of Technology http://biomodels.caltech.edu

BioModels AT SourceForge http://sourceforge.net/projects/biomodels/

Web Services http://www.ebi.ac.uk/biomodels-main/webservices

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Model of the month

August, 2010

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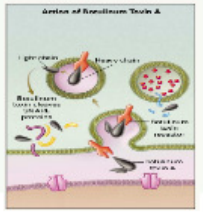
Read more...



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The Virtual Cell recently released a new version of the SBML to VCML converter...

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Browse - Curated models

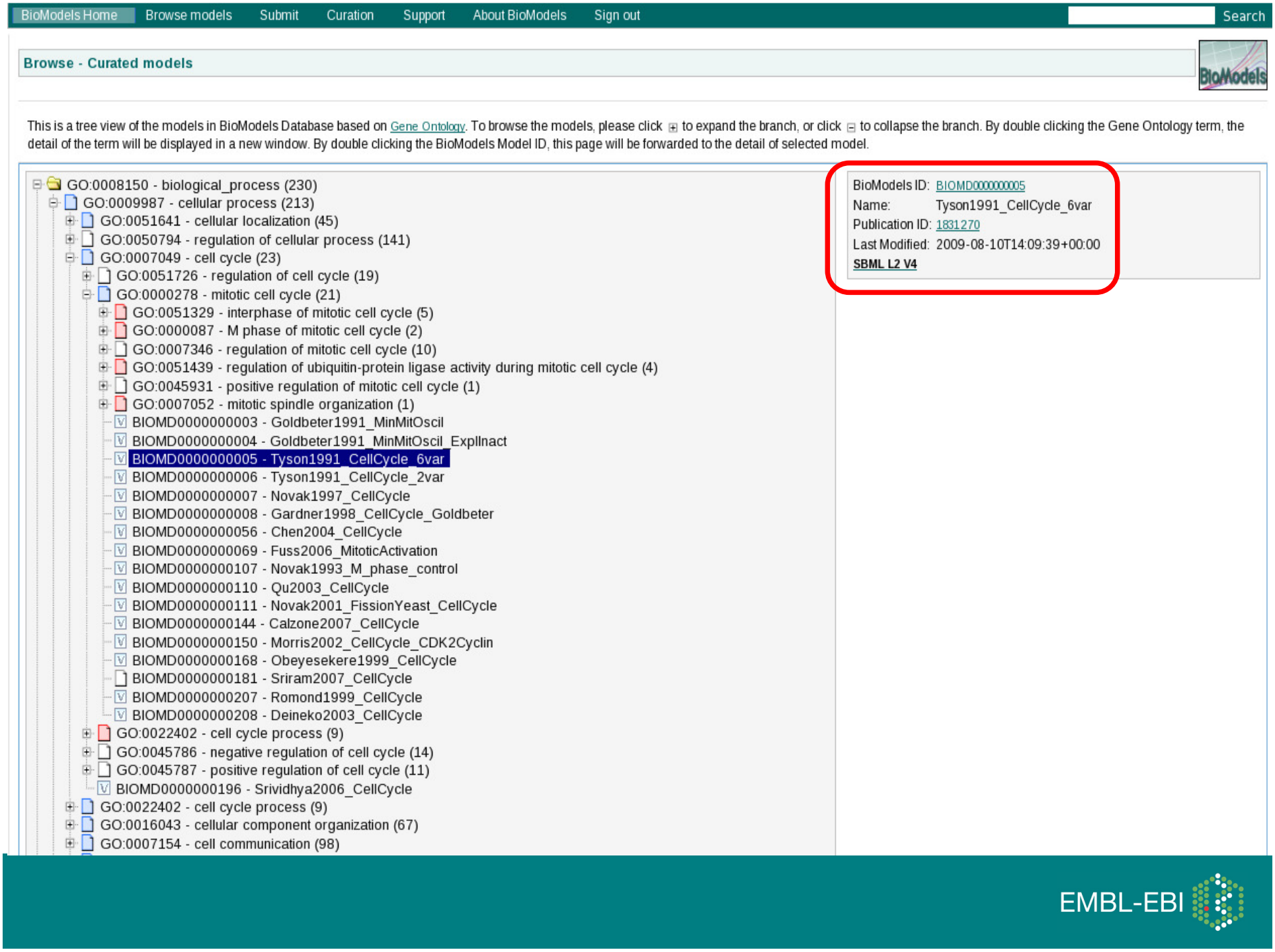
This is a tree view of the models in BioModels Database based on Gene Ontology. To browse the models, please click ⊞ to expand the branch, or click ⊟ to collapse the branch. By double clicking the Gene Ontology term, the detail of the term will be displayed in a new window. By double clicking the BioModels Model ID, this page will be forwarded to the detail of selected model.

- GO:0008150 - biological_process (230)
- GO:0005575 - cellular_component (200)
- GO:0003674 - molecular_function (154)

BioModels ID: *Unspecified*
Name: *N/A*
Publication ID: *N/A*
Last Modified: *N/A*

The relationships between terms are represented by different icons.

- BioModels qualifiers:
  - bqbiol:is
  - bqbiol:isVersionOf
  - bqbiol:hasPart
- Gene Ontology relationships:
  - is a
  - part of
  - develops from
  - other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GO:0008150 - biological_process (230)
GO:0009987 - cellular process (213)
GO:0051641 - cellular localization (45)
GO:0050794 - regulation of cellular process (141)
GO:0007049 - cell cycle (23)
GO:0051726 - regulation of cell cycle (19)
GO:0000278 - mitotic cell cycle (21)
GO:0051329 - interphase of mitotic cell cycle (5)
GO:0000087 - M phase of mitotic cell cycle (2)
GO:0007346 - regulation of mitotic cell cycle (10)
GO:0051439 - regulation of ubiquitin-protein ligase activity during mitotic cell cycle (4)
GO:0045931 - positive regulation of mitotic cell cycle (1)
GO:0007052 - mitotic spindle organization (1)
BIOMD0000000003 - Goldbeter1991_MinMitOscil
BIOMD0000000004 - Goldbeter1991_MinMitOscil_ExplInact
BIOMD0000000005 - Tyson1991_CellCycle_6var
BIOMD0000000006 - Tyson1991_CellCycle_2var
BIOMD0000000007 - Novak1997_CellCycle
BIOMD0000000008 - Gardner1998_CellCycle_Goldbeter
BIOMD0000000056 - Chen2004_CellCycle
BIOMD0000000069 - Fuss2006_MitoticActivation
BIOMD0000000107 - Novak1993_M_phase_control
BIOMD0000000110 - Qu2003_CellCycle
BIOMD0000000111 - Novak2001_FissionYeast_CellCycle
BIOMD0000000144 - Calzone2007_CellCycle
BIOMD0000000150 - Morris2002_CellCycle_CDK2Cyclin
BIOMD0000000168 - Obeyesekere1999_CellCycle
BIOMD0000000181 - Sriram2007_CellCycle
BIOMD0000000207 - Romond1999_CellCycle
BIOMD0000000208 - Deineko2003_CellCycle
GO:0022402 - cell cycle process (9)
GO:0045786 - negative regulation of cell cycle (14)
GO:0045787 - positive regulation of cell cycle (11)
BIOMD0000000196 - Srividhya2006_CellCycle
GO:0022402 - cell cycle process (9)
GO:0016043 - cellular component organization (67)
GO:0007154 - cell communication (98)
BioModels ID: BIOMD0000000005
Name: Tyson1991_CellCycle_6var
Publication ID: 1831270
Last Modified: 2009-08-10T14:09:39+00:00
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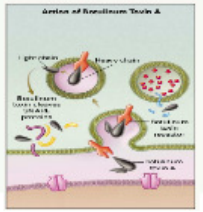

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Search - Models

Text Search

You can search BioModels Database for models using one or more of the following criteria:

- *BioModels ID* → Search BioModels Database for *exact* BioModels identifiers (for example *BIOMD0000000001* or *BIOMD0000000022*).
- *Person* → Search BioModels Database for model submitter and/or creator(s) names, or model reference publication author(s) names (for example *Nicolas Le Novère*, *Nicolas*, *Bruce Shapiro* or *Shapiro*, *Edelstein* or *Novak*).
- *SBML Elements* → Search BioModels Database using the content of either "name" or "*notes*" SBML elements (for example *Edelstein* or *nicotinic*). Select the checkbox behind, if you want to find documents which matches the exact phrase; otherwise, all words will be searched as default.
- *Resource* → Search BioModels Database for related information found in the models reference publication or third-party resources, by either publication/resource identifier or text (for example *9256450* or *cyclin* for publication, *GO:0000278* or *cell cycle* for Gene Ontology, *P04551* or *cell division* for UniProt).
- *Resource ID* → Search BioModels Database for annotations, by third-party resource identifiers (for example *IPR002394* for InterPro, *hsa04080* for KEGG Pathway, *68910* for Reactome).

A part from the *BioModels ID* -based search, for every other criteria the search operates on a *contains the entered string basis*, case-insensitive. That is, searching *Person* for *Shapi* or *shapi* will return the same results as searching for *Shapiro* or *shapiro*. In addition, since search strings are treated as words, do not enter regular expressions.

Multiple criteria can be combined with either *and* or *or*. If *and* is selected, only those models satisfying all the criteria will be returned. If instead *or* is selected, all the models satisfying at least one of the criteria will be returned.

BioModels ID:

Person:

SBML Elements: match the **exact phrase**

Resource: Publication

Resource: Publication

Resource: Publication

Resource ID: Enzyme Nomenclature

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Resource ID: Enzyme Nomenclature

Compose by: and or

Search Reset

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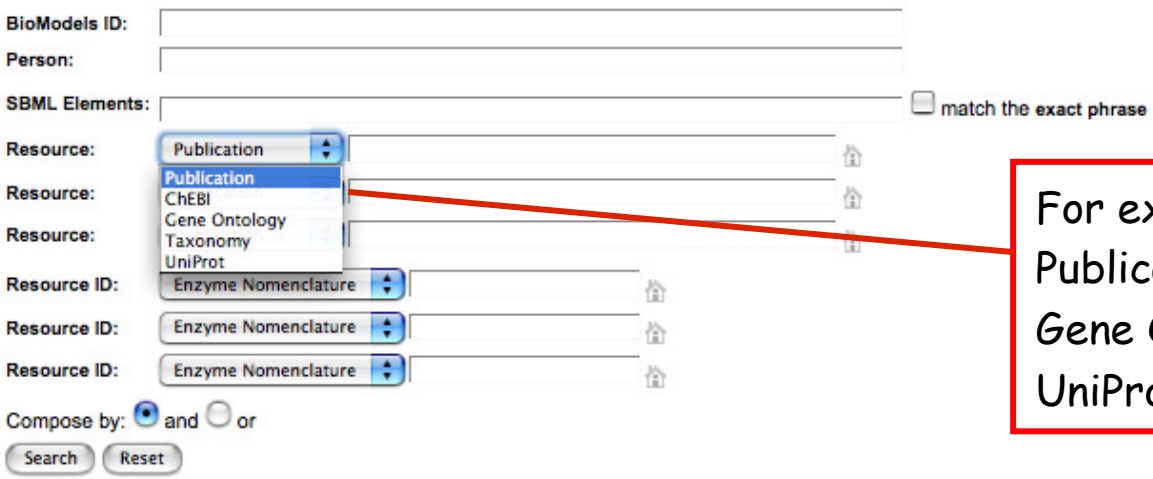

For example,
Publication: *PubMed or Cyclin*
Gene Ontology: *GO:0000278 or cell cycle*
UniProt: *P04551 or cell division*

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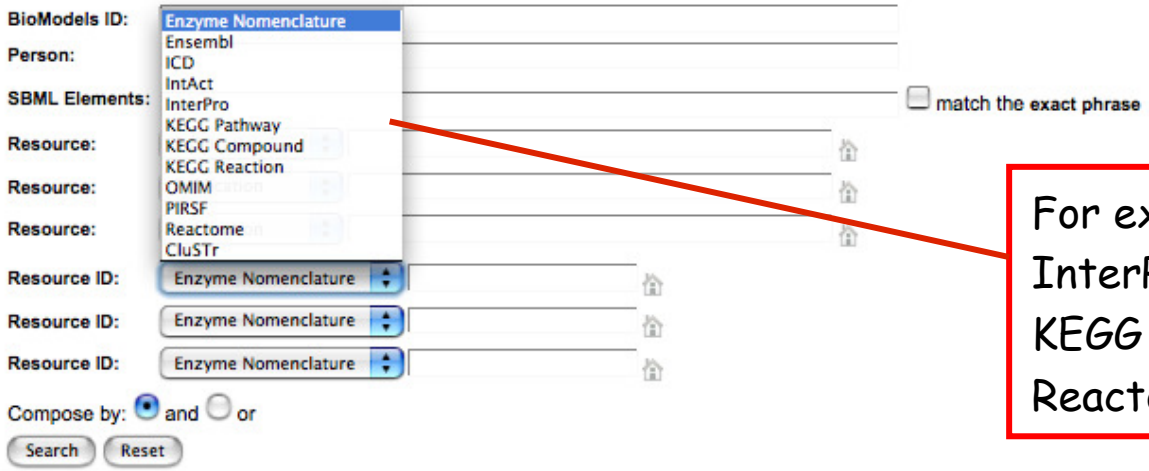
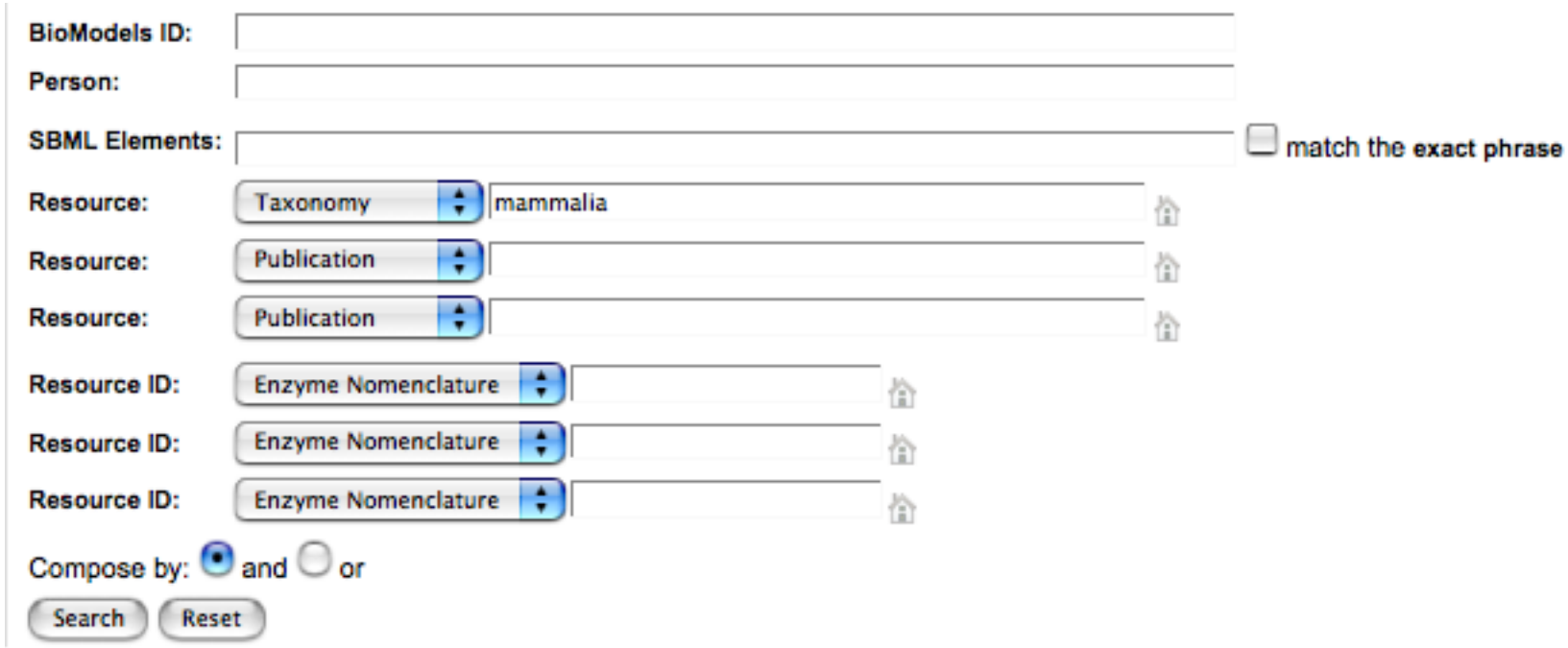


For example,
InterPro: *IPR002394*
KEGG Pathway: *hsa04080*
Reactome: *68910*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Person:
SBML Elements:
match the exact phrase
Resource:
Taxonomy
mammalia
Resource:
Publication
Resource:
Publication
Resource ID:
Enzyme Nomenclature
Resource ID:
Enzyme Nomenclature
Resource ID:
Enzyme Nomenclature
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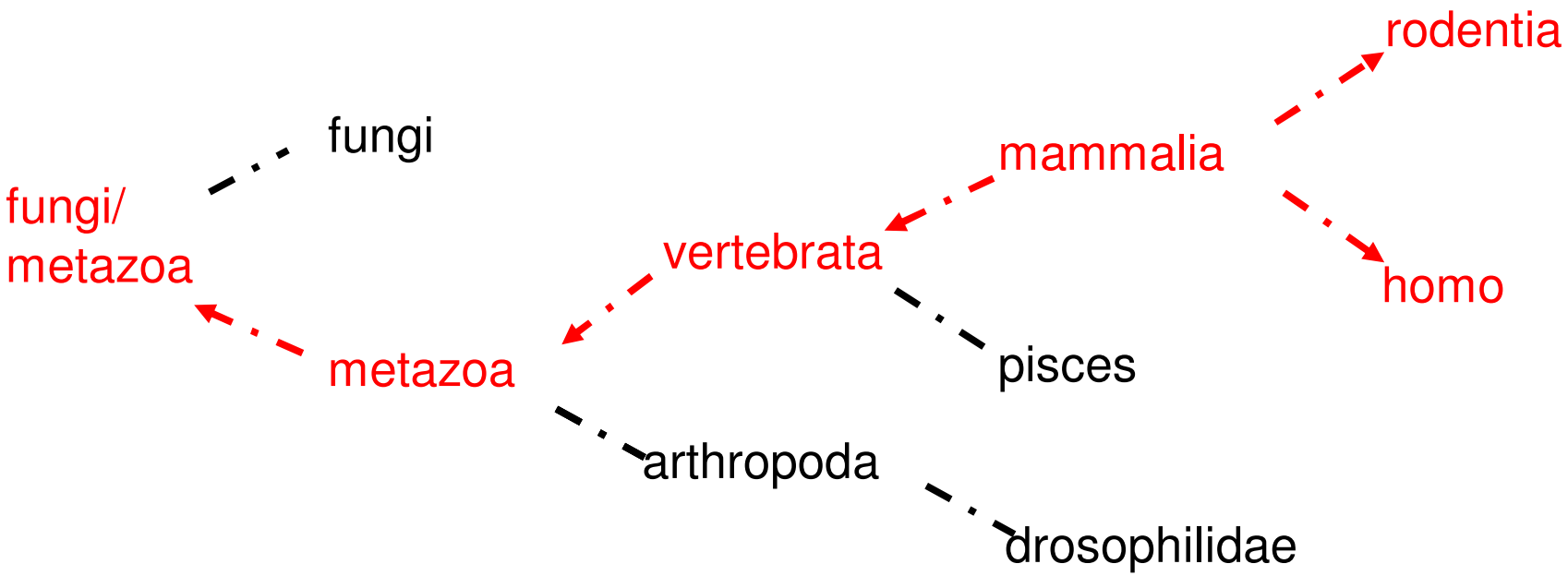
Taxonomic Searches

linking to hierarchical controlled vocabularies allows for more elaborate searching:
e.g.: searching BioModels DataBase for all models fitting mammals



Resource: Taxonomy mammalia

Resource: Publication oscillations

26 Curated Models returned.

BioModels ID	Name	Publication ID	Last Modified
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BIOMD0000000006	Tyson1991_CellCycle_2var	1831270	2009-02-25T14:41:44+00:00
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BIOMD0000000158	Zatorsky2006_p53_Model2	16773083	2008-01-14T21:40:04+00:00
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BIOMD0000000201	Goldbeter2008_Somite_Segmentation_Clock_Notch_Wnt_FGF	18308339	2009-03-16T14:34:11+00:00

hamster

metazoa/fungi

rattus

homo sapiens

mammalia

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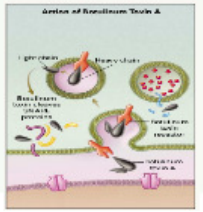
Model of the month

August, 2010

Botulinum neurotoxin serotype A (BoNT/A) causes flaccid paralysis by a multi-step mechanisim. Two mathematical models that has been developed, to estimate upper limits of the time during which antitoxin and other impermeable inhibitors of BoNT/A can exert an effect, is described here.
Read more...



News

30 September 2010 **Eighteenth Release!**
Download All Models Under SBML Format

29 June 2010 **New BioModels Database publication**
New BioModels Database paper published in *BMC Systems Biology*: BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models.

2nd June 2010 **SBML to VCML converter updated**
The Virtual Cell recently released a new version of the SBML to VCML converter...

EMBL-EBI

Lebeda et. al. (2008), Onset dynamics of type A botulinum neurotoxin-induced paralysis.

July 2010, model of the month by *Vijayalakshmi Chelliah*
Original model: BIOMD0000000178, BIOMD0000000267

The deadly naturally occurring neurotoxin, Botulinum neurotoxin (BoNT) produced by an anaerobic and spore forming bacterium Clostridium botulinum (and rarely by other Clostridium species such as C. butyricum, C. baratii and C. argentinense), induces a potentially fatal paralysis known as botulism. Botulism is characterized by symmetric, descending, flaccid paralysis of motor and autonomic nerves, usually beginning with the cranial nerves. Blurred vision, dysphagia, and dysarthria are common initial complaints. C. botulinum produces seven antigenitically and serologically distint but structurally similar toxins (A to G) that are found in soil and ocean sediment. Human botulism is mainly caused by types A, B, E and F. Types C, D and G cause toxicity in birds, horses, cattle and primates.

BoNT enters through 1) Ingestion of preformed toxin, 2) Inhalation of preformed toxin, 3) Local production of toxin by C botulinum organisms in the gastrointestinal tract 4) Local production of toxin by C botulinum organisms in devitalized tissue at the site of a wound.

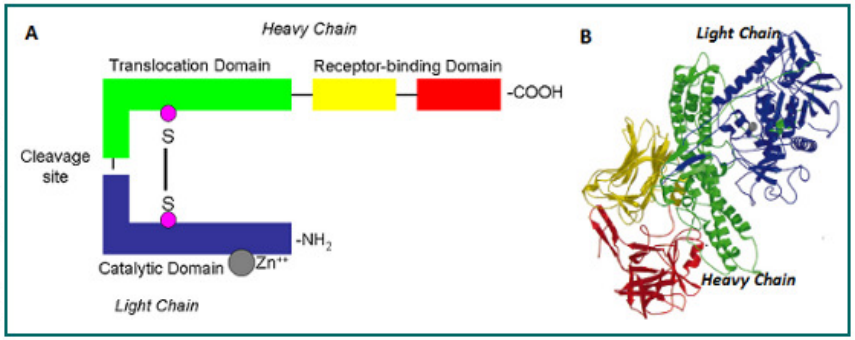


Figure 1: Botulinum toxin structure A) schematic representation of BoNT, B) Crystal structure of BoNT/A - PDBcode:3BTA. Figure B - taken from [1]. The Light chain catalytic domain is coloured in blue. The heavy chain translocation domain is coloured in green, N-terminal and the C-terminal receptor binding domains are coloured in yellow and red respectively. The catalytic zinc is represented as a ball in gray. The colour code is same for Figures 1A and 1B.

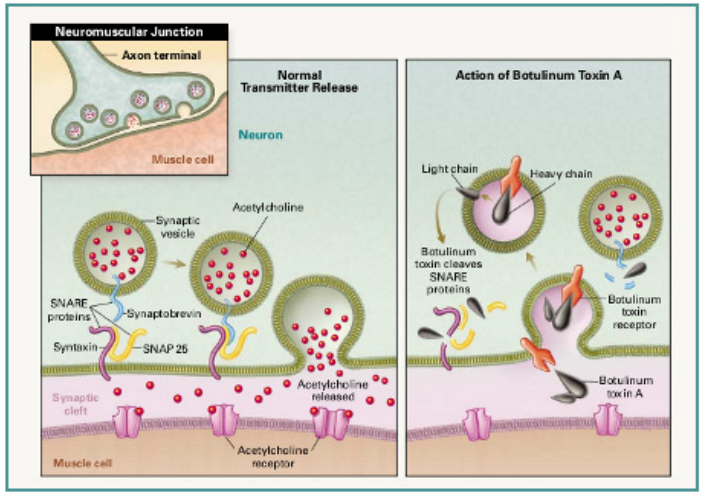


Figure 2: Mechanism of action of BoNTs (right) compared to the normal cell (left). Shown are the individual stages of BoNT intoxication, including cell surface recognition, vesicle internalization, translocation of the catalytic domain (light chain) into the cytosol, and proteolytic cleavage of one of the proteins of the SNARE complex. These steps lead to inhibition of neurotransmitter-containing vesicle release. BoNT/B, D, F, and G cleave proteins of the VAMP family (blue), and BoNT/A, C, and E cleave SNAP-25 (yellow). BoNT/C can also cleave syntaxin (purple). Figure taken from [2]

The underlying mechanism of BoNT that causes diseases also provides clinical benefits. BoNT/A and B are used as medication to treat patients with nerve and muscle disorders. The toxin has been tested and adopted for therapeutic use in four clinical areas 1) ophthalmology (for treating blepharospasm and strabismus), 2) neurology (for treating dystonias (focal and some segmental)), 3) otolaryngology (for treating spasmodic dysphonia) and gastroenterolgy that focus on smooth muscle and sphincter control (for treating achalasia). For details [click here]. Apart from its medical use, it is also used as cosmetic agents for the treatment of facial wrinkles. For details [click here]. In spite of all these beneficial effect, BoNTs is considered among the most dangerous biological weapon due to their extreme toxicity and easy production. For details [click here]

BoNT is expressed as a single polypeptide chain (~150kDa) which is activated by proteolytic cleavage to form two chains (a heavy chain (100kDa) and a light chain (50kDa)) that are connected by a single disulphide bond. The heavy chain comprises of translocation domain and receptor-binding domain. The light chain (catalytic domain) is a zinc-containing metalloproteinase. Schematic representation and crystal structure of BoNT/A is shown in Figure 1.

BoNT enters the blood stream and is transported to the neuromuscular junction. The receptor-binding domain provides cholinergic specificity and binds the toxin to the presynaptic receptors. The toxin then enters the neuronal cell via receptor-mediated endocytosis. The translocation domain of the heavy chain promotes the entry of light chain (toxic moiety) to neuroplasm, that cleaves one ore more of the proteins that form SNARE protein complex (complex formed by SNAP-25, Syntaxin and VAMP) depending on the BoTN serotype. SNARE protein complex normally allow neurotransmitter, Acetylcholine to leave the cell and transmits a nerve impulse to a muscle, signalling the muscle to contract. As BoNT prevents the formation of the SNARE protein complex by cleaving the proteins that form SNARE protein complex, the Acetylcholine release is blocked. As the result, signal transmission between the nerve and muscle is stopped causing botulism (paralysis). The mechanism of neurotransmitter release in normal cell and cells that are affected by BoNT/A is shown in (Figure 2).

Model components & Sub-model creation

BIOMD0000000005 - Tyson1991_CellCycle_6var

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Reference Publication

Publication ID: 1831270

Proc Natl Acad Sci U S A 1991 Aug;88(16):7328-32.
Modeling the cell division cycle: cdc2 and cyclin interactions.
Tyson JJ.
Department of Biology, Virginia Polytechnic Institute and State University, Blacksburg 24061. [more]

Model

Original Model: *BIOMD0000000005.xml.origin*

Submitter: Nicolas Le Novère

Submission ID: MODEL6614644188

Submission Date: 13 Sep 2005 12:31:08 UTC

Last Modification Date: 10 Aug 2009 14:09:39 UTC

Creation Date: 08 Feb 2005 18:28:27 UTC

Encoders: Bruce Shapiro
Vijayalakshmi Chelliah

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	bqmodel:is	Taxonomy Fungi/Metazoa group

Notes

This a model from the article:
Modeling the cell division cycle: cdc2 and cyclin interactions.
Tyson JJ *Proc. Natl. Acad. Sci. U.S.A.* 1991; 88(16); 7328-32 1831270,
Abstract:
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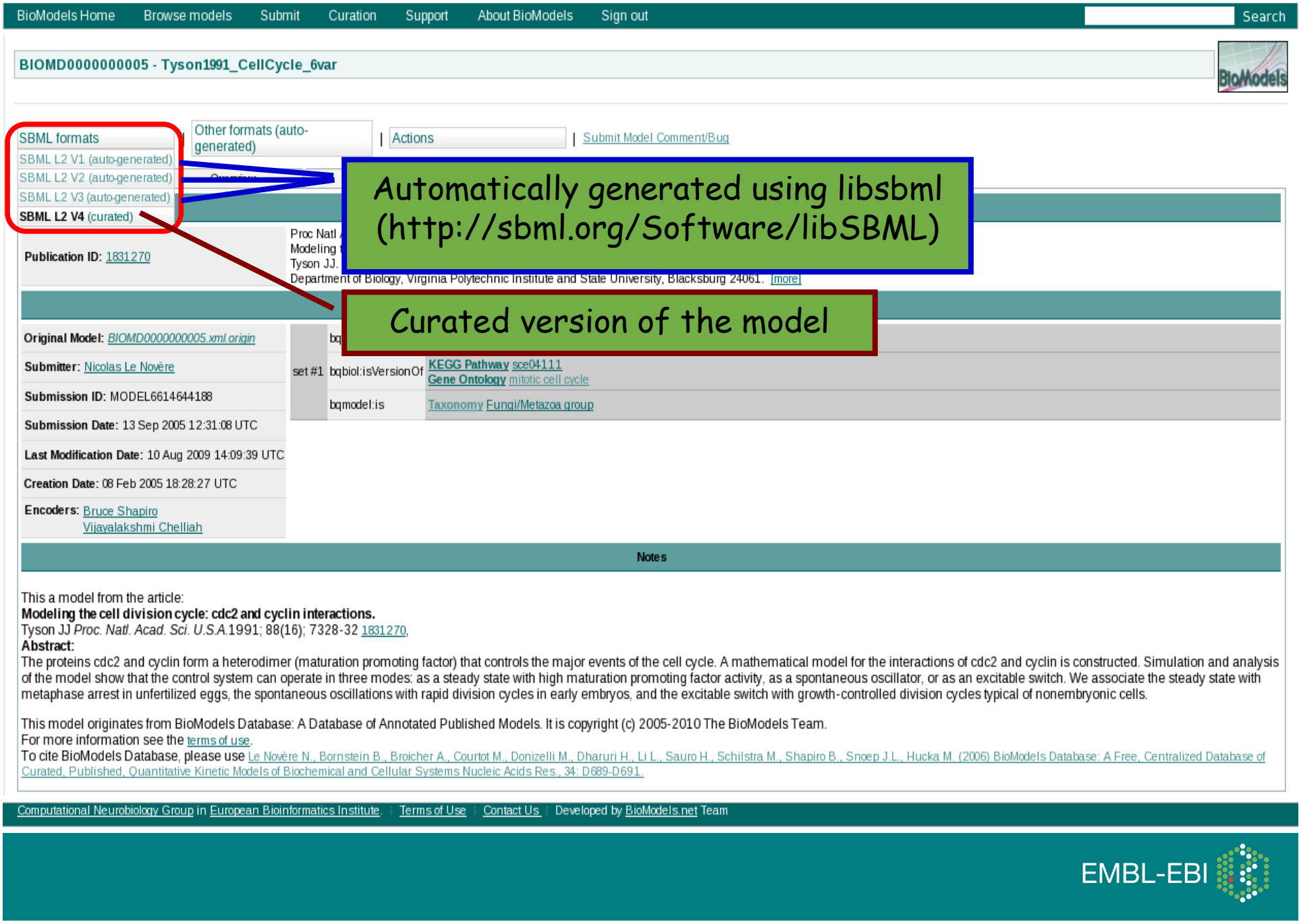
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Curated version of the model
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Department of Biology, Virginia Polytechnic Institute and State University, Blacksburg 24061. [more]
Original Model: BIOMD0000000005.xml.origin
Submitter: Nicolas Le Novère
Submission ID: MODEL6614644188
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Gene Ontology mitotic cell cycle
bqmodel:is
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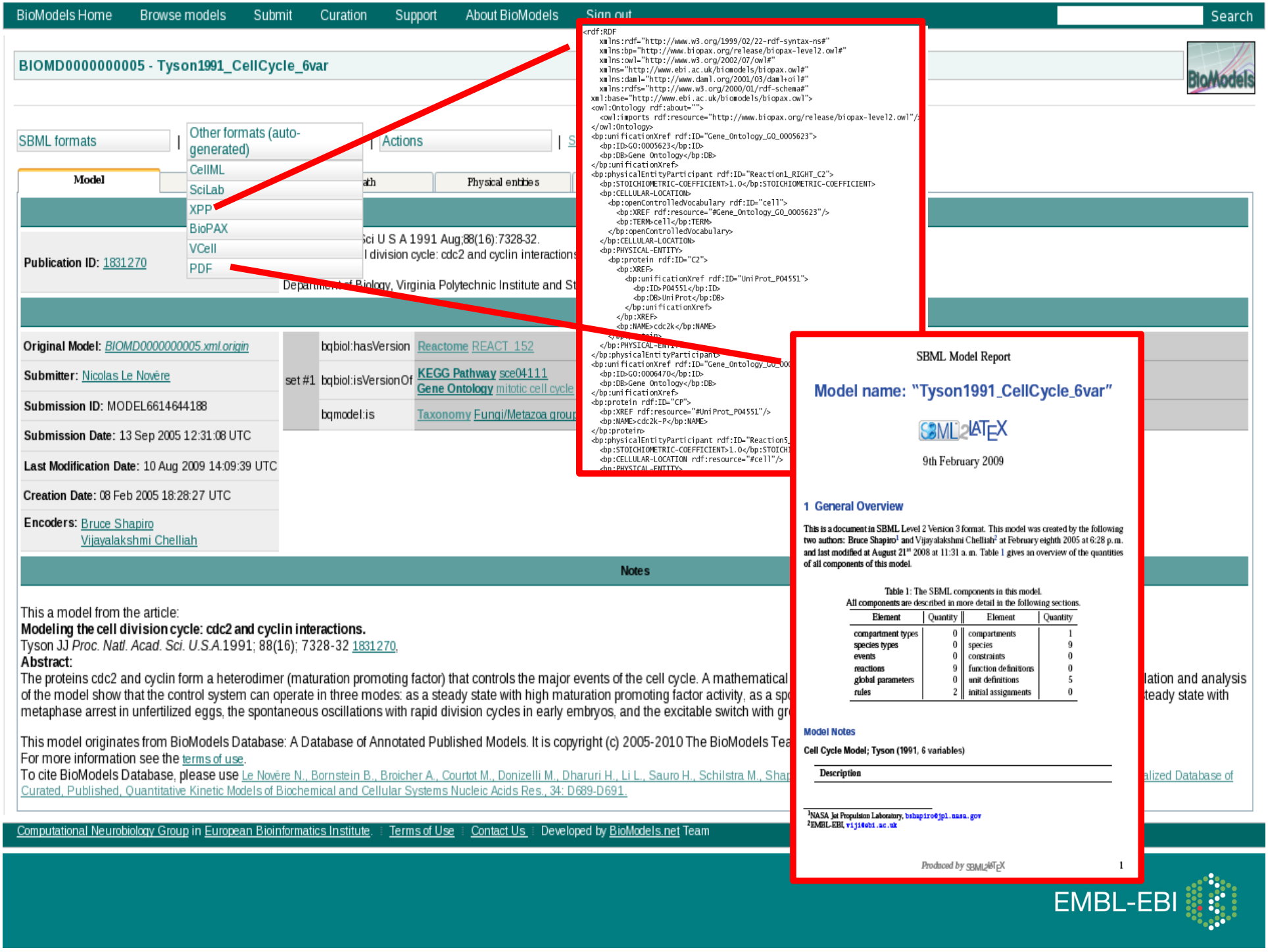
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Publication ID: 1831270
Original Model: BIOMD0000000005.xml.origin
Submitter: Nicolas Le Novère
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Vijayalakshmi Chelliah
set #1
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Reactome REACT_152
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KEGG Pathway sce04111
Gene Ontology mitotic cell cycle
bqmodel:is
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Computational Neurobiology Group in European Bioinformatics Institute.
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Developed by BioModels.net Team
SBML Model Report
Model name: "Tyson1991_CellCycle_6var"
9th February 2009
1 General Overview
This is a document in SBML Level 2 Version 3 format. This model was created by the following two authors: Bruce Shapiro[1] and Vijayalakshmi Chelliah[2] at February eighth 2005 at 6:28 p.m. and last modified at August 21st 2008 at 11:31 a.m. Table 1 gives an overview of the quantities of all components of this model.
Table 1: The SBML components in this model.
All components are described in more detail in the following sections.
Element | Quantity | Element | Quantity
compartment types | 0 | compartments | 1
species types | 0 | species | 9
events | 0 | constraints | 0
reactions | 9 | function definitions | 0
global parameters | 0 | unit definitions | 5
rules | 2 | initial assignments | 0
Model Notes
Cell Cycle Model; Tyson (1991, 6 variables)
Description
[1]NASA Jet Propulsion Laboratory, bshapiro@jpl.nasa.gov
[2]EMBL-EBI, vijl@ebi.ac.uk
Produced by SBML2LaTeX
1
EMBL-EBI

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Reference Publication

Publication ID: 1831270

Proc Natl Acad Sci
Modeling the cell di ctions.
Tyson JJ.
Department of Biology, Virginia Polytechnic Institute and State University, Black

Model

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Submitter: Nicolas Le Novère

Submission ID: MODEL6614644188

Submission Date: 13 Sep 2005 12:31:08 UTC

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Encoders: Bruce Shapiro
Vijayalakshmi Chelliah

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	bqmodel:is	Taxonomy Fungi/Metazoa group

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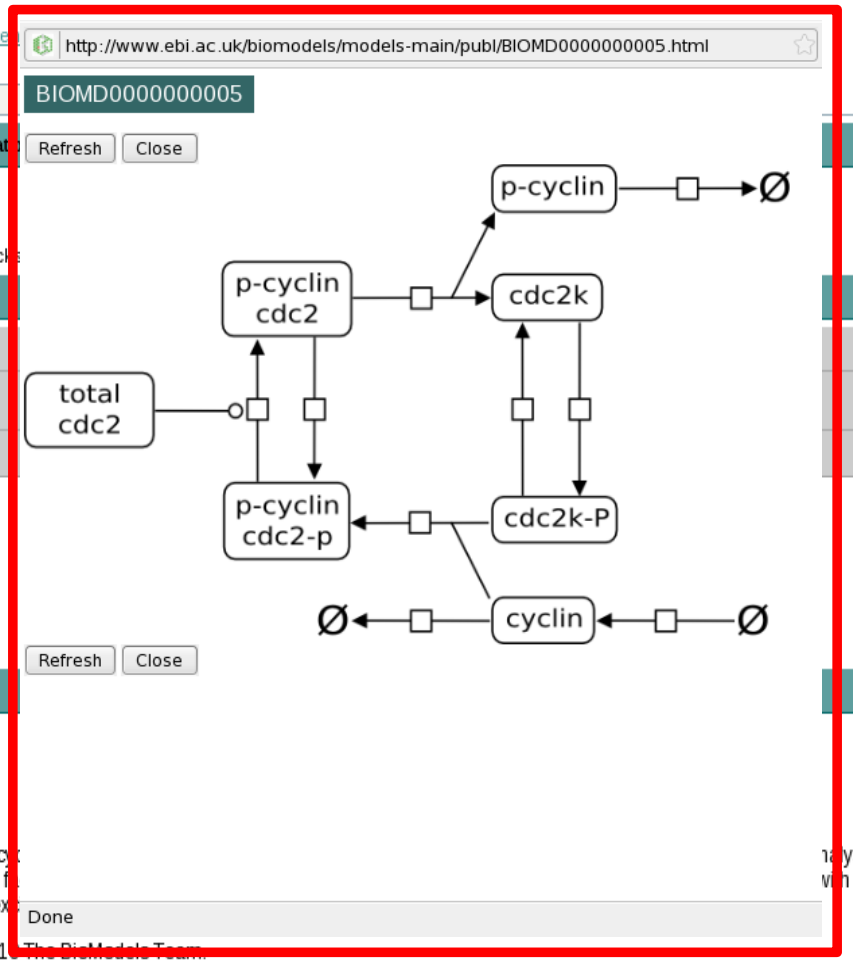

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BIOMD0000000005 - Tyson (1991), modelling cell division

by Nicolas Le Novère

One of the characteristics of life is autopoiesis, that is the auto-production. The biological cell is the archetypal example of an autopoietic systems. One of the key events of cell reproduction is the division of a cell into two descendants. In population formed of unicellular organisms, but also in many tissues of pluricellular organisms, this processus is a periodic one, called cell cycle. The mechanisms underlying eukaryotic cell cycle have been extensively studied, and have been found remarkably conserved throughout evolution. Their elucidation has been awarded the Nobel prize of physiology and medecine in 2001. Cell division is not only the basic mechanism by which a human is built from the egg, when altered it also triggers diseases such as cancers.

With his model published in 1991 [1], John Tyson played a pioneer role in what would become one of the most prolific fields of quantitative modeling in cell biology. One of the crucial events deciding the cell division is the formation of the Maturation Promoting Factor (MPF), from oscillating proteins called cyclin and specific protein kinases. With only 6 reacting species and 9 reactions (figure 1), Tyson built a mechanistic model explaining a very complex cellular behaviour from simple molecular events. The model is based on the creation and degradation of cyclin, its binding to and dissociation from cyclin dependent kinase CDC2, and the phosphorylation of both proteins. Although his model was primarily devoted to explain yeast cell cycle, its explanatory power covered the whole metazoa/fungi group.

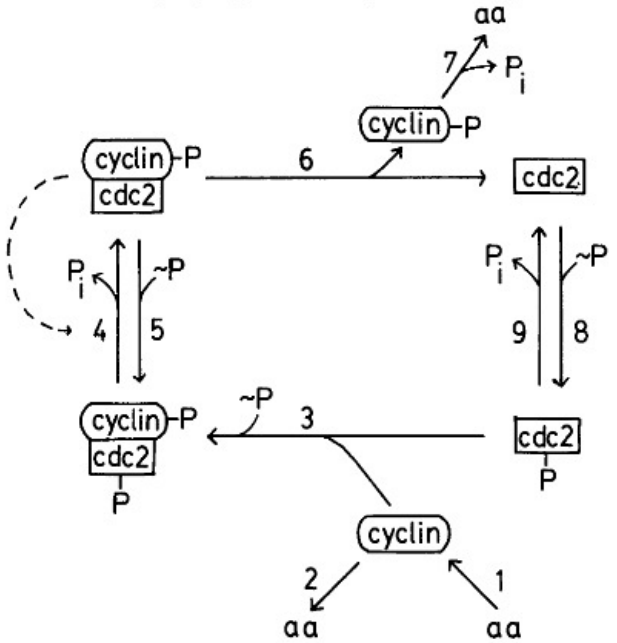

Figure 1: Reaction graph of the model from Tyson 1991.

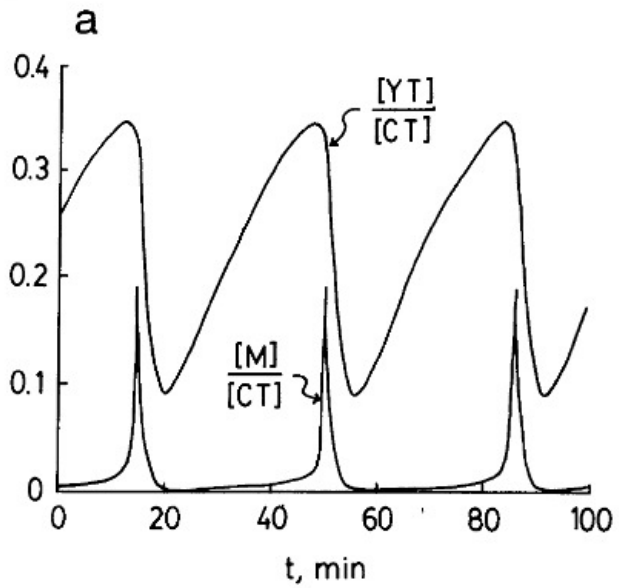

Figure 2: Oscillations of the total cyclin (YT) and the total MPF, relative to the total cyclin dependent kinase CDC2.

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Tyson JJ.
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Creation Date: 08 Feb 2005 18:28:27 U

Encoders: Bruce Shapiro, Vijayalakshmi Chelliah

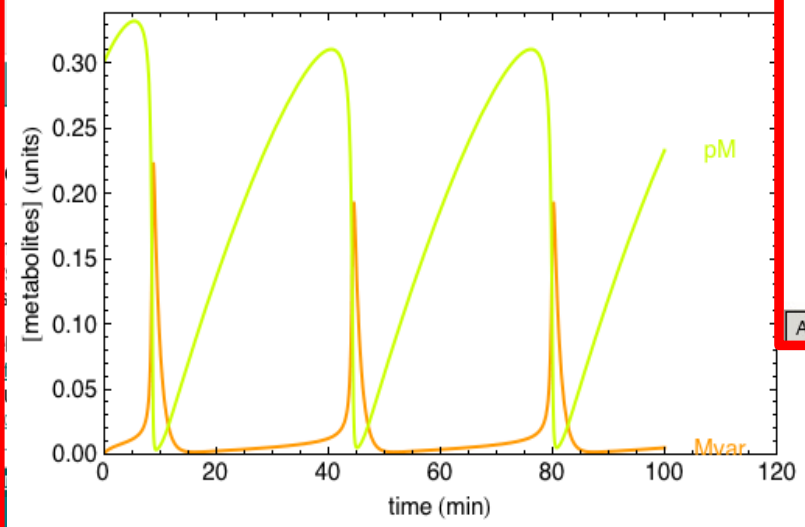
	bqbiol:hasVersion	Reactome REACT_152
set #1	bqbiol:isVersionOf	KEGG Pathway sce04111 Gene Ontology mitotic cell cycle
	bqmodel:is	Taxonomy Fungi/Metazoa group

This a model from the article:
Modeling the cell division cycle: c
Tyson JJ *Proc. Natl. Acad. Sci. U.S.A.*
Abstract:
The proteins cdc2 and cyclin form a
of the model show that the control s
metaphase arrest in unfertilized egg

This model originates from BioMod
For more information see the terms
To cite BioModels Database, please
Curated, Published, Quantitative Kine

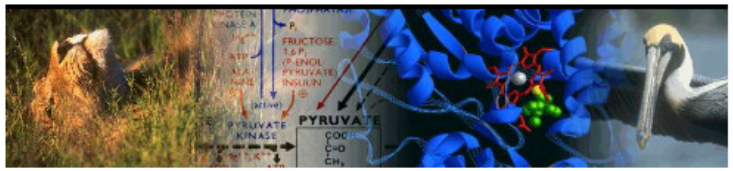
Computational Neurobiology Group in E

http://jjj.mib.ac.uk/webMathematica/Examples/PlotScript11.jsp?fun="JWS



Download the results in text or comma separated value format (e.g. for Excel import):

http://jjj.mib.ac.uk/biomodels/Tyson1991/index.html



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Biomodels: BIOMD0000000005
Tyson1991
Powered by JWS Online

JWSApplet – ver 5.0.3 Tyson1991

	Parameter	Value
P1_v1	cell	1
P2_v1	k6	1
P3_v1	k8notP	1.0e6
P4_v1	k9	1000
P5_v1	k3	200
P6_v1	k5notP	0.
P7_v1	k1aa	0.015
P8_v1	k2	0.
P9_v1	k7	0.6
P10_v1	k4	180
P11_v1	k4prime	0.018
E1	EmptySet	0.
I1	C2[0]	0.
I2	CP[0]	1
I3	Mvar[0]	0.
I4	Y[0]	0.
I5	YP[0]	0.
I6	pM[0]	0.3

Evaluate Model

Sim | State

StartTime 0 EndTime 100

Rates Metabolites

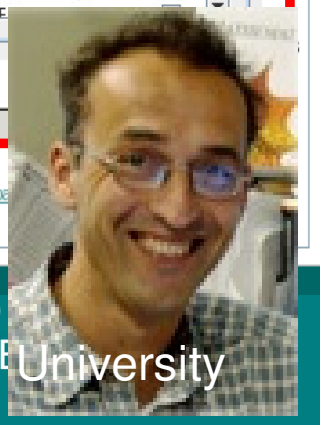
Type	Output	Plot
M1	C2	☐
M2	CP	☐
M3	Mvar	☑
M4	Y	☐
M5	YP	☐
M6	pM	☑
F1	v[Rea...	☐
F2	v[Rea...	☐
F3	v[Rea...	☐
F4	v[Rea...	☐
F5	v[Rea...	☐
F6	v[Rea...	☐
F7	v[Rea...	☐

POWERED BY webMATHEMATICA2

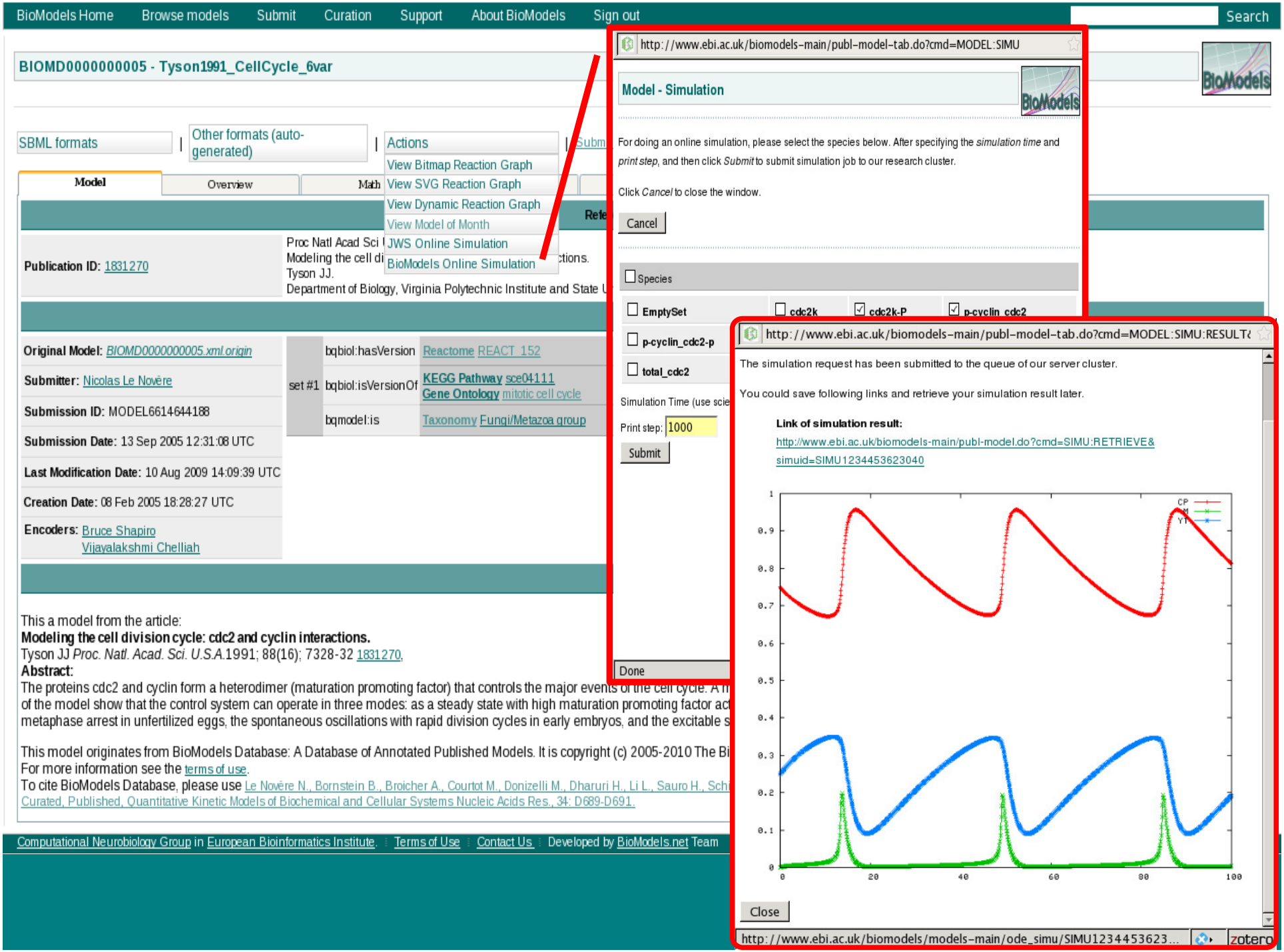
Reset

Applet jjjApplet started

Snoep J.L., Hucka M. (2006) BioModels Databa



Jacky Snoep
Stellenbosch University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View Dynamic Reaction Graph
View Model of Month
JWS Online Simulation
BioModels Online Simulation
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Publication ID: 1831270
Tyson JJ.
Original Model: BIOMD0000000005.xml.origin
Submitter: Nicolas Le Novère
Submission ID: MODEL6614644188
Submission Date: 13 Sep 2005 12:31:08 UTC
Last Modification Date: 10 Aug 2009 14:09:39 UTC
Creation Date: 08 Feb 2005 18:28:27 UTC
Encoders: Bruce Shapiro
Vijayalakshmi Chelliah
bqbiol:hasVersion
Reactome REACT_152
set #1
bqbiol:isVersionOf
KEGG Pathway sce04111
Gene Ontology mitotic cell cycle
bqmodel:is
Taxonomy Fungi/Metazoa group
This a model from the article:
Modeling the cell division cycle: cdc2 and cyclin interactions.
Tyson JJ Proc. Natl. Acad. Sci. U.S.A.1991; 88(16); 7328-32 1831270,
Abstract:
This model originates from BioModels Database: A Database of Annotated Published Models. It is copyright (c) 2005-2010 The Bi
For more information see the terms of use.
To cite BioModels Database, please use Le Novère N., Bornstein B., Broicher A., Courtot M., Donizelli M., Dharuri H., Li L., Sauro H., Schi
Curated, Published, Quantitative Kinetic Models of Biochemical and Cellular Systems Nucleic Acids Res., 34: D689-D691.
Computational Neurobiology Group in European Bioinformatics Institute.
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Developed by BioModels.net Team
http://www.ebi.ac.uk/biomodels-main/publ-model-tab.do?cmd=MODEL:SIMU
Model - Simulation
For doing an online simulation, please select the species below. After specifying the simulation time and print step, and then click Submit to submit simulation job to our research cluster.
Click Cancel to close the window.
Cancel
Species
EmptySet
cdc2k
cdc2k-P
p-cyclin_cdc2
p-cyclin_cdc2-p
total_cdc2
Simulation Time (use scie
Print step: 1000
Submit
Done
http://www.ebi.ac.uk/biomodels-main/publ-model-tab.do?cmd=MODEL:SIMU:RESULT
The simulation request has been submitted to the queue of our server cluster.
You could save following links and retrieve your simulation result later.
Link of simulation result:
http://www.ebi.ac.uk/biomodels-main/publ-model.do?cmd=SIMU:RETRIEVE&simuid=SIMU1234453623040
CP
M
YT
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
20
40
60
80
100
Close
http://www.ebi.ac.uk/biomodels/models-main/ode_simu/SIMU1234453623...
zotero

BIOMD0000000005 - Tyson1991_CellCycle_6var

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Reference Publication

Publication ID: 1831270

Proc Natl Acad Sci U S A 1991 Aug;88(16):7328-32.
Modeling the cell division cycle: cdc2 and cyclin interactions.
Tyson JJ.
Department of Biology, Virginia Polytechnic Institute and State University, Blacksburg 24061. [more]

Model

Original Model: *BIOMD0000000005.xml.origin*

Submitter: Nicolas Le Novère

Submission ID: MODEL6614644188

Submission Date: 13 Sep 2005 12:31:08 UTC

Last Modification Date: 10 Aug 2009 14:09:39 UTC

Creation Date: 08 Feb 2005 18:28:27 UTC

Encoders: Bruce Shapiro
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	bqbiol:hasVersion	Reactome REACT_152
set #1	bqbiol:isVersionOf	KEGG Pathway sce04111 Gene Ontology mitotic cell cycle
	bqmodel:is	Taxonomy Fungi/Metazoa group

Notes

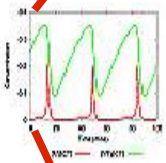
This a model from the article:
Modeling the cell division cycle: cdc2 and cyclin interactions.
Tyson JJ *Proc. Natl. Acad. Sci. U.S.A.*1991; 88(16); 7328-32 1831270,
Abstract:
The proteins cdc2 and cyclin form a heterodimer (maturation promoting factor) that controls the major events of the cell cycle. A mathematical model for the interactions of cdc2 and cyclin is constructed. Simulation and analysis of the model show that the control system can operate in three modes: as a steady state with high maturation promoting factor activity, as a spontaneous oscillator, or as an excitable switch. We associate the steady state with metaphase arrest in unfertilized eggs, the spontaneous oscillations with rapid division cycles in early embryos, and the excitable switch with growth-controlled division cycles typical of nonembryonic cells.

BIOMD0000000005 - Tyson1991_

SBML formats | Other fo generat

Model | Overv

Curation result



2010-02-08T10:29:04

Comment: The mo

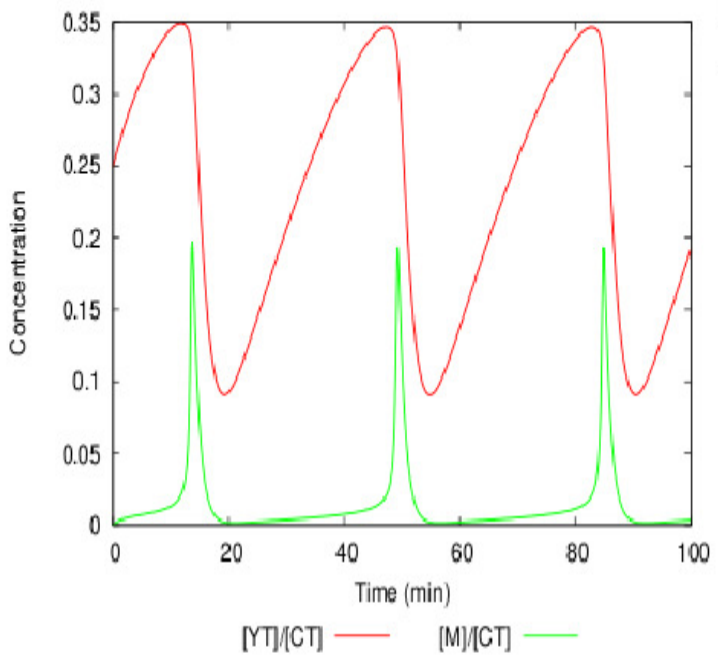
Model history

Rev	Log message
36	changed to SBML l2_v4 a
3	the latest version when im
2	original models.

Compare Revisions

Curation Result - Mozilla Firefox

http://www.ebi.ac.uk/biomodels-main/simulation-result.do?uri=anno-r



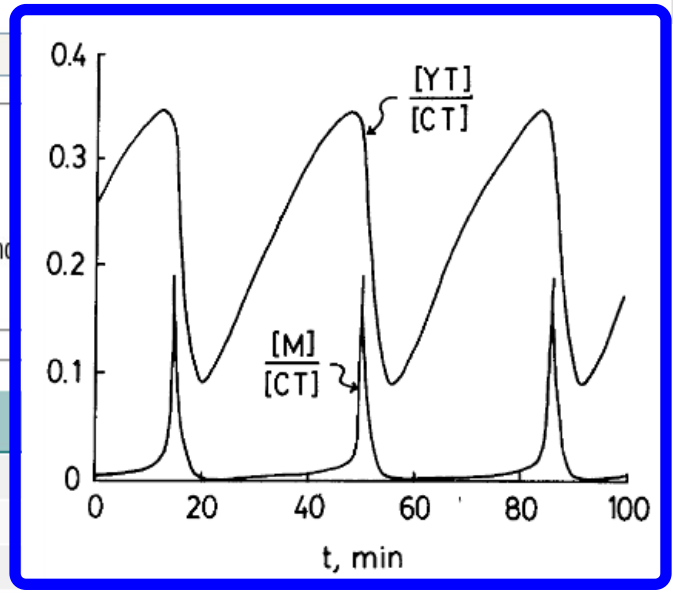
2010-02-08T10:29:04+00:00

Comment: The model reproduces figure 3A of the reference publication. The model was integrated and simulated using Copasi v4.5 (Build 30).

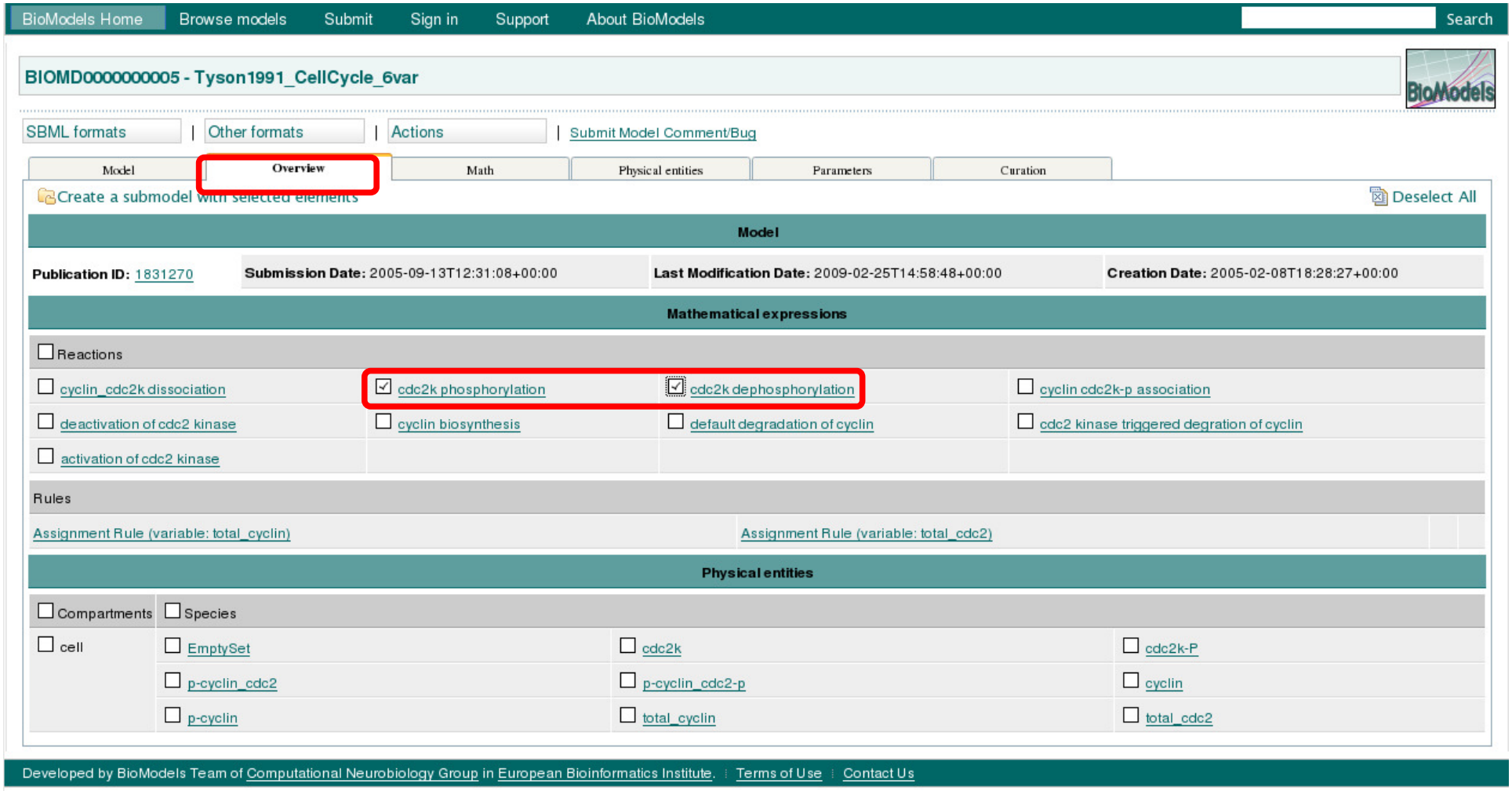
Figure reproduced using COPASI

Close

Done



original article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Creation Date: 2005-02-08T18:28:27+00:00
Mathematical expressions
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cyclin_cdc2k dissociation
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cdc2k dephosphorylation
cyclin cdc2k-p association
deactivation of cdc2 kinase
cyclin biosynthesis
default degradation of cyclin
cdc2 kinase triggered degration of cyclin
activation of cdc2 kinase
Rules
Assignment Rule (variable: total_cyclin)
Assignment Rule (variable: total_cdc2)
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Species
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EmptySet
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cdc2k-P
p-cyclin_cdc2
p-cyclin_cdc2-p
cyclin
p-cyclin
total_cyclin
total_cdc2
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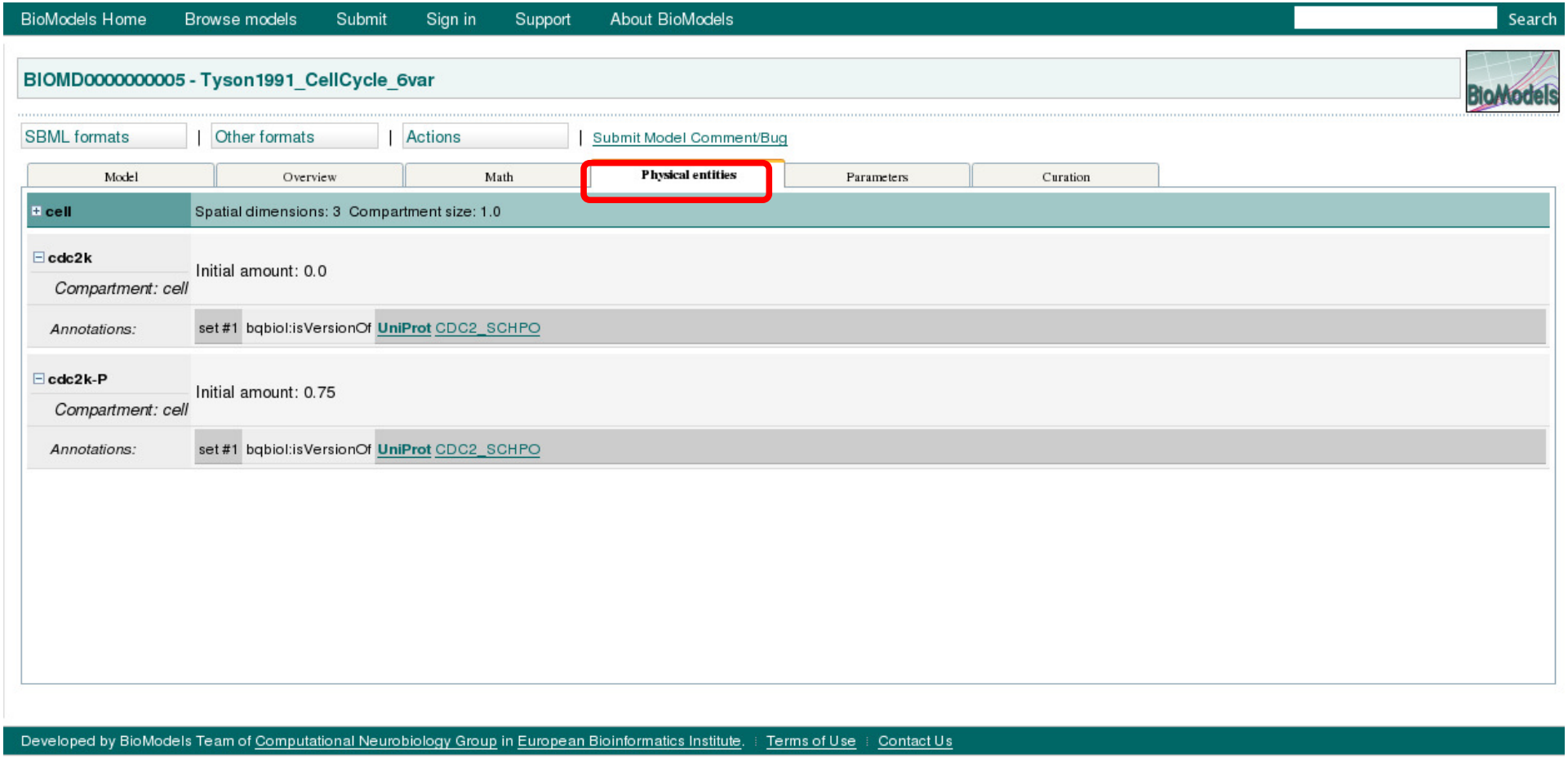
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cell
Spatial dimensions: 3 Compartment size: 1.0
cdc2k
Compartment: cell
Initial amount: 0.0
Annotations:
set #1 bqbiol:isVersionOf UniProt CDC2_SCHPO
cdc2k-P
Compartment: cell
Initial amount: 0.75
Annotations:
set #1 bqbiol:isVersionOf UniProt CDC2_SCHPO
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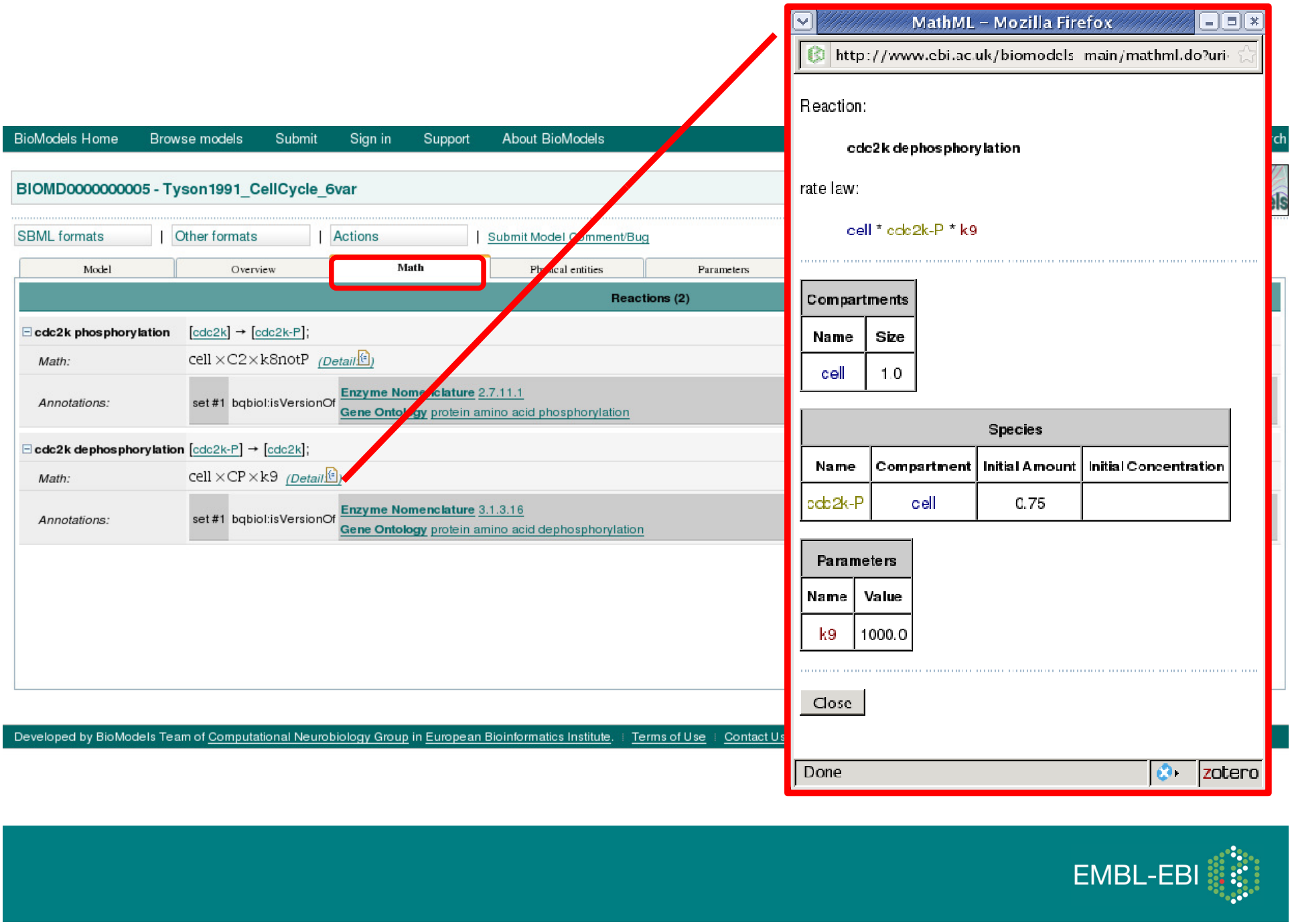
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cdc2k phosphorylation [cdc2k] → [cdc2k-P];
Math: cell ×C2×k8notP (Detail)
Annotations: set #1 bqbiol:isVersionOf Enzyme Nomenclature 2.7.11.1
Gene Ontology protein amino acid phosphorylation
cdc2k dephosphorylation [cdc2k-P] → [cdc2k];
Math: cell ×CP×k9 (Detail)
Annotations: set #1 bqbiol:isVersionOf Enzyme Nomenclature 3.1.3.16
Gene Ontology protein amino acid dephosphorylation
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http://www.ebi.ac.uk/biomodels main/mathml.do?uri
Reaction:
cdc2k dephosphorylation
rate law:
cell * cdc2k-P * k9
Compartments
Name
Size
cell
1 0
Species
Name
Compartment
Initial Amount
Initial Concentration
cdc2k-P
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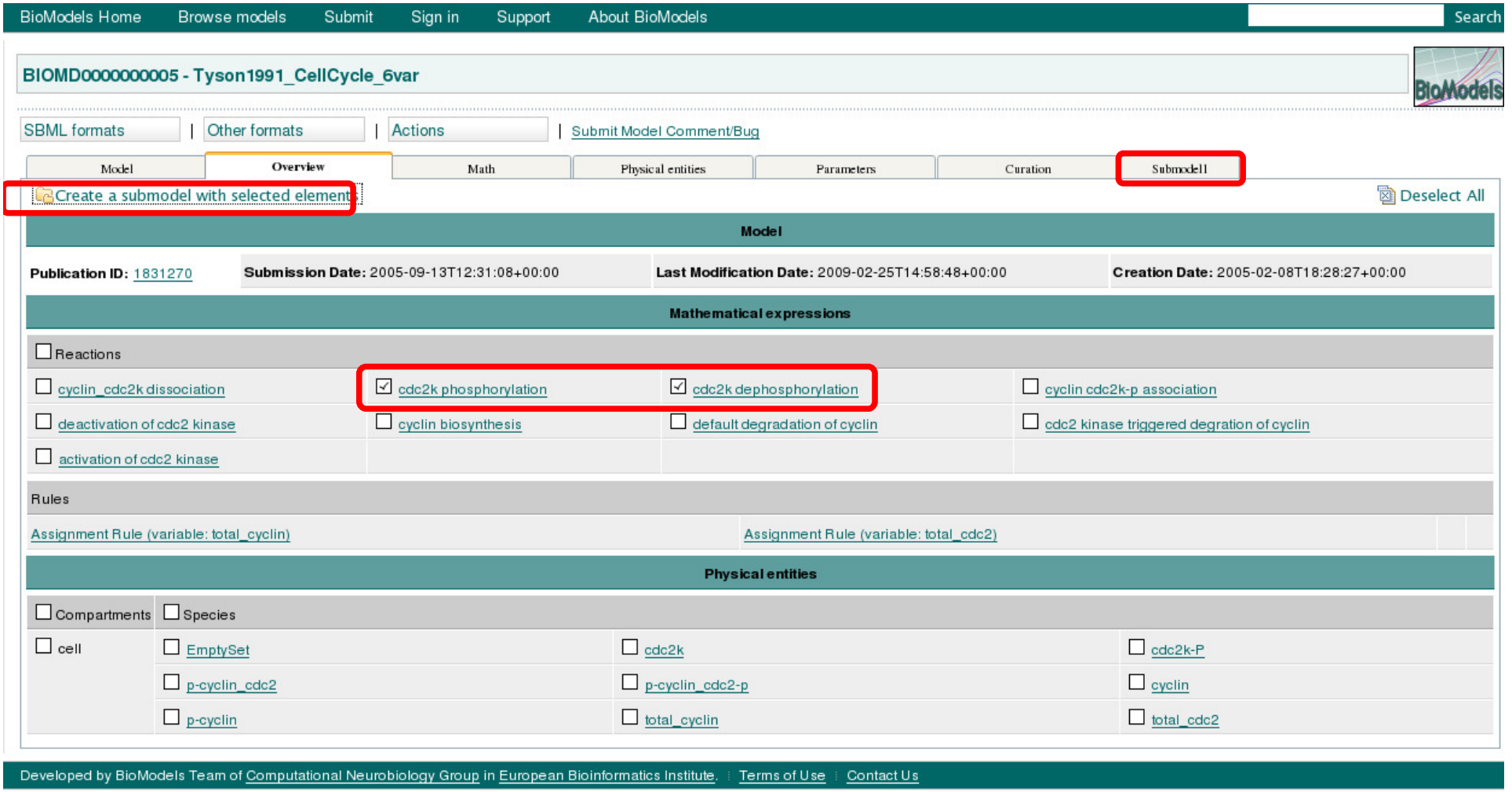
Parameters
Name
Value
k9
1000.0
Close
Done
zotero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Deselect All
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p-cyclin_cdc2-p
cyclin
p-cyclin
total_cyclin
total_cdc2
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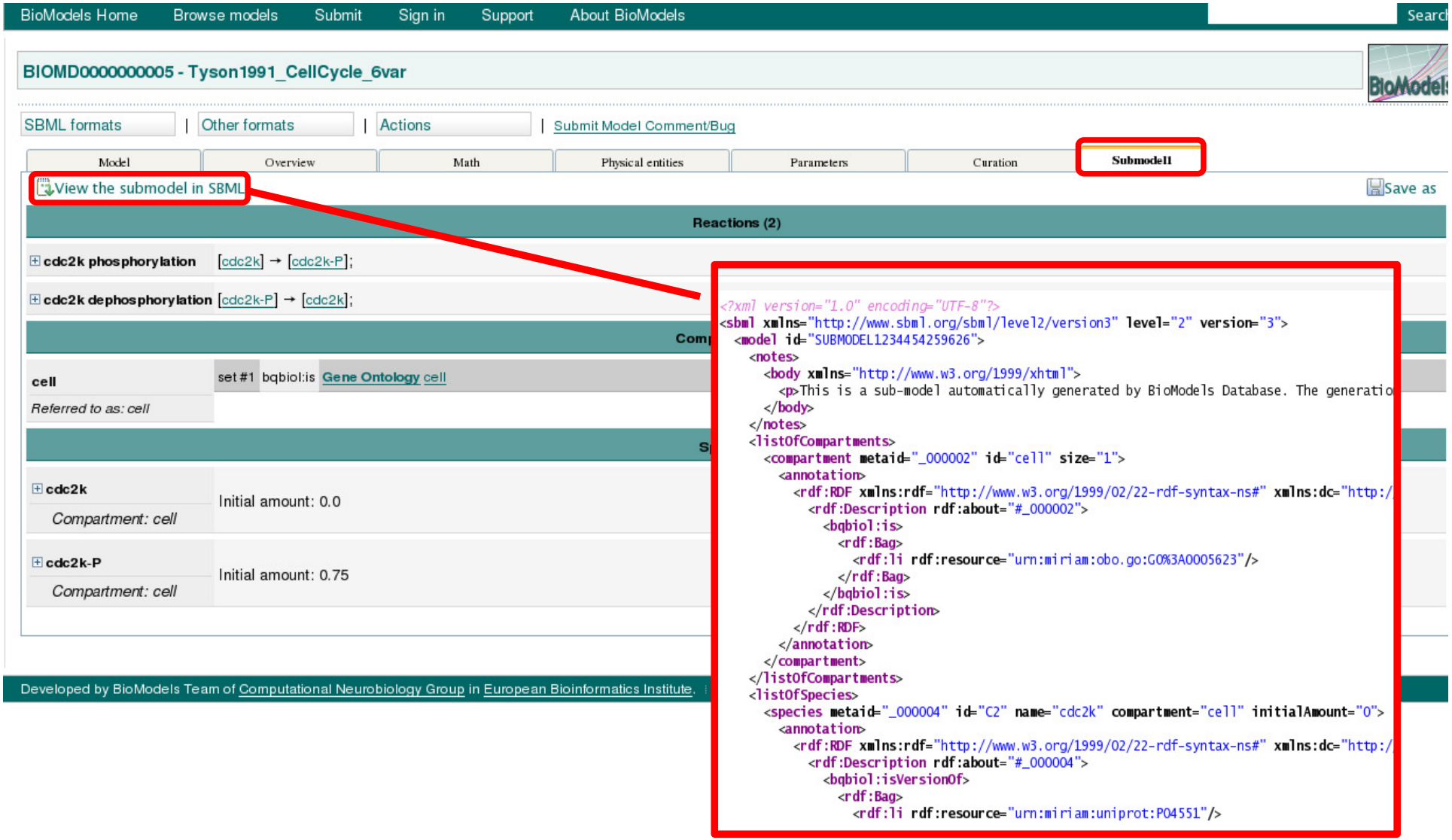
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Reactions (2)
cdc2k phosphorylation [cdc2k] → [cdc2k-P];
cdc2k dephosphorylation [cdc2k-P] → [cdc2k];
cell
set #1 bqbiol:is Gene Ontology cell
Referred to as: cell
cdc2k
Compartment: cell
Initial amount: 0.0
cdc2k-P
Compartment: cell
Initial amount: 0.75
Developed by BioModels Team of Computational Neurobiology Group in European Bioinformatics Institute.
<?xml version="1.0" encoding="UTF-8"?>
<sbml xmlns="http://www.sbml.org/sbml/level2/version3" level="2" version="3">
<model id="SUBMODEL1234454259626">
<notes>
<body xmlns="http://www.w3.org/1999/xhtml">
<p>This is a sub-model automatically generated by BioModels Database. The generatio
</body>
</notes>
<listOfCompartments>
<compartment metaid="_000002" id="cell" size="1">
<annotation>
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<bqbiol:is>
<rdf:Bag>
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</rdf:Description>
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</annotation>
</compartment>
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<listOfSpecies>
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<annotation>
<rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#" xmlns:dc="http:/
<rdf:Description rdf:about="#_000004">
<bqbiol:isVersionOf>
<rdf:Bag>
<rdf:li rdf:resource="urn:miriam:uniprot:P04551"/>
EMBL-EBI

BioModels Web Services

Available features

With BioModels Web Services, users can access the up-to-date resources in BioModels Database without installing a local copy of the database. There are a range of available features for searching and retrieving models. Furthermore, some features can help users to extract interesting parts from a large model and construct them into a submodel. For any comments or new feature enquiries, please feel free to contact us.

- Available features
- javadoc
- WSDL

The WSDL (Web Services Description Language) defines and describes the available features in an XML format file. This enables third-party sofware to automate parsing all available features of BioModels Web Services. Comparing with WSDL, Javadoc is API documentation which provides more information to the developers.

Download

According to different cases, we provide two kinds of libraries for using BioModels Web Services. For downloading, please right click on the link and "*Save Target As*" or "*Save Link As*".

Description	Size	Link
Standalone and includes all external dependencies and ready for use	1.9M	biomodelswslib-standalone-1.11.jar
Light-weight, but needs other dependencies to work together	6.4K	biomodelswslib-single-1.11.jar

These are the dependencies only needed by light-weight library.

- axis.jar
- jaxrpc.jar
- commons-logging-1.1.jar
- commons-discovery-0.2.jar
- saaj.jar
- wsdl4j-1.5.1.jar

Basics - Getting Started

Firstly, download the library we provided. I guess you already done it.

Assuming that you downloaded the biomodelswslib-standalone.jar, let's write a simple HelloBioModels.java to test if it works on your environment.

```
import uk.ac.ebi.biomodels.*;

public class HelloBioModels
{
  public static void main(String args[]) throws Exception
  {
    BioModelsWSClient client = new BioModelsWSClient();

    /* uncomment when a proxy is needed
    client.setProperty("http.proxyHost", "your.http.proxy.host");
    client.setProperty("http.proxyPort", "yourHttpProxyPort");
    client.setProperty("socks.proxyHost", "your.socks.proxy.host");
    client.setProperty("socks.proxyPort", "yourSocksProxyPort");
    */
```

BioModels Database widely used

- For benchmarking the modeling and simulation tools.
- Models are downloaded by researches to generate more elaborate models (i.e. including more reactions, etc.).
- Clustering and Merging models using annotations.

and many more....

BioModels Team at EBI

Nicolas
Le Novère

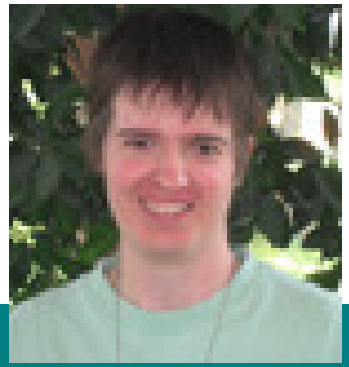
Camille Laibe

Nicolas Rodriguez

Lukas Endler

Vijayalakshmi Chelliah

Sarah Keating



Nick Juty

Sarala Wimalaratne