BioModels Database, a curated resource of annotated published models

Nicolas Le Novère, EMBL-EBI
on the behalf of the BioModels.net team

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

The models I am not going to talk about

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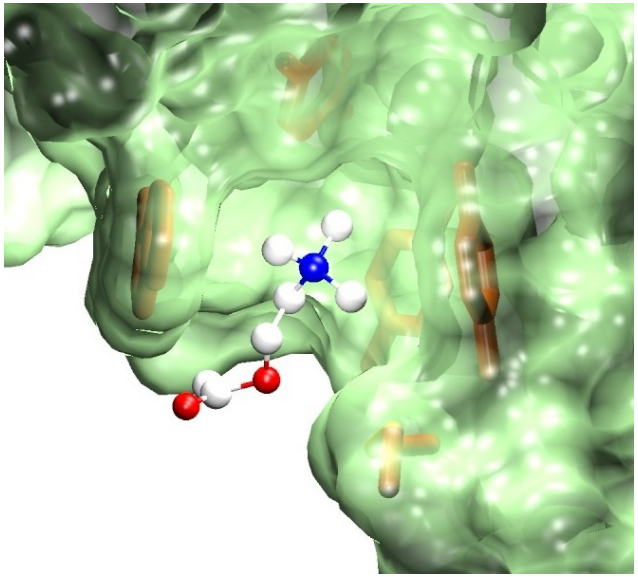
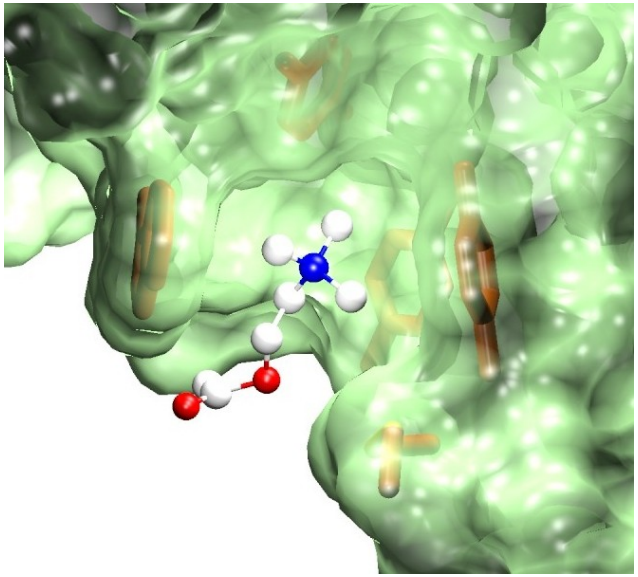
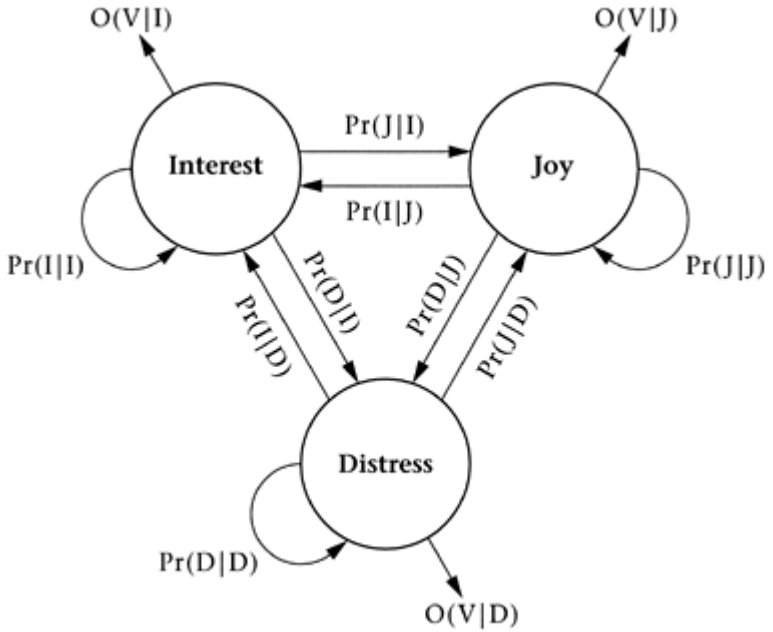
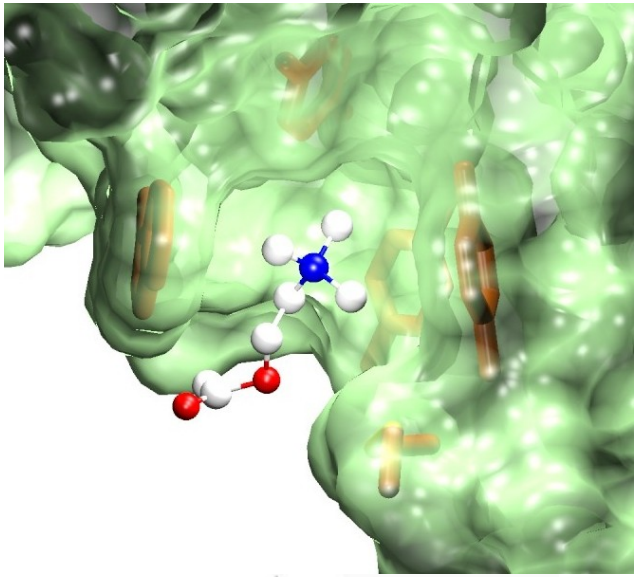


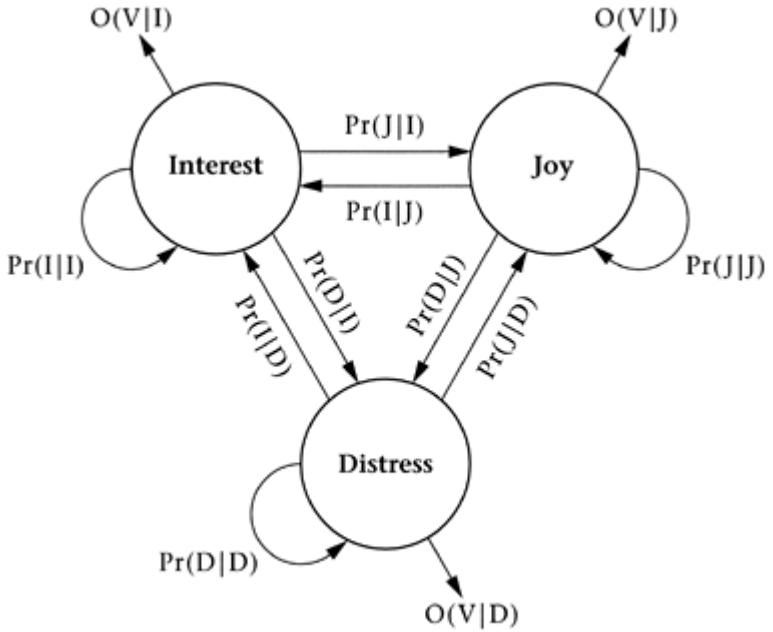
The models I am not going to talk about





The models I am not going to talk about





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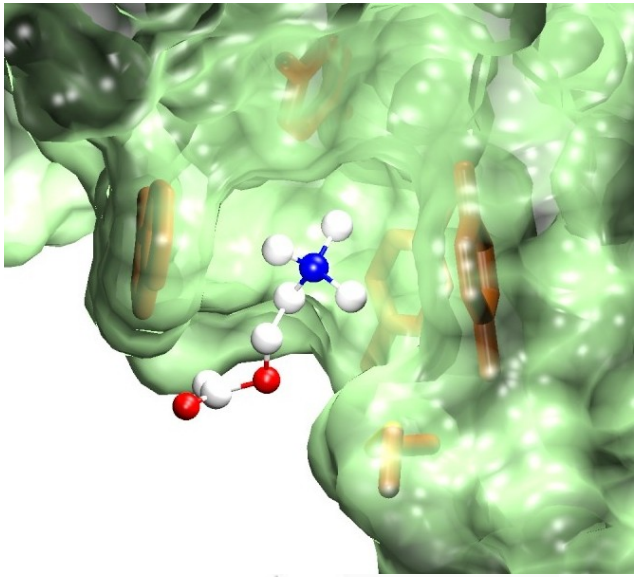
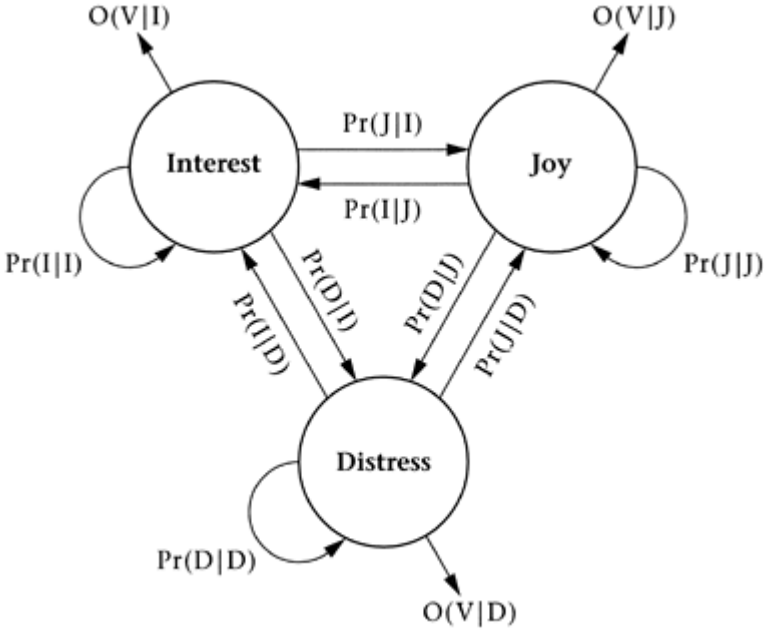




“Model”, for here and now

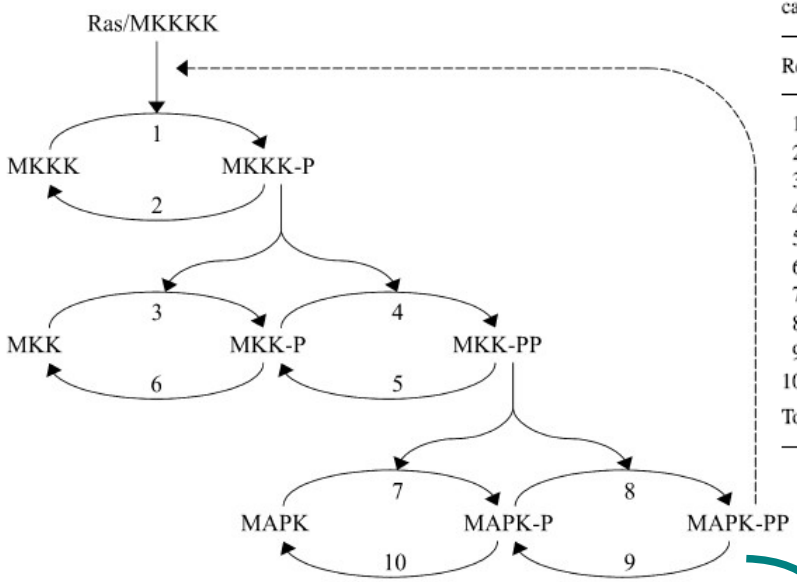


Table 2. Rate equations and parameter values of the MAPK cascade model. Concentrations and the Michaelis constants (K_1–K_{10}) are given in nM. The catalytic rate constants (k_3, k_4, k_7, k_8) and the maximal enzyme rates (V_1, V_2, V_5, V_6, V_9, V_{10}) are expressed in s^{-1} and nM·s^{-1}, respectively.

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	$V_{10} \cdot [MAPK\text{-}P]/(K_{10} + [MAPK\text{-}P])$	$V_{10} = 0.5$; $K_{10} = 15$;

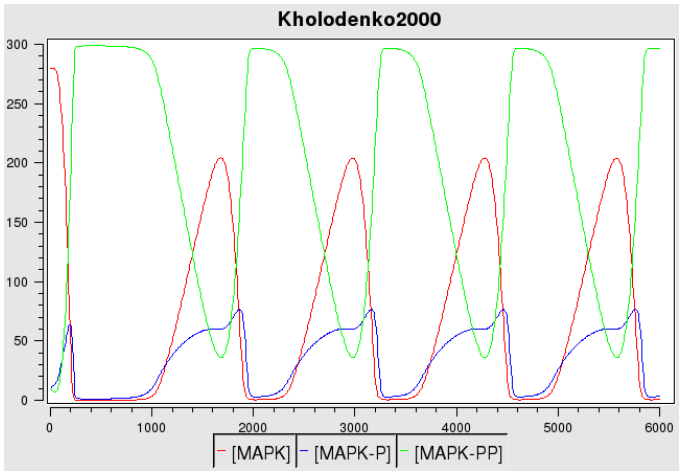
Total concentrations: $[MKKK]_{total} = 100$; $[MKK]_{total} = 300$; $[MAPK]_{total} = 300$

computer readable format, eg.

SBML

simulation software eg. COPASI

numerical output eg. time course



Motivation and requirements

- 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 must be accessible, as well as their detailed description.
  - Modelers must be able to rely on the accuracy of the models.
  - Models should be available in common formats eg.:
    - SBML (http://www.sbml.org)
    - CellML (http://www.cellml.org)
  - Resource should be searchable for different criteria.
  - Resource should neither focussed on a particular biological substrate, process or species, nor specialised on a given modelling approach

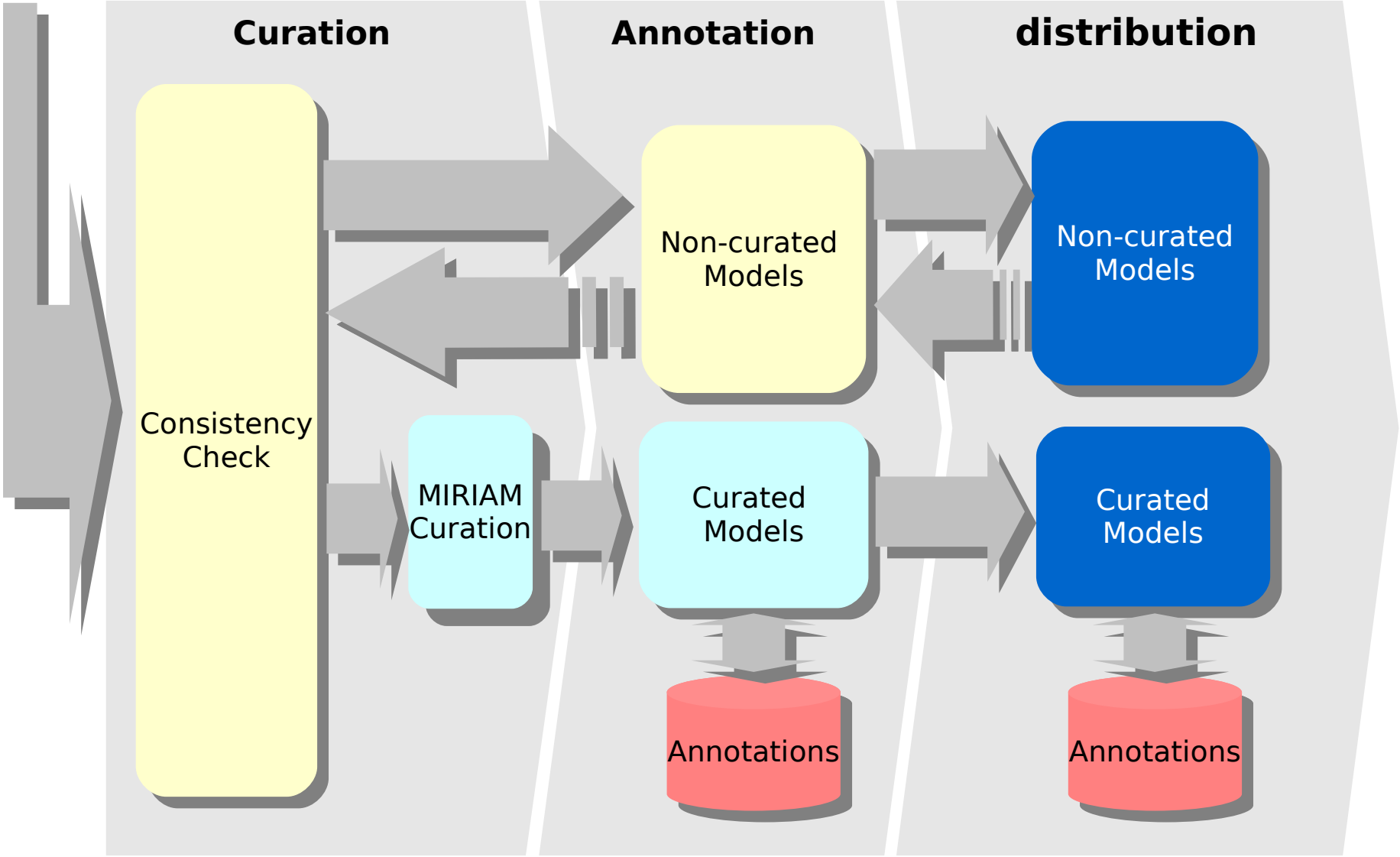
What is BioModels Database?

- Store and serve quantitative models of biomedical interest
- Only models described in the peer-reviewed scientific literature.
- Models are curated: computer software check the syntax, while human curators check the semantics.
- Models are simulated to ensure they provide the expected results
- Model components are annotated, to improve identification and retrieval.
- Models are accepted in several formats, and served in several others.

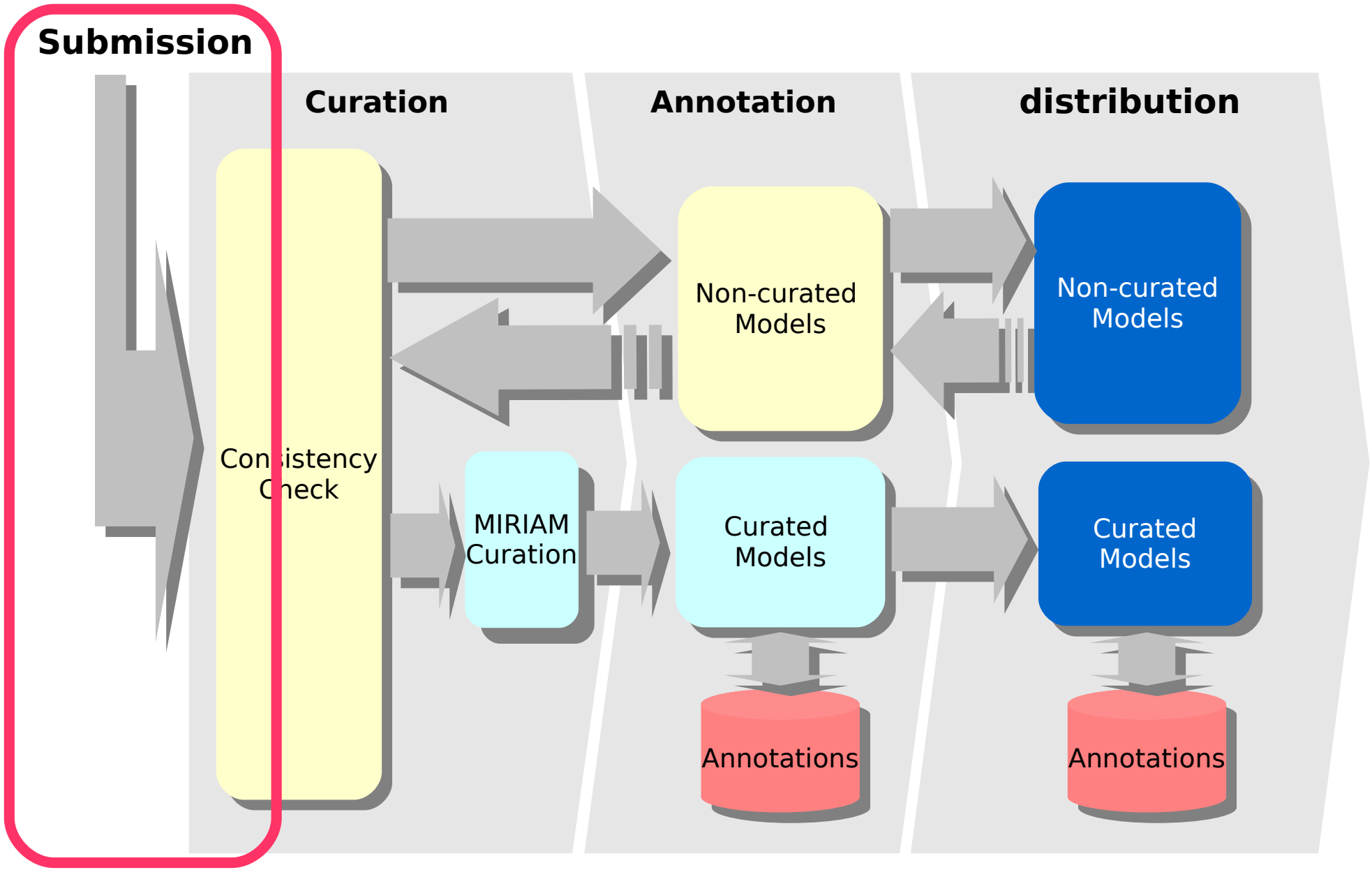
Production of the resource

Production pipeline

Submission



Submission of new models



Where do models come from?

- Submitted by curators
  - imported from other repositories (DOQCS, CellML)
  - imported from journals webpages
  - reimplemented from literature
- From authors before grant application or publication
- Some journals advocate submission to BioModels DB:
  - Molecular Systems Biology
  - PLoS journals
  - BioMedCentral journals
- Various people curated models out of interest.

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 pathways, controlled vocabularies, etc.

Search | Go to the model | Advanced search

Browse models

- Curated models (216)
- Browse models using GO
- Non-curated models (196)

Deposition of models into BioModels Database gives convenience to users to exchange and reuse models. BioModels Database currently accepts models encoded in two formats: SBML and CellML.

Simulate in JWS Online

Submit a model

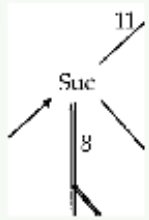
Mirror at California Institute of Technology http://biomodels.caltech.edu

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

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

Model of the month

May, 2009



Sucrose accumulation is accompanied by continuous synthesis and degradation processes in the developing sugar cane, *Saccharum officinarum*. Sugar cane internode maturation coincides with increased sucrose storage, but is not dependent purely on time. In addition, cane varieties accumulate sucrose to quite divergent extents.

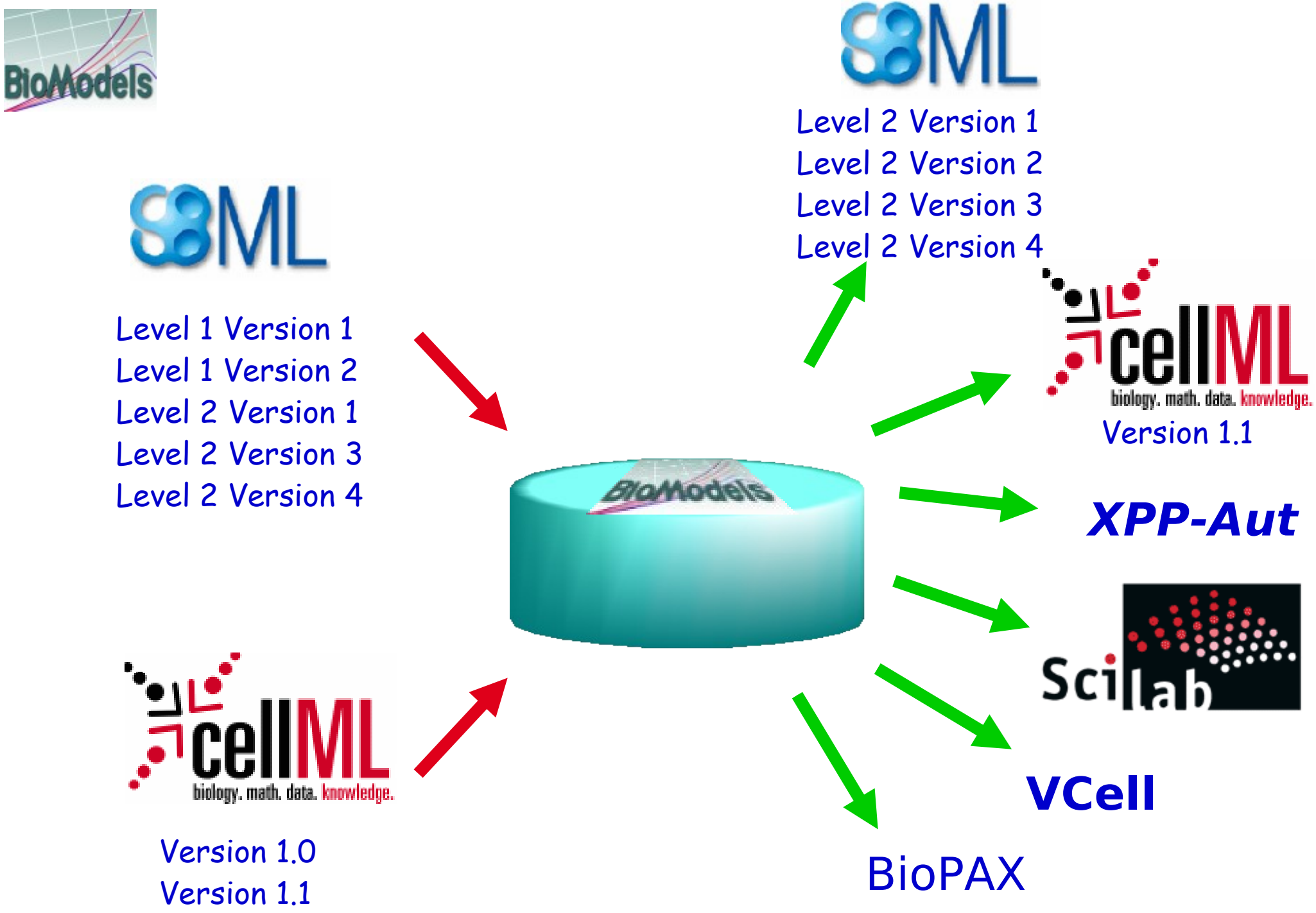
Read more...

News

16th June 2009 **Fourteenth release**
Download All Models Under SBML Format

25th March 2009 **Thirteenth release**
Download All Models Under SBML Format

28th-30th March 2009 **BioModels meeting 2009**
The Fourth BioModels Meeting will be held from March 28 to 30, 2009, at the EBI in Cambridge (United Kingdom).


BioModels
SBML
Level 2 Version 1
Level 2 Version 2
Level 2 Version 3
Level 2 Version 4
SBML
Level 1 Version 1
Level 1 Version 2
Level 2 Version 1
Level 2 Version 3
Level 2 Version 4
cellML
biology. math. data. knowledge.
Version 1.1
BioModels
XPP-Aut
Scilab
cellML
biology. math. data. knowledge.
Version 1.0
Version 1.1
VCell
BioPAX

>170 tools supporting SBML

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.

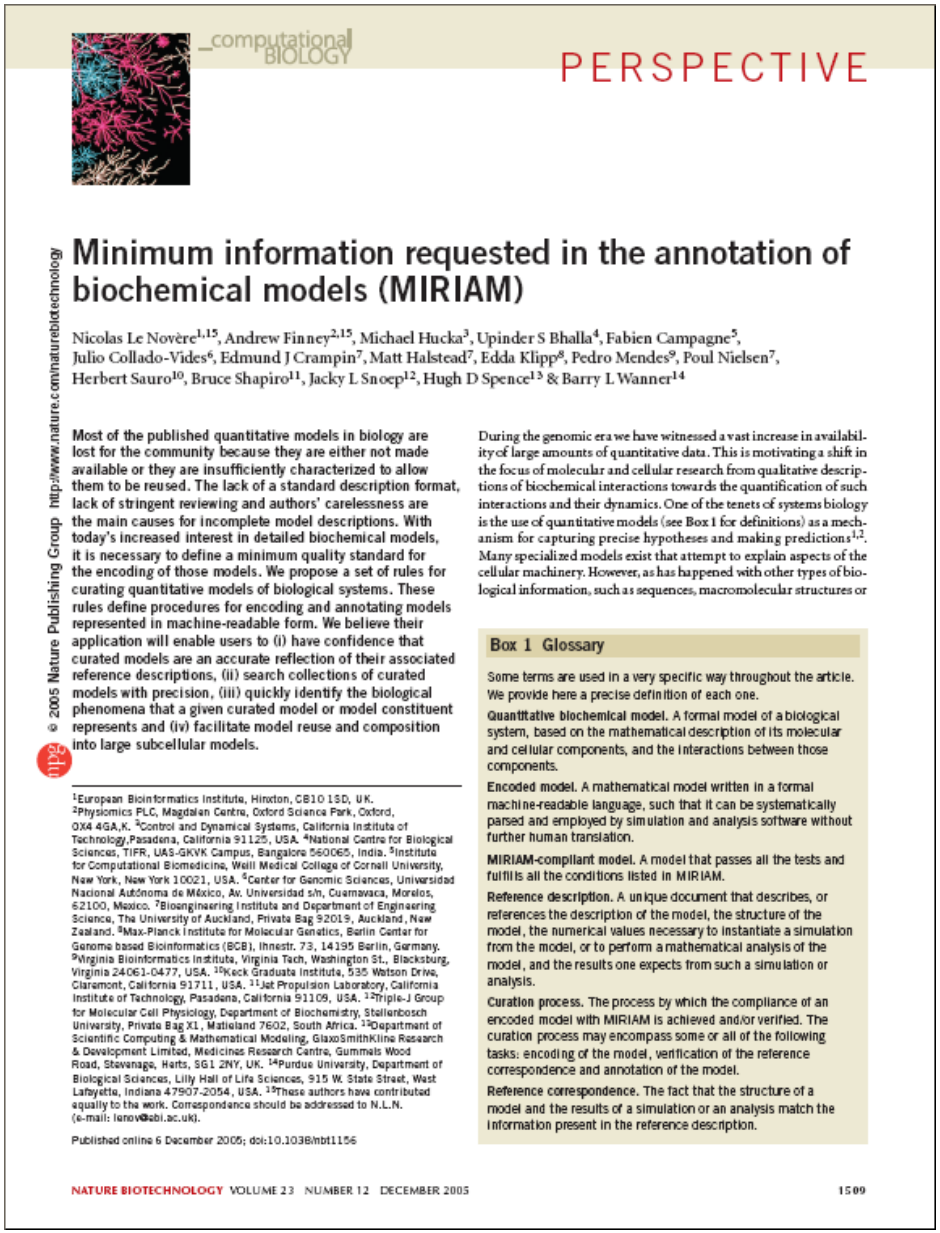
	Capabilities					Frameworks							API	Dep.	Platforms	SBML		Availabil.		
	Creation	Simulation	Analysis	Database	Utility	ODE	DAE	PDE	Stochastic	Events	Logical	Other				Import	Export	Open source	Academic use	Commercial use
acslXtreme	•														W	•			$	$
ALC	•					•	•		•			•			L, W, M, B		•	•	F	F
Asmparts	•				•	•									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
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	$
BioGrid																				

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

MIRIAM guidelines

- Reporting guidelines for curation of quantitative models
  - Specifically about encoding & annotation
  - 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.

[1]European Bioinformatics Institute, Hinxton, CB10 1SD, UK. [2]Physiomics PLC, Magdalen Centre, Oxford Science Park, Oxford, OX4 4GA,K. [3]Control and Dynamical Systems, California Institute of Technology,Pasadena, California 91125, USA. [4]National Centre for Biological Sciences, TIFR, UAS-GKVK Campus, Bangalore 560065, India. [5]Institute for Computational Biomedicine, Weill Medical College of Cornell University, New York, New York 10021, USA. [6]Center for Genomic Sciences, Universidad Nacional Autónoma de México, Av. Universidad s/n, Cuernavaca, Morelos, 62100, Mexico. [7]Bioengineering Institute and Department of Engineering Science, The University of Auckland, Private Bag 92019, Auckland, New Zealand. [8]Max-Planck Institute for Molecular Genetics, Berlin Center for Genome based Bioinformatics (BCB), Ihnestr. 73, 14195 Berlin, Germany. [9]Virginia Bioinformatics Institute, Virginia Tech, Washington St., Blacksburg, Virginia 24061-0477, USA. [10]Keck Graduate Institute, 535 Watson Drive, Claremont, California 91711, USA. [11]Jet Propulsion Laboratory, California Institute of Technology, Pasadena, California 91109, USA. [12]Triple-J Group for Molecular Cell Physiology, Department of Biochemistry, Stellenbosch University, Private Bag X1, Matieland 7602, South Africa. [13]Department of Scientific Computing & Mathematical Modeling, GlaxoSmithKline Research & Development Limited, Medicines Research Centre, Gunnels Wood Road, Stevenage, Herts, SG1 2NY, UK. [14]Purdue University, Department of Biological Sciences, Lilly Hall of Life Sciences, 915 W. State Street, West Lafayette, Indiana 47907-2054, USA. [15]These authors have contributed equally to the work. Correspondence should be addressed to N.L.N. (e-mail: lenov@ebi.ac.uk).

Published online 6 December 2005; doi:10.1038/nbt1156

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

Models must :

- be encoded in a public machine-readable format (community standard in the case of BioModels Database).
- be clearly linked to a single reference description (peer-reviewed in the case of BioModels Database)
- reflect the structure of the biological processes described in the reference paper (list of reactions etc.)
- be instantiable in a simulation (possess initial conditions etc.)
- be able to reproduce the results given in the reference paper
- contain creator's contact details
- annotation to unambiguously identify each model constituent

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 4
- 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 4* 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 *AuthorNameYear_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

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- SBML Level 2 Version 3
- SBML Level 2 Version 2
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Publication ID: 1831270 (●) **PubMed** (Search Medline) ( ) **DOI** (Resolve a DOI) ( ) **URL** ( ) **Unpublished**

Continue Reset

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- 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 the curation step (underlined fields are required), and then click *Submit*.

First name:

Last name:

Organisation:

Email:

Comment:

Original model:

Model file: Browse...

Submit Reset

Submit - Step 4

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

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

MODEL8232600906

Submit Another Model

Subject: **BioModels Database - Notification of New Model Submission**
From: biomodels-database-mailer@ebi.ac.uk
Date: 09:30
To: vijj@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
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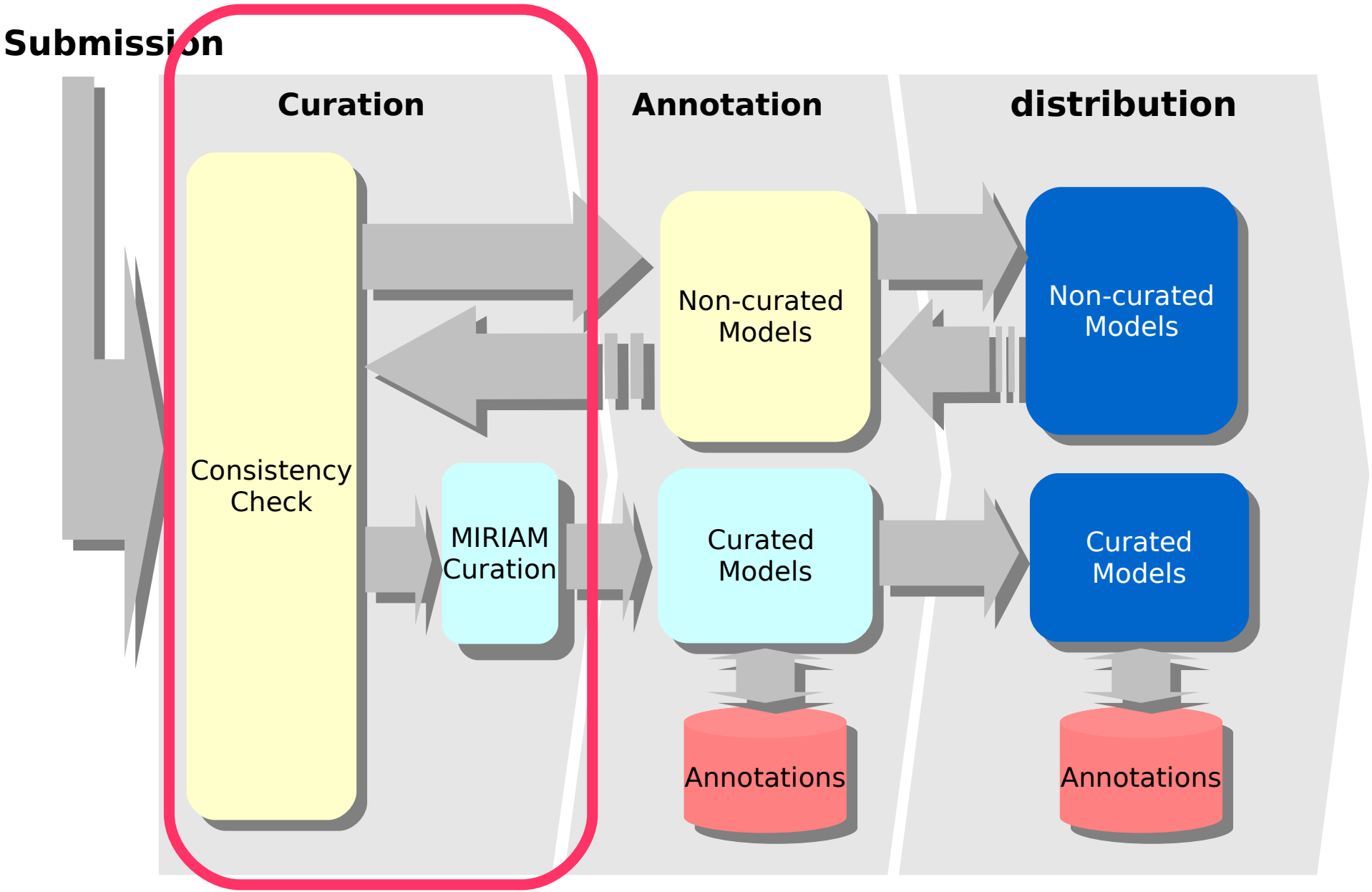
Thank you,
The BioModels Database Team

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.

Curation


Submission
Curation
Annotation
distribution
Consistency Check
MIRIAM Curation
Non-curated Models
Curated Models
Annotations
Non-curated Models
Curated Models
Annotations

BioModels Database - SeaMonkey

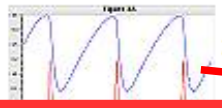
BioModels Home | Browse models | Submit | Sign in | Support | About BioModels | Search

BIOMD0000000005 - Tyson1991_CellCycle_6var

SBML formats | Other formats | Actions | Submit Model

Model | Overview | Math | Physical entities

Curation result

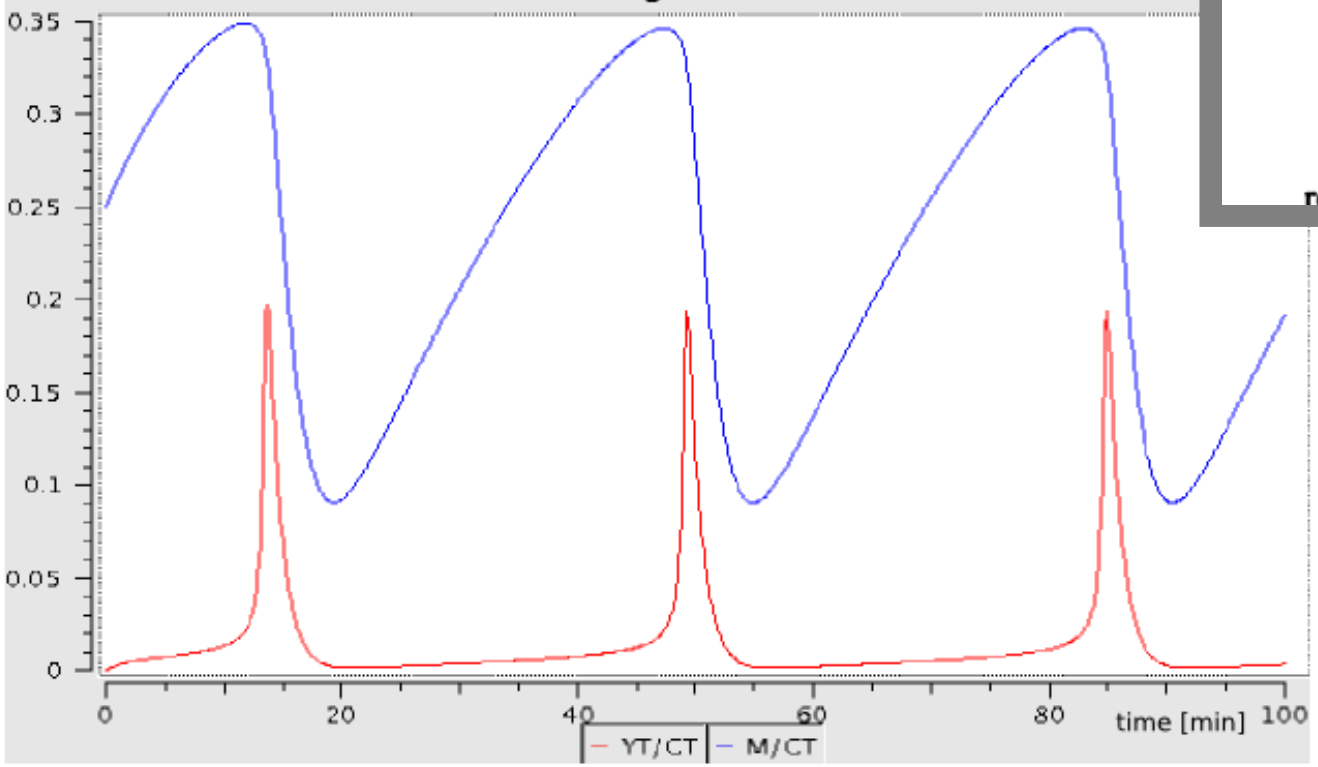


2008-08-15T12:01:18+00:00

Comment: The model was simulated using Copasi v.4.4

http://www.ebi.ac.uk - Curation Result - SeaMonkey

Figure 3A



Comment: Reproduction of Fig3A from the original publication (Tyson JJ 1991). Integrated and plot using Copasi v.4.4.

Done

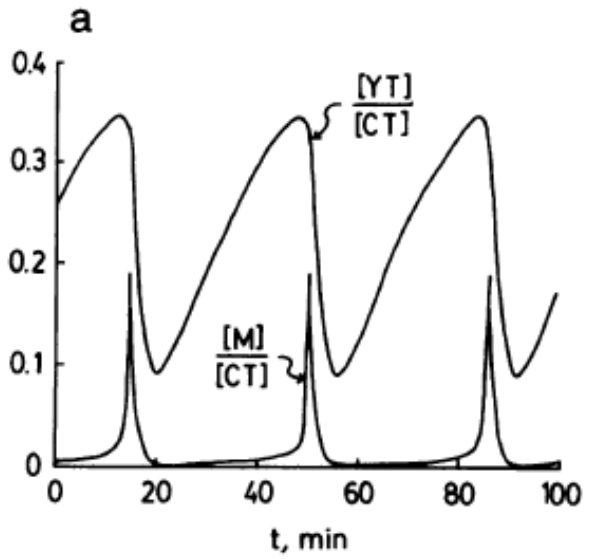


FIG. 3. Dynamical behavior of the cdc2–cycli
relative to total cdc2 ([CT] = [C2] + [CP] + [pM]

Curated and Non-curated Models

- Curated models – MIRIAM compliance successfully checked
- Non-Curated models – valid SBML, not curated or annotated
  - Not MIRIAM compliant:

    cannot reproduce results published in the paper.

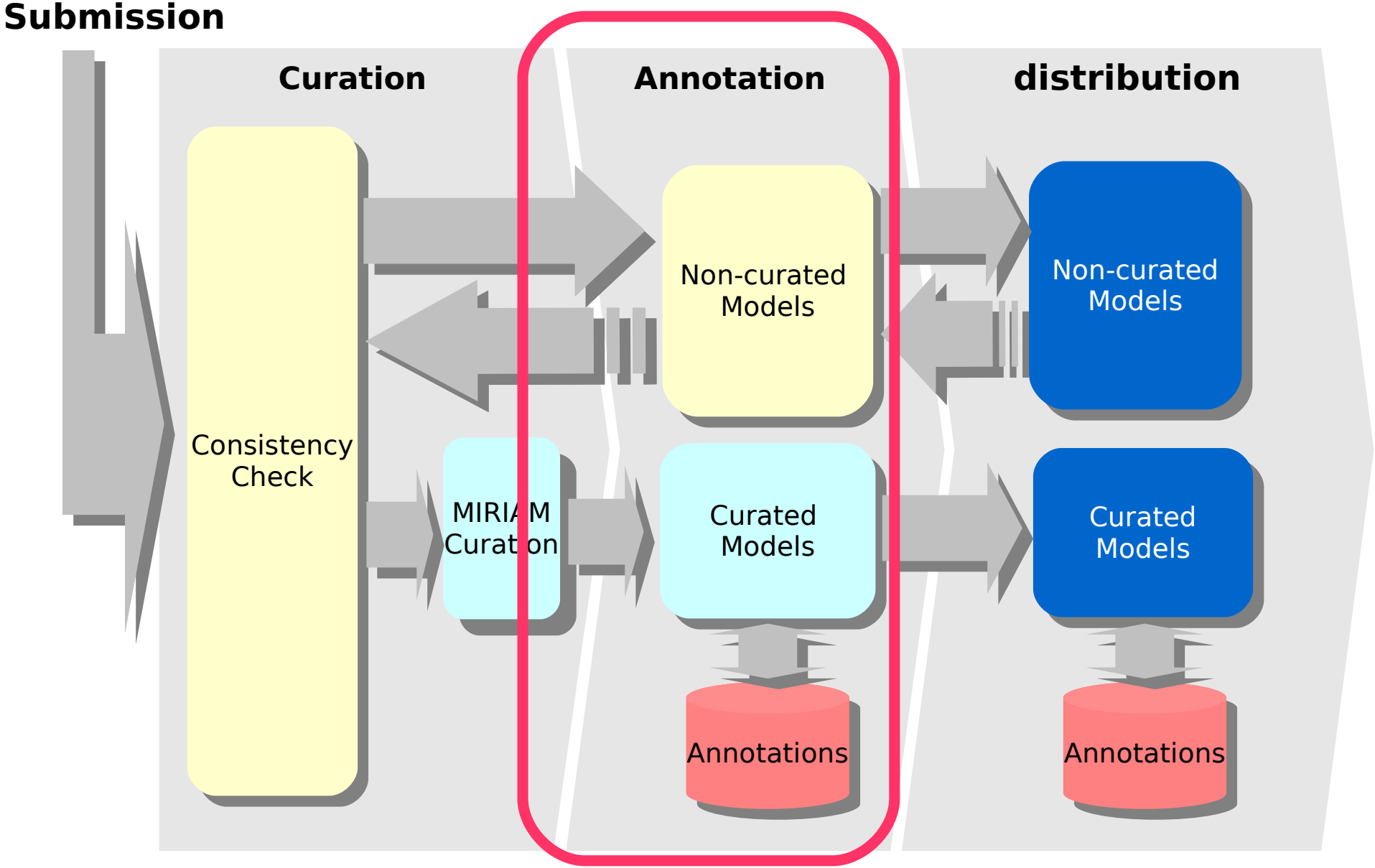
    differ in model structure

    non-kinetic models (eg. FBA, stoichiometric maps)
  - MIRIAM compliant:

    models contain kinetics that we cannot curate at present.

    models are yet to be curated

Annotation


Submission
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MIRIAM annotations

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

- enhances model quality
- is essential for search criteria.

External information are represented as a triplet which consists of:

- resource (eg. Enzyme Nomenclature)
- identifier (eg. 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/)

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 Date: 2005-09-13T12:31:08+00:00

Last Modification Date: 2009-02-25T14:58:48+00:00

Creation Date: 2005-02-08T18:28:27+00:00

Encoders: Bruce Shapiro
Vijayalakshmi Chelliah

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

Notes

Cell Cycle Model; Tyson (1991, 6 variables)

Description

A model of the cell cycle based on the interactions between cdc2 and cyclin. The model has six dynamic variables: C2 (cdc2); CP (cdc2-P complex); pM (P-cyclin-cdc2-P complex); M (active MPF, P-cyclin-cdc2 complex); Y (cyclin); and YP (cyclin-P). Total cyclin concentration (YT) is the sum [YT]=[Y]+[YP]+[pM]+[M]

Reaction

Variable	ODE
C2	0
CP	1
pM	0.3
M	0
Y	0
YP	0

BioModels Home | Browse models | Submit | Sign in | Support | About BioModel

BIOMD0000000005 - Tyson1991_CellCycle_6var

SBML formats | Other formats | Actions | Submit M

Model | Overview | Math | Physical entit

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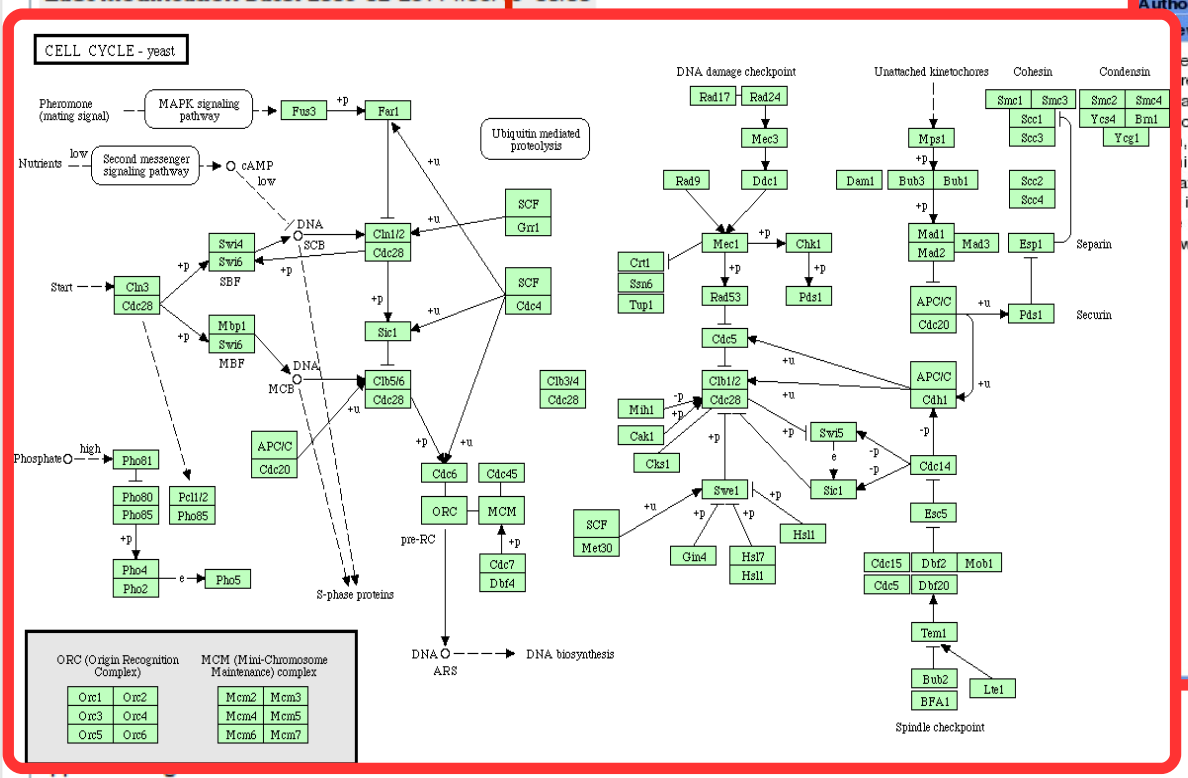
set #1	bqbiol:isVersionOf	**KEGG Pathway** sce04111
		Gene Ontology mitotic cell cycle
	bqbiol:hasVersion	**Reactome** REACT_152

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

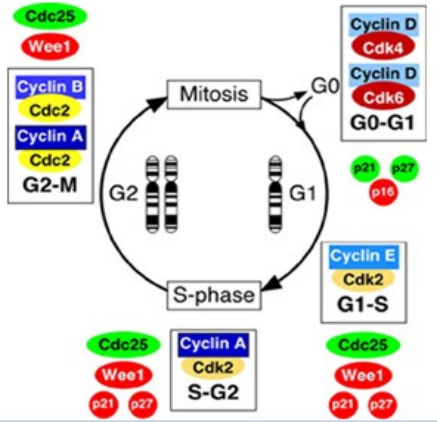
Up taxonomy tree	Down taxonomy tree
Eukaryota	● Choanoflagellida ● Fungi ● Fungi/Metazoa incertae sedis ● Metazoa



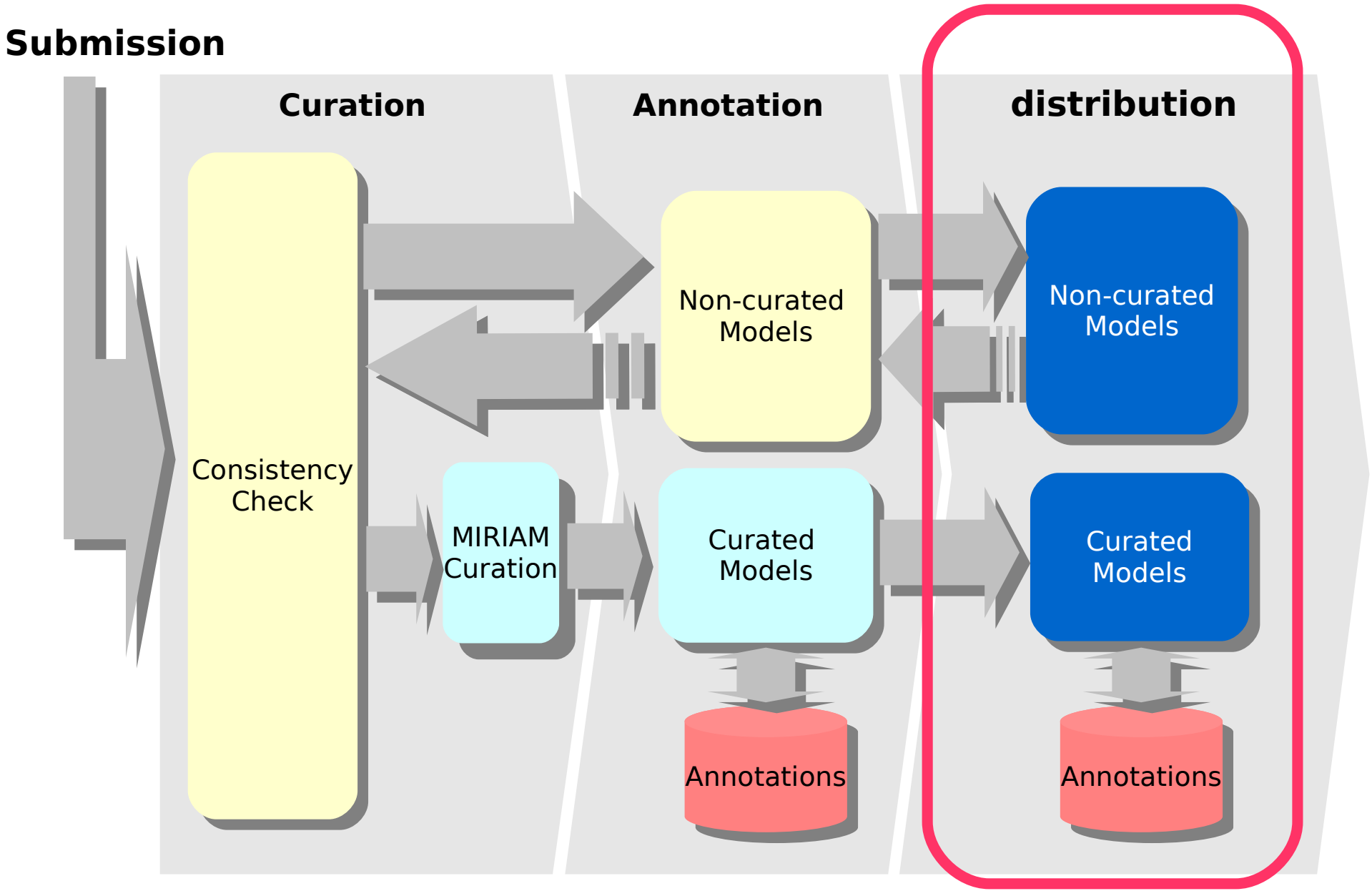
Cell Cycle, Mitotic

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

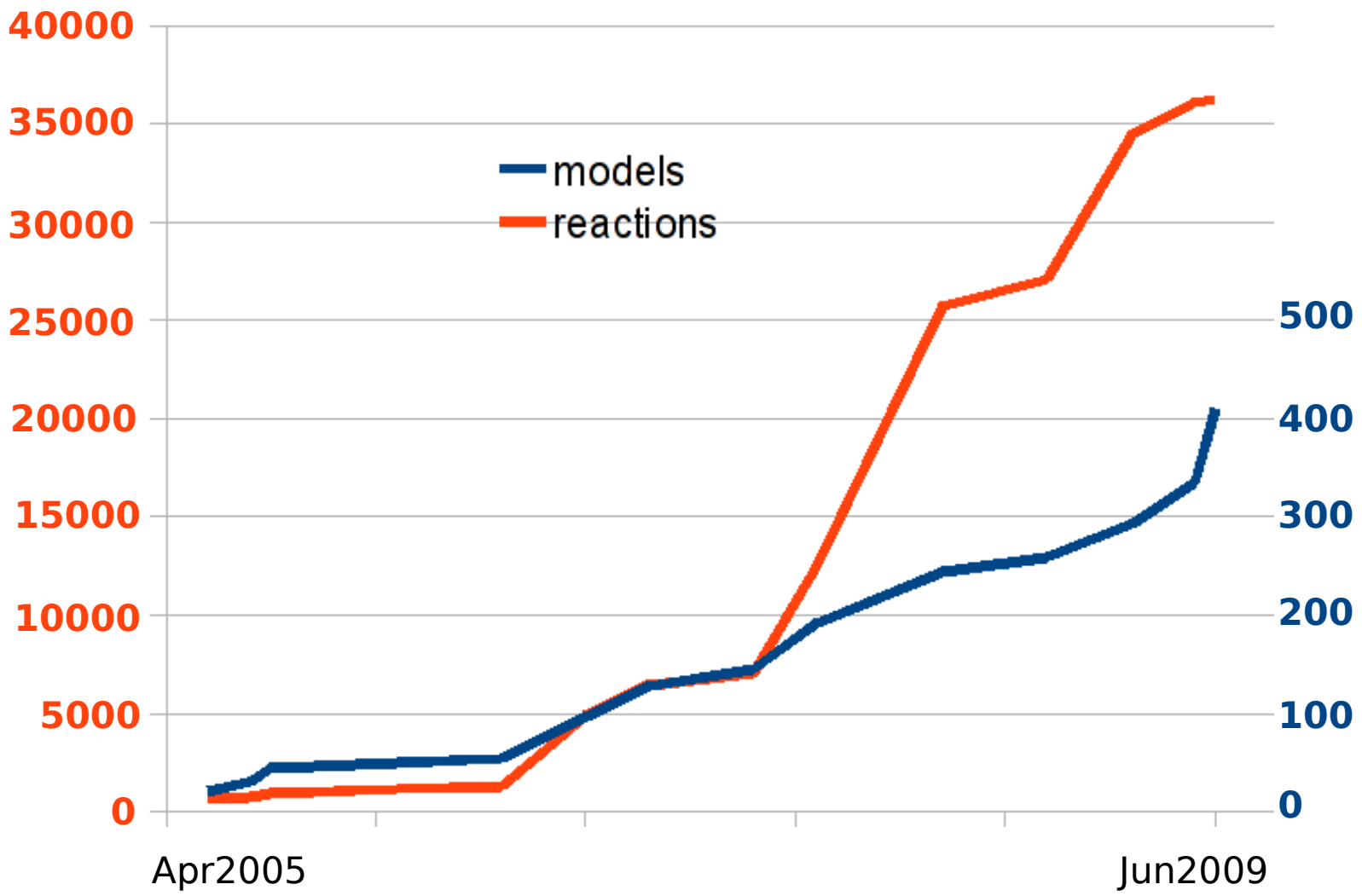
eplication of the genome and the subsequent segregation of chromosomes into daughter cells are controlled by
replication is carried out during a discrete temporal period known as the S (synthesis)-phase, and chromosome
ar architecture at mitosis. Two gap-phases separate these major cell cycle events: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



Distribution



Steady-increase of BioModels Database



Retrieving Models

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 pathways, controlled vocabularies, etc.

Search | Go to the model | Advanced search

Browse models

- Curated models (216)
- Browse models using GO
- Non-curated models (196)

Browse the models in the curated branch. These models have been thoroughly curated, and model elements have been annotated with terms from controlled vocabularies as well as links to relevant data resources.

Simulate in JWS Online

Submit a model

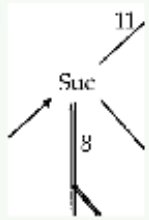
Mirror at California Institute of Technology http://biomodels.caltech.edu

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

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

Model of the month

May, 2009



Sucrose accumulation is accompanied by continuous synthesis and degradation processes in the developing sugar cane, *Saccharum officinarum*. Sugar cane internode maturation coincides with increased sucrose storage, but is not dependent purely on time. In addition, cane varieties accumulate sucrose to quite divergent extents.

Read more...

News

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Browse - Curated models

The following fields are used to describe a model:

- *BioModels ID* → A unique string of characters associated with the model, which will never be re-used even if the model is deleted from the BioModels Database.
- *Name* → The name of the model, as written in the model itself by its creator(s).
- *Publication ID* → The unique identifier of the reference publication describing the model, specified either as a PubMed identifier (linked to the EBI Medline database), or as a DOI (linked to the original publication through a DOI resolver), or as an URL. Being all published, all models must have one publication identifier, and the same identifier can be shared amongst several models if they have been described in the same publication.
- *Last Modified* → The date when the model was last modified.

To view a model, simply click on the correspondant BioModels ID provided within the leftmost column of the row corresponding to the model.

1 2 3 4 5

10 | 50 | 100 | All

BioModels ID	Name	Publication ID	Last Modified
BIOMD0000000169	Aguda1999_CellCycle	10619492	2008-08-20T19:05:46+00:00
BIOMD0000000214	Akman2008_Circadian_Clock_Model2	18277380	2009-06-19T16:39:50+00:00
BIOMD0000000211	Albert2005_Glycolysis	15955817	2009-04-08T16:54:47+00:00
BIOMD0000000054	Ataullahkhanov1996_Adenylate	8733433	2008-08-21T11:57:42+00:00
BIOMD0000000071	Bakker2001_Glycolysis	11415442	2008-10-30T18:11:41+00:00
BIOMD0000000197	Bartholome2007_MDCKII	17548463	2008-12-02T14:36:00+00:00
BIOMD0000000128	Bertram2006_Endothelin	16434725	2007-10-17T14:16:27+00:00
BIOMD0000000062	bhartiya2003 tryptophan operon	12787031	2008-08-21T12:00:28+00:00
BIOMD0000000058	Bindschadler2001_coupled_Ca_oscillators	12779457	2008-08-21T11:59:06+00:00
BIOMD0000000175	Birtwistle2007_ErbB_Signalling	18004277	2009-04-21T20:13:48+00:00
BIOMD0000000077	Blum2000_LHsecretion_1	10662710	2009-04-21T18:53:25+00:00
BIOMD0000000043	Borghans1997_CaOscillation_model1	17029867	2009-04-21T12:52:44+00:00
BIOMD0000000044	Borghans1997_CaOscillation_model2	17029867	2008-08-21T11:53:55+00:00
BIOMD0000000045	Borghans1997_CaOscillation_model3	17029867	2008-08-21T11:54:12+00:00

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Browse the models in the curated branch using the Gene Ontology tree. The number that appears between brackets next to each GO branch represents how many models are related to that GO term.

Simulate in JWS Online

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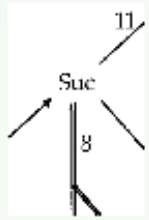
Model of the month

May, 2009



Sucrose accumulation is accompanied by continuous synthesis and degradation processes in the developing sugar cane, *Saccharum officinarum*. Sugar cane internode maturation coincides with increased sucrose storage, but is not dependent purely on time. In addition, cane varieties accumulate sucrose to quite divergent extents.

Read more...

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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 (209)
- GO:0005575 - cellular_component (187)
- GO:0003674 - molecular_function (146)

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 (209)
  - GO:0009987 - cellular process (195)
    - GO:0051641 - cellular localization (39)
    - GO:0050794 - regulation of cellular process (131)
    - GO:0007049 - cell cycle (22)
      - GO:0051726 - regulation of cell cycle (18)
      - GO:0000278 - mitotic cell cycle (20)
        - GO:0051329 - interphase of mitotic cell cycle (4)
        - 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 mit
        - 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

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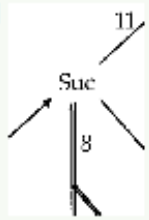

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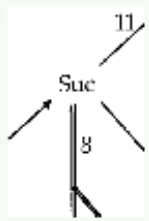

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Search - Models

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

Resource ID: Enzyme Nomenclature

Resource ID: Enzyme Nomenclature

Compose by: and or

Search Reset

Search - Models

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BioModels ID:
Person:
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Resource:
Resource:
Resource:
Resource ID: Enzyme Nomenclature
Resource ID: Enzyme Nomenclature
Resource ID: Enzyme Nomenclature

Enzyme Nomenclature
Ensembl
ICD
IntAct
InterPro
KEGG Pathway
KEGG Compound
KEGG Reaction
OMIM
PIRSF
Reactome
CluSTr
FMA

Compose by: and or

Search Reset

For example,
InterPro: *IPR002394*
KEGG Pathway: *hsa04080*
Reactome: *68910*

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:

Resource:

Publication
ChEBI
Gene Ontology
Taxonomy
UniProt

Resource ID: Enzyme Nomenclature

Resource ID: Enzyme Nomenclature

Resource ID: Enzyme Nomenclature

Compose by: and or

Search Reset

For example,

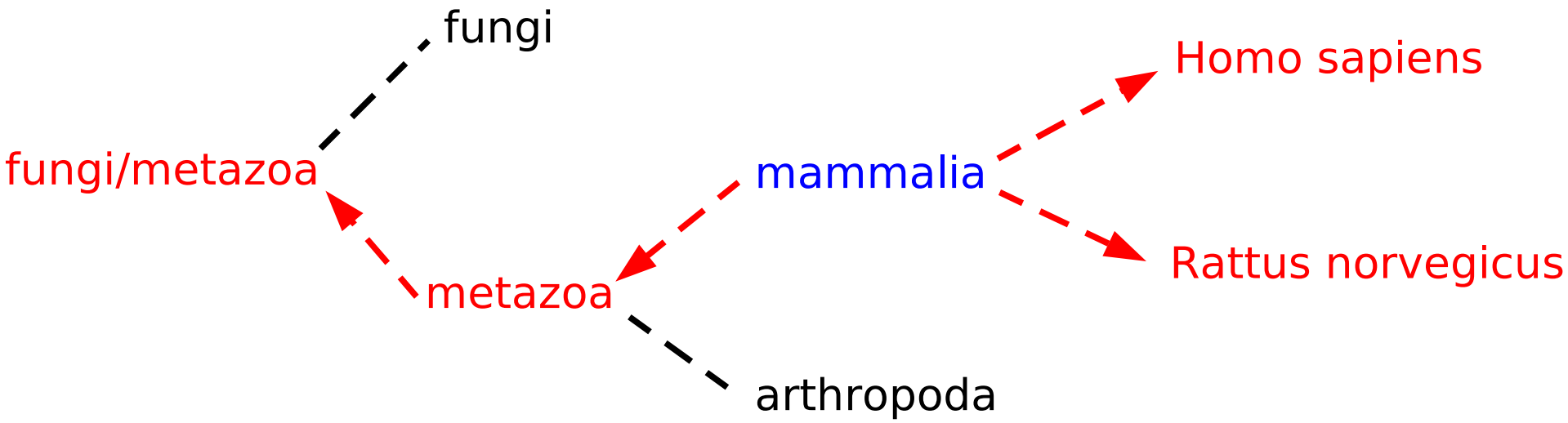
Publication: *1831270* or *Cyclin*

Gene Ontology: *GO:0000278* or *cell cycle*

UniProt: *P00533* or *EGFR*

Taxonomic search

searching for mammalia
→ a model valid for all metazoa is valid for all mammals
→ a model of homo sapiens is also a model of mammal



88 Curated Models returned.

BioModels ID	Name	Publication ID	Last Modified
BIOMD0000000005	Tyson1991_CellCycle_6var	1831270	2009-02-25T14:58:48+00:00
BIOMD0000000006	Tyson1991_CellCycle_2var	1831270	2009-02-25T14:41:44+00:00
BIOMD0000000015	Curto1998_purineMetabol	9664759	2009-04-20T17:46:30+00:00
BIOMD0000000018	Morrison1989_FolateCycle	2732237	2008-08-21T11:44:21+00:00
BIOMD0000000019	Schoeberl2002_EGF_MAPK	11923843	2009-04-20T18:01:25+00:00
BIOMD0000000024	Scheper1999_CircClock	9870936	2008-08-21T11:46:43+00:00
BIOMD0000000041	Kongas2001_creatine	10.1038/npre.2007.13...	2009-04-21T16:36:29+00:00
BIOMD0000000043	Borghans1997_CaOscillation_model1	17029867	2009-04-21T12:52:44+00:00
BIOMD0000000044	Borghans1997_CaOscillation_model2	17029867	2008-08-21T11:53:55+00:00
BIOMD0000000045	Borghans1997_CaOscillation_model3	17029867	2008-08-21T11:54:12+00:00
BIOMD0000000047	Oxhamre2005_Ca_oscillation	15596518	2008-08-21T11:54:50+00:00
BIOMD0000000048	Kholodenko1999_EGFRsignaling	10514491	2008-08-21T11:55:14+00:00
BIOMD0000000049	Sasagawa2005_MAPK	15793571	2009-04-21T16:53:15+00:00
BIOMD0000000054	Ataullahkhanov1996_Adenylate	8733433	2008-08-21T11:57:42+00:00
BIOMD0000000057	Sneyd2002_IP3_Receptor	11842185	2008-08-21T11:58:43+00:00
BIOMD0000000059	Fridlyand2003_Calcium_flux	12644446	2008-10-01T17:23:42+00:00
BIOMD0000000069	Fuss2006_MitoticActivation	16873466	2008-08-21T12:03:13+00:00
BIOMD0000000070	Holzhutter2004_Erythrocyte_Metabolism	15233787	2008-08-21T12:03:41+00:00
BIOMD0000000073	Leloup2003_CircClock_DD	12775757	2008-08-21T12:04:54+00:00
BIOMD0000000081	Suh2004_KCNQ_Regulation	15173220	2008-08-21T12:07:50+00:00
BIOMD0000000088	Maeda2006_MyosinPhosphorylation	16923126	2008-08-21T12:10:40+00:00
BIOMD0000000093	Yamada2003_JAK_STAT_pathway	12527385	2008-08-21T12:12:24+00:00

metazoa/fungi

homo sapiens

rattus

rattus norvegicus

mammalia

Model, model components & Submodels

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 Date: 2005-09-13T12:31:08+00:00

Last Modification Date: 2009-02-25T14:58:48+00:00

Creation Date: 2005-02-08T18:28:27+00:00

Encoders: Bruce Shapiro
Vijayalakshmi Chelliah

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

Notes

Cell Cycle Model; Tyson (1991, 6 variables)

Description

A model of the cell cycle based on the interactions between cdc2 and cyclin. The model has six dynamic variables: C2 (cdc2); CP (cdc2-P complex); pM (P-cyclin-cdc2-P complex); M (active MPF, P-cyclin-cdc2 complex); Y (cyclin); and YP (cyclin-P). Total cyclin concentration (YT) is the sum [YT]=[Y]+[YP]+[pM]+[M]

Reaction

Variable	ODE
C2	0
CP	1
pM	0.3
M	0
Y	0
YP	0

BIOMD0000000005 - Tyson1991_CellCycle_6var

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

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

Create a submodel with selected elements | Deselect All

Model

Publication ID: 1831270 **Submission Date:** 2005-09-13T12:31:08+00:00 **Last Modification Date:** 2009-02-25T14:58:48+00:00 **Creation Date:** 2005-02-08T18:28:27+00:00

Mathematical expressions

Reactions

cyclin_cdc2k dissociation	cdc2k phosphorylation	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)

Physical entities

Compartments	Species		
cell	EmptySet	cdc2k	cdc2k-P
	p-cyclin_cdc2	p-cyclin_cdc2-p	cyclin
	p-cyclin	total_cyclin	total_cdc2

BIOMD0000000005 - Tyson1991_CellCycle_6var

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

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

Reactions (9)

cyclin_cdc2k dissociation	[p-cyclin_cdc2] → [cdc2k] + [p-cyclin];
Math:	$cell \times k6 \times M$ *(Detail)*
Annotations:	set #1 — bqbiol:isVersionOf **Gene Ontology** regulation of cyclin-dependent protein kinase activity; bqbiol:hasVersion **Reactome** REACT_6308
cdc2k phosphorylation	[cdc2k] → [cdc2k-P];
cdc2k dephosphorylation	[cdc2k-P] → [cdc2k];
cyclin cdc2k-p association	[cdc2k-P] + [cyclin] → [p-cyclin_cdc2-p];
deactivation of cdc2 kinase	[p-cyclin_cdc2] → [p-cyclin_cdc2-p];
cyclin biosynthesis	[EmptySet] → [cyclin];
default degradation of cyclin	[cyclin] → [EmptySet];
cdc2 kinase triggered degration of cyclin	[p-cyclin] → [EmptySet];
activation of cdc2 kinase	[p-cyclin_cdc2-p] → [p-cyclin_cdc2]; {*total_cdc2*}

Rules (2)

Assignment Rule	total_cyclin = Y + YP + M + pM
Assignment Rule	total_cdc2 = C2 + CP + M + pM

BIOMD0000000005 - Tyson1991_CellCycle_6var

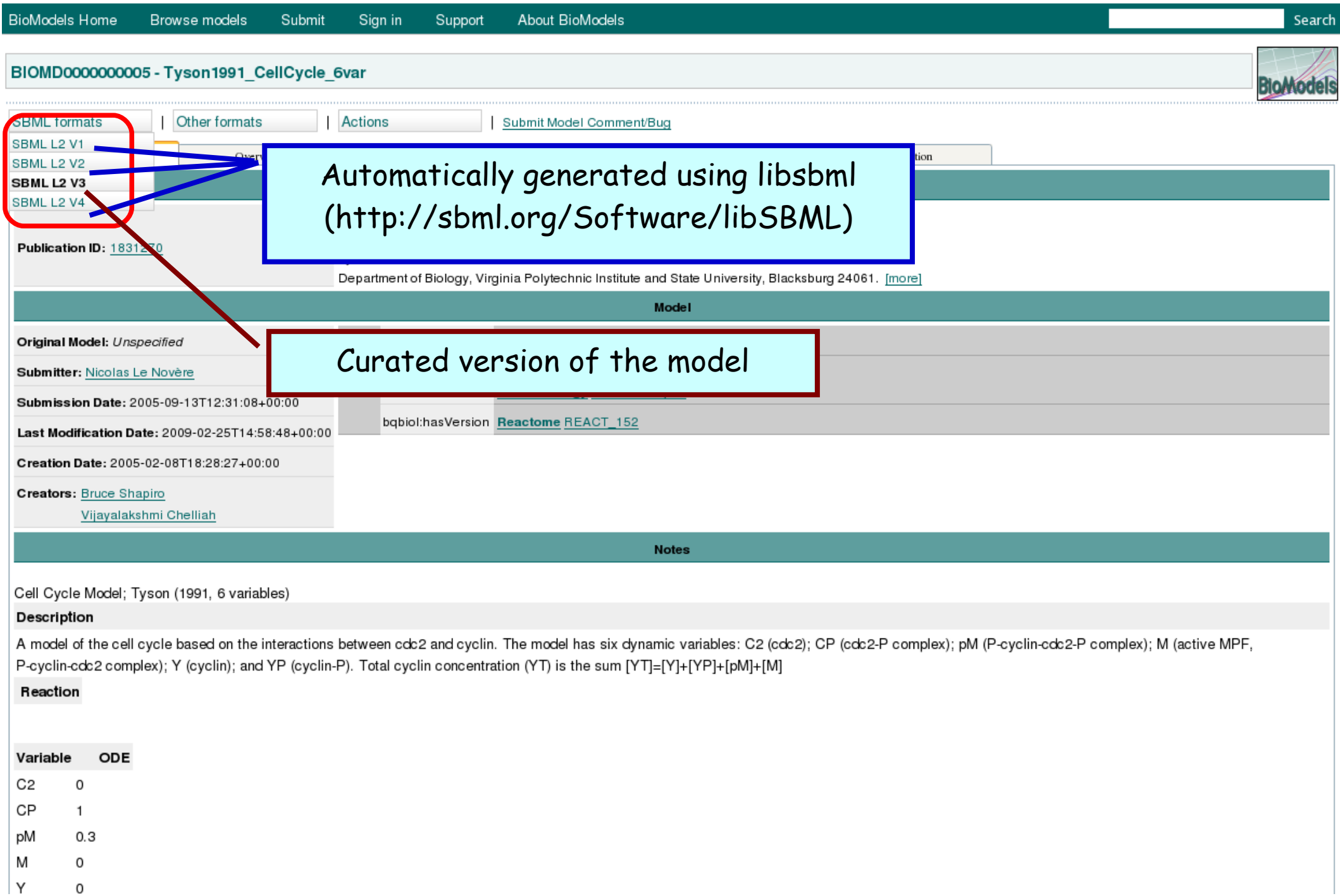
SBML formats | Other formats | Actions | Submit Model Comment/Bug

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

cell	Spatial dimensions: 3 Compartment size: 1.0
Annotations:	set #1 bqbiol:is Gene Ontology cell
EmptySet *Compartment: cell*	Initial amount: 0.0
cdc2k *Compartment: cell*	Initial amount: 0.0
cdc2k-P *Compartment: cell*	Initial amount: 0.75
p-cyclin_cdc2 *Compartment: cell*	Initial amount: 0.0
p-cyclin_cdc2-p *Compartment: cell*	Initial amount: 0.25
cyclin *Compartment: cell*	Initial amount: 0.0
p-cyclin *Compartment: cell*	Initial amount: 0.0
total_cyclin *Compartment: cell*	
total_cdc2 *Compartment: cell*	

BIOMD0000000005 - Tyson1991_CellCycle_6var

cyclin_cdc2k dissociation (1)	
k6	Value: 1.0 *Constant*
cdc2k phosphorylation (1)	
k8notP	Value: 1000000.0 *Constant*
cdc2k dephosphorylation (1)	
k9	Value: 1000.0 *Constant*
cyclin cdc2k-p association (1)	
k3	Value: 200.0 *Constant*
deactivation of cdc2 kinase (1)	
k5notP	*Constant*
cyclin biosynthesis (1)	
k1aa	Value: 0.015 *Constant*
default degradation of cyclin (1)	
k2	*Constant*
cdc2 kinase triggered degration of cyclin (1)	
k7	Value: 0.6 *Constant*
activation of cdc2 kinase (2)	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SBML L2 V1
SBML L2 V2
SBML L2 V3
SBML L2 V4
Automatically generated using libsbml
(http://sbml.org/Software/libSBML)
Curated version of the model
Publication ID: 1831270
Department of Biology, Virginia Polytechnic Institute and State University, Blacksburg 24061. [more]
Model
Original Model: Unspecified
Submitter: Nicolas Le Novère
Submission Date: 2005-09-13T12:31:08+00:00
Last Modification Date: 2009-02-25T14:58:48+00:00
Creation Date: 2005-02-08T18:28:27+00:00
Creators: Bruce Shapiro
Vijayalakshmi Chelliah
bqbiol:hasVersion
Reactome REACT_152
Notes
Cell Cycle Model; Tyson (1991, 6 variables)
Description
A model of the cell cycle based on the interactions between cdc2 and cyclin. The model has six dynamic variables: C2 (cdc2); CP (cdc2-P complex); pM (P-cyclin-cdc2-P complex); M (active MPF, P-cyclin-cdc2 complex); Y (cyclin); and YP (cyclin-P). Total cyclin concentration (YT) is the sum [YT]=[Y]+[YP]+[pM]+[M]
Reaction
Variable
ODE
C2 0
CP 1
pM 0.3
M 0
Y 0

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BIOMD0000000005 - Tyson1991_CellCycle_6var

SBML formats | Other formats | Actions | Submit Model Comm

- CellML
- SciLab
- XPP
- BioPAX
- VCell
- PDF

Model | Math | Physical entities

Publication ID: 1831270

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

Modeling the cell division cycle: cdc2 and cyclin

Tyson JJ.

Department of Biology, Virginia Polytechnic Insti

Original Model: *Unspecified*

Submitter: Nicolas Le Novère

Submission Date: 2005-09-13T12:31:08+00:00

Last Modification Date: 2009-02-25T14:58:48+00:00

Creation Date: 2005-02-08T18:28:27+00:00

Creators: Bruce Shapiro
Vijayalakshmi Chelliah

set #1	bqmodel:is	Taxonomy Fungi/Me
	bqbiol:isVersionOf	KEGG Pathway sce0
		Gene Ontology mitot
	bqbiol:hasVersion	Reactome REACT_

Notes

Cell Cycle Model; Tyson (1991, 6 variables)

Description

A model of the cell cycle based on the interactions between cdc2 and cyclin. The model has six dynamic variables: C2 (cdc2); CP (c MPF, P-cyclin-cdc2 complex); Y (cyclin); and YP (cyclin-P). Total cyclin concentration (YT) is the sum [YT]=[Y]+[YP]+[pM]+[M]

Reaction

Variable	ODE
C2	0
CP	1
pM	0.3
M	0
Y	0

```
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    xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#"
    xmlns:bp="http://www.biopax.org/release/biopax-level2.owl#"
    xmlns:owl="http://www.w3.org/2002/07/owl#"
    xmlns="http://www.ebi.ac.uk/biomodels/biopax.owl#"
    xmlns:daml="http://www.daml.org/2001/03/daml+oil#"
    xmlns:rdfs="http://www.w3.org/2000/01/rdf-schema#"
xml:base="http://www.ebi.ac.uk/biomodels/biopax.owl">
<owl:Ontology rdf:about="">
  <owl:imports rdf:resource="http://www.biopax.org/release/biopax-level2.owl"/>
</owl:Ontology>
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  <bp:ID>GO:0005623</bp:ID>
  <bp:DB>Gene Ontology</bp:DB>
</bp:unificationXref>
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  <bp:CELLULAR-LOCATION>
    <bp:openControlledVocabulary rdf:ID="cell">
      <bp:XREF rdf:resource="#Gene_Ontology_GO_0005623"/>
      <bp:TERM>cell</bp:TERM>
    </bp:openControlledVocabulary>
  </bp:CELLULAR-LOCATION>
  <bp:PHYSICAL-ENTITY>
    <bp:protein rdf:ID="C2">
      <bp:XREF>
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          <bp:DB>UniProt</bp:DB>
        </bp:unificationXref>
      </bp:XREF>
      <bp:NAME>cdc2k</bp:NAME>
    </bp:protein>
  </bp:PHYSICAL-ENTITY>
</bp:physicalEntityParticipant>
<bp:unificationXref rdf:ID="Gene_Ontology_GO_000
  <bp:ID>GO:0006470</bp:ID>
  <bp:DB>Gene Ontology</bp:DB>
</bp:unificationXref>
<bp:protein rdf:ID="CP">
  <bp:XREF rdf:resource="#UniProt_P04551"/>
  <bp:NAME>cdc2k-P</bp:NAME>
</bp:protein>
<bp:physicalEntityParticipant rdf:ID="Reaction5_
  <bp:STOICHIOMETRIC-COEFFICIENT>1.0</bp:STOICHI
  <bp:CELLULAR-LOCATION rdf:resource="#cell"/>
  <bp:PHYSICAL-ENTITY>
```

SBML Model Report

Model name: "Tyson1991_CellCycle_6var"

SBML2LaTeX

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

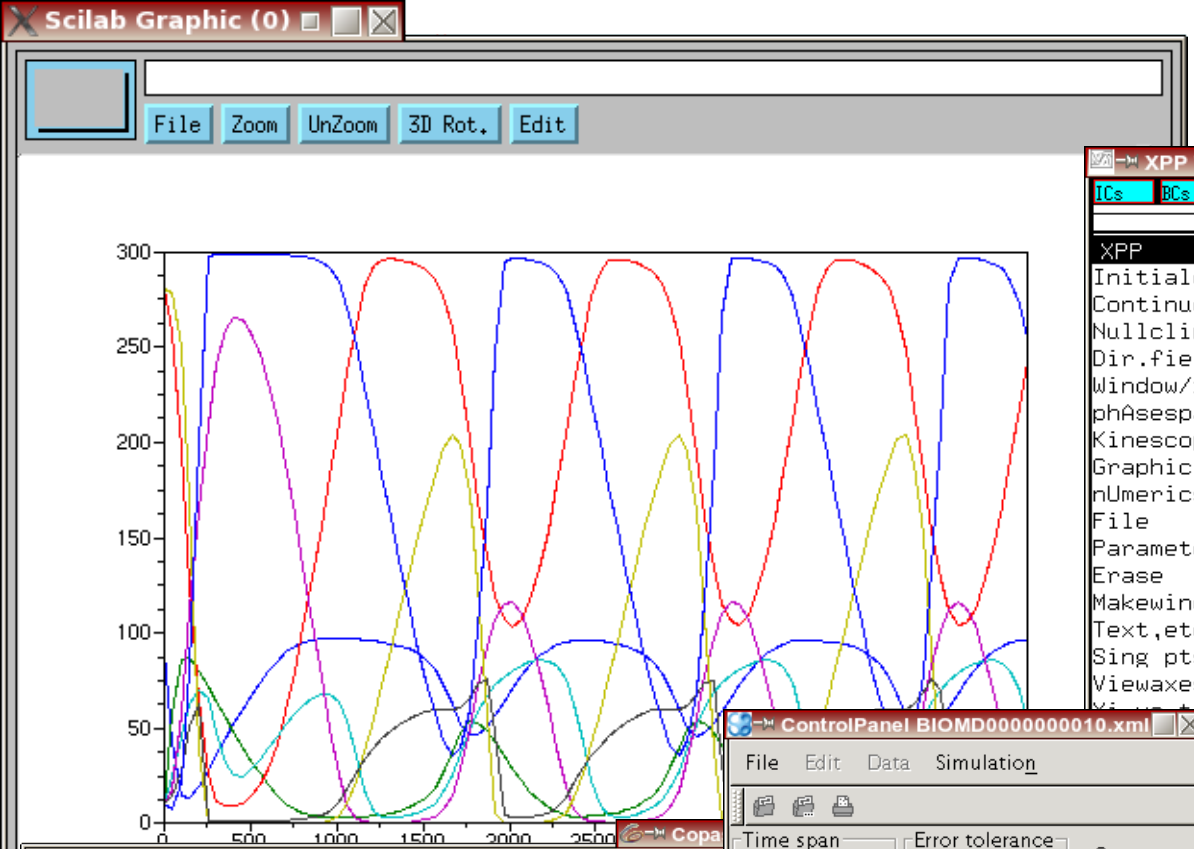
Cell Cycle Model; Tyson (1991, 6 variables)

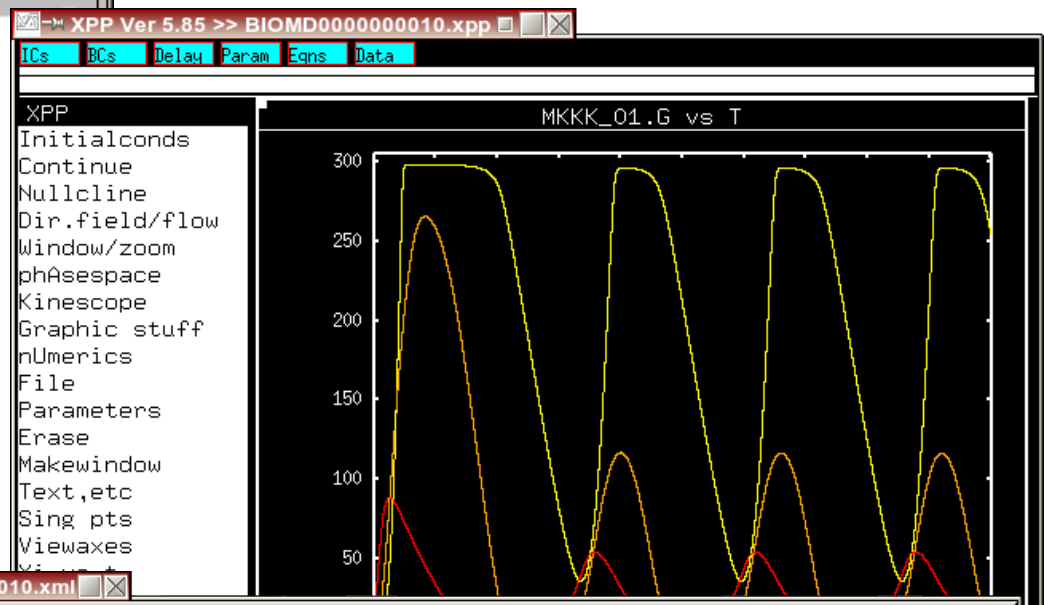
Description

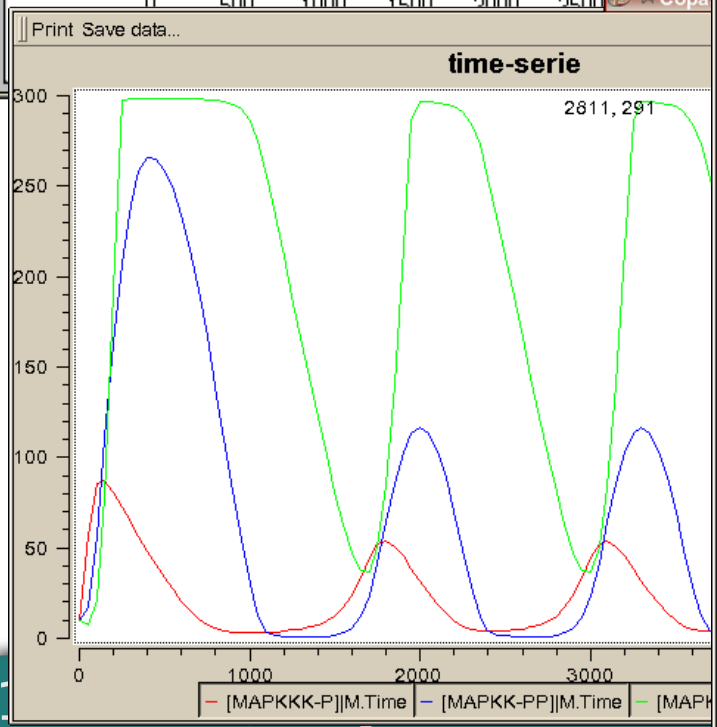
[1]NASA Jet Propulsion Laboratory, bshapiro@jpl.nasa.gov
[2]EMBL-EBI, viji@ebi.ac.uk

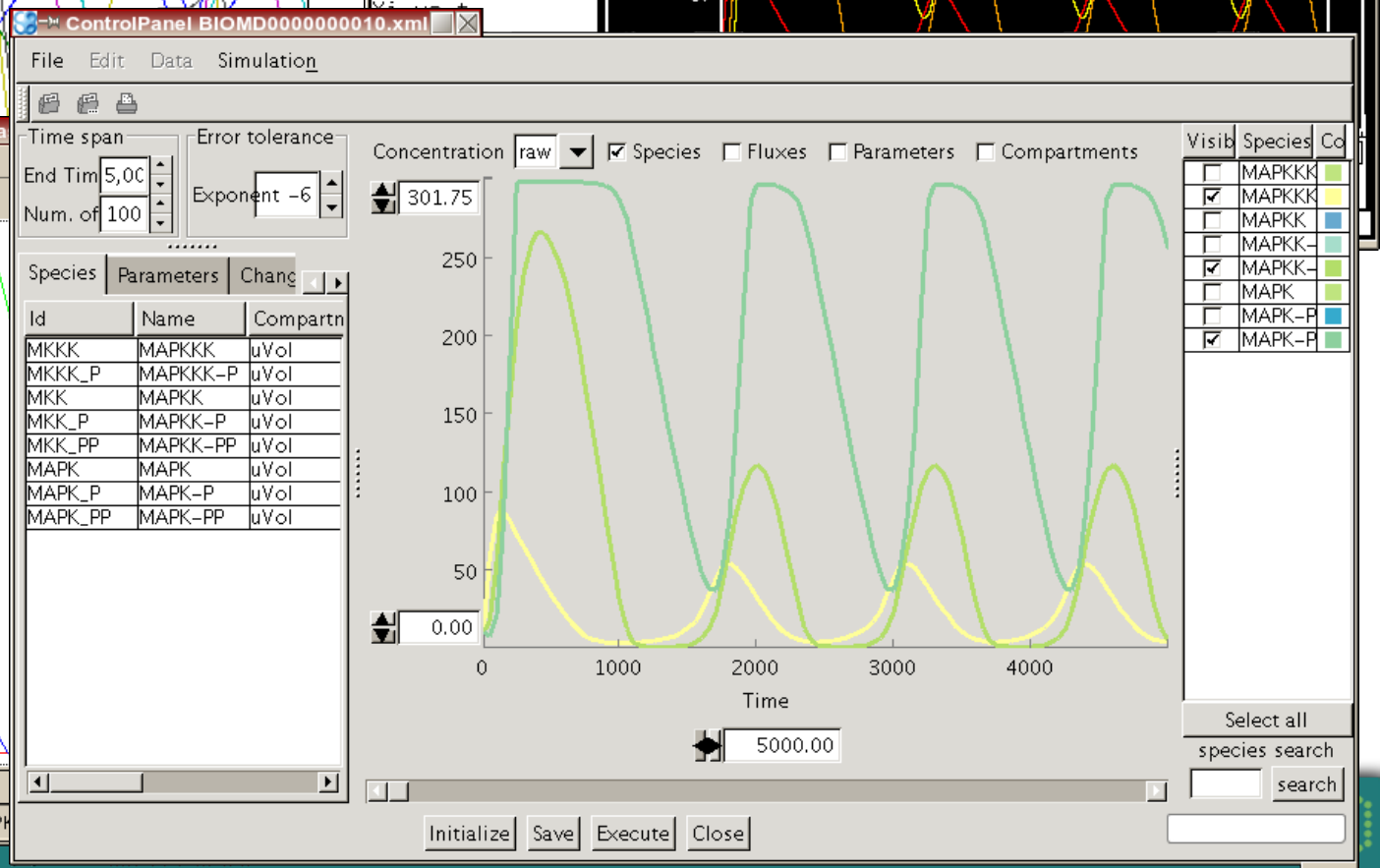
Produced by SBML2LaTeX 1

BIOMD0000000010









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Document describing the structure of a model. This document is quoted within the model.
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The individuals who wrote the model present in the BioModels Database, based on the reference publication. Model creators are listed within the model.
"Complete Dataset"
The entire content of the BioModels Database, including the models and their annotations.

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b. Contact BioModels team to include your modifications in the standard version of the model.
c. Rename the modified model, and remove both the BioModels Database identifier and any mention of the model creators.

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BioModels Database

BioModels Database is a data resource providing quantitative models of biological processes ...more.

SBML

The Systems Biology Markup Language (SBML) is a computer-readable format for representing models of biochemical reaction networks ...more.

Here is a list of all the conversions to and from SBML that we are developing and maintaining.

SBML to XPP

XPP-Aut is a numerical analysis software. It permits to solve differential equations, difference equations, delay equations, functional equations, boundary value problems, and stochastic equations.

SBML to SciLab

SciLab is a scientific software package for numerical computations providing a powerful open computing environment for engineering and scientific applications.

SBML to CellML CellML to SBML

CellML is an open standard based on the XML markup language like SBML. CellML is being developed by the Bioengineering Institute at the University of Auckland and affiliated research groups. The main difference between CellML and SBML is that the former is based on modules while the latter is based on hierarchical components.

SBML to BioPax

The main objective of the BioPAX initiative is to develop a data exchange format for biological pathways that is flexible, extensible, optionally encapsulated and compatible with other standards and can be widely adopted in a timely manner.

SBML to Dot

GraphViz is an open source graph visualization software. The language used to encode the graphics processed by GraphViz is called DOT. Note that a "dot" file can be used with other graphical software.

SBML to SVG

Scalable Vector Graphics (SVG) is a language for describing two-dimensional graphics and graphical applications in XML. It is an open standard created by the World Wide Web Consortium.

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BIOMD0000000005 - Tyson1991_CellCycle_6var

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

- View GIF Reaction Graph
- View SVG Reaction Graph
- View Dynamic Reaction Graph
- View Model of Month
- JWS Online Simulation
- BioModels Online Simulation

Model | Overview | Physical entities | Parameters | Curation

Reference Publication

Publication ID: 1831270

1991 Aug;88(16):7328-32.

cycle: cdc2 and cyclin interactions.

irginia Polytech

Original Model: *Unspecified*

Submitter: Nicolas Le Novère

Submission Date: 2005-09-13T12:31:08+00:00

Last Modification Date: 2009-02-25T14:58:48+00:00

Creation Date: 2005-02-08T18:28:27+00:00

Creators: Bruce Shapiro, Vijayalakshmi Chelliah

set #1	bqmodel:is	Taxonomy
	bqbiol:isVersionOf	KEGG Pathw, Gene Ontolo
	bqbiol:hasVersion	Reactome

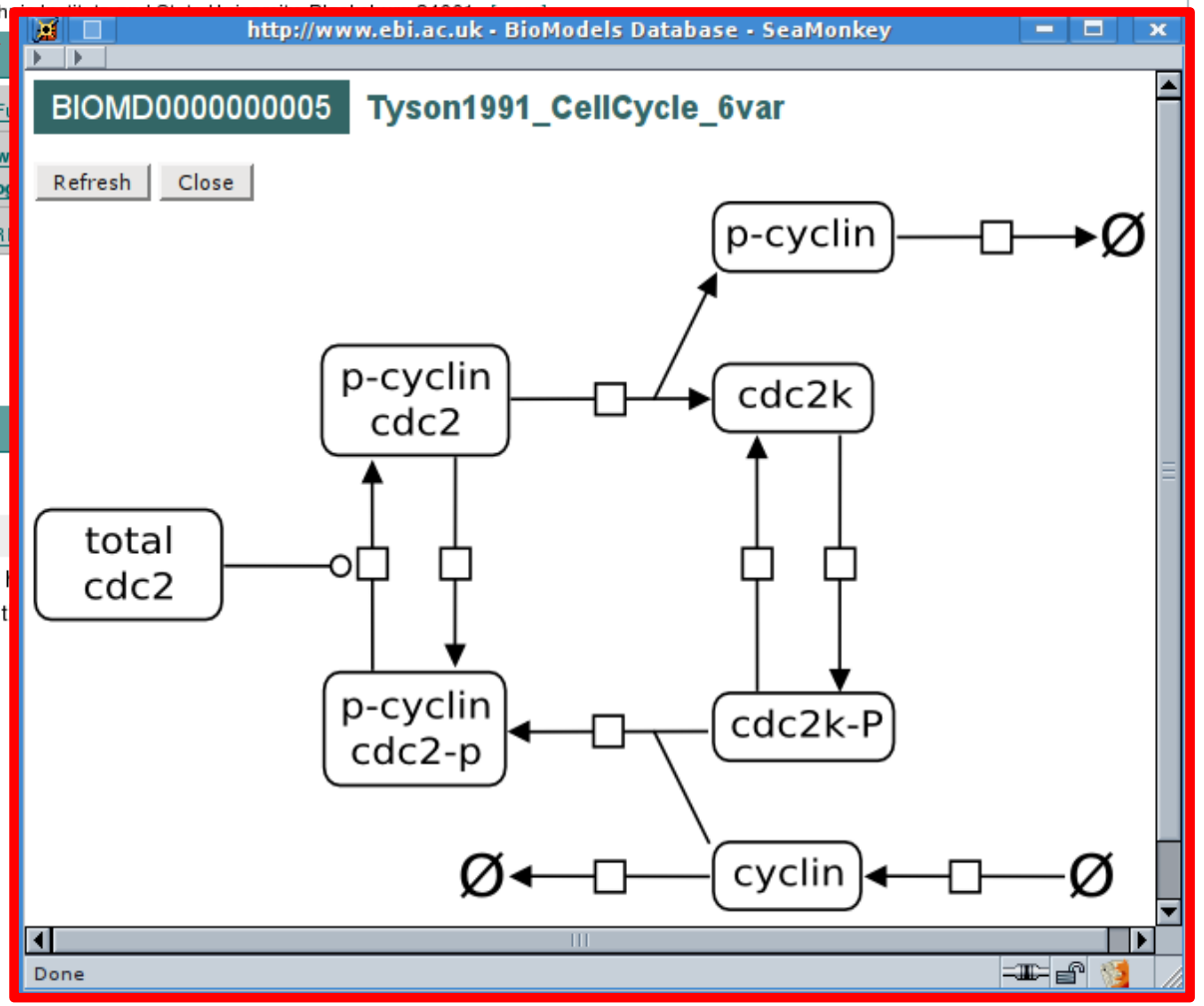
Cell Cycle Model; Tyson (1991, 6 variables)

Description

A model of the cell cycle based on the interactions between cdc2 and cyclin. The model
P-cyclin-cdc2 complex); Y (cyclin); and YP (cyclin-P). Total cyclin concentration (YT) is t

Reaction

Variable	ODE
C2	0
CP	1
pM	0.3
M	0
Y	0



BIOMD0000000005 - Tyson1991_CellCycle_6var

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

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Model | Overview | Physical entities | Parameters | Curation

Reference Publication

Publication ID: 1831270

1991 Aug;88(16):7328-32.

cycle: cdc2 and cyclin interactions.

irginia Polytechnic Institute and State University, Blacksburg 24061. [more]

Model

Original Model: *Unspecified*

Submitter: Nicolas Le Novère

Submission Date: 2005-09-13T12:31:08+00:00

Last Modification Date: 2009-02-25T14:58:48+00:00

Creation Date: 2005-02-08T18:28:27+00:00

Creators: Bruce Shapiro, Vijayalakshmi Chelliah

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

Notes

Cell Cycle Model; Tyson (1991, 6 variables)

Description

A model of the cell cycle based on the interactions between cdc2 and cyclin. The model has six dynamic variables: C2 (cdc2); CP (cdc2-P complex); pM (P-cyclin-cdc2-P complex); M (active MPF, P-cyclin-cdc2 complex); Y (cyclin); and YP (cyclin-P). Total cyclin concentration (YT) is the sum [YT]=[Y]+[YP]+[pM]+[M]

Reaction

Variable	ODE
C2	0
CP	1
pM	0.3
M	0
Y	0

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.

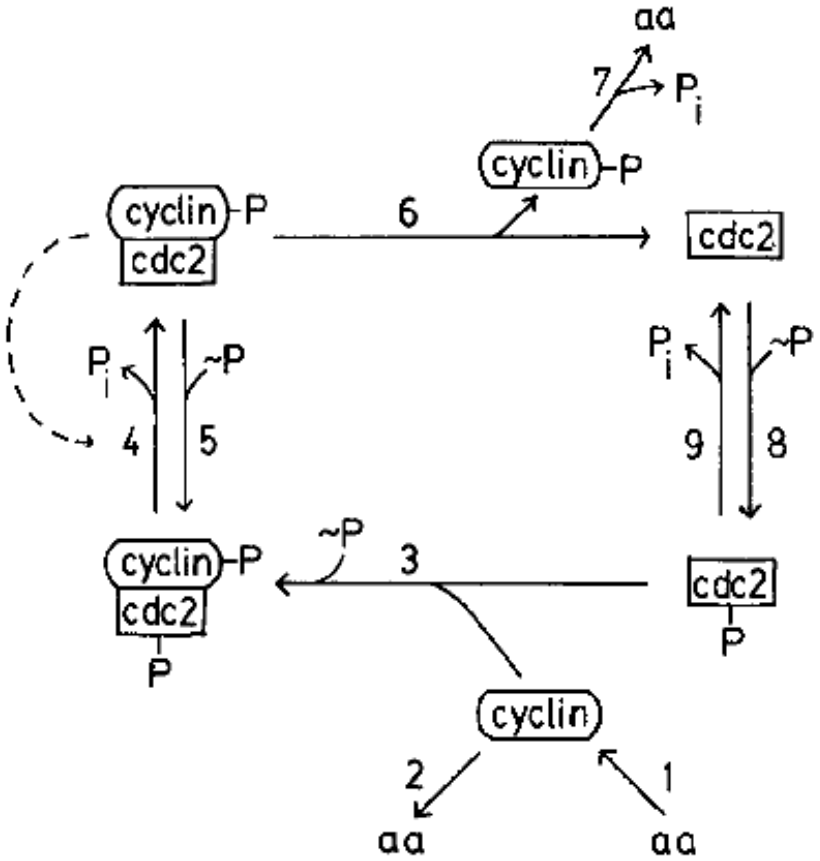


Figure 1: Reaction graph of the model from Tyson 1991.

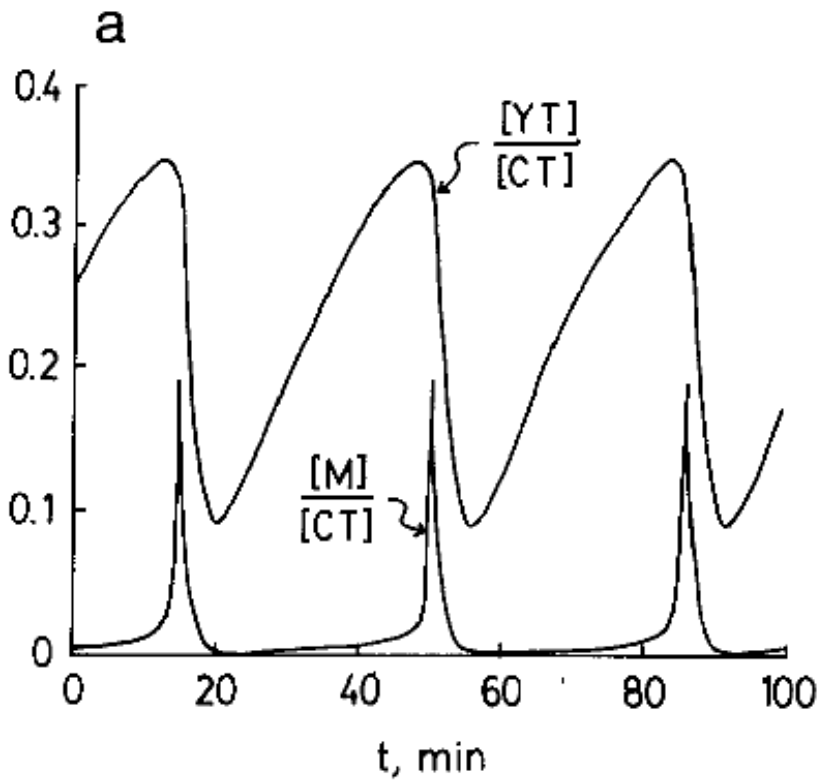


Figure 2: Oscillations of the total cyclin (YT) and the total MPF, relative to the total cyclin dependent kinase CDC2.

BioModels Home | Browse models | Submit | Sign in | Support | About | Search

BIOMD0000000005 - Tyson1991_CellCycle_6var

SBML formats | Other formats | Actions | Submit M

Model | Overview

Actions:
- View GIF Reaction Graph
- View SVG Reaction Graph
- View Dynamic Reaction Graph
- View Model of Mo
- JWS Online Simulation
- BioModels Online Simulation

Publication ID: 1831270

1991 Aug;8
cycle: cdc2
irginia Polyt

Original Model: *Unspecified*

Submitter: Nicolas Le Novère

Submission Date: 2005-09-13T12:31:08+00:00

Last Modification Date: 2009-02-25T14:58:48+00:00

Creation Date: 2005-02-08T18:28:27+00:00

Creators: Bruce Shapiro
Vijayalakshmi Chelliah

set #1	bqmodel:is	Taxonom
	bqbiol:isVersionOf	KEGG Pa / Gene Ont
	bqbiol:hasVersion	Reactom

Cell Cycle Model; Tyson (1991, 6 variables)

Description

A model of the cell cycle based on the interactions between cdc2 and cyclin. The mod
P-cyclin-cdc2 complex); Y (cyclin); and YP (cyclin-P). Total cyclin concentration (YT)

Reaction

Variable	ODE
C2	0
CP	1
pM	0.3
M	0
Y	0

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	☐ cyclin	☐ p-cyclin	☑ total_cyclin
☐ total_cdc2			

Simulation Time (use scientific notation e.g. 1

Print step: 1000

Submit

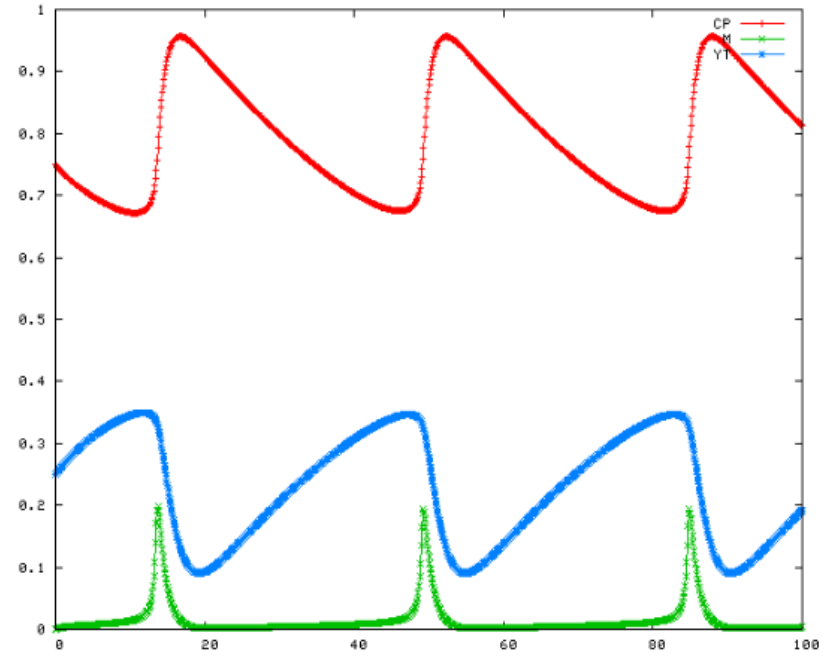
Done

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



Close

http://www.ebi.ac.uk/biomodels/models-main/ode_simu/SIMU1234453623... zotero

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BIOMD0000000005 - Tyson1991_CellCycle_6var

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

- View GIF Reaction Graph
- View SVG Reaction Graph
- View Dynamic Reaction Graph
- View Model of Month
- JWS Online Simulation
- BioModels Online Simulation

Model | Overview | Physical Entities | Parameters

Publication ID: 1831270

Reference Publication

1991 Aug;88(16):7328-32.

cycle: cdc2 and cyclin interactions.

irginia Polytechnic Institute and State University, BI

Original Model: *Unspecified*

Submitter: Nicolas Le Novère

Submission Date: 2005-09-13T12:31:08+00:00

Last Modification Date: 2009-02-25T14:58:48+00:00

Creation Date: 2005-02-08T18:28:27+00:00

Creators: Bruce Shapiro, Vijayalakshmi Chelliah

Model

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

Cell Cycle Model; Tyson (1991, 6

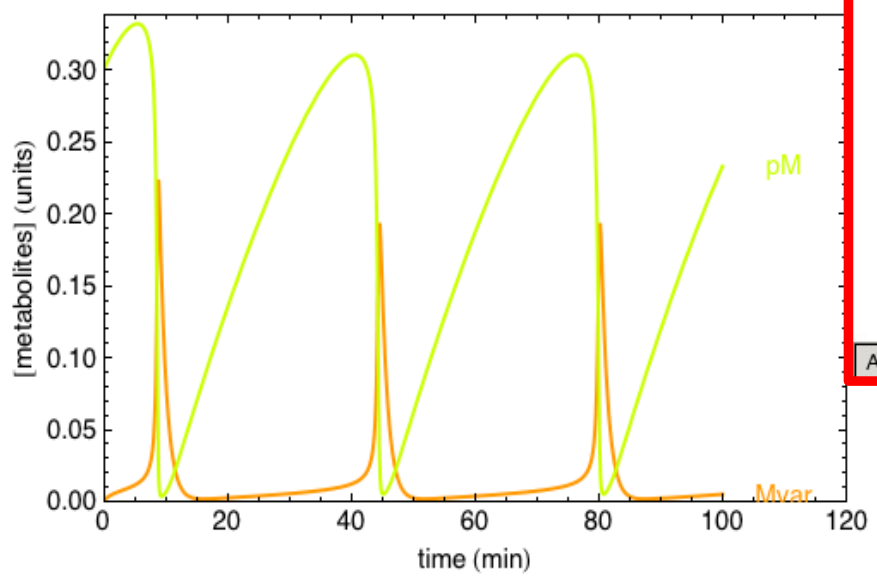
Description

A model of the cell cycle based or
P-cyclin-cdc2 complex); Y (cyclin)

Reaction

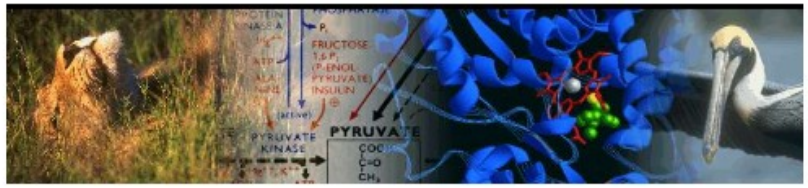
Variable	ODE
C2	0
CP	1
pM	0.3
M	0
Y	0

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



Biomodels Home | Index | JWS Online

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

zotero

BIOMD0000000005 - Tyson1991_CellCycle_6var

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

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

Create a submodel with selected elements | Deselect All

Model

Publication ID: 1831270 **Submission Date:** 2005-09-13T12:31:08+00:00 **Last Modification Date:** 2009-02-25T14:58:48+00:00 **Creation Date:** 2005-02-08T18:28:27+00:00

Mathematical expressions

Reactions

cyclin_cdc2k dissociation	cdc2k phosphorylation	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)

Physical entities

Compartments	Species		
cell	EmptySet	cdc2k	cdc2k-P
	p-cyclin_cdc2	p-cyclin_cdc2-p	cyclin
	p-cyclin	total_cyclin	total_cdc2

BIOMD0000000005 - Tyson1991_CellCycle_6var

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

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

Create a submodel with selected elements — Deselect All

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Reactions

☐ cyclin_cdc2k dissociation	☑ cdc2k phosphorylation	☑ cdc2k dephosphorylation	☐ cyclin cdc2k-p association
☐ deactivation of cdc2 kinase	☐ cyclin biosynthesis	☐ default degradation of cyclin	☐ cdc2 kinase triggered degration of cyclin
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Rules

Assignment Rule (variable: total_cyclin)	Assignment Rule (variable: total_cdc2)

Physical entities

Compartments	Species		
☐ cell	☐ EmptySet	☐ cdc2k	☐ cdc2k-P
	☐ p-cyclin_cdc2	☐ p-cyclin_cdc2-p	☐ cyclin
	☐ p-cyclin	☐ total_cyclin	☐ total_cdc2

BIOMD0000000005 - Tyson1991_CellCycle_6var

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

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

Reactions (2)

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

BIOMD0000000005 - Tyson1991_CellCycle_6var

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

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

cell	Spatial dimensions: 3 Compartment size: 1.0
Annotations:	set #1 bqbiol:is **Gene Ontology** cell
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

BIOMD0000000005 - Tyson1991_CellCycle_6var

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

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

Create a submodel with selected elements | Deselect All

Model

Publication ID: 1831270 **Submission Date:** 2005-09-13T12:31:08+00:00 **Last Modification Date:** 2009-02-25T14:58:48+00:00 **Creation Date:** 2005-02-08T18:28:27+00:00

Mathematical expressions

Reactions

cyclin_cdc2k dissociation	cdc2k phosphorylation	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)

Physical entities

Compartments	Species		
cell	EmptySet	cdc2k	cdc2k-P
	p-cyclin_cdc2	p-cyclin_cdc2-p	cyclin
	p-cyclin	total_cyclin	total_cdc2

BIOMD0000000005 - Tyson1991_CellCycle_6var

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

Overview | Math | Physical entities | Parameters | Curation | Submodel1

View the submodel in SBML | Save as

Reactions (2)

cdc2k phosphorylation	[cdc2k] → [cdc2k-P];
cdc2k dephosphorylation	[cdc2k-P] → [cdc2k];

Compartments (1)

cell	set #1	bqbiol:is	Gene Ontology cell
Referred to as: cell			

Species (2)

cdc2k *Compartment: cell*	Initial amount: 0.0
cdc2k-P *Compartment: cell*	Initial amount: 0.75

BIOMD0000000005 - Tyson1991_CellCycle_6var

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

Overview | Math | Physical entities | Parameters | Curation | Submodel1

View the submodel in SBML | Save as

Reactions (2)

cdc2k phosphorylation	[cdc2k] → [cdc2k-P];
cdc2k dephosphorylation	[cdc2k-P] → [cdc2k];

Compar

cell	set #1 bqbiol:is	Gene Ontology cell
Referred to as: cell		

Spe

cdc2k *Compartment: cell*	Initial amount: 0.0
cdc2k-P *Compartment: cell*	Initial amount: 0.75


```
<?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>
          <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#" xmlns:dc="http:/
            <rdf:Description rdf:about="#_000002">
              <bqbiol:is>
                <rdf:Bag>
                  <rdf:li rdf:resource="urn:miriam:obo.go:GO%3A0005623"/>
                </rdf:Bag>
              </bqbiol:is>
            </rdf:Description>
          </rdf:RDF>
        </annotation>
      </compartment>
    </listOfCompartments>
    <listOfSpecies>
      <species metaid="_000004" id="C2" name="cdc2k" compartment="cell" initialAmount="0">
        <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"/>
```

BioModels Web Services

Available features

Following are the currently available features in BioModels Web Services. In order to make using data in BioModels Database more conveniently, we will consider all requirements about new features.

```
java.lang.String helloBioModels()
          Say hello to BioModels
java.lang.String[] getAllCuratedModelsId()
```

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*".

Name	Description	Size	Link
biomodelswslib-standalone.jar	standalone and includes all external dependencies and ready for use;	1.9M	http://www.ebi.ac.uk/compneur-srv/biomodels/softwares/biomodelswslib-standalone-1.11.jar
biomodelswslib.jar	light-weight, but needs other dependencies to work togeter.	6.4K	http://www.ebi.ac.uk/compneur-srv/biomodels/softwares/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{
```

BioModels

Nicolas Le Novère

Michael Hucka

Development

Camille Laibe

Chen Li

Nicolas Rodriguez

Curation

Lukas Endler

Vijayalakshmi Chelliah

Melanie Stefan

Nick Juty

An international collaboration

- EBI
  - Nicolas Le Novère
  - Alexander Broicher
  - Mélanie Courtot
  - Marco Donizelli
  - Arnaud Henry
  - Chen Li
  - Lu Li
  - Camille Laibe
  - Nicolas Rodriguez
- SBML team (Caltech)
  - Michael Hucka
  - Andrew Finney
  - Benjamin Borstein
  - Harish Dharuri
  - Enuo He
  - Sarah Keating
  - Maria Schilstra
  - Bruce Shapiro
- NCBS (Bangalore)
  - Upinder Bhalla
  - Harsha Rani
- University of Washington
  - Herbert Sauro
- Vienna TBI
  - Rainer Machne
- Systems Biology Institute (Tokyo)
  - Hiroaki Kitano
  - Akira Funahashi
- JWS Online (Stellenbosh)
  - Jacky Snoep
- Virtual Cell (UCHC)
  - Ion Moraru
- Journals supporting BioModels Database
  - Molecular Systems Biology
  - All PLoS Journals
  - All BioMedCentral Journals
- Programs used for curation
  - CellDesigner/SBMLodeSolver
  - COPASI
  - Jarnac/JDesigner
  - MathSBML
  - RoadRunner
  - SBMLeditor
  - XPP-Aut

The community of Systems Biology for their contributions of models and comments.

An international collaboration

- EBI
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  - Alexander Broicher
  - Mélanie Courtot
  - Marco Donizelli
  - Arnaud Henry
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  - MathSBML
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For more discussion come at the EMBL-EBI exhibition booth during the coffee break