

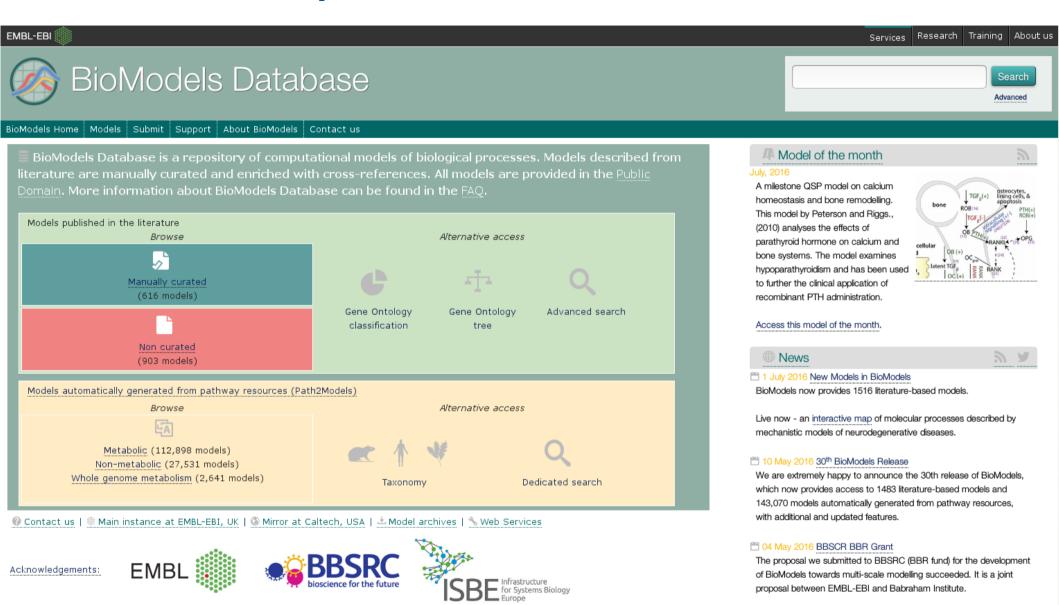
Sharing and re-using computational models of biological processes

Nicolas Le Novère, Babraham Institute





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







What is BioModels?

- Store and serve quantitative models of biological interest
- Models described in the peer-reviewed scientific literature + models automatically generated from pathway resources
- 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



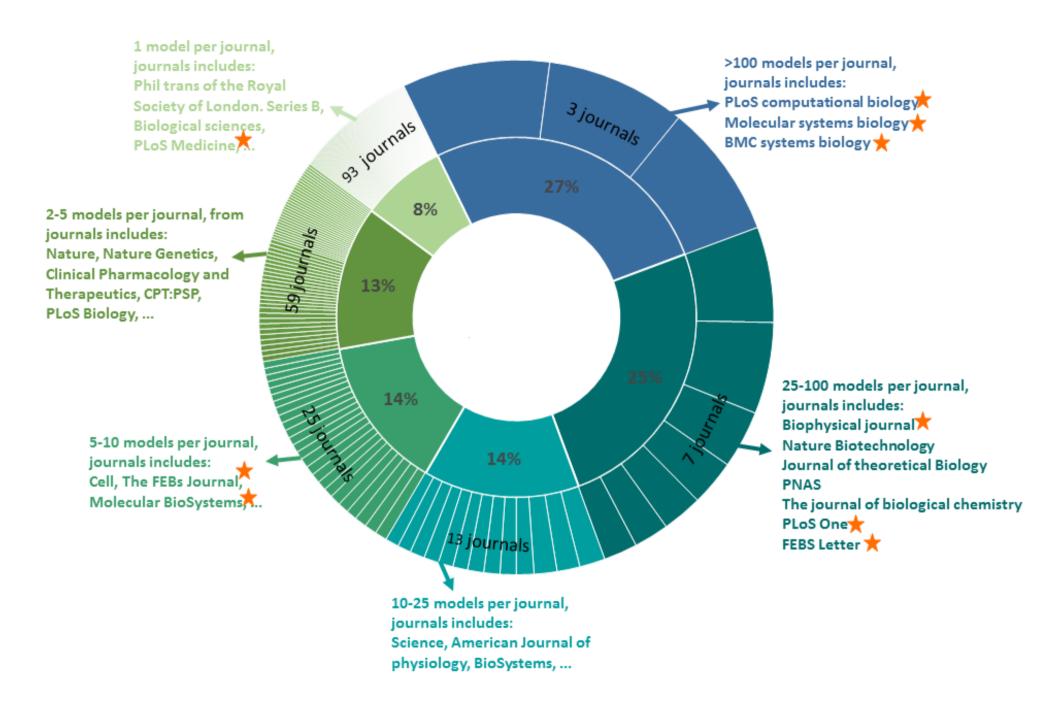
What can-we do with BioModels Database?

- Search and retrieve relevant quantitative or qualitative models
- Explore the variables and the structure of the model
- Run timecourse simulations of the model
- Download the model in many formats
- Do all the above via Web Services
- Learn about significant models using the Model of the Month



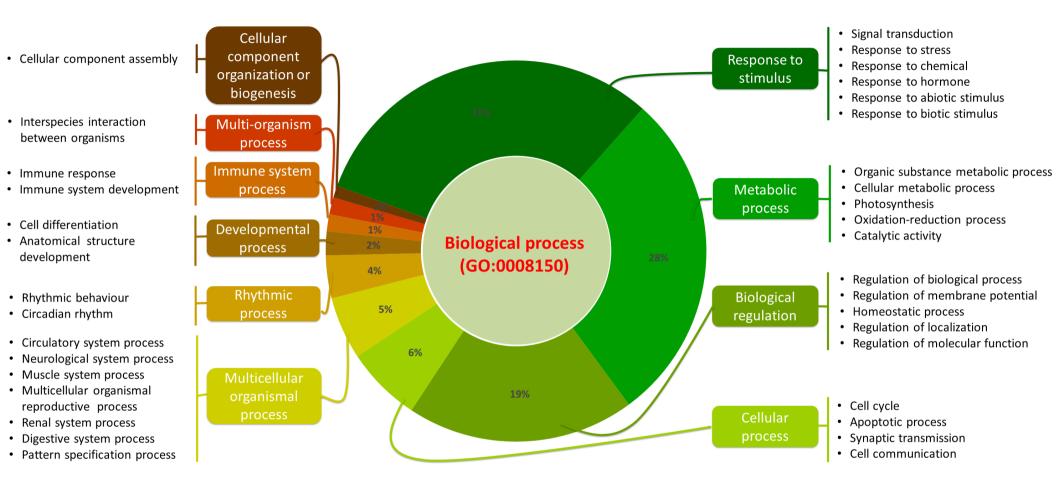
Where do models come from?

- Submitted by curators
 - imported from other repositories (DOQCS, CellML)
 - reimplemented from literature
- Various people curated models out of interest.
- From authors before grant applications or publications
- Over 300 scientific journals advise submission to BioModels Db:
 - Molecular Systems Biology
 - Public Library of Science journals
 - BioMedCentral journals
 - Royal Society of Chemistry journals





What models can you see in BioModels?



Interactive chart available at https://www.ebi.ac.uk/biomodels-main/gochart





BioModels is not limited to biochemistry!

Is it about bio[logy|chemistry|medicine]?

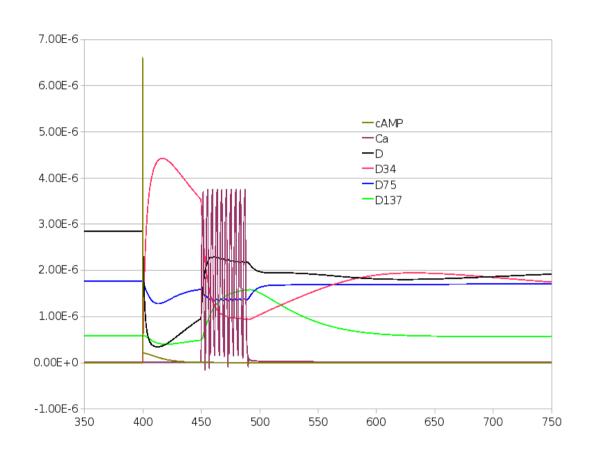
Is it a computational model?

Is it published?

Then it should be in BioModels

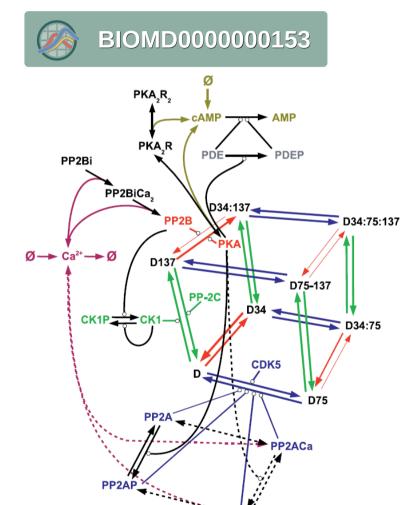


Process based biochemical models



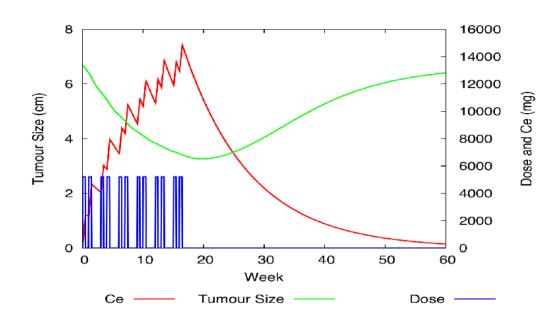
reaction: $v_{\rm on} = k_{\rm on} \times [{\rm D}] \times [{\rm CDK5}] \times {\rm Vol}$

Fernandez et al. DARPP-32 is a robust integrator of dopamine and glutamate signals *PLoS Comput Biol* (2006) 2: e176.





Pharmacometrics models



Tham et al (2008) A pharmacodynamic model for the time course of tumor shrinkage by gemcitabine + carboplatin in non-small cell lung cancer patients.

Clin Cancer Res. 2008 14(13): 4213-8.



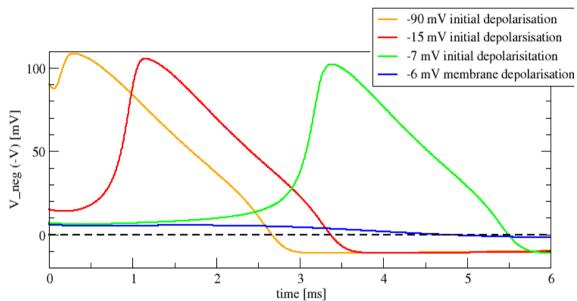
$$\frac{dSize}{dt} = (Rate_{in} \times Effect - K_{over} \times Size) \times Size$$

$$Effect = 1 - \frac{E_{max} \times Ce}{Amt_{50} + Ce}$$





Conductance-based model

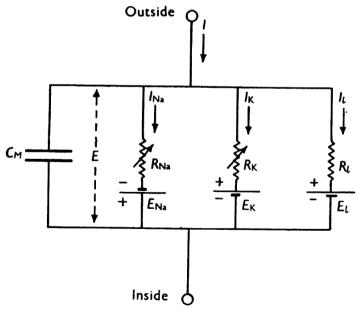


Hodgkin AL, Huxley AF. A quantitative description of membrane current and its application to conduction and excitation in nerve. *J Physiol* (1952) 117:500-544.



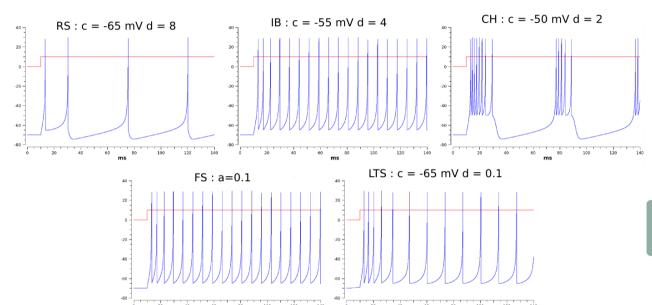
rate rule:
$$\frac{dv}{dt} = \frac{I - (i_{Na} + i_{K} + i_{L})}{C_{m}}$$

assignment rule: $i_{Na} = g_{Na} \times m^3 \times h \times (V - E_{Na})$





Neuroscience models



Izhikevich EM. Simple model of spiking neurons. IEEE Trans Neural Netw (2003) 14(6):1569-1572.

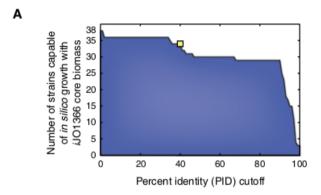


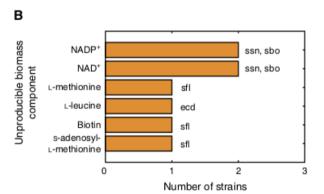
rate rule:
$$\frac{dv}{dt} = 0.04^2 + 5 \times V + 140 - U + i$$

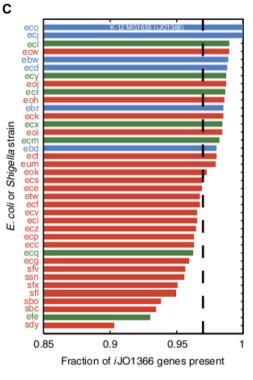
event: when
$$v > V_{\rm thresh} \left\{ \begin{array}{l} v = c \\ U = U + d \end{array} \right.$$



Flux Balance Analysis models





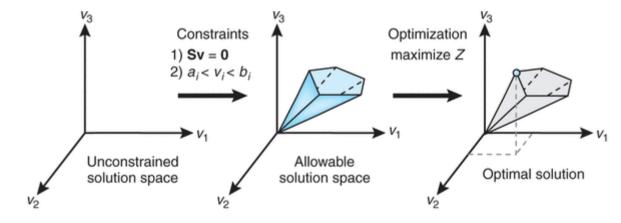


Orth et al. A comprehensive genomescale reconstruction of Escherichia coli metabolism.

Mol Syst Biol (2011);7:535

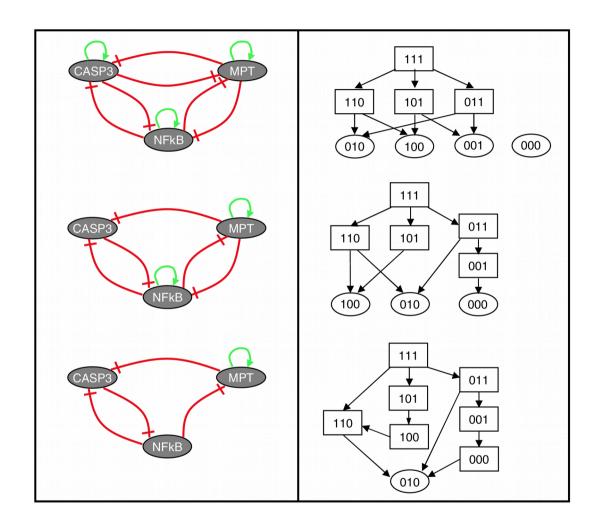


reaction: $v_i = \mathrm{flux}_i$





Logic models



Calzone et al. Mathematical modelling of cell-fate decision in response to death receptor engagement. *PLoS Comput Biol* (2010);6:e1000702



Logic function:

 $\neg MPT \land \neg NF\kappa B \Rightarrow CASP3$





BioModels Db does not belong to anyone!

CC0 1.0 Universal (CC0 1.0) Public Domain Dedication

This is a human-readable summary of the **Legal Code (read the full text)**.

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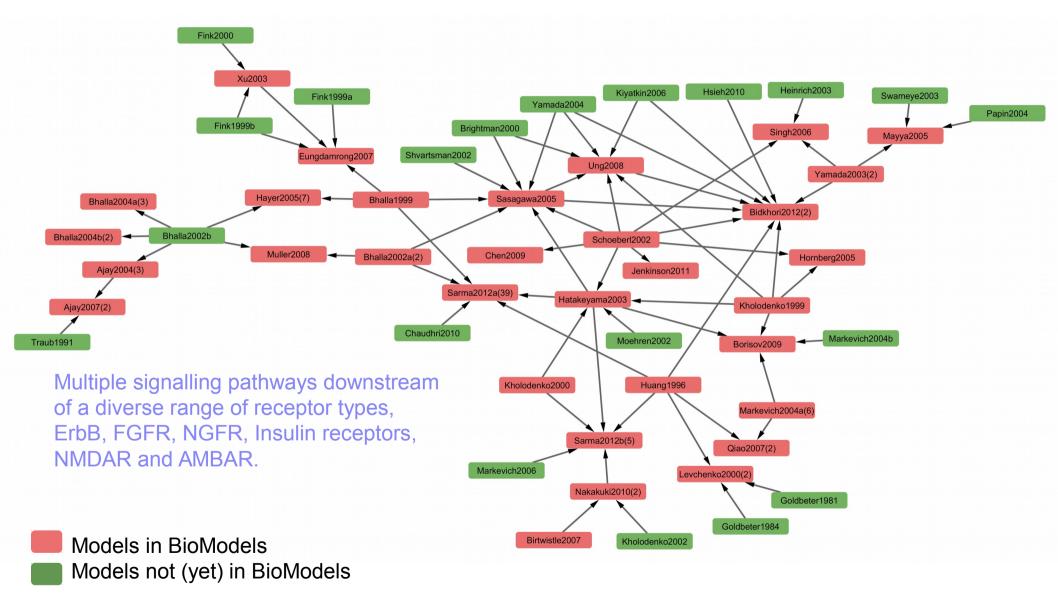
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Culture of model reuse - model evolution











Curated and Non-curated Models

- Curated models Comply with the MIRIAM guidelines
- 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 (e.g. reaction-diffusion models)
 models are yet to be curated

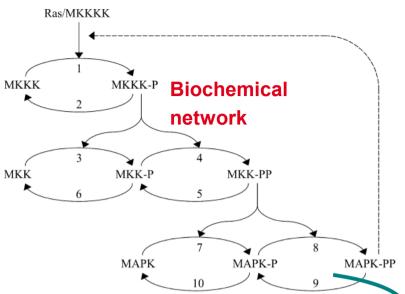


Table 2. Rate equations and parameter values of the MAPK cascade model. Concentrations and the Michaelis constants (K_1-K_{10}) are given in nm. The catalytic rate constants (k_3, k_4, k_7, k_8) and the maximal enzyme rates $(V_1, V_2, V_5, V_6, V_9, V_{10})$ are expressed in s⁻¹ and nm·s⁻¹, respectively.

Reaction number	Rate equation	Parameter values
1	$V_1 \cdot [MKKK]/((1 + ([MAPK-PP]/K_I)^n) \cdot (K_1 + [MKKK]))$	$V_1 = 2.5; n = 1; K_I = 9; K_1 = 10;$
2	$V_2 \cdot [MKKK-P]/(K_2 + [MKKK-P])$	$V_2 = 0.25; K_2 = 8;$
3	$k_3 \cdot [MKKK-P] \cdot [MKK]/(K_3 + [MKK])$	$k_3 = 0.025; K_3 = 15;$
4	k_4 ·[MKKK- P]·[MKK- P]/(K_4 + [MKK- P])	$k_4 = 0.025; K_4 = 15;$
5	$V_5 \cdot [MKK-PP]/(K_5 + [MKK-PP])$	$V_5 = 0.75$; $K_5 = 15$;
6	$V_6 \cdot [MKK-P]/(K_6 + [MKK-P])$	$V_6 = 0.75$; $K_6 = 15$;
7	$k_7 \cdot [MKK-PP] \cdot [MAPK]/(K_7 + [MAPK])$	$k_7 = 0.025; K_7 = 15;$
8	$k_8 \cdot [MKK-PP] \cdot [MAPK-P]/(K_8 + [MAPK-P])$	$k_8 = 0.025$; $K_8 = 15$;
9	$V_9 \cdot [MAPK-PP]/(K_9 + [MAPK-PP])$	$V_9 = 0.5$; $K_9 = 15$;
10	V_{10} [MAPK- P]/ $(K_{10} + [MAPK-P])$	$V_{10} = 0.5; K_{10} = 15;$
Total concentrations: [MKK	$K]_{total} = 100; [MKK]_{total} = 300; [MAPK]_{total} = 300$	

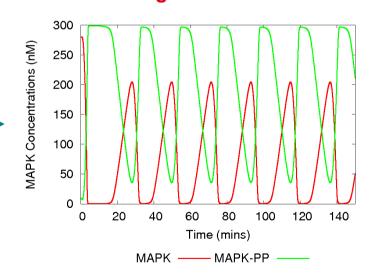
Biochemical network - mathematical representation

computer readable format, eg. Model simulation using simulation tools Eg. Copasi Annotations:

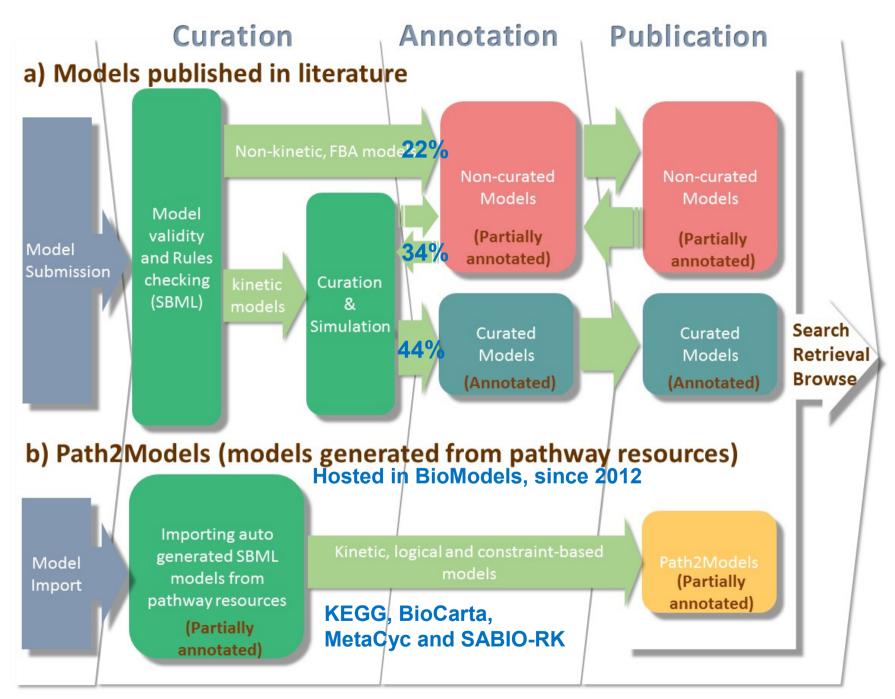
Cross-references

and ontology terms

Simulation result eg. time course



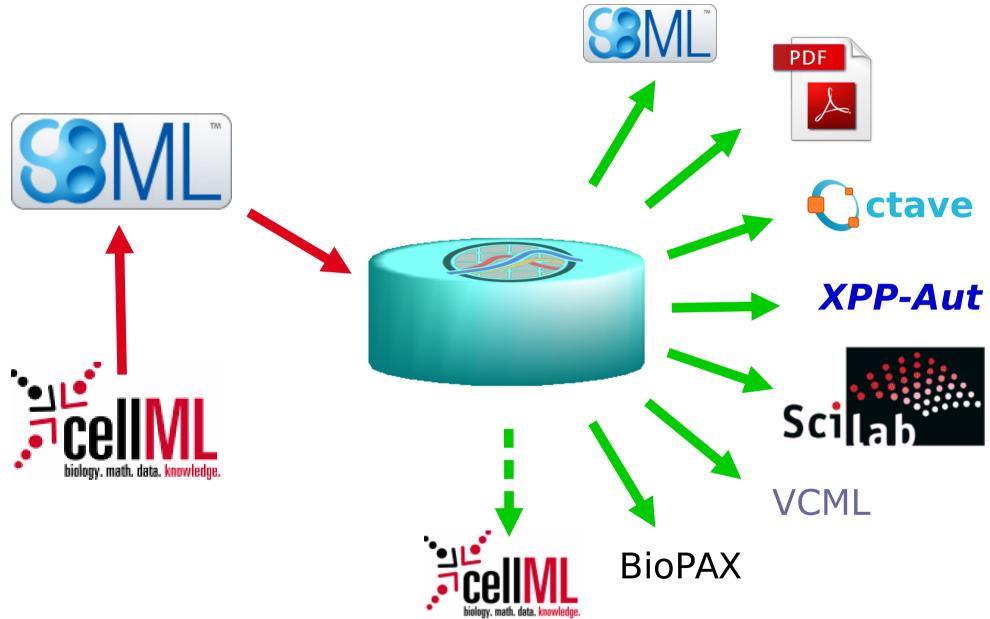








Input and output formats









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BioModels Database is a repository of computational models of biological processes. Models described from literature are manually curated and enriched with cross-references. All models are provided in the Public Domain. More information about BioModels Database can be found in the FAQ.

Models published in the literature Browse



Manually curated (530 models)



Non curated (655 models) Alternative access



Gene Ontology classification



Gene Ontology tree



Advanced search

Models automatically generated from pathway resources (Path2Models)

Browse

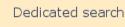


Metabolic (112,898 models) Non-metabolic (27,531 models) Whole genome metabolism (2,641 models) Alternative access









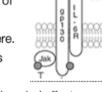
Taxonomy

🕜 Contact us | 🏶 Main instance at EMBL-EBI, UK | 🚳 Mirror at Caltech, USA | 🚣 Model archives | 🔧 Web

Model of the month

September, 2014

A mathematical model describing the inhibition of IL6 signalling in Crohn's Disease is presented here. Several antibody ligands were simulated with



different targets and their varied effects upon IL6 signalling is observed.

Access this model of the month.

Mews



and display

BioModels' homepage has been updated to provide a clearer view of the content of the repository. Also, a GO classification is a new browsing tool for models from the literature. Finally, various updates have been implemented for non-curated models.

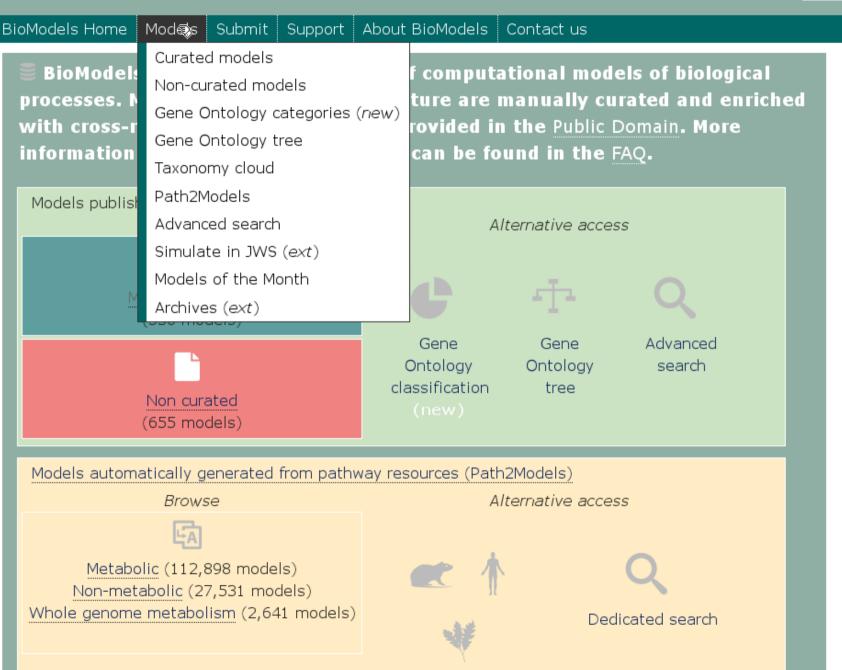
25 April 2014 Our recent diabetes review most downloaded in April on CPT:PSP

Our recent review "The impact of mathematical modeling on the understanding of diabetes and related complications" has been the most downloaded this month from the CPT: Pharmacometrics & Systems Pharmacology website!





BioModels Database



Taxonomy

Model of the r

September, 2014

A mathematical model describing the inhibition of IL6 signalling in Crohn's Disease is presented her Several antibody ligands were simulated with different targets and their

Access this model of the

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25 April 2014 Our rece downloaded in April on CF Our recent review "The ir

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modeling on the understarelated complications had been downloaded this month to

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Submit a new model Annotation information Curation guidelines Annotation guidelines

computational models of biological ture are manually curated and enriched rovided in the Public Domain. More can be found in the FAQ.

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(530 models)



Non curated (655 models) Alternative access



Gene Ontology classification



Gene Ontology tree



Advanced search

Models automatically generated from pathway resources (Path2Models)

Browse



Metabolic (112,898 models) Non-metabolic (27,531 models) Whole genome metabolism (2,641 models) Alternative access









Taxonomy

Dedicated search

A Model

September, 2014

A mathematical describing the in IL6 signalling in Disease is prese Several antibod were simulated different targets signalling is obs

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8 August 2014 and display

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Models automatically generated from pathway resources (Path2Models)

Models published in the literature

Browse

(530 models)

Non curated

(655 models)

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Metabolic (112,898 models) Non-metabolic (27,531 models)

Whole genome metabolism (2,641

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tree

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Advanced

search

Dedicated search



September, 2014

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8 August 2014 Updated I access and display

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25 April 2014 Our recent most downloaded in April on Our recent review "The imp mathematical modeling on of diabetes and related con been the most downloaded the CPT: Pharmacometrics Pharmacology website!



🛿 Contact us | 🕪 Main instance at EMBL-EBI, UK | 🚳 Mirror at Caltech, USA | 📥 Model archives |

Taxonomy

Neb Services

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Curator Sign in

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Models published in the literature

Browse Alternative access



Manually curated

(530 models)



Non curated (655 models)



Gene Ontology classification



Gene Ontology tree



Advanced search

Models automatically generated from pathway resources (Path2Models)

Browse



Metabolic (112,898 models)
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Whole genome metabolism (2,641 models)

Alternative access









Dedicated search

Taxonomy

September, 2014
A mathematical model

Model of the mo

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Access this model of the mo



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BioModels' homepage has a provide a clearer view of the repository. Also, a GO class browsing tool for models fro Finally, various updates have implemented for non-curate

most downloaded in April on a Our recent review "The imparathematical modeling on the of diabetes and related combeen the most downloaded the CPT: Pharmacometrics & Pharmacology website!





Submit - Step 1

You can submit here models to be included in BioModels Database.

The following formats are currently accepted:

- SBML Level 3: Version 1 (Including any packages)
- SBML Level 2: Version 1, Version 2, Version 3 and Version 4
- SBML Level 1: Version 1 and Version 2

CellML: 1.0 and 1.1

Contact us, if you have your model in formats other than SBML or CellML

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

If you wish to provide additional files with your submission, please contact us.

The submitted model will not be publicly available from BioModels Database straightaway. If you wish to know more about the submission, curation and annotation pro sections of the Frequently Asked Questions.

To ensure a prompt processing of your model, please follow those simple guidelines:

- Check that your model is valid according to the format you chose. If your model is encoded in SBML, you can use the official online validator.
- Enter all relevant information which could help the work of our curators (relation between the model and publication, modifications or clarifications of the model example using the notes elements if your model is encoded in SBML), or in the Comment field provided in step 2 of this form.
- If you created the model (or collaborated to its creation) but are not an author of the associated publication, please add your personnal information (first and la In the model, so that your contribution can be acknowledged. If you used SBML, this can be done by adding to the model element a dc:creator annotation, as I the blue part if already present).
- Choose a meaningful name for your model. You can follow the pattern AuthorNameYear Topic, Method, for example: Levchenko2000 MAPK, noScaffold or

All models in BioModels Database are available under the terms of the Creative Commons CC0 1.0 (Public Domain Dedication). Therefore you need to agree to relea Domain before submitting it to BioModels Database.

Thank you for contributing to BioModels Database!

Please enter the identifier of the scientific publication associated with the model, and then click Continue. If the model has not been published, please select the 'Unpul

Publication Identifier:

Type of identifier:

- PubMed ID (Search Medline)
 DOI (Resolve a DOI)
 URL

Unpublished





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 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* are 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.
- Choose a meaningful value for the attribute name of the model element. Examples of good model names are NameAuthorYear_Topic_Method, Levcher Edelstein1996_EPSP_AChEvent.
- Check the validity of the model (for example by using this online validator if your model is encoded in the SBML format). All the models undergo a primar 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 U repository. Refrain from entering a generic URL to the repository itself.

Please enter you	personal details and any comment useful for the curation step (underlined fields are	required) and then click Submit
First name:	personal details and any comment useful for the curation step (underlined fields are	required), and then click <i>Submit</i> .
Last name:		<u> </u>
Organisation:		
Email:		
Comment:		
Original model:		
Model file:	Browse No file selected.	
Submit Res	et	

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Browse - Curated models

H The following fields are used to describe a model: ...

← 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 ←

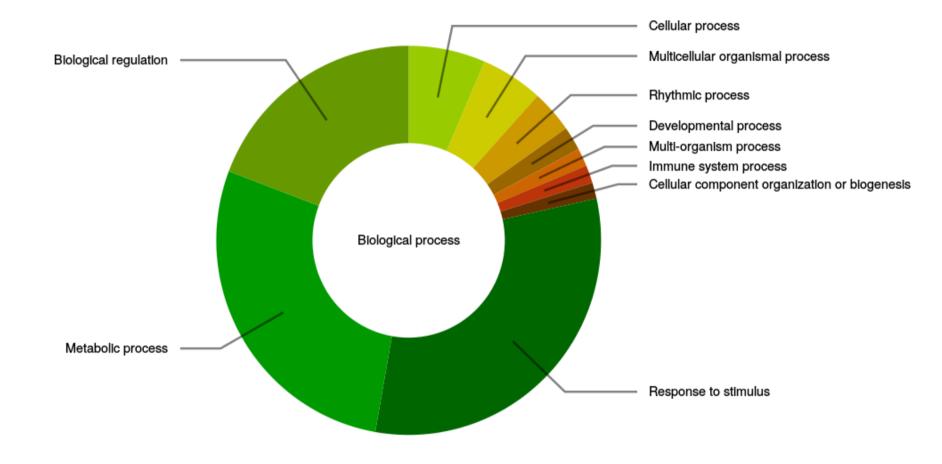
10 | 50 | 100 | All

- 15 5 4 5 0 1 0 5 10 11 15 10 14 10 10 11 10 15 50 51 55 50 51 50 50 51 50 50 54 50 50 51 50 51			
BioModels ID	<u>Name</u> ▽	Publication ID	Last Modified
BIOMD000000355	Abell2011_CalciumSignaling_WithAdaptation	<u>21844332</u>	2011-09-08T12:03:57+00:00
BIOMD000000354	Abell2011_CalciumSignaling_WithoutAdaptation	21844332	2011-09-08T12:16:51+00:00
BIOMD000000428	Achcar2012 - Glycolysis in bloodstream form T. brucei	22379410	2013-06-10T13:41:07+00:00
BIOMD000000476	Adams2012 - Locke2006 Circadian Rhythm model refined with Input Signal Light Function	22855577	2013-09-11T15:39:47+00:00
BIOMD000000169	Aguda1999_CellCycle	10619492	2012-07-05T14:42:01+00:00
BIOMD000000295	Akman2008_Circadian_Clock_Model1	18277380	2014-05-28T01:56:26+00:00
BIOMD000000214	Akman2008_Circadian_Clock_Model2	18277380	2014-05-28T01:57:42+00:00
BIOMD0000000220	Albeck2008_extrinsic_apoptosis	18406323	2012-07-05T14:42:40+00:00
BIOMD0000000211	Albert2005_Glycolysis	<u>15955817</u>	2014-05-27T23:52:38+00:00
BIOMD000000289	Alexander2010_Tcell_Regulation_Sys1	20195912	2014-03-11T13:38:50+00:00



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Classification of models published in the literature, based on GO







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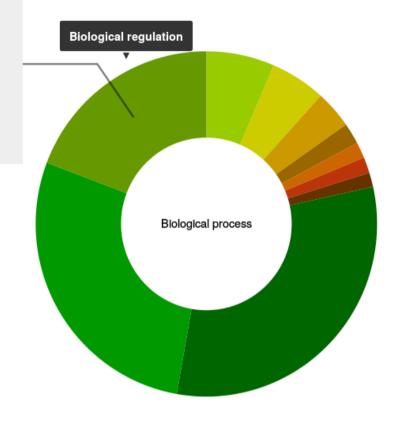
Clas e literature, based on GO

Regulation of biological process (109)

Biological regulation (232)

- · Regulation of membrane potential

- Homeostatic process (27)
 Regulation of localization (21)
 Regulation of molecular function (10)



Selected GO term: Regulation of biological process

Curated Models

BioModels ID	Name Name	Publication ID	Last Modified
BIOMD000000012	Elowitz2000 - Repressilator	10659856	2013-07-10
BIOMD000000065	Yildirim2003_Lac_Operon	12719218	2014-02-12
BIOMD0000000067	Fung2005_Metabolic_Oscillator	<u>15875027</u>	2012-05-16
BIOMD0000000079	Goldbeter2006_weightCycling	<u>16595882</u>	2012-07-05
PIOMPOODOODO	Thomson1090_AdopylateCycleso	paprafiaTi ⁴ 902	2014 02 12

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BioModels Database: GO tree

This is a tree view of the curated models based on their Gene Ontology & annotation.

To browse the models, please click the local control is icon on the left of the term to expand the related branch and similarly click on the local control is icon to collapse an already opened branch. By clicking on a term's name, the list of models annotated with this term (or one of its descendant) will be displayed on the right panel.

- ▼ GO:0008150 biological_process (529)
 - ▶ GO:0022610 biological adhesion (1)
 - ▼ GO:0065007 biological regulation (373)
 - ▼ GO:0050789 regulation of biological process (316)
 - ▼ GO:0048519 negative regulation of biological process (77)
 - ▼ GO:0051129 negative regulation of cellular component organization (5)
 - ▼ GO:0010639 negative regulation of organelle organization (5)
 - ▼ GO:0051784 negative regulation of nuclear division (5)
 - ▼ GO:0045839 negative regulation of mitosis (5)
 - ▼ GO:0045841 negative regulation of mitotic metaphase/anaphase transition (5)

GO:0007094 - mitotic spindle assembly checkpoint (5)

- GO:0048523 negative regulation of cellular process (71)
- ▶ GO:0051093 negative regulation of developmental process (1)
- ▶ GO:0045926 negative regulation of growth (1)
- ▶ GO:0002683 negative regulation of immune system process (1)
- GO:0009892 negative regulation of metabolic process (54)
- ▶ GO:0043901 negative regulation of multi-organism process (5)
- GO:0051241 negative regulation of multicellular organismal process (1)
- ▶ GO:0048585 negative regulation of response to stimulus (32)
- ▶ GO:0051283 negative regulation of sequestering of calcium ion (7)
- ▶ GO:0023057 negative regulation of signaling (33)
- ► GO:0051051 negative regulation of transport (8)
- ► GO:0048518 positive regulation of biological process (91)
- ▶ GO:0044087 regulation of cellular component biogenesis (2)
- ► GO:0051128 regulation of cellular component organization (12)
- GO:0050794 regulation of cellular process (274)

Model(s) annotated with the GO term $\underline{GO:0007094}$ \blacksquare or one of its descendant(s):

- Chen2004 Cell Cycle Regulation (BIOMD0000000056)
- <u>Ibrahim2008 Mitotic Spindle Assembly Checkpoint Convey variant</u> (BIOMD000000187)
- <u>Ibrahim2008 Mitotic Spindle Assembly Checkpoint Dissociation</u>
 variant (BIOMD000000186)
- <u>Ibrahim2008 Cdc20 Sequestring Template Model</u>
 (BIOMD0000000194)
- Ibrahim2008 MCC assembly model KDM (BIOMD0000000193)





- Person → Search BioModels Database for model submitter and/or creator(s) names, or model reference publication author(s) names (for example Nicolas L 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
 you want to find documents which matches the exact phrase; otherwise, all words will be searched as default.
- Annotation (full text) → Search BioModels Database for related information found in the models reference publication or third-party resources, by either publidentifier or text (for example 9256450 or cyclin for publication, GO:0000278 or cell cycle for Gene Ontology, P04551 or cell division for UniProt).
- Annotation (identifier) → Search BioModels Database for annotations, by third-party resource identifiers (for example IPR002394 for InterPro, hsa04080 for 68910 for Reactome).

A part from the *BioModels Identifier* -based search, for every other criteria the search operates on a *contains the entered string basis*, case-insensitive *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 nexpressions.

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 smodels satisfying at least one of the criteria will be returned.

		k
BioModels identifier:		
Person:		
SBML elements:		match the exact phrase
Annotation (full text): UniF	Prot Knowledgebase 🗸	
Annotation (full text): Publ	lication v cell cycle	
Annotation (full text): Gen	e Ontology 🔻	
Annotation (identifier): Pub	Chem-compound 🗸	
Annotation (identifier): KEG	G Reaction 🗸	
Annotation (identifier): Enzy	me Nomenclature	
Compose by: • and • or		
Search Reset		

Search - Models

Query: Publication cell cycle [resources]

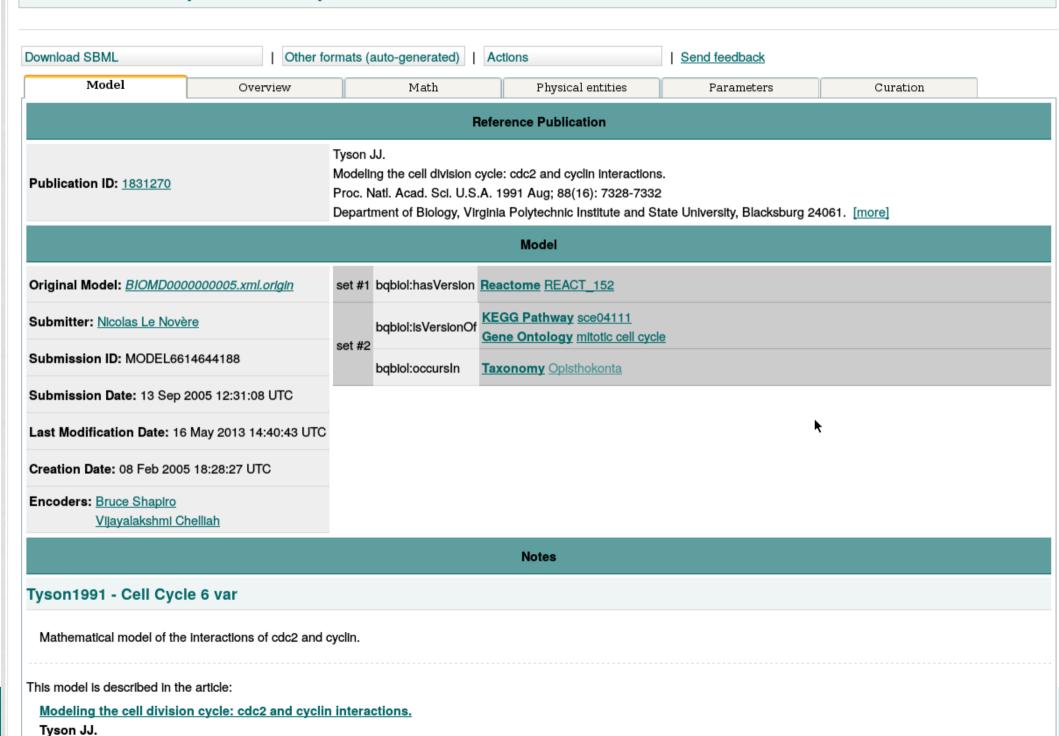
The search returned 44 models.

New Search

■ 33 Curated models returned:

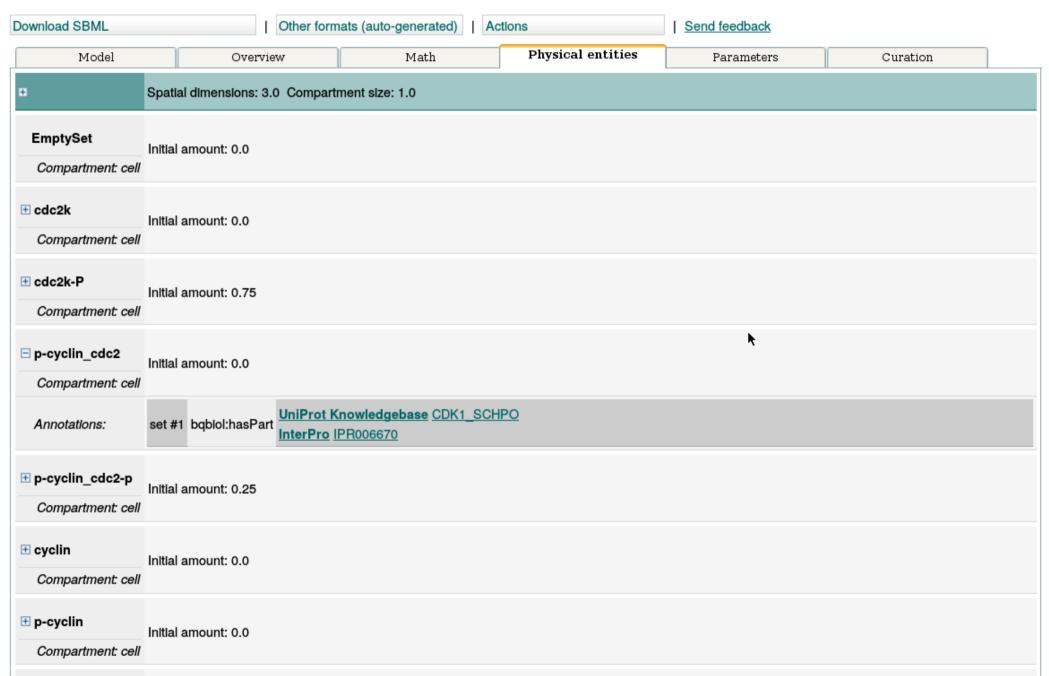
BioModels ID _▽	<u>Name</u>	Publication ID	<u>Last Modified</u>
BIOMD000000003	Goldbeter1991 - Min Mit Oscil	<u>1833774</u>	2013-05-16T14:38:01+00:00
BIOMD000000004	Goldbeter1991 - Min Mit Oscil, Expl Inact	<u>1833774</u>	2012-12-11T15:30:15+00:00
BIOMD000000005	Tyson1991 - Cell Cycle 6 var	<u>1831270</u>	2013-05-16T14:40:43+00:00
BIOMD000000006	Tyson1991 - Cell Cycle 2 var	1831270	2013-05-16T14:38:56+00:00
BIOMD000000007	Novak1997 - Cell Cycle	<u>9256450</u>	2014-03-26T14:20:21+00:00
BIOMD000000008	Gardner1998 - Cell Cycle Goldbeter	<u>9826676</u>	2014-07-24T10:59:34+00:00
BIOMD000000018	Morrison1989_FolateCycle	<u>2732237</u>	2012-07-05T14:40:37+00:00
BIOMD000000056	Chen2004 - Cell Cycle Regulation	<u>15169868</u>	2013-06-07T10:59:38+00:00
BIOMD000000109	Haberichter2007_cellcycle	17299420	2012-07-05T14:49:20+00:00
BIOMD000000110	Qu2003_CellCycle	14645053	2012-05-16T10:13:14+00:00
BIOMD000000111	Novak2001_FissionYeast_CellCycle	12779461	2012-07-05T16:47:55+00:00
BIOMD000000150	Morris2002_CellCycle_CDK2Cyclin	11959850 Babrah	2010-12-01T22:10:11+00:00

BIOMD000000005 - Tyson1991 - Cell Cycle 6 var

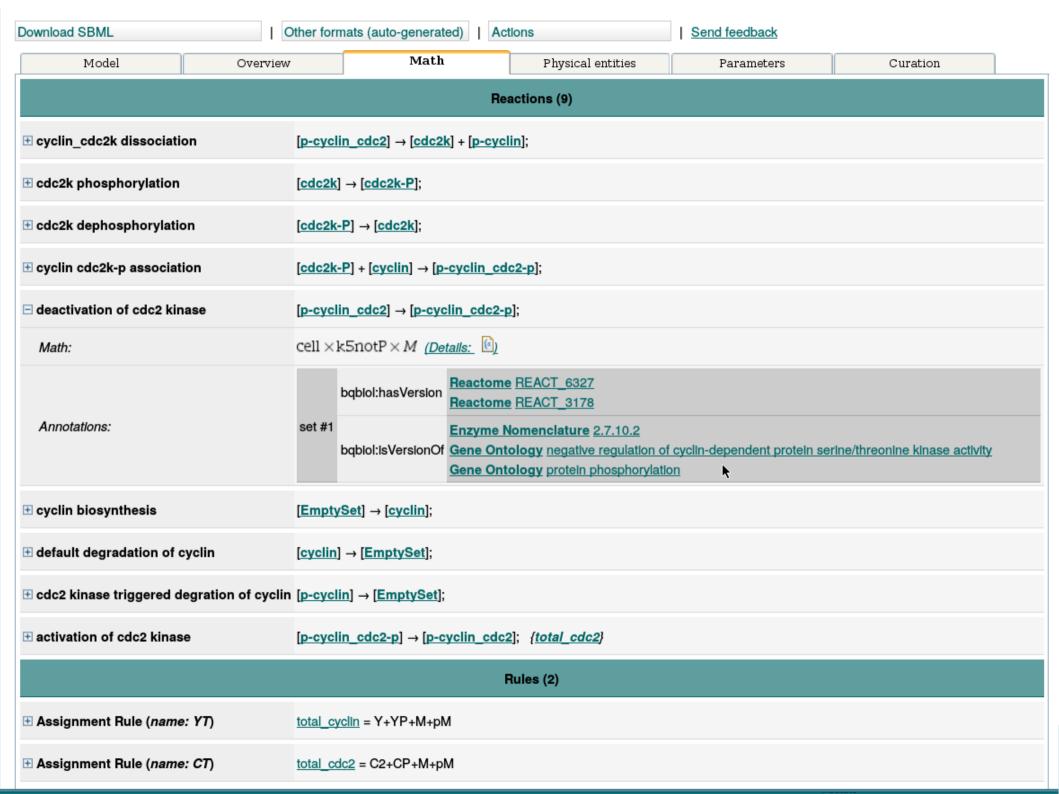


Proc. Natl. Acad. Sci. U.S.A. 1991; 88(16); 7328-32

BIOMD000000005 - Tyson1991 - Cell Cycle 6 var



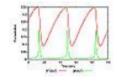




BIOMD000000005 - Tyson1991 - Cell Cycle 6 var



Representative curation result(s)



Curator's comment: (updated: 08 Feb 2010 10:29:04 GMT)

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

Additional file(s)

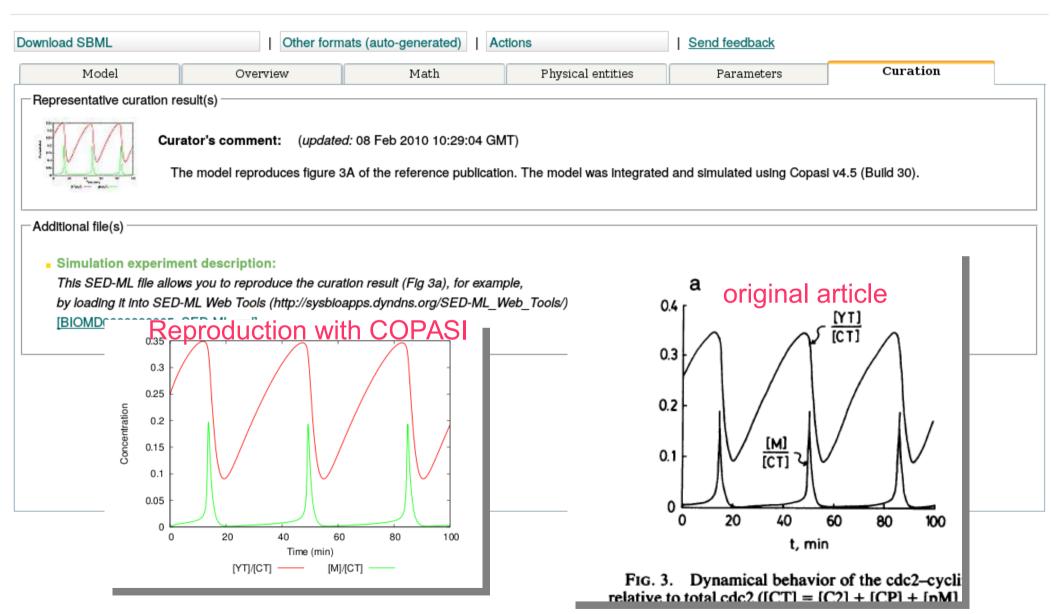
Simulation experiment description:

This SED-ML file allows you to reproduce the curation result (Fig 3a), for example, by loading it into SED-ML Web Tools (http://sysbloapps.dyndns.org/SED-ML_Web_Tools/).

[BIOMD000000005_SED-ML.xml]

×

BIOMD000000005 - Tyson1991 - Cell Cycle 6 var



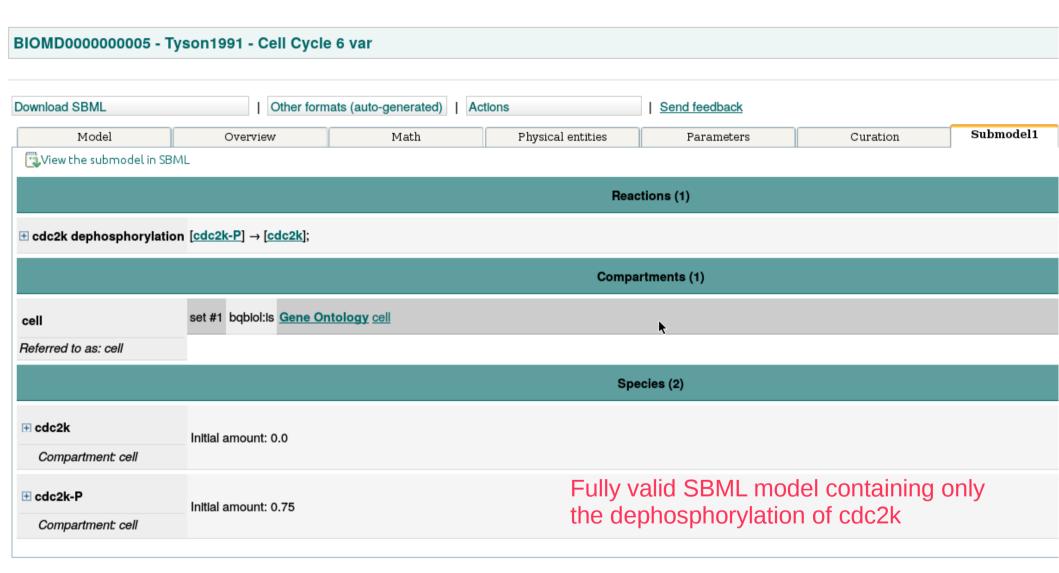


BIOMD00000005 - Tyson1991 - Cell Cycle 6 var								
Download SBML	Other formats (auto-genera	ated)	Actions	Send feedback				
Model Overview			ı	Physical entities	Parameters	S	Curation	
© Create a submodel with selected elements						lect All		
				Model				
Publication ID: 183	31270 Submission	Date: 13 Sep 2005 12:31:08 UT	C La	st Modification Date: 16 May 20	13 14:40:43 UTC	Creation	Date: 08 Feb 2005 18:28:2	7 UTC
			Math	ematical expressions				
Reactions								
cyclin_cdc2k dissociation cdc2k phosphorylation				cdc2k dephosphorylation	<u>cyclin o</u>	cyclin cdc2k-p association		
deactivation of cdc2 kinase cyclin biosynthesis				default degradation of cyclin	cdc2 ki	cdc2 kinase triggered degration of cyclin		
activation of cdc2 kinase								
Rules								
Assignment Rule	(variable: total_cyc	<u>lin)</u>		Assignment Rule (varial	ole: total_cdc2)			
Physical entities								
□ Compartments □ Species								
cell	<u>EmptySet</u>		<u> </u>	edc2k		<u>cd</u>	c2k-P	
	p-cyclin_cdc2		<u> </u>	p-cyclin_cdc2-p		<u>cyclin</u>		
p-cyclin			<u> </u>	total_cyclin			total_cdc2	
COMBINE tutorial, 16 Sept 2016								

BIOMD00000000	05 - Tyson1991 -	Cell Cycle 6	var						
Download SBML		Other formats	(auto-generated)	Actions	Send feed	lback			
Model	Over	view	Math	Physical entities	Para	meters	Curat	on	Submodel1
Create a submod	el with selected elem	ents							Deselect All
				Model					
Publication ID: 183	1270 Submission	Date: 13 Sep 200	05 12:31:08 UTC	Last Modification Date: 16 Ma	ay 2013 14:40	:43 UTC	Creation Date:	08 Feb 2005	18:28:27 UTC
				Mathematical expressions					
Reactions									
cyclin_cdc2k d	lissociation	cdc2k pho	<u>sphorylation</u>	cdc2k dephosphorylatio	<u>on</u>	cyclin o	cdc2k-p associa	tion_	
deactivation of cdc2 kinase cyclin biosynthesis			synthesis	default degradation of cyclin cdc2 kinase triggered degration of cyclin			cyclin		
activation of c	dc2 kinase								
Rules					h				
Assignment Rule (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		











BIOMD000000005 - Tyson1991 - Cell Cycle 6 var



Publication ID: 1831270

Automatically generated using libsbml (http://sbml.org/Software/libSBML)

<u>lback</u>

meters

Curation

Reference Publication

Curated version of the model

ate University, Blacksburg 24061. [more]

Original Model: BIOMD000000005.xml.origin set #1 bqblol:hasVersion Reactome REACT_152 Submitter: Nicolas Le Novère Submission ID: MODEL6614644188 Submission Date: 13 Sep 2005 12:31:08 UTC Model Model KEGG Pathway sce04111 Gene Ontology mitotic cell cycle bqblol:occursin Taxonomy Opisthokonta

Encoders: Bruce Shapiro

Vijayalakshmi Chelliah

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

Last Modification Date: 16 May 2013 14:40:43 UTC

Notes

Tyson1991 - Cell Cycle 6 var

Mathematical model of the interactions of cdc2 and cyclin.

This model is described in the article:

Modeling the cell division cycle: cdc2 and cyclin interactions.

Tyson JJ.

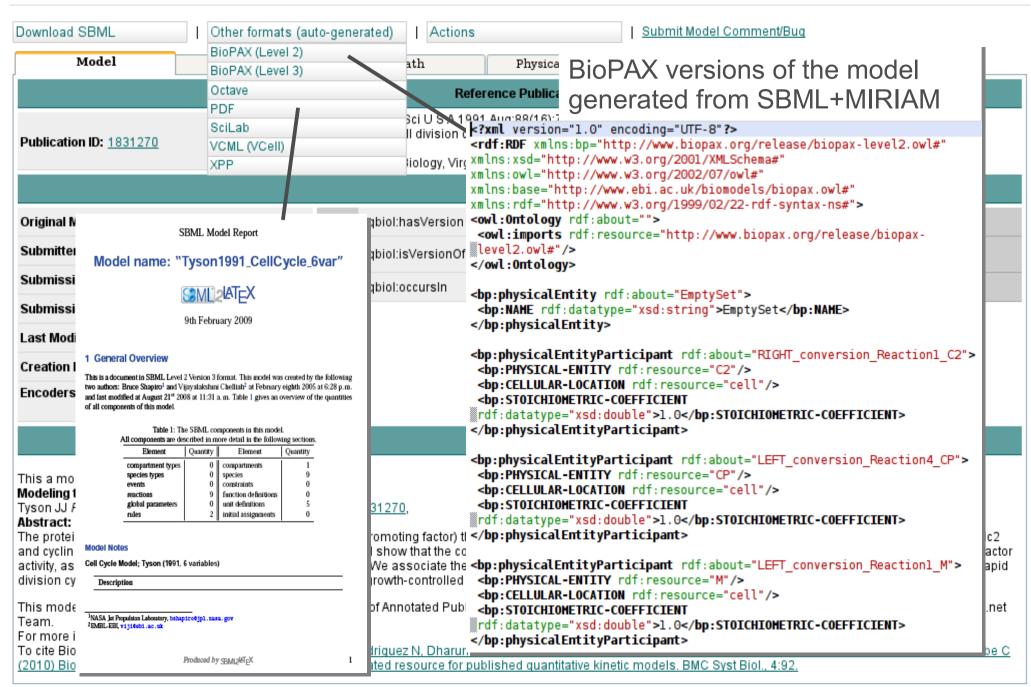
Proc Notl Acad Sci 11 S A 1001 - 88/16 - 7308-30

Institu

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BIOMD000000005 - Tyson1991_CellCycle_6var



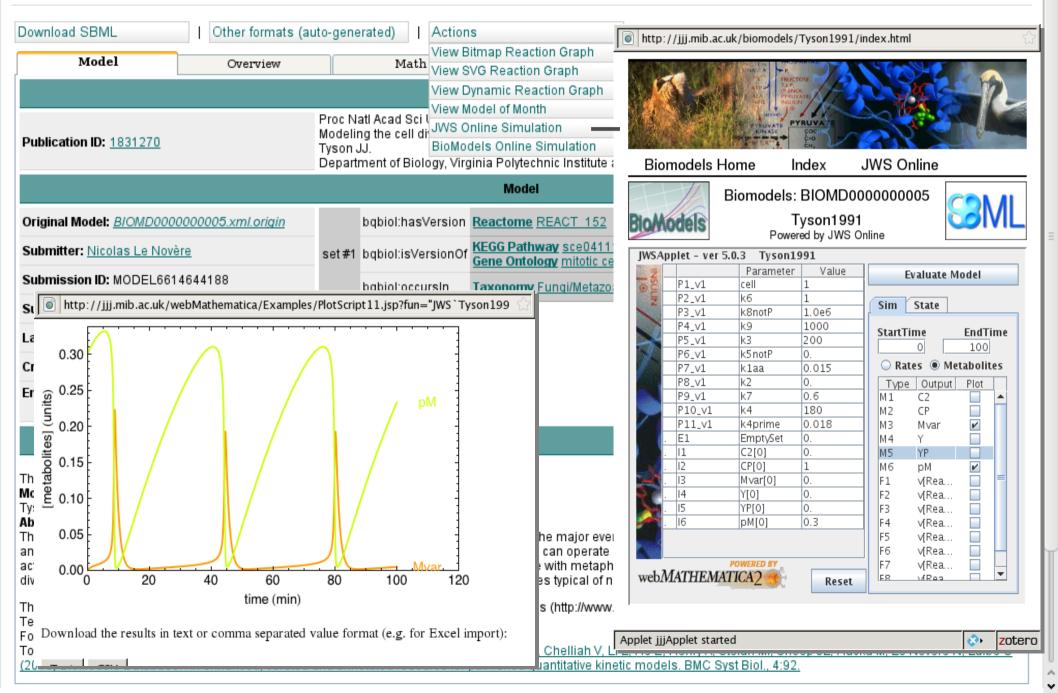


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BIOMD000000005 - Tyson1991_CellCycle_6var





From pathways to models ... Path2Models





PathwavInteractionDatabase



Logical models of individual signalling pathways





Chemical kinetics models of individual metabolic pathways







Flux Balance Analysis of whole genome reconstructions



Path2Models

Path2Models is a branch of BioModels Database dedicated to hosting models automatically generated from pathway resources, such as <u>KEGG</u>, <u>BioCarta</u>, <u>MetaCyc</u>, <u>PID</u> and <u>SABIO-RK</u>.

Browse models

Models from this branch are classified in 3 distinct categories:

- · metabolic models
- non-metabolic models
- · whole genome metabolism models

One can also browse those models by organism:

list of all organisms

Search models

The following search will only look for models coming from the path2models project:

N

Help about the search

- The keywords AND or OR (in upper cases) are available to refine the search. By default, if more than one word is present in a query, OR will be used to combine them.
- Double quotes (") can be used to force the search engine to match a whole expression containing several words.

Search

• The colon character (:) must be escaped in the queries; one can use a backslash for this purpose (1:).

Download all models

• Archives of all models (from the latest release)

Additional information

Those automatically generated models are only partially parameterized. In the case of KEGG signaling pathways for which no mechanistic details are provided, the models (with qual constructs) contain only topological relationships together with interaction signs. No logical rules specify the effects of (combined) interactions, and these models should be seen as confident to be further parameterized before use in simulation. This can be done either by considering default, yet biologically magningful, logical functions.

Path2Models:

Here are all the whole genome metabolism models available:

- [Eubacterium] cylindroides T2-87
- Acaryochloris marina (strain MBIC 11017)
- Accumulibacter phosphatis (strain UW-1)
- Acetobacter pasteurianus (strain NBRC 3283 / LMG 1513 / CCTM 1153)
- Acetobacter pasteurianus IFO 3283-01-42C
- Acetobacter pasteurianus IFO 3283-03
- Acetobacter pasteurlanus IFO 3283-07
- Acetobacter pasteurianus IFO 3283-12
- Acetobacter pasteurianus IFO 3283-22
- Acetobacter pasteurianus IFO 3283-26
- Acetobacter pasteurianus IFO 3283-32
- Acetobacterium woodii (strain ATCC 29683 / DSM 1030 / JCM 2381 / KCTC 1655)
- Acetohalobium arabaticum (strain ATCC 49924 / DSM 5501 / Z-7288)
- Acholeplasma laidlawii (strain PG-8A)
- Achromobacter xylosoxidans (strain A8)
- Acidaminococcus fermentans (strain ATCC 25085 / DSM 20731 / VR4)
- Acidaminococcus intestini (strain RyC-MR95)
- Acidianus hospitalis (strain W1)
- Acidilobus saccharovorans (strain DSM 16705 / VKM B-2471 / 345-15)
- Acidimicrobium ferrooxidans (strain DSM 10331 / JCM 15462 / NBRC 103882 / ICP)
- Acidiphilium cryptum (strain JF-5)
- Acidiphilium multivorum (strain DSM 11245 / JCM 8867 / AIU301)
- Acidithiobacillus caldus (strain SM-1)
- Acidithiobacillus ferrivorans SS3
- Acidithiobacillus ferrooxidans (strain ATCC 23270 / DSM 14882 / NCIB 8455)
- Acidithiobacillus ferrooxidans (strain ATCC 53993)
- Acidobacterium capsulatum (strain ATCC 51196 / DSM 11244 / JCM 7670)
- Acidothermus cellulolyticus (strain ATCC 43068 / 11B)
- Acidovorax avenae (strain ATCC 19860 / DSM 7227 / JCM 20985 / NCPPB 1011)
- Acidovorax citrulli (strain AAC00-1)
- Acidovorax ebreus (strain TPSY)
- Acidovorax sp. (strain JS42)

k

Whole Genome Metabolism - Homo sapiens

Download SBML SBML L2 V4

SBML L2 V4 (with Identifiers.org URLs)

Send feedback

Model information

Identifier: BMID000000140905

Project:

path2models

Submission: 19 May 2012 15:48:00 UTC

Format: SBML L2 V4 Categories: genome-scale

Last modified: 04 Oct 2013 04:05:27 UTC

Published: 19 May 2012 23:49:21 UTC

Annotations

occursIn	Homo sapiens	Taxonomy
IsDerivedFrom	Homo saplens (human)	KEGG Genome
isDescribedBy	Initial sequencing and analysis of the human genome.	PubMed
isDescribedBy	The sequence of the human genome.	PubMed
isDescribedBy	Finishing the euchromatic sequence of the human genome.	PubMed
isDescribedBy	The DNA sequence and biological annotation of human chromosome 1.	PubMed
isDescribedBy	Generation and annotation of the DNA sequences of human chromosomes 2 and 4.	PubMed
isDescribedBy	The DNA sequence, annotation and analysis of human chromosome 3.	PubMed
isDescribedBy	The DNA sequence and comparative analysis of human chromosome 5.	PubMed
isDescribedBy	The DNA sequence and analysis of human chromosome 6.	PubMed
isDescribedBy	Human chromosome 7: DNA sequence and biology.	PubMed
isDescribedBy	The DNA sequence of human chromosome 7.	PubMed
isDescribedBy	DNA sequence and analysis of human chromosome 8.	PubMed
isDescribedBy	DNA sequence and analysis of human chromosome 9.	PubMed
isDescribedBy	The DNA sequence and comparative analysis of human chromosome 10.	PubMed
isDescribedBy	Human chromosome 11 DNA sequence and analysis including novel gene identification.	PubMed
isDescribedBy	The finished DNA sequence of human chromosome 12.	PubMed
isDescribedBy	The DNA sequence and analysis of human chromosome 13.	PubMed
isDescribedBy	The DNA sequence and analysis of human chromosome 14.	PubMed
isDescribedBy	Analysis of the DNA sequence and duplication history of human chromosome 15.	PubMed
isDescribedBy	The sequence and analysis of duplication-rich human chromosome 16.	PubMed

BioModels Web Services

With BioModels Web Services, users can programmatically access up-to-date information from BioModels Database without installing a local copy of the database. They provide a wide range of features for searching and retrieving models. Furthermore, some features can help users to extract interesting parts from a large model and assemble them into a fully valid submodel. For any comments or new feature enquiries, please feel free to contact us.

Available features

- Available features
- WSDL

The list of available features's page describes all the available services in a nice human readable way, included a detailed description of all methods. The WSDL (Web Services Description Language) defines the provided services in an XML format file. This enables third-party software to automatically generate clients for accessing the services.

Java library

The Java library provides a very convenient way to use the web services. It gives access to improved methods (for example giving access to 'SimpleModel' objects rather than raw XML) in order to make the use of the web services easier.

k

Documentation

The library documentation gives information for developers wishing to use the API:

Java library documentation (Javadoc)

Get the library via Maven

The library is available from the EBI Maven repository.

You just need to add the following to your pom.xml to get it and all its dependencies:

Index of ftp://ftp.ebi.ac.uk/pub/databases/biomodels/weekly_archives/2012/

♣ Up to higher level directory

Name	Size	Last Modified
p BioModels-Database-weekly-2012-01-02-sbmls.tar.gz	11734 KB	22/03/12 00:00:00
p BioModels-Database-weekly-2012-01-09-sbmls.tar.gz	11735 KB	22/03/12 00:00:00
BioModels-Database-weekly-2012-01-16-sbmls.tar.gz	11734 KB	22/03/12 00:00:00

Index of ftp://ftp.ebi.ac.uk/pub/databases/biomodels/releases/

♠ Up to higher level directory

Name	Size	Last Modified	
2005-04-11		08/02/12	00:00:00
2005-06-01		08/02/12	00:00:00
2005-07-28		08/02/12	00:00:00
2006-01-31		08/02/12	00:00:00

Index of ftp://ftp.ebi.ac.uk/pub/databases/biomodels/releases/latest/

♠ Up to higher level directory

Name	Size	Last Modified
BioModels_Database-r23_p2m-metabolic.tar.bz2	1966032 KB	10/08/12 15:19:00
BioModels_Database-r23_p2m-non_metabolic.tar.bz2	78726 KB	10/08/12 15:19:00
BioModels_Database-r23_p2m-whole_genome_metabolism.tar.bz2	509109 KB	10/08/12 15:20:00
BioModels_Database-r23_pub-all_files.tar.bz2	601968 KB	10/08/12 21:03:00
BioModels_Database-r23_pub-sbml_files.tar.bz2	10992 KB	11/08/12 13:10:00





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Nicolas Le Novère Babraham Institute EMBL-EBI (2003-2012) Founder of BioModels in 2005



Maciei Swat



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Tung Nguyen



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Shukanto Das

External curation collaborator:

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Sarah Keating



Vincent Knight-Schrijver



Nicolas Rodriguez



Corina

Dueñas Roca

All past members of the team,

Systems Modelling Community

&

Funders



















