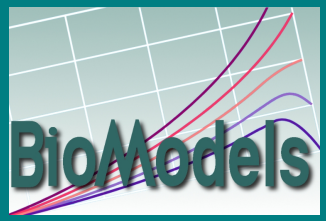
BioModels Database, a public model-sharing resource

WTAC: In Silico Systems Biology

EMBL-EBI

27th April 2012

Viji Chelliah
viji@ebi.ac.uk



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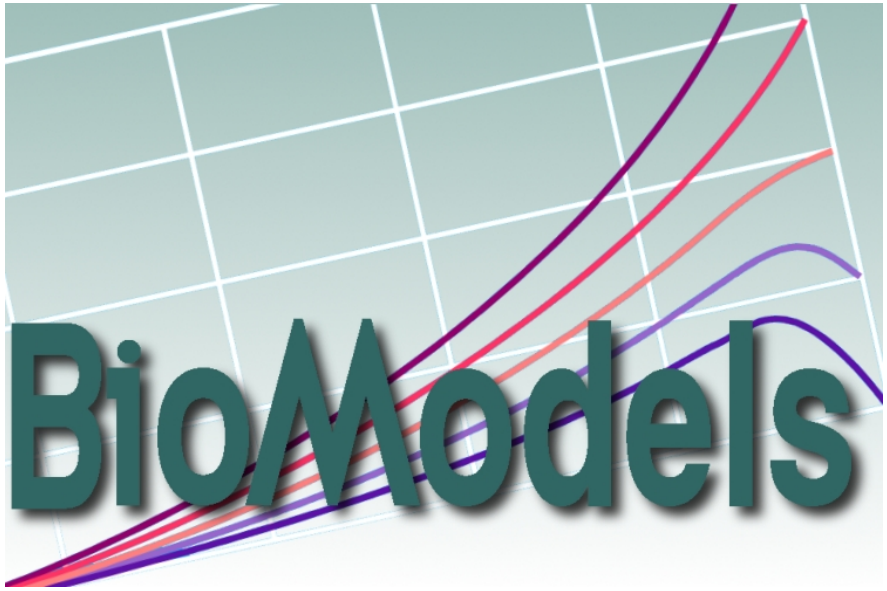
Outline

BioModels Database:

- In general (Growth, Model Diversity, Source of Models)
- Model Production Pipeline
  - Submission
  - Curation & Simulation
  - Annotation
  - Browse, Search & Retrieval
- Model components, features and Submodel creation.

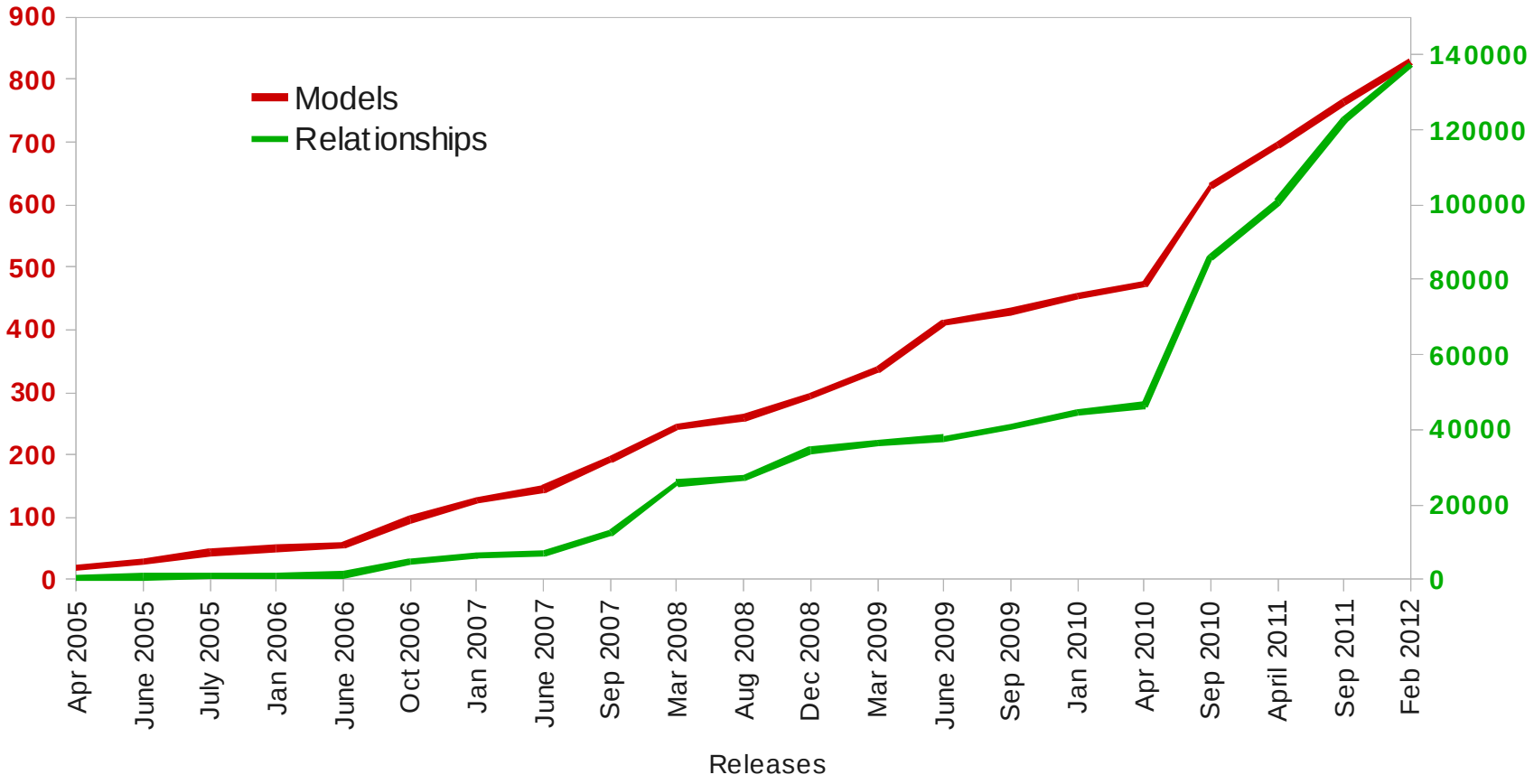


- In General.....

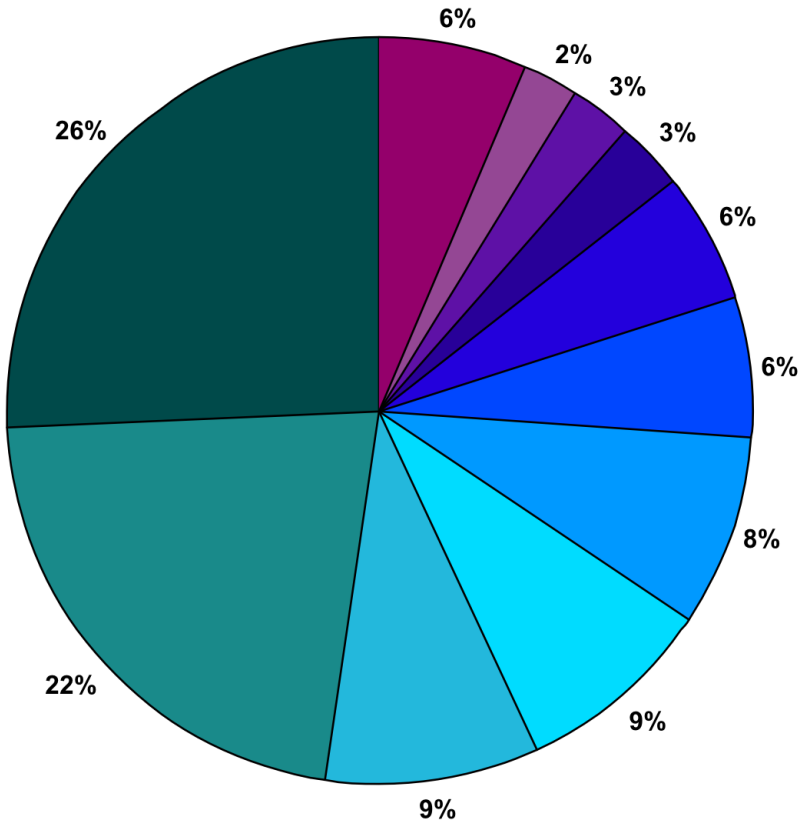
BioModels Database

- 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 curated and then annotated by linking the model elements to relevant data resources, such as publications, databases of compounds and pathways, etc. to improve identification and retrieval.
- Models are accepted in certain 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



BioModels Database: interface

BIOMD0000000271 - Becker2010_EpoR_CoreModel

Download SBML | Other formats (auto-generated) | Actions | Curation Comment

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

Reference Publication

Publication ID: 20488988

Becker V, Schilling M, Bachmann J, Baumann U, Raue A, Maiwald T, Timmer J, Klingmüller U
Covering a broad dynamic range: information processing at the erythropoietin receptor.
Science 2010 Jun;328(5984):1404-8.
Division Systems Biology of Signal Transduction, DKFZ-ZMBH Alliance, German Cancer Research Center, 69120 Heidelberg, Germany. [more]

Model

Original Model: *BIOMD0000000271.xml.origin*

Submitter: Verena Becker

Submission ID: MODEL1005260000

Submission Date: 26 May 2010 13:59:38 UTC

Last Modification Date: 29 Oct 2010 11:58:13 UTC

Creation Date: 26 May 2010 16:12:55 UTC

Encoders: Vijayalakshmi Chelliah
Marcel Schilling
Verena Becker

set #1	bqbiol:occursIn	**Taxonomy** Murinae **Brenda Tissue Ontology** BTO:0001035
	bqbiol:isVersionOf	**Gene Ontology** erythropoietin receptor activity
	bqbiol:isPartOf	**KEGG Pathway** ko04640 **KEGG Pathway** ko04630

Notes

This is the core model described in the article:
Covering a Broad Dynamic Range: Information Processing at the Erythropoietin Receptor
Verena Becker, Marcel Schilling, Julie Bachmann, Ute Baumann, Andreas Raue, Thomas Maiwald, Jens Timmer and Ursula Klingmüller; *Science* Published Online May 20, 2010; DOI:10.1126/science.1184913 PMID:20488988
Abstract:
Cell surface receptors convert extracellular cues into receptor activation, thereby triggering intracellular signaling networks and controlling cellular decisions. A major unresolved issue is the identification of receptor properties that criti
processing of ligand-encoded information. We show by mathematical modeling of quantitative data and experimental validation that rapid ligand depletion and replenishment of cell surface receptor are characteristic features of the e
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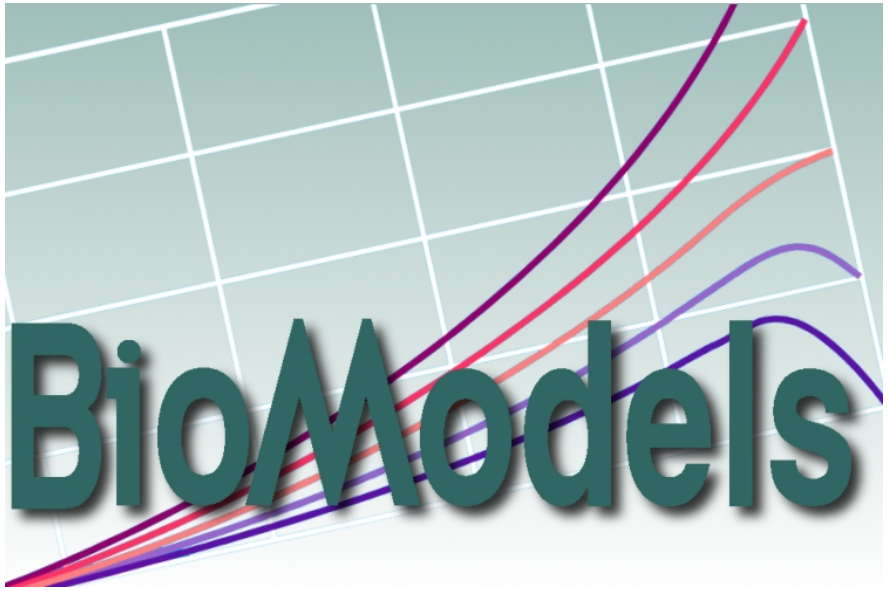
binding, suggesting an essential role of large intracellular receptor pools. These receptor properties enable the system to cope with basal and acute demand in the hematopoietic system.

SBML model exported from PottersWheel.

```
% PottersWheel model definition file

function m = BeckerSchilling2010_EpoR_CoreModel()
```

EMBL-EBI



-Production Pipeline.....

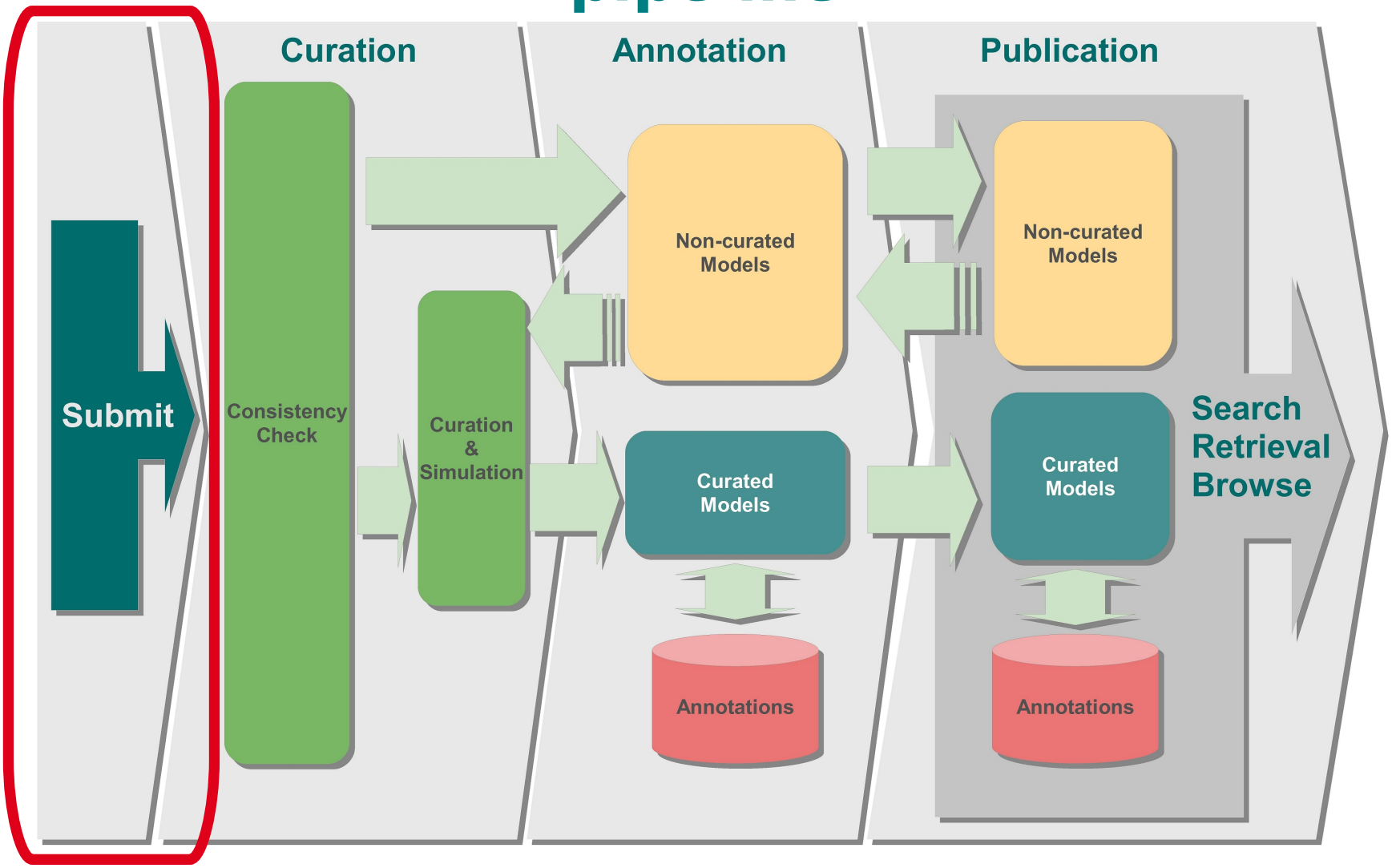
Submission

Curation

Annotation

Search

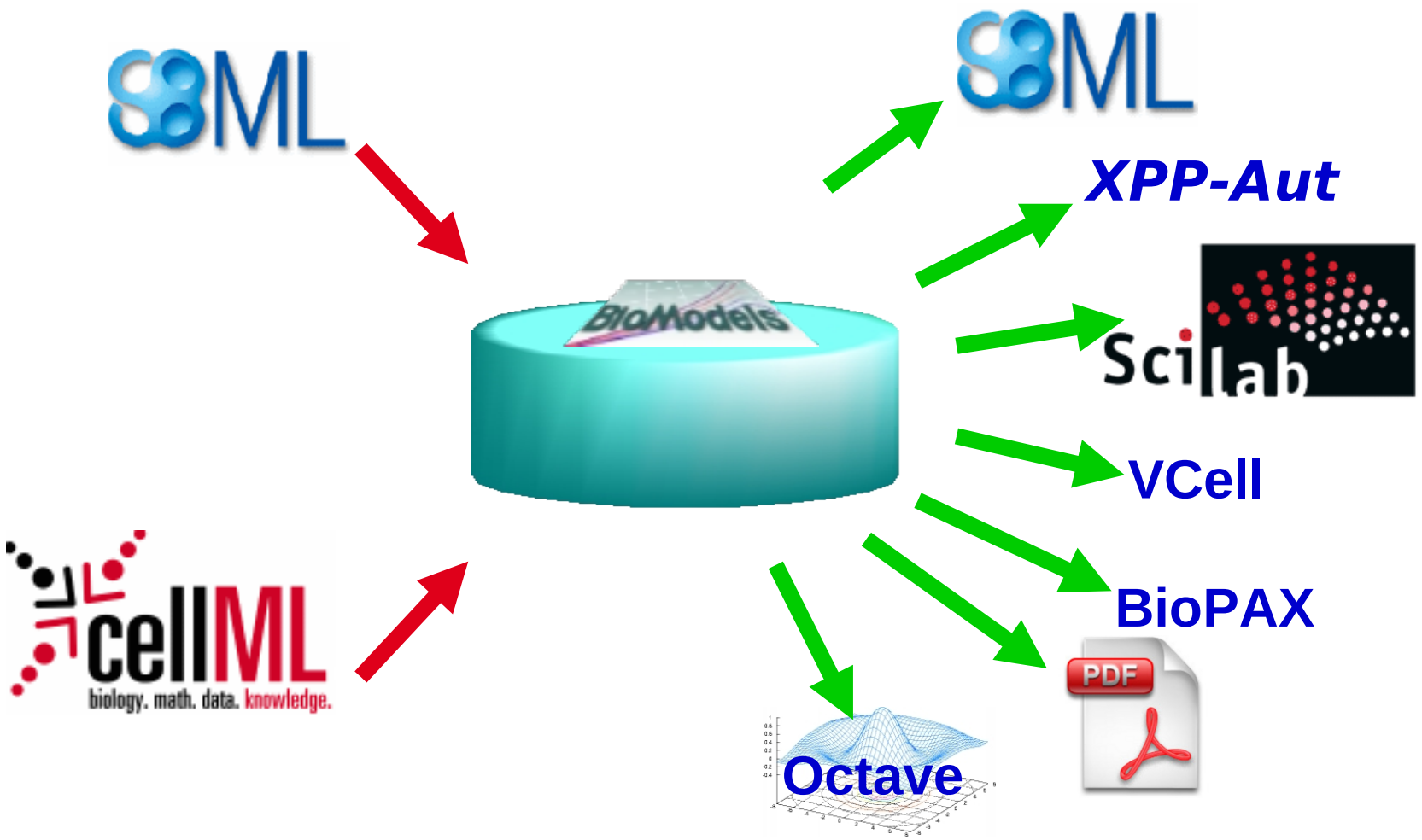
BioModels Database: Production pipeline



Where do models come from?

- From authors prior to publication
  supported (advocate submission to BioModels Database in instructions for authors) by journals that includes:
  - Molecular Systems Biology
  - PLoS journals
  - BioMedCentral journals
  - RSC journals
- Submitted by curators
  - reimplemented from literature
  - imported from supplementary materials of the article
  - Exchanged with other repositories (DOQCS, CellML, JWS online..)
- Provided by other people encoding models for their research.

Model import/export format



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

BioModels Database - A Database of Annotated Published Models

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

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

Search | Go to model | Advanced Search

Browse models

- Curated models (409)
- Browse models using GO
- Non-curated models (420)

Simulate in JWS Online

Submit a model

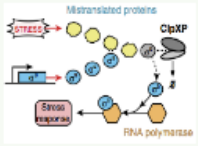
Links

- Main instance at EMBL-EBI, UK
- Mirror at Caltech, USA
- Project on SourceForge
- Web Services
- Download archived models

Model of the month

April, 2012

The implication of quering theory in biological processes, has been demonstrated quantitatively by Cookson et al. (2011), by observing significant cross-talk between two networks that are indirectly coupled through a common set of processors.. *Read more...*



News

12 April 2012 **New web services available!**
New methods are now provided and the version 1.20 of the Java library has been released.
Read more...

8th February 2012 **Twenty-first Release of BioModels Database!**
Important changes are happening or announced, please read more...
Download models archives

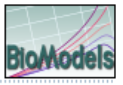
1st September 2011 **Twentieth Release of BioModels Database!**
Download all models in the SBML format

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

Funded by: bbsrc biotechnology and biological sciences research council | EMBL

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 *Edelstein1998_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: 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
EMBL-EBI
Wellcome-Trust Genome Campus
Hinxton Cambridge
CB10 1SD
United-Kingdom

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

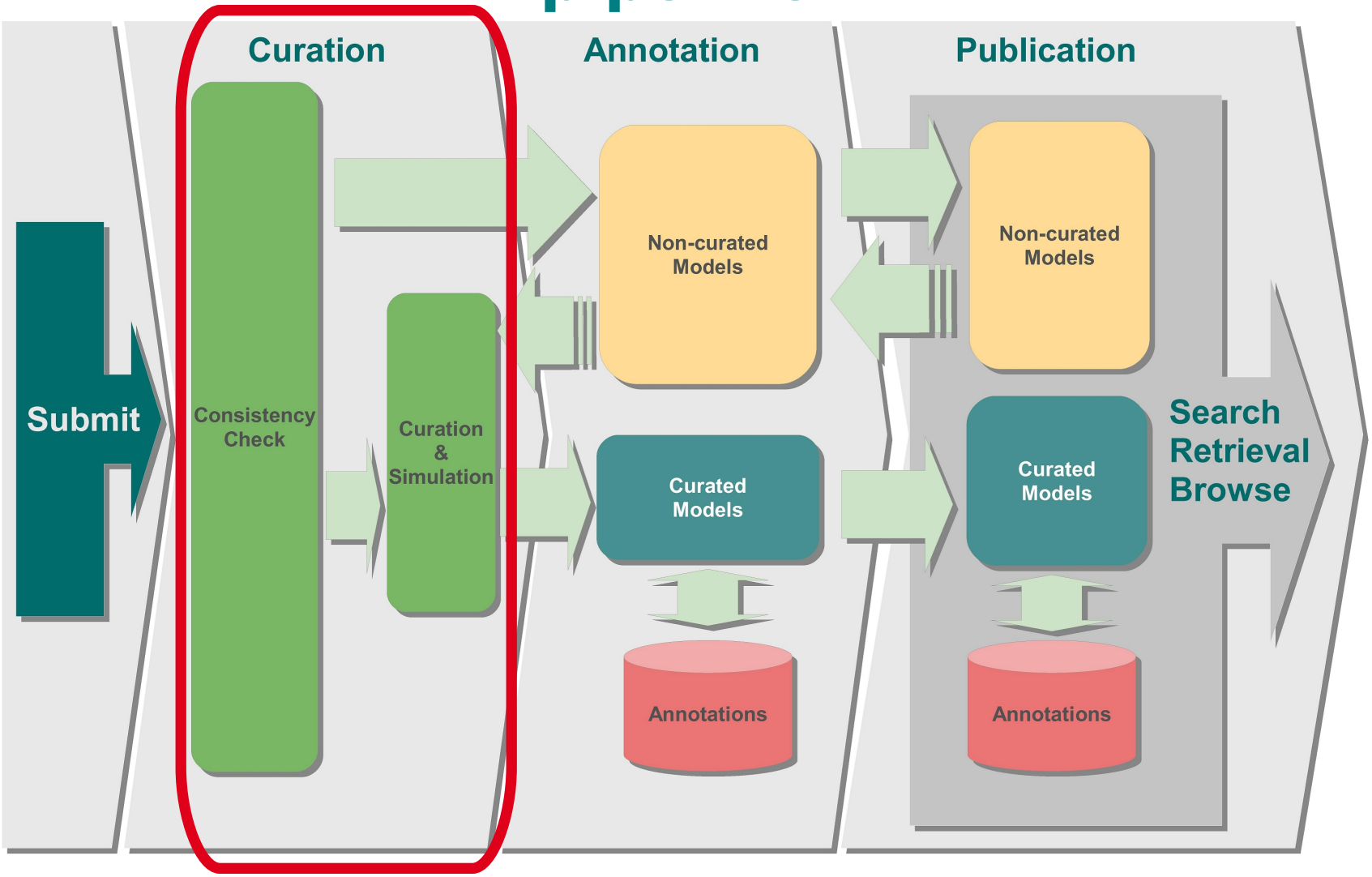
Tel: +44 (0)1223 494521
Fax: +44 (0)1223 494468

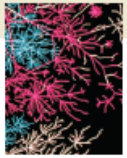
Thank you,
The BioModels Database Team

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.

BioModels Database: Production pipeline





_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 Modelling, 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.

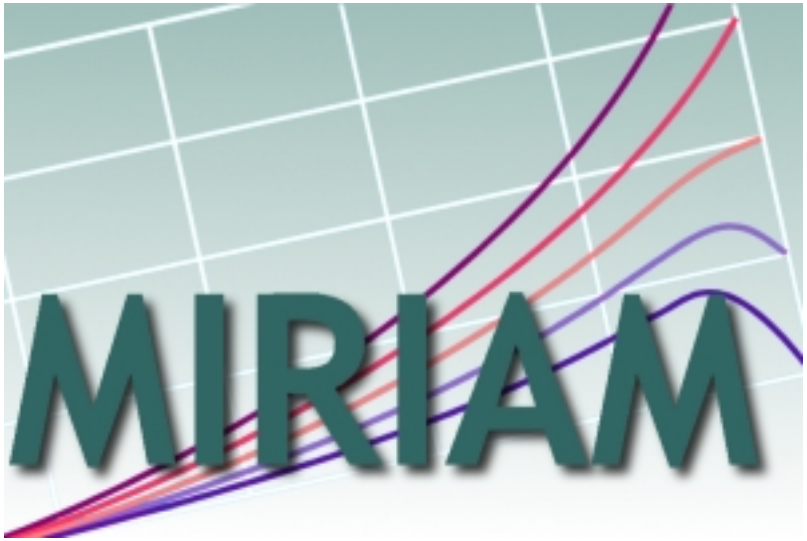
Reference description. A unique document that describes, or references the description of the model, the structure of the model, the numerical values necessary to instantiate a simulation from the model, or to perform a mathematical analysis of the model, and the results one expects from such a simulation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

The Minimum Information Required In the Annotation of a Model



https://biomodels.net/miriam

EMBL-EBI

MIRIAM compliance

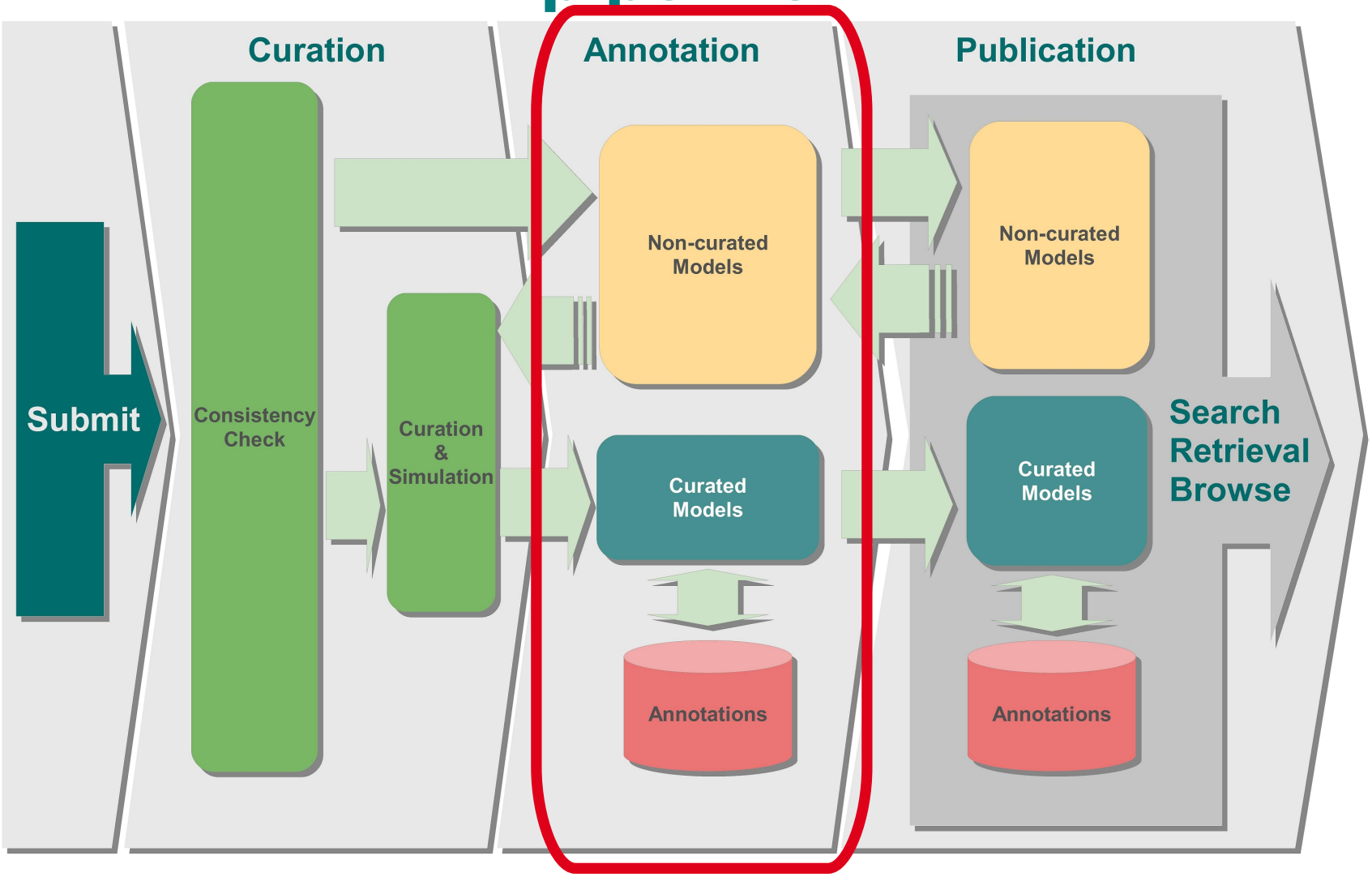
Minimum Information Requested In the Annotation of Models

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.

BioModels Database: Production pipeline



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

BIOMD0000000271 - Becker2010_EpoR_CoreModel

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Reference Publication

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Submission ID: MODEL1005260000

Submission Date: 26 May 2010 13:59:38 UTC

Last Modification Date: 29 Oct 2010 11:58:13 UTC

Creation Date: 26 May 2010 16:12:55 UTC

Encoders: Vijayalakshmi Chelliah
Marcel Schilling
Verena Becker

set #1	bqbiol:occursIn	**Taxonomy** Murinae Brenda Tissue Ontology BTO:0001035
	bqbiol:isVersionOf	**Gene Ontology** erythropoietin receptor activity
	bqbiol:isPartOf	**KEGG Pathway** ko04640 **KEGG Pathway** ko04630

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Covering a Broad Dynamic Range: Information Processing at the Erythropoietin Receptor
Verena Becker, Marcel Schilling, Julie Bachmann, Ute Baumann, Andreas Raue, Thomas Maiwald, Jens Timmer and Ursula Klingmüller; *Science* Published Online May 20, 2010; DOI:10.1126/science.1184913 PMID:20488988
Abstract:
Cell surface receptors convert extracellular cues into receptor activation, thereby triggering intracellular signaling networks and controlling cellular decisions. A major unresolved issue is the identification of receptor properties that criti
processing of ligand-encoded information. We show by mathematical modeling of quantitative data and experimental validation that rapid ligand depletion and replenishment of cell surface receptor are characteristic features of the e
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Science 2010 Jun;328(5984):1404-8.
Division Systems Biology of Signal Transduction, DKFZ-ZMBH Alliance, German Cancer Res

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Encoders: Vijayalakshmi Chelliah
Marcel Schilling
Verena Becker

	bqbiol:occursIn	Taxonomy Murinae Brenda Tissue Ontology BTO:0001035
set #1	bqbiol:isVersionOf	Gene Ontology erythropoietin receptor activity
	bqbiol:isPartOf	KEGG Pathway ko04640 KEGG Pathway ko04630

Notes

This is the core model described in th
Covering a Broad Dynamic Range: In
Verena Becker, Marcel Schilling, Juli
Abstract:
Cell surface receptors convert extrace
processing of ligand-encoded informa
receptor (EpoR). The amount of Epo-E
binding, suggesting an essential role

SBML model exported from PottersWh

```
% PottersWheel model definiti

function m = BeckerSchilling2
```

d Ursula Kli

works and co
validation th
ligand input
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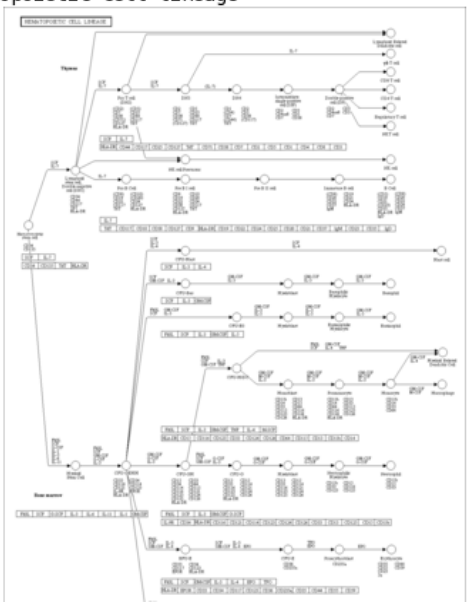
ko04640 Hematopoietic cell lineage



UniProt › Taxonomy

Search | Blast | Align | Retrieve | ID Mapping

Search in: Taxonomy — Query

SUBFAMILY **Murinae**

UniProtKB (120,403) | Branch (606) | Taxonomy help

Mnemonic	9MURI
Taxon identifier	39107
Scientific name	Murinae
Common name	-
Synonym	-
Other names	› Otomyinae
Rank	SUBFAMILY
Lineage	› cellular organisms › Eukaryota › Fungi/Metazoa group

Taxonomy navigation

› Muridae
› Abeomelomys
› Aethomys
› Anisomys
› Apodemus
› Apomys
› Archboldomys
› Arvicanthis
› Bandicota
› Batomys
› Berylmys
› Bullimus
› Bunomys
› Carpomys

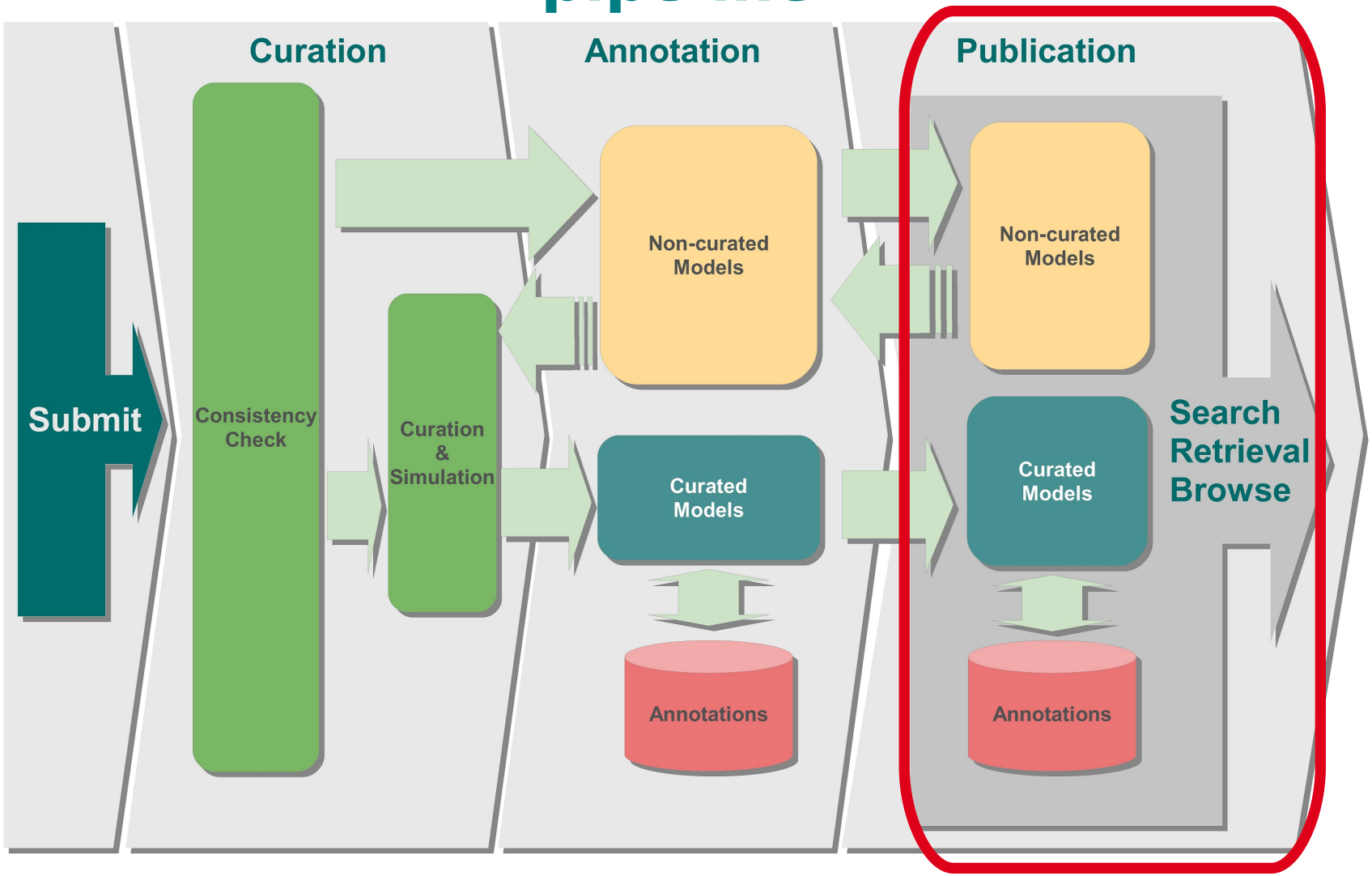
QuickGO — Click for example search — Search! — Web Services — Datas

Term Information | Ancestor Chart | Child Terms | Protein Annotation | Co-occu

ID	GO:0004900
Name	erythropoietin receptor activity
Ontology	Molecular Function
Definition	Combining with erythropoietin to initiate a change in cell activity.
Comment	
GONUTS	GO:0004900 Wiki Page

EMBL-EBI

BioModels Database: Production pipeline



Model browsing..

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Submit a model

Links

- Main instance at EMBL-EBI, UK
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April, 2012

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Read more...

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1st September 2011 **Twentieth Release of BioModels Database!**
Download all models in the SBML format

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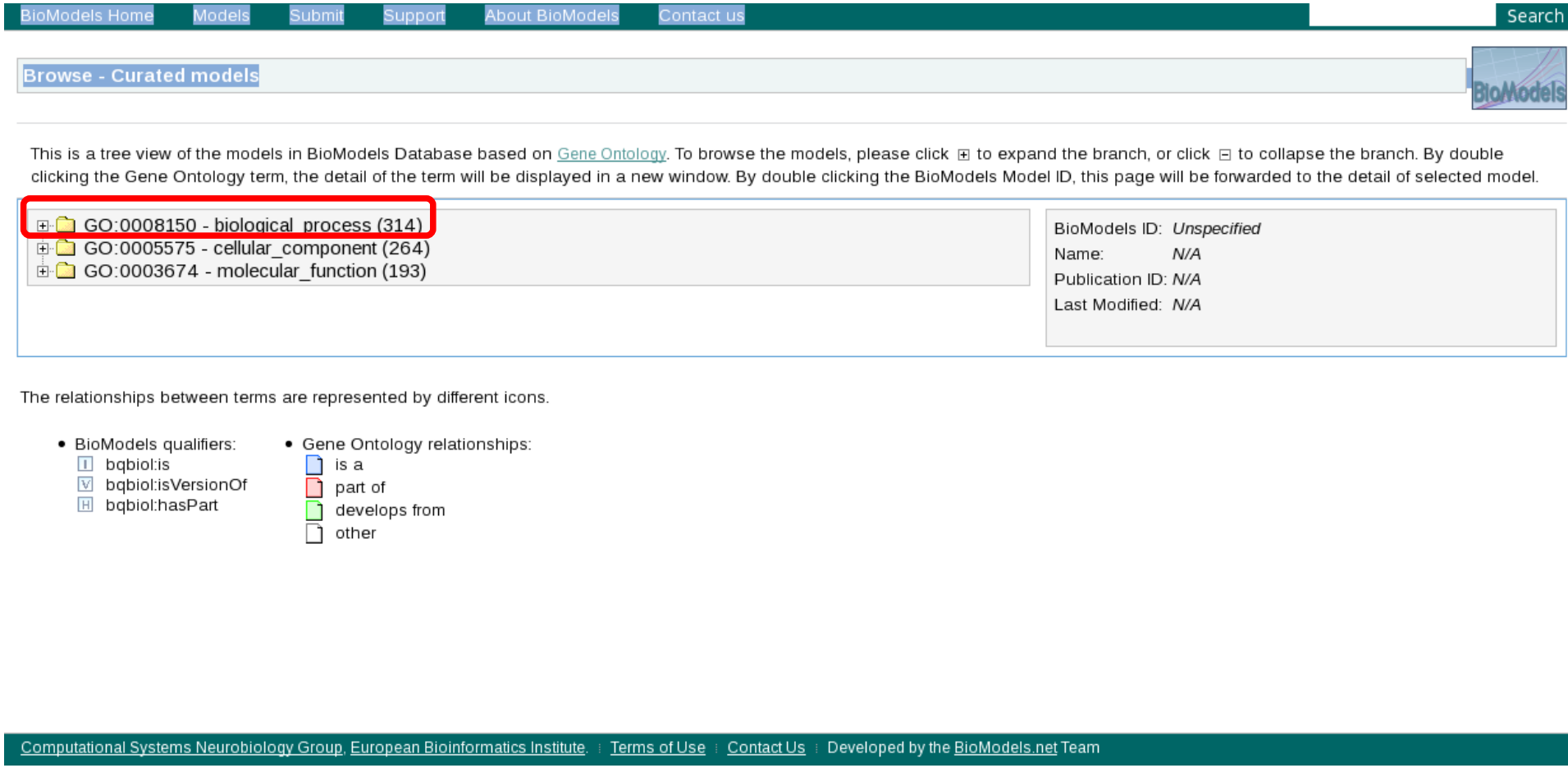

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Browse - Curated models

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 (314)
  - GO:0009987 - cellular process (280)
    - GO:0051641 - cellular localization (48)
    - GO:0050794 - regulation of cellular process (172)
    - GO:0007049 - cell cycle (27)
      - GO:0051726 - regulation of cell cycle (23)
      - GO:0000278 - mitotic cell cycle (23)
        - GO:0051329 - interphase of mitotic cell cycle (7)
        - GO:0000087 - M phase of mitotic cell cycle (2)
        - GO:0007346 - regulation of mitotic cell cycle (13)
        - GO:0051439 - regulation of ubiquitin-protein ligase activity involved in 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 (11)
      - GO:0045786 - negative regulation of cell cycle (15)
      - GO:0045787 - positive regulation of cell cycle (12)
      - GO:0004693 - cyclin-dependent protein kinase activity (9)
        - BIOMD0000000196 - Srividhya2006_CellCycle

BioModels ID: BIOMD0000000005
Name: Tyson1991_CellCycle_6var
Publication ID: 1831270
Last Modified: 2010-05-24T16:33:07+00:00
SBML L2 V4

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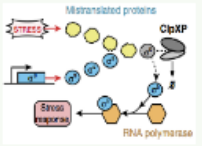

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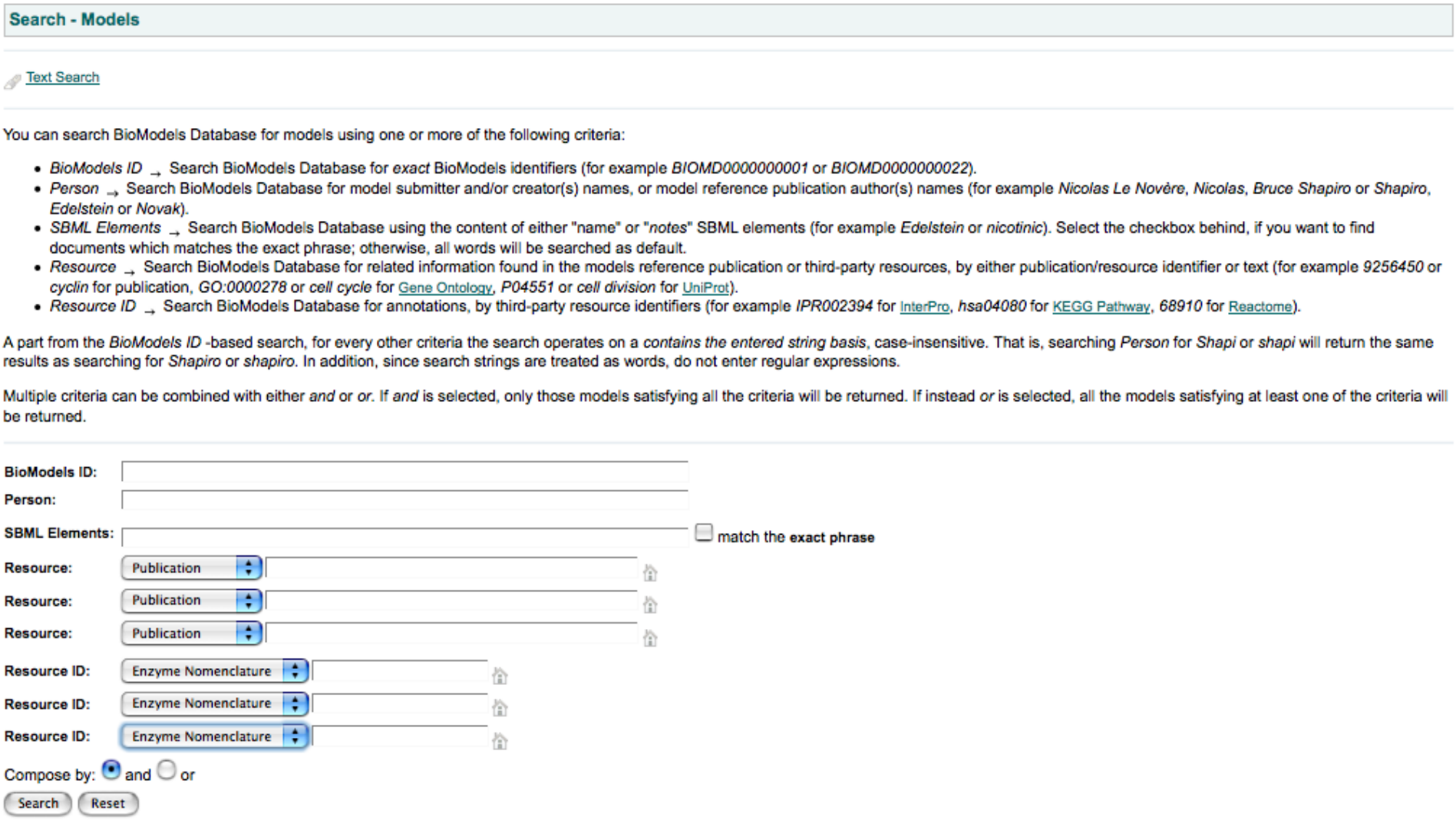
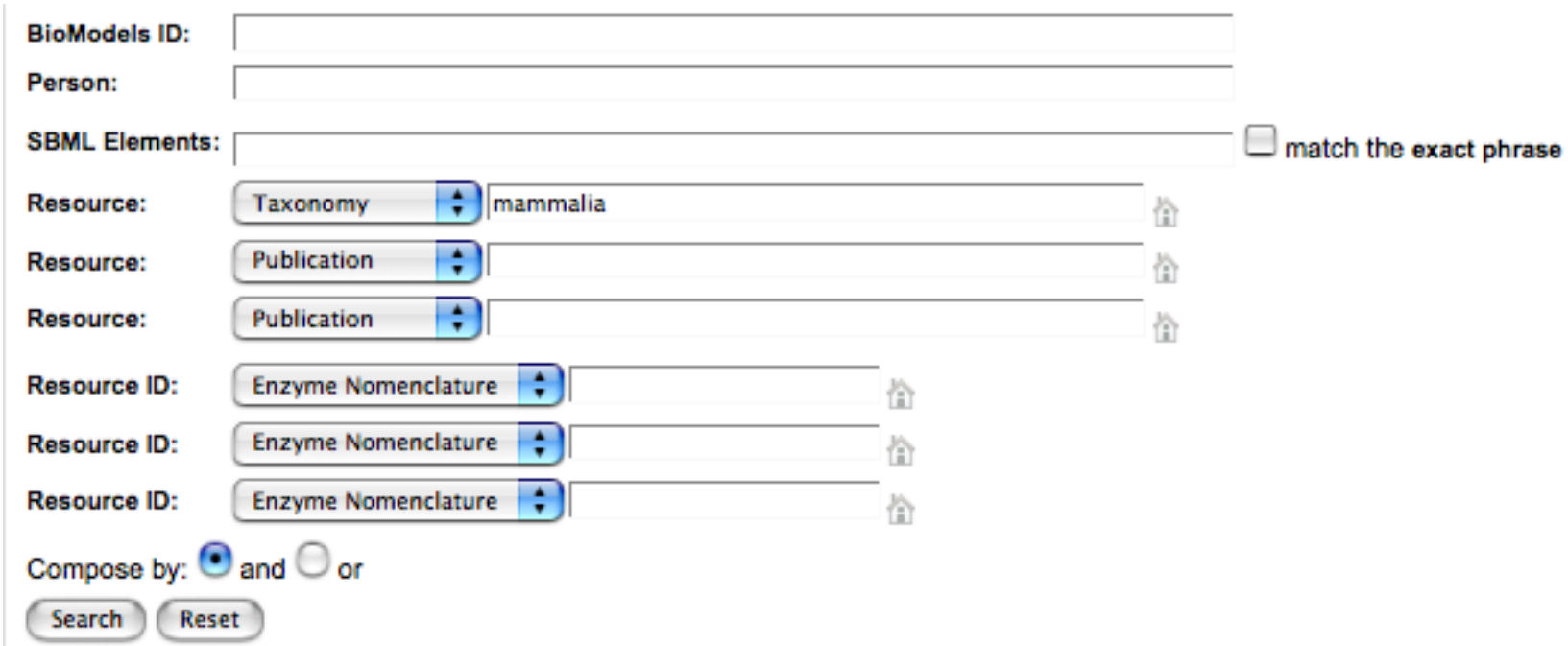
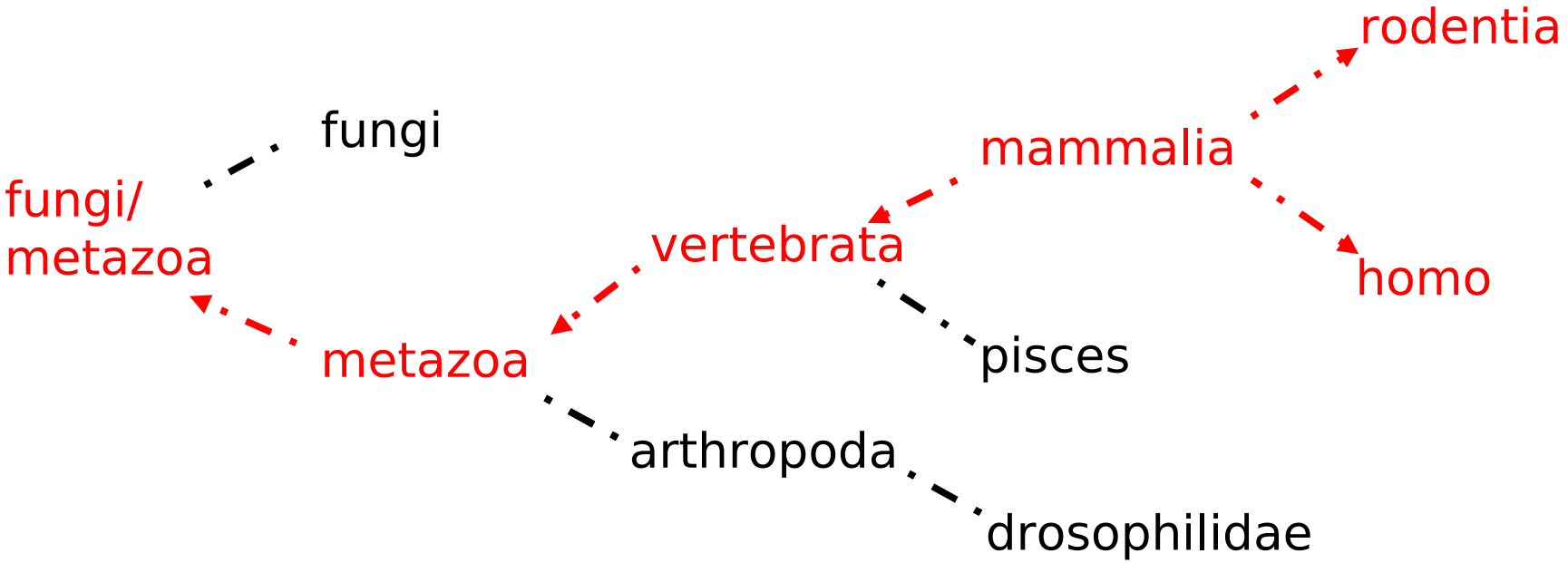


Model searching..



Taxonomic Searches

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



Model retrieving..

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

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

Notes

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Tyson JJ *Proc. Natl. Acad. Sci. U.S.A.* 1991; 88(16); 7328-32 1831270,
Abstract:
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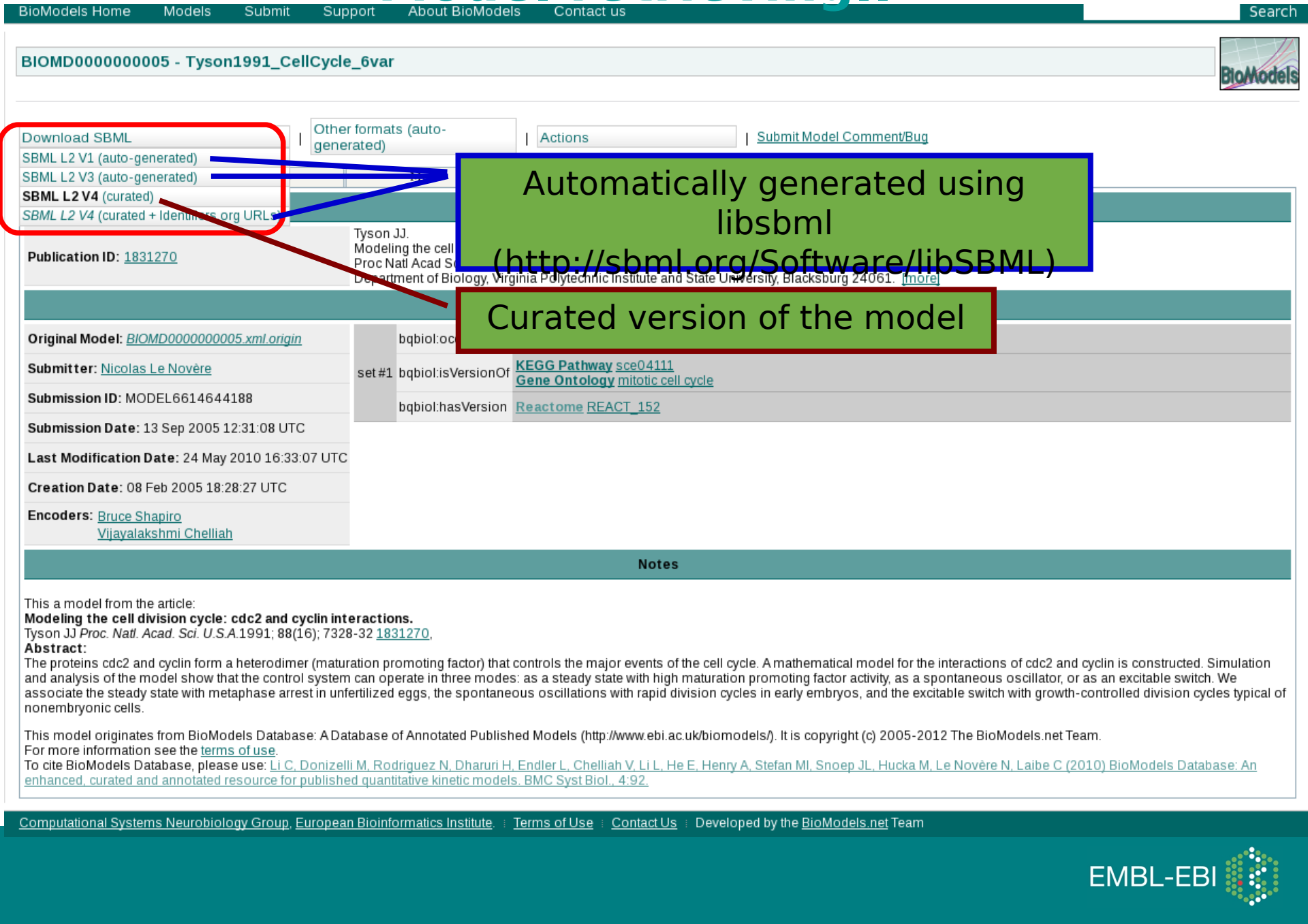
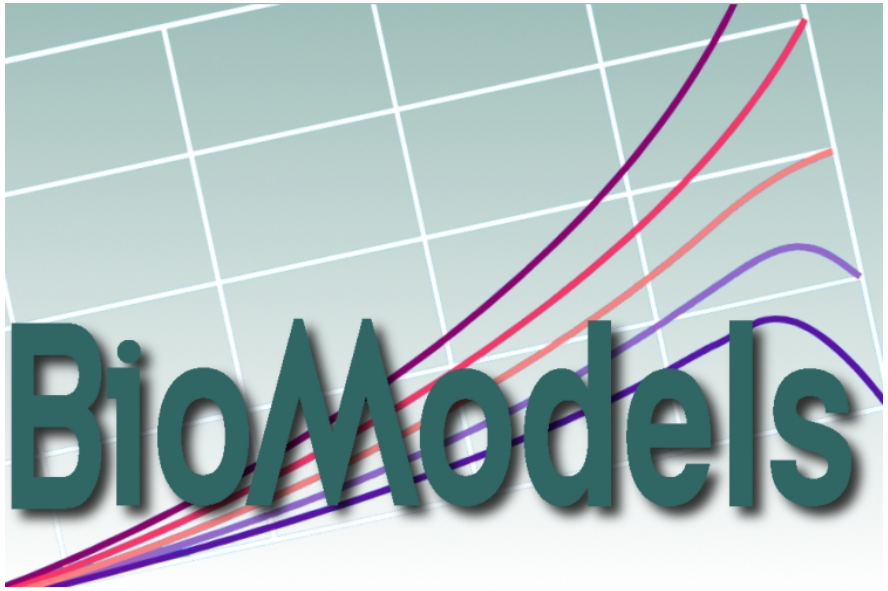
Model retrieving..





Model components, Features & Sub-model creation

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BIOMD0000000005 - Tyson1991_CellCycle_6var

Download SBML | Other formats (auto-generated) | Actions

- BioPAX (Level 2)
- BioPAX (Level 3)
- Octave (m-file)
- PDF
- SciLab
- VCML (VCell)
- XPP

Model | ath | Physical entities

Publication ID: 1831270

ci U S A 1991 Aug;88(16):7328-32.
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ology, Virginia Polytechn… Institute and S

Original Model: *BIOMD0000000005.xml.origin*

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Submission ID: MODEL6614644188

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

Last Modification Date: 24 May 2010 16:33:07 UTC

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

Encoders: Bruce Shapiro
Vijayalakshmi Chelliah

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	bqbiol:isVersionOf	KEGG Pathway sce04111 Gene Ontology mitotic cell cycl
	bqbiol:occursIn	Taxonomy Fungi/Metazoa grou

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To cite BioModels Database, please use: Li C, Donizelli M, Rodriguez N, Dharuri H, Endler L, Chelliah V, Li L, He E, Henry A, Stefan MI, Snoep JL, H… hanced, curated and annotated resource for published quantitative kinetic models. BMC Syst Biol., 4:92.

Computational Systems Neurobiology Group, European Bioinformatics Institute. | Terms of Use | Contact Us | Developed by the BioModels.net T…


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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, vij1@ebi.ac.uk

Produced by SBML2LaTeX 1

EMBL-EBI

BIOMD0000000005 - Tyson1991_CellCycle_6var

SBML formats | Other formats (auto-generated) | Actions | Submit Model Comment

Actions:
- View Bitmap Reaction Graph
- View SVG Reaction Graph
- View Dynamic Reaction Graph
- View Model of Month
- JWS Online Simulation
- BioModels Online Simulation

Model | Overview | Math | Parameters

Reference Publication

Publication ID: 1831270

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	bqbiol:hasVersion	Reactome REACT_152
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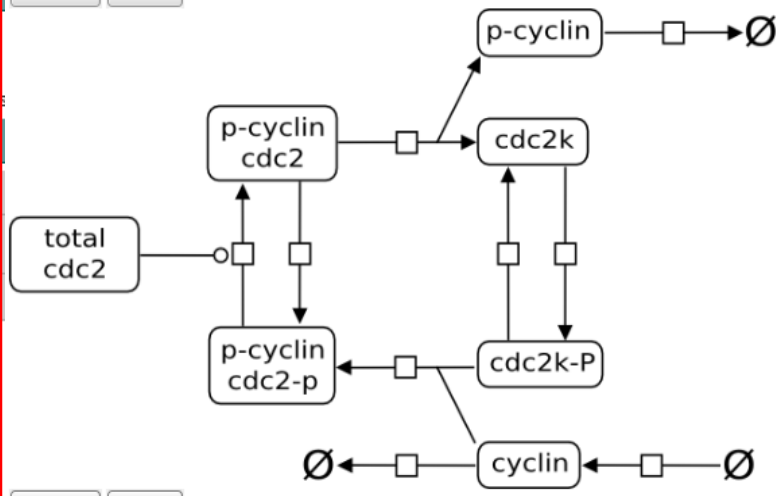
To cite BioModels Database, please use Le Novère N., Bornstein B., Broicher A., Courtot M., Donizelli M., Dharuri H., Li L., Sauro H., Schilstra M., Shapiro B., Snoep J.L., Hucka M. (2006) BioModels Database: A Free, Centralized Database of Curated, Published, Quantitative Kinetic Models of Biochemical and Cellular Systems Nucleic Acids Res., 34: D689-D691.

http://www.ebi.ac.uk/biomodels/models-main/publ/BIOMD0000000005.html

BIOMD0000000005

Refresh | Close



Refresh | Close

Graphical export (SBGN)

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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.

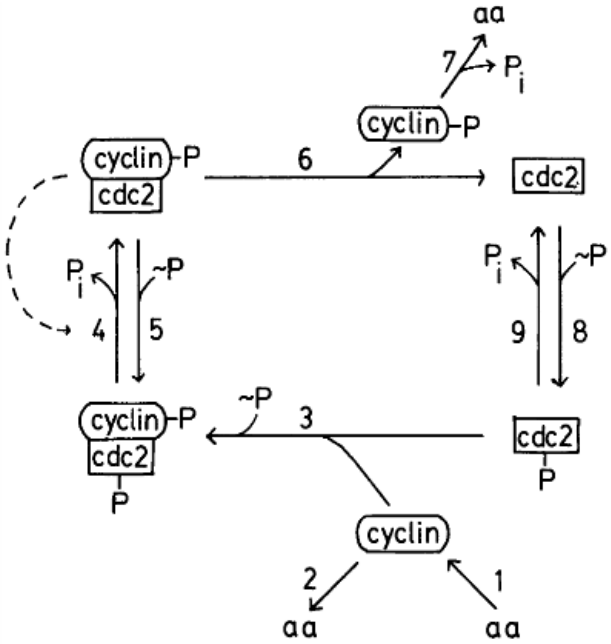

Figure 1: Reaction graph of the model from Tyson 1991.

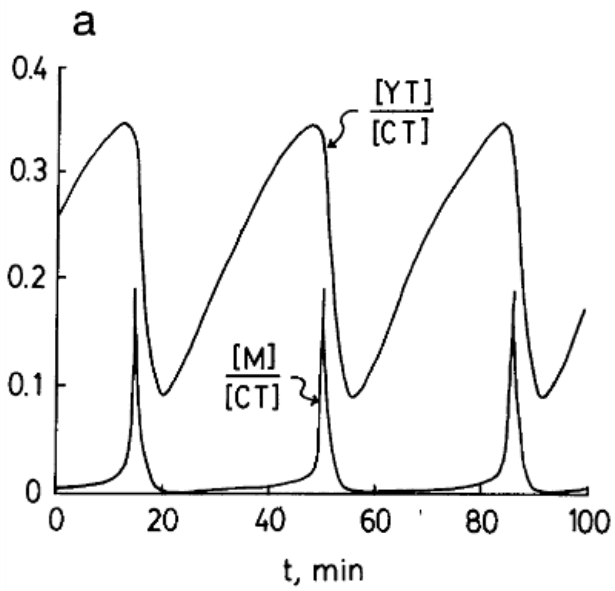

Figure 2: Oscillations of the total cyclin (YT) and the total MPF, relative to the total cyclin dependent kinase CDC2.

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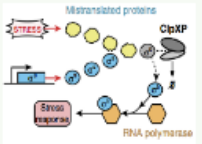

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8th February 2012 **Twenty-first Release of BioModels Database!**
Important changes are happening or announced, please read more...
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1st September 2011 **Twentieth Release of BioModels Database!**
Download all models in the SBML format

View - Models of the month

Each "Model of the Month" is an article which explores the biological significance of a particular model from BioModels Database. Every article includes elements such as:

- the description of the model itself and its results
- the biological background of the model
- a brief description of the biological processes that are encoded as a mathematical model
- the biological role of each of the model elements
- the diseases that are caused due to the malfunction of these elements
- the presenters own view on the model

Direct access to the models of the month for a given year: 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012

2012

- April: BIOMD0000000405
  Cookson et al. (2011). Queueing up for enzymatic processing: correlated signaling through coupled degradation. - *Benedetta Frida Baldi*
- March: BIOMD0000000118, BIOMD0000000119
  Golomb et al. (2006). Contribution of persistent Na+ current and M-type K+ current to somatic bursting in CA1 pyramidal cells: combined experimental and modeling study. - *Youwei Zheng*
- February: BIOMD0000000328
  Bucher et al. 2011. A systems biology approach to dynamic modeling and inter-subject variability of statin pharmacokinetics in human hepatocytes. - *Christine Hoyer*
- January: BIOMD0000000401, BIOMD0000000402, BIOMD0000000403
  Ayati et al. (2010). A mathematical model of bone remodeling dynamics for normal bone cell populations and myeloma bone disease. - *Vijayalakshmi Chelliah*

2011

- December: BIOMD0000000364
  Lee et al. (2010). A revisit to the one form kinetic model of prothrombinase. - *Massimo Lai*
- November: BIOMD0000000356
  Nyman et al. (2011). A Hierarchical Whole-body Modeling Approach Elucidates the Link between in Vitro Insulin Signaling and in Vivo Glucose Homeostasis. - *Ishan Ajmera*
- October: BIOMD0000000271, BIOMD0000000272
  Becker et al. (2010). Covering a broad dynamic range: information processing at the erythropoietin receptor. - *Nick Juty*
- September: BIOMD0000000069
  Fuss et al. (2006). Bistable switching and excitable behaviour in the activation of Src at mitosis. - *Denis Brun*
- August: BIOMD0000000239
  Jiang et al. (2007). A kinetics core model of the Glucose-simulated insulin secretion network of pancreatic beta cells. - *Ishan Ajmera*
- July: BIOMD0000000338, BIOMD0000000339, BIOMD0000000340
  Wajima et al. (2009). A comprehensive model for the humoral coagulation network in human. - *Michael Schubert*
- June: BIOMD0000000301
  Friedland et al., (2009). Synthetic gene networks that count. - *Gael Jalowicki*
- May: BIOMD0000000296
  Balagaddé et al., (2008). A synthetic Escherichia coli predator-prey ecosystem. - *Michele Mattioni*
- April: BIOMD0000000306, BIOMD0000000307, BIOMD0000000308, BIOMD0000000309, BIOMD0000000310, BIOMD0000000311, BIOMD0000000312

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BIOMD0000000005 - Tyson1991_CellCycle_6var

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- View SVG Reaction Graph
- View Dynamic Reaction Graph
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- JWS Online Simulation
- BioModels Online Simulation

Model | Overview | Math | Parameters

Reference Publication

Publication ID: 1831270

Proc Natl Acad Sci U
Modeling the cell di ctions.
Tyson JJ.
Department of Biology, Virginia Polytechnic Institute and State University, Blacksburg 24

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 U

Encoders: Bruce Shapiro, Vijayalakshmi Chelliah

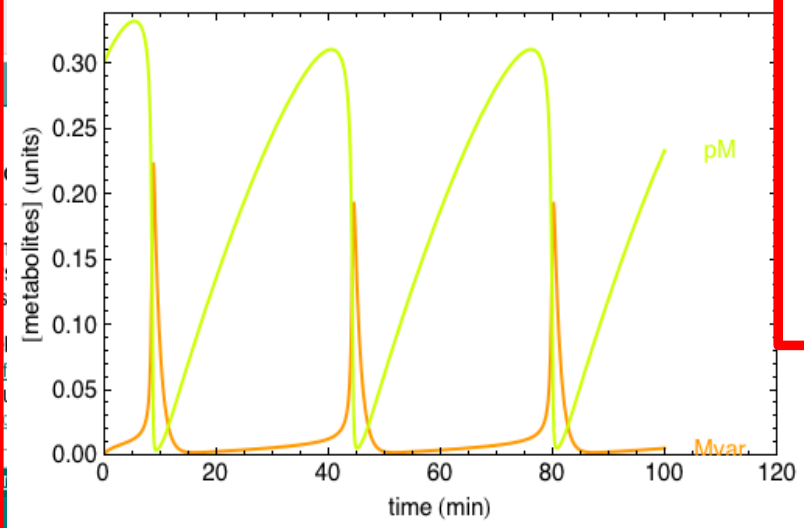
	bqbiol:hasVersion	Reactome REACT_152
set #1	bqbiol:isVersionOf	KEGG Pathway sce04111 Gene Ontology mitotic cell cycle
	bqmodel:is	Taxonomy Fungi/Metazoa group

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

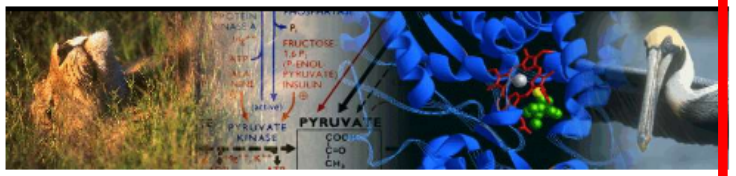
Computational Neurobiology Group in E

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]	0.
.	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 Database: A Free, Centralized Database of

Jacky Snoep
Stellenbosch University
EMBL-EBI

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BIOMD0000000005 - Tyson1991_CellCycle_6var

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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 n
of the model show that the control system can operate in three modes: as a steady state with high maturation promoting factor act
metaphase arrest in unfertilized eggs, the spontaneous oscillations with rapid division cycles in early embryos, and the excitable s

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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.

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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

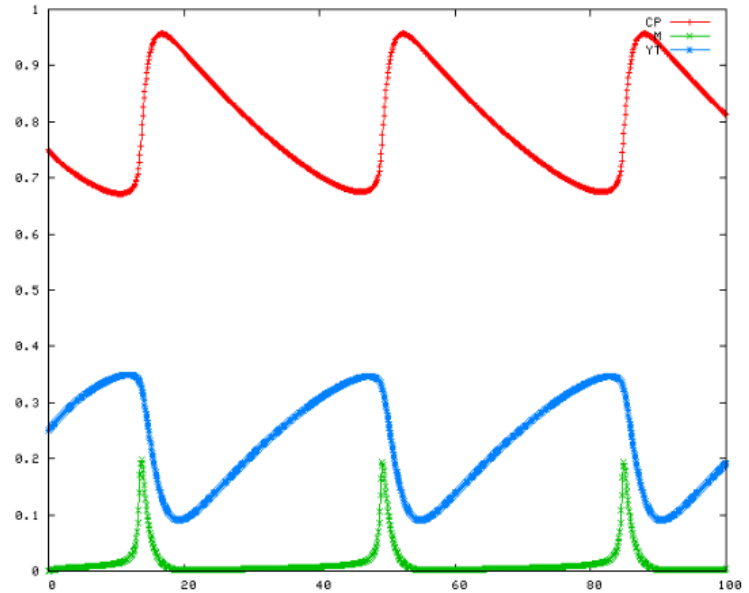
Done

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



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.
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Tyson JJ.
Department of Biology, Virginia Polytechnic Institute and State University, Blacksburg 24061. [more]

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Encoders: Bruce Shapiro
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	bqbiol:isVersionOf	KEGG Pathway sce04111 Gene Ontology mitotic cell cycle
	bqmodel:is	Taxonomy Fungi/Metazoa group

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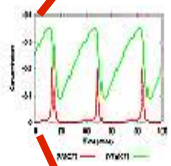
BIOMD0000000005 - Tyson1991

SBML formats | Other fo generat

Model | Overv

Curation result



2010-02-08T10:29:04

Comment: The mo

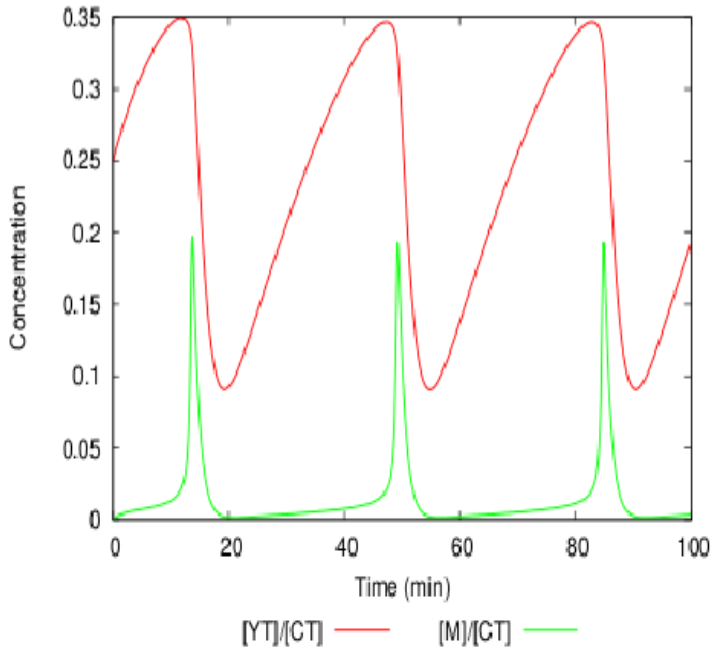
Model history

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



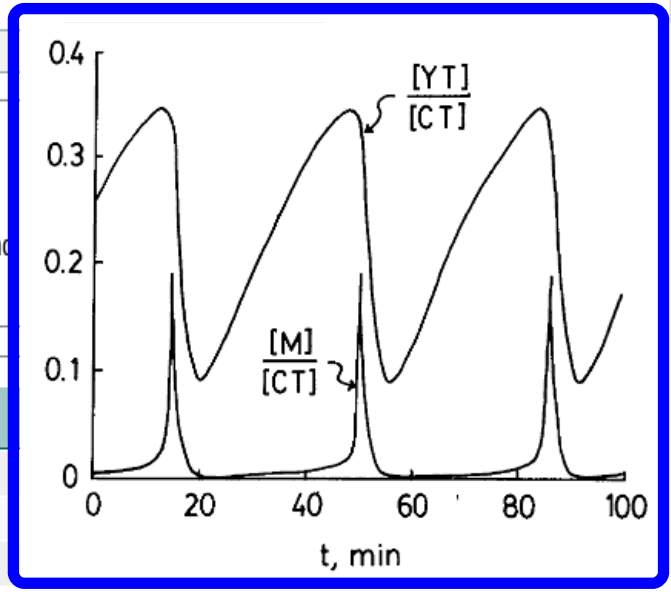
2010-02-08T10:29:04+00:00

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

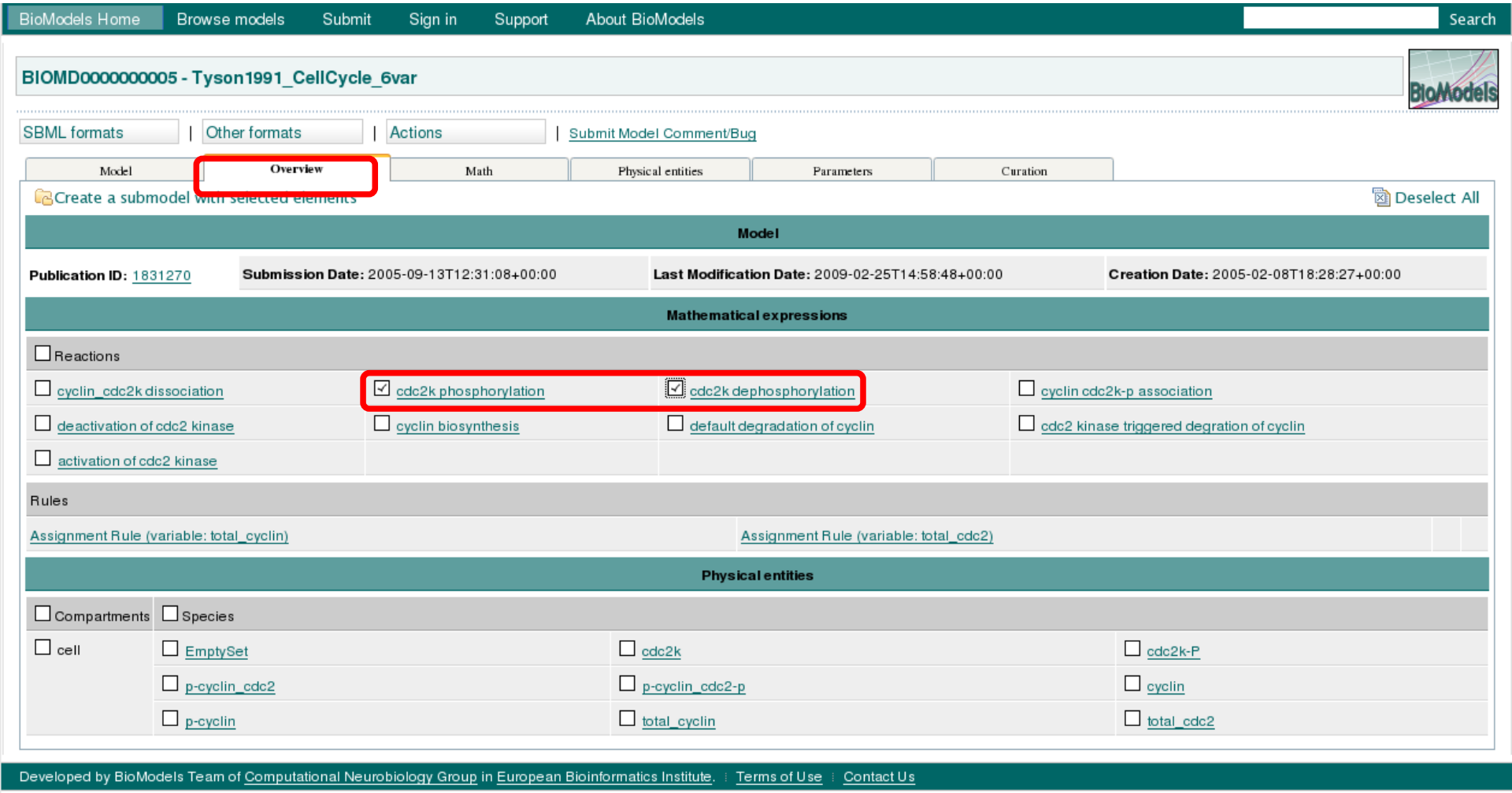
Figure reproduced using COPASI

Close

Done



original article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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
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Assignment Rule (variable: total_cdc2)
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cdc2k-P
p-cyclin_cdc2
p-cyclin_cdc2-p
cyclin
p-cyclin
total_cyclin
total_cdc2
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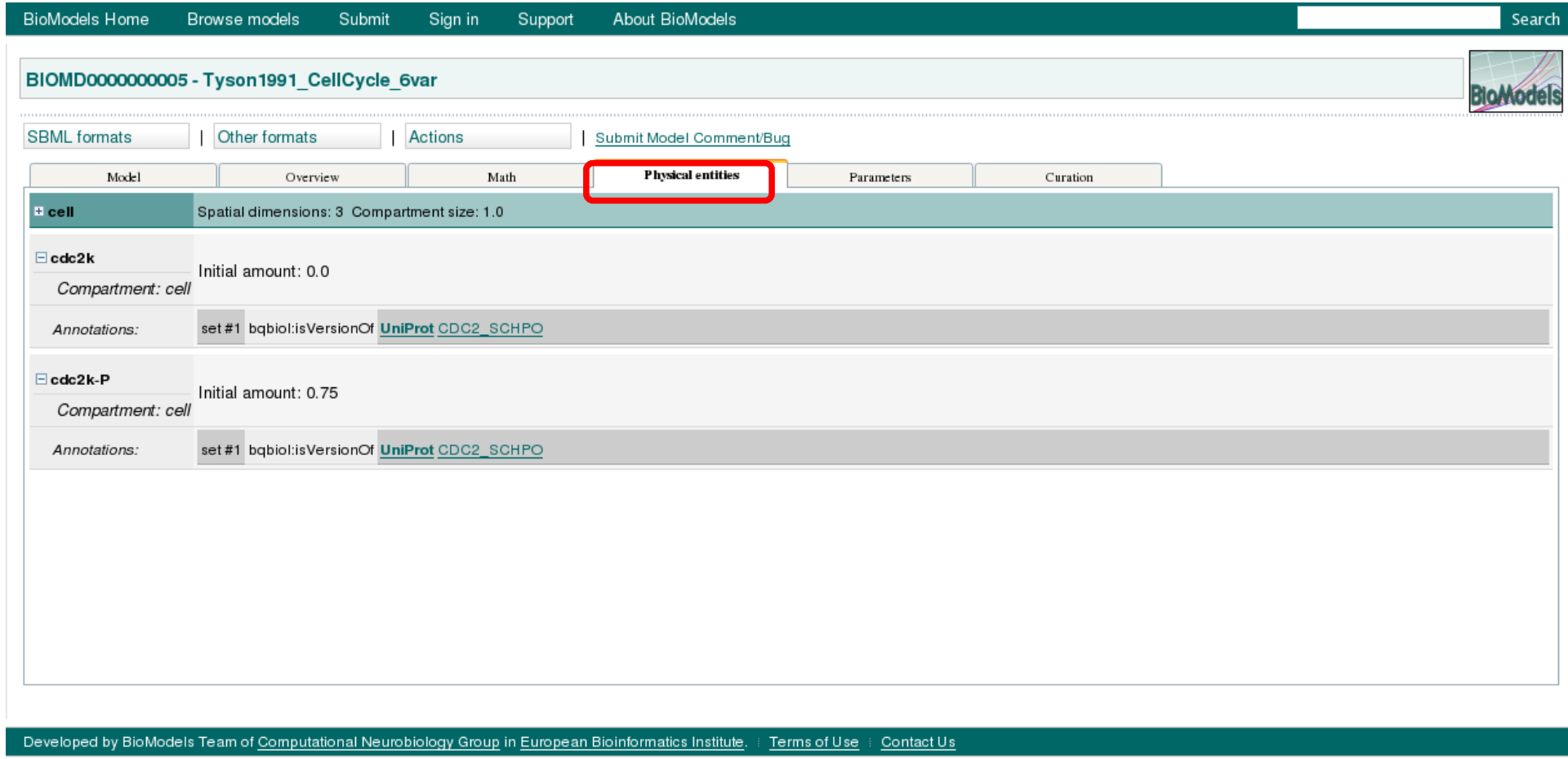
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Spatial dimensions: 3 Compartment size: 1.0
cdc2k
Compartment: cell
Initial amount: 0.0
Annotations:
set #1 bqbiol:isVersionOf UniProt CDC2_SCHPO
cdc2k-P
Compartment: cell
Initial amount: 0.75
Annotations:
set #1 bqbiol:isVersionOf UniProt CDC2_SCHPO
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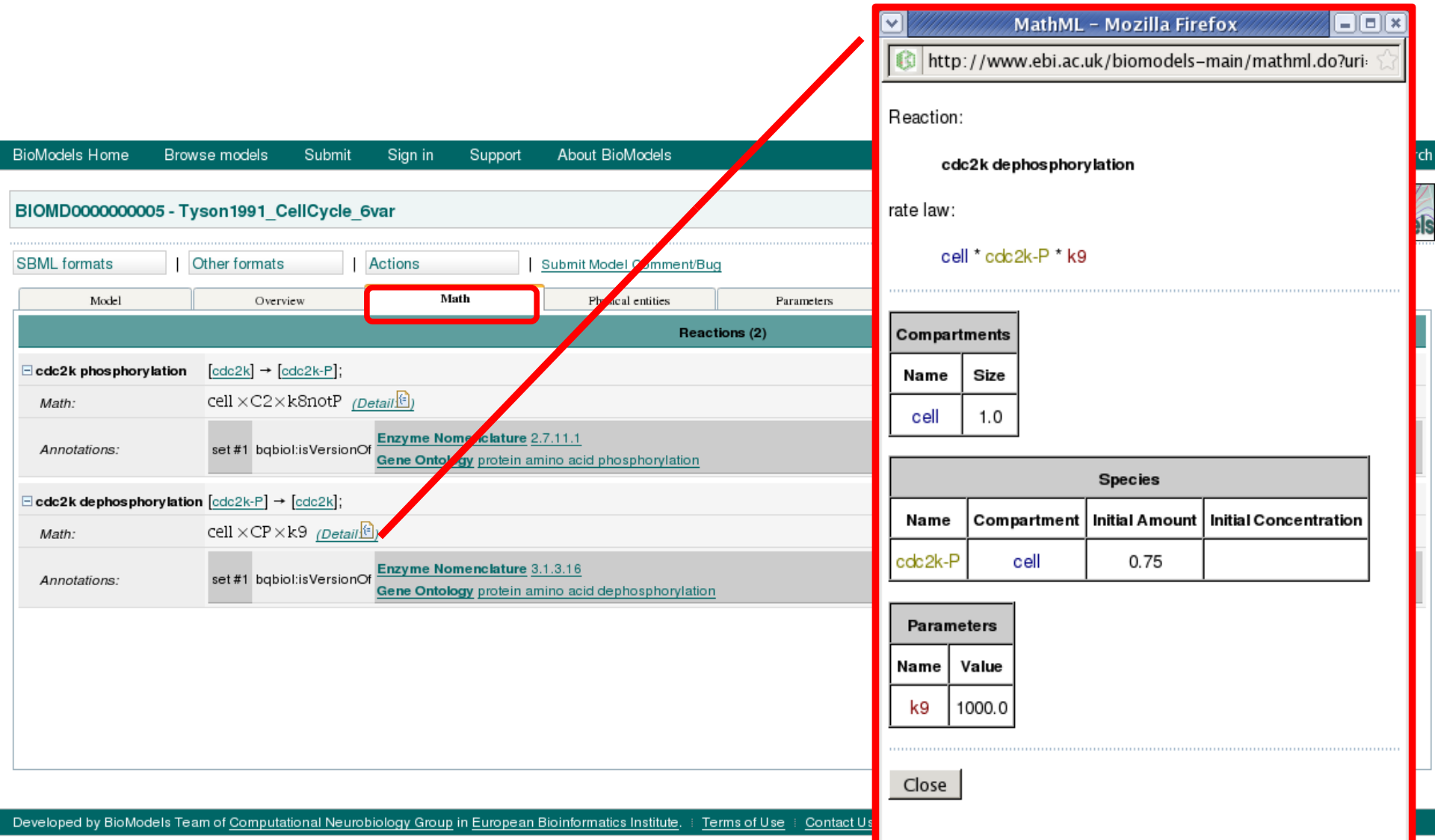
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cdc2k phosphorylation
[cdc2k] → [cdc2k-P];
Math:
cell ×C2×k8notP (Detail)
Annotations:
set #1
bqbiol:isVersionOf
Enzyme Nomenclature 2.7.11.1
Gene Ontology protein amino acid phosphorylation
cdc2k dephosphorylation
[cdc2k-P] → [cdc2k];
Math:
cell ×CP×k9 (Detail)
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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
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cdc2k dephosphorylation
rate law:
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Size
cell
1.0
Species
Name
Compartment
Initial Amount
Initial Concentration
cdc2k-P
cell
0.75
Parameters
Name
Value
k9
1000.0
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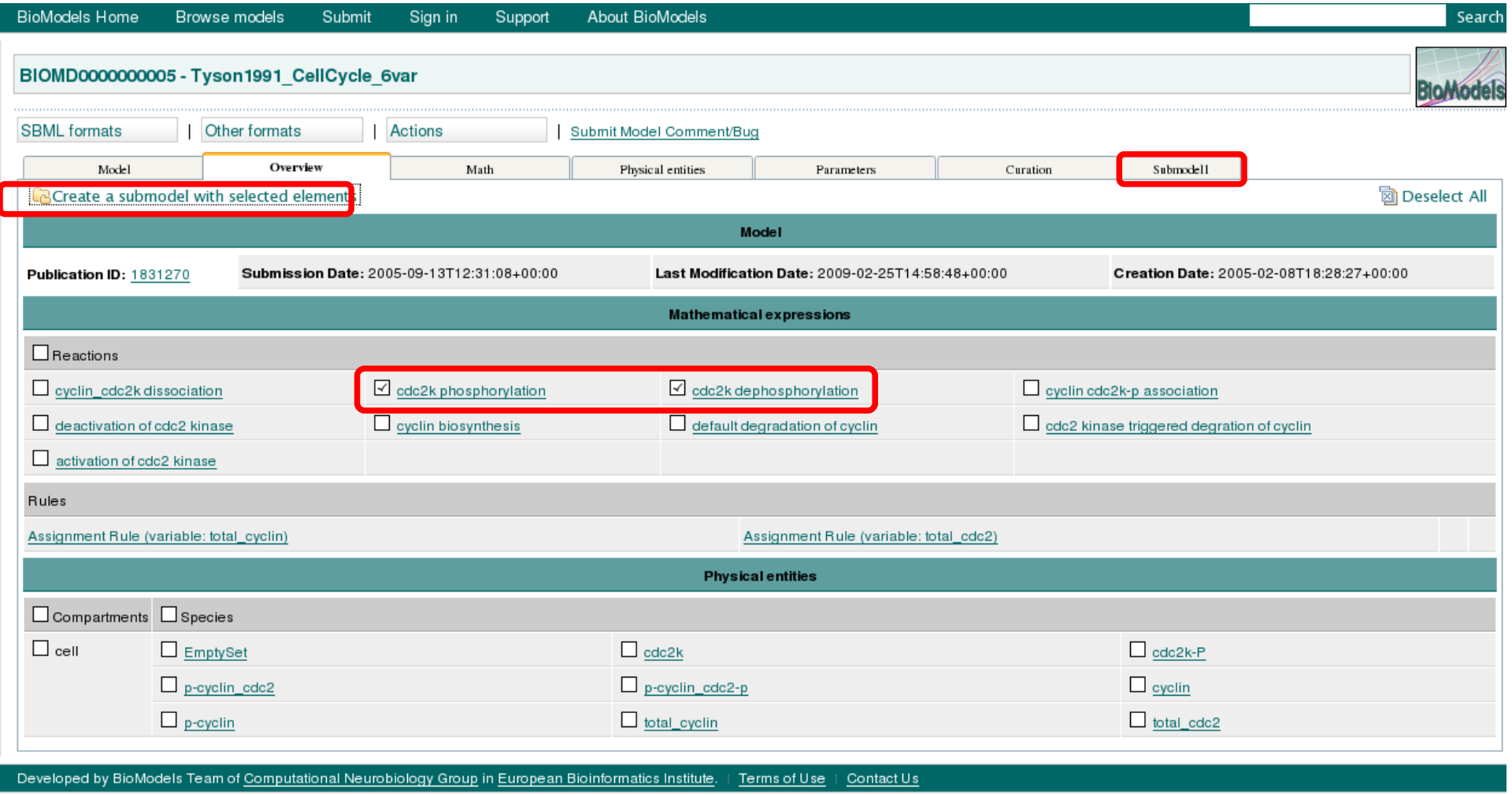
Done
zotero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p-cyclin_cdc2-p
cyclin
p-cyclin
total_cyclin
total_cdc2
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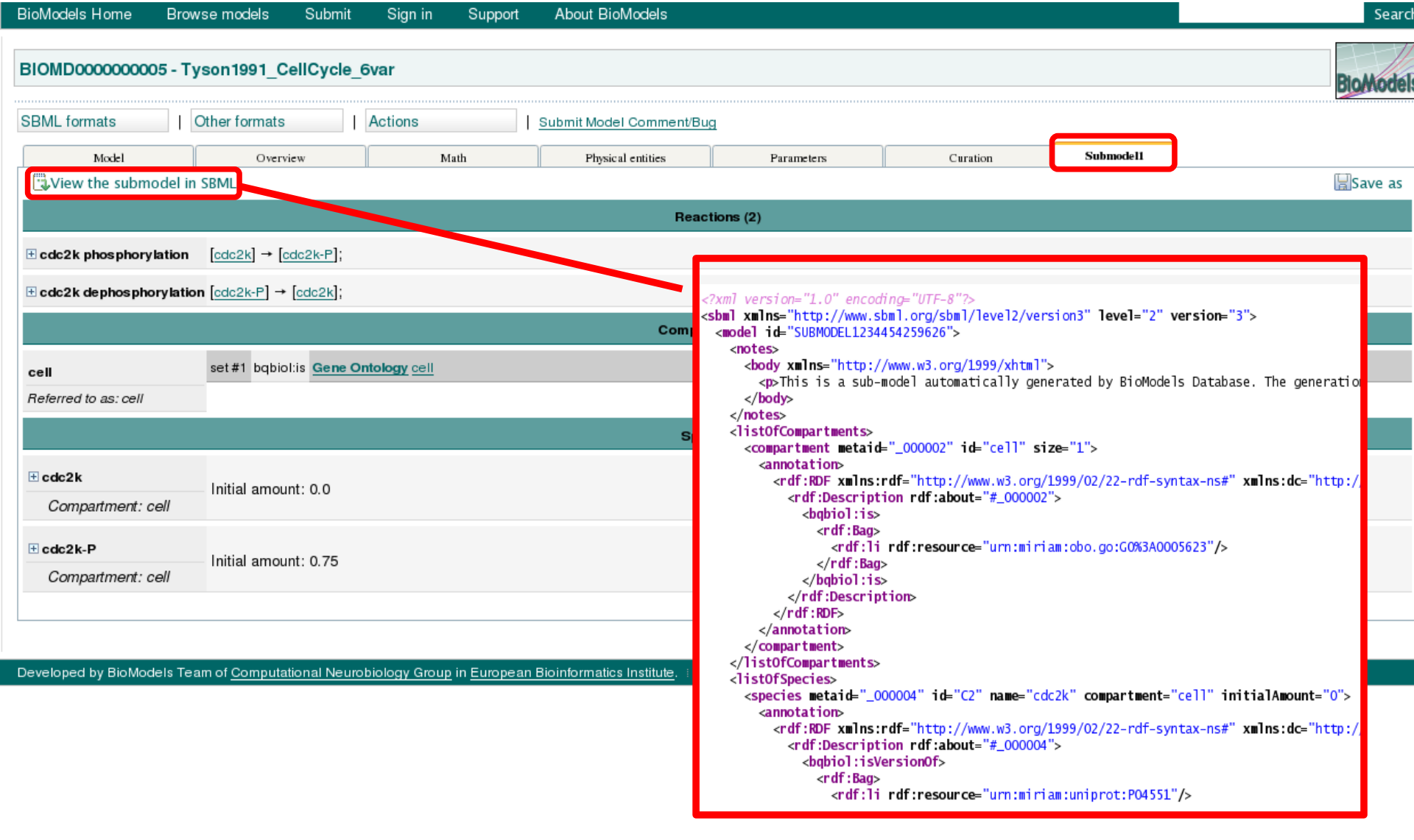
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Reactions (2)
cdc2k phosphorylation [cdc2k] → [cdc2k-P];
cdc2k dephosphorylation [cdc2k-P] → [cdc2k];
cell
set #1 bqbiol:is Gene Ontology cell
Referred to as: cell
cdc2k
Compartment: cell
Initial amount: 0.0
cdc2k-P
Compartment: cell
Initial amount: 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>
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<annotation>
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<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>
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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"/>

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 modelling 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.net Team

&

Systems Biology Community