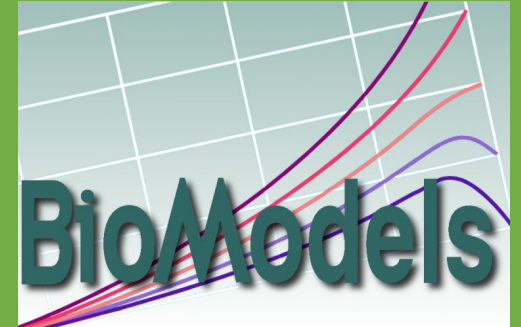


BioModels Database



Camille Laibe



COMBINE 2012, 15-19th August 2012, Toronto

EBI is an Outstation of the European Molecular Biology Laboratory.

Modellers need to:

- **find**
- **understand**
- **reuse**
- **combine**

existing models



Modellers need to:

- **find**
- **understand**
- **reuse**
- **combine**

existing models

This requires:

- **standard formats**
- access to **published** models
- provision of **reliable** models: **curated and annotated**



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](#).

[Advanced Search](#)

Models published in the literature

- [Browse curated models](#)
- [Browse curated models using GO](#)
- [Browse curated models using Taxonomy](#)
- [Browse non-curated models](#)

Path2Models (new)

Submit a model

Links

- [Main instance at EMBL-EBI, UK](#)
- [Mirror at Caltech, USA](#)
- [Project on SourceForge](#)
- [Web Services](#)
- [Download archived models](#)

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

Model of the month

July, 2012

The proinflammatory cytokine Tumour Necrosis Factor (TNF), by binding to its membrane receptor TNF receptor type 1 (TNF-R1), activates pro-apoptotic signalling via caspase activation, besides stimulating NF- κ B-mediated survival pathway at the same time. Schliemann et al. (2011), have analyzed the crosstalk between the pro- and anti-apoptotic signalling pathways induced by TNF-R1, based on an experimentally validated mathematical model.



[Please read more...](#)

News

11th August 2012 **Twenty-third Release of BioModels Database!**

With this release, several new models have been published and numerous have been updated. Moreover new services are now available (for example related to the access to models from the Path2Models project) while others have been improved (such as the model browsing feature based on a tree of Gene Ontology terms or the BioPAX export). Please read the [release notes](#) for more information.

[Download models archives](#)

1st July 2012 **Updated GO tree model browsing**
 The new GO tree model browsing feature allows you to browse the curated models via Gene Ontology terms has been updated. The tree now fully works on all main web browsers. Moreover, when clicking on one GO term, the list of relevant models is displayed in the right panel.

- Biochemical models
 - interactions between molecules in multiple cellular compartments
- Pharmacometrics models
 - tumor growth and treatment response
- Single-compartment neurons
 - membrane voltage, current flow, concentrations of various ions intra- and extracellularly
- Spread of infectious diseases
 - outbreak of zombie infection
- Ecosystem models
 - interaction of living organisms in a given environment
- ...



- From **authors** prior to publication

Supported (listed in instructions for authors) by > **300 journals**, including:

(Molecular Systems Biology, PLoS journals, BioMedCentral journals, ...)

- Submitted by **curators**

- implemented from literature
- imported from journal supplementary materials
- exchanged with other repositories

(DOQCS, CellML Model Repository, JWS Online, ...)

- **Projects** generating large numbers of quantitative models

(Path2Models, ...)

- Provided by other **people** curating models out of interest





CC0 1.0 Universal (CC0 1.0) Public Domain Dedication

This is a human-readable summary of the [Legal Code \(read the full text\)](#).

[Disclaimer](#)

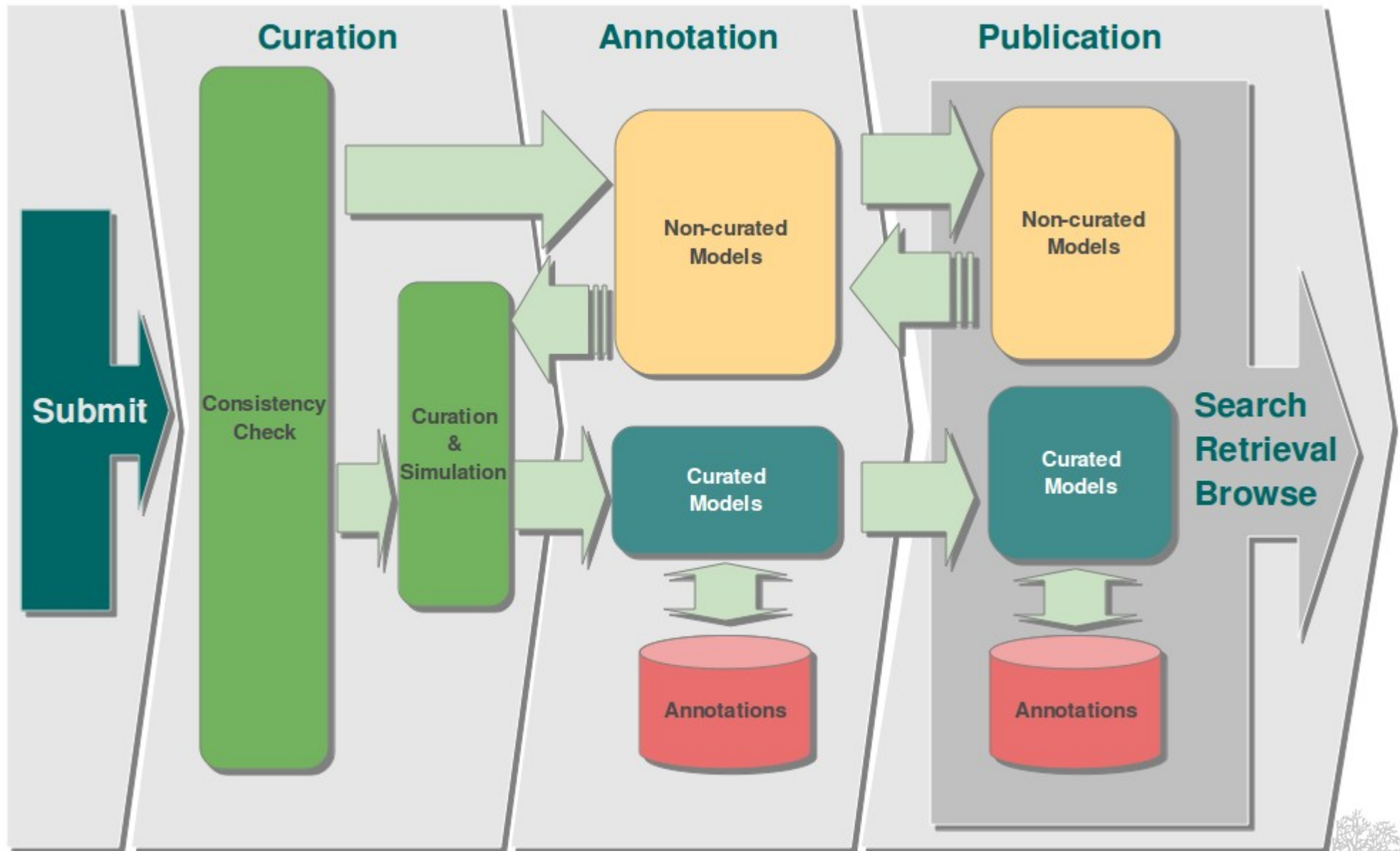
No Copyright



The person who associated a work with this deed has **dedicated** the work to the public domain by waiving all of his or her rights to the work worldwide under copyright law, including all related and neighboring rights, to the extent allowed by law.

You can copy, modify, distribute and perform the work, even for commercial purposes, all without asking permission. See **Other Information** below.





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

The following formats are currently accepted:

- [SBML Level 3: Version 1](#)
- [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](#)

If you wish to submit a model under a different format, 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](#) processes, please refer to the relevant 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, etc.) either directly into the model file (for 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 personal information (first and last name, organisation and email address) 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 in this [example](#) which you can re-use (skip 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 *Edelstein1996_EPSP_AChEvent*.

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 release the encoded model in the **Public Domain** before submitting it to BioModels Database.

Thanks a lot for your contribution 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 'Unpublished' option.

Publication Identifier:

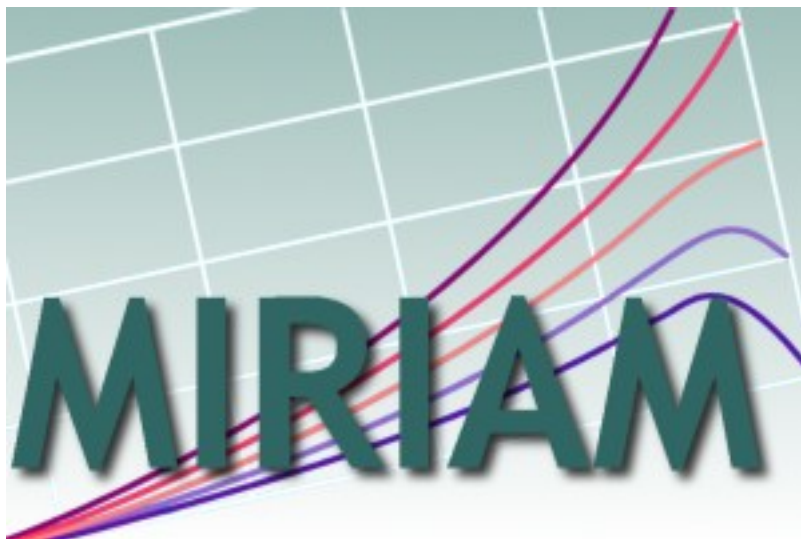
Type of identifier:

- ☒ PubMed ID ([Search Medline](#)) ☐ DOI ([Resolve a DOI](#)) ☐ URL
☐ Unpublished

Continue

Reset





- Minimum Information Required In the Annotation of a Model
- set of guidelines for the curation and annotation of quantitative models
- about encoding and annotation
- applicable to **any structured model format**

<http://biomodels.net/miriam/>

cf. Nicolas Le Novère *et al.* Minimum Information Requested in the Annotation of biochemical Models (MIRIAM). *Nature Biotechnology*, 2005



■ MIRIAM Registry

- catalogue of **data collections** and their associated **namespace**
- provides **perennial identifiers** for annotation and cross-referencing purposes

Identifiers.org

identifiers^o_g

- built on the information stored in the **Registry**
- provides **directly resolvable URIs**

Human calmodulin: **P62158** in **UniProt**

➡ <http://identifiers.org/uniprot/P62158>


Alcohol dehydrogenase: **1.1.1.1** in **Enzyme Nomenclature**

➡ <http://identifiers.org/ec-code/1.1.1.1>

Activation of MAPKK activity: **GO:0000186** in **Gene Ontology**


➡ <http://identifiers.org/obo.go/GO:0000186>



This is a tree view of the curated models based on their [Gene Ontology](#)  annotation.


To browse the models, please click the ► icon on the left of the term to expand the related branch and similarly click on the ▼ 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](#) (422)
 - [GO:0065007 - biological regulation](#) (299)
 - [GO:0008283 - cell proliferation](#) (11)
 - [GO:0071840 - cellular component organization or biogenesis](#) (96)
 - ▼ [GO:0009987 - cellular process](#) (358)
 - [GO:0030029 - actin filament-based process](#) (2)
 - [GO:0001775 - cell activation](#) (3)
 - [GO:0007569 - cell aging](#) (2)
 - [GO:0007154 - cell communication](#) (170)
 - ▼ [GO:0007049 - cell cycle](#) (37)
 - [GO:0022402 - cell cycle process](#) (19)
 - [GO:0004693 - cyclin-dependent protein kinase activity](#) (19)
 - [GO:0000278 - mitotic cell cycle](#) (31)
 - [GO:0045786 - negative regulation of cell cycle](#) (18)
 - [GO:0045787 - positive regulation of cell cycle](#) (13)
 - [GO:0051726 - regulation of cell cycle](#) (25)
 - [GO:0022402 - cell cycle process](#) (19)
 - [GO:0008219 - cell death](#) (17)
 - [GO:0051301 - cell division](#) (4)
 - [GO:0016049 - cell growth](#) (7)
 - [GO:0006928 - cellular component movement](#) (1)
 - [GO:0071841 - cellular component organization or biogenesis at cellular level](#) (38)
 - [GO:0048869 - cellular developmental process](#) (11)
 - [GO:0019725 - cellular homeostasis](#) (38)
 - [GO:0051641 - cellular localization](#) (66)
 - [GO:0044237 - cellular metabolic process](#) (283)
 - [GO:0071804 - cellular potassium ion transport](#) (17)
 - [GO:0051716 - cellular response to stimulus](#) (150)
 - [GO:0007059 - chromosome segregation](#) (2)
 - [GO:0000910 - cytokinesis](#) (1)
 - [GO:0003001 - generation of a signal involved in cell-cell signaling](#) (14)
 - [GO:0016037 - light absorption](#) (1)
 - [GO:0051651 - maintenance of location in cell](#) (5)
 - [GO:0007017 - microtubule-based process](#) (3)
 - [GO:0048523 - negative regulation of cellular process](#) (67)
 - [GO:0048522 - positive regulation of cellular process](#) (84)
 - [GO:0050794 - regulation of cellular process](#) (223)
 - [GO:0032940 - secretion by cell](#) (14)
 - [GO:0023061 - signal release](#) (14)

Model(s) annotated with the GO term [GO:0022402](#)  or one of its descendant(s):


- [Aguda1999_CellCycle](#) (BIOMD00000000169)
- [Bai2003_G1phaseRegulation](#) (BIOMD00000000242)
- [Borisov2009_EGF_Insulin_Crosstalk](#) (BIOMD00000000223)
- [Calzone2007_CellCycle](#) (BIOMD00000000144)
- [Chen2004_CellCycle](#) (BIOMD00000000056)
- [Ciliberto2003_Morphogenesis_Checkpoint](#) (BIOMD00000000297)
- [Conradie2010_RPControl_CellCycle](#) (BIOMD00000000265)
- [Deineko2003_CellCycle](#) (BIOMD00000000208)
- [Haberichter2007_cellcycle](#) (BIOMD00000000109)
- [Ibrahim2008_Cdc20_Sequestering_Template_Model](#) (BIOMD00000000194)
- [Ibrahim2008_MCC_assembly_model_KDM](#) (BIOMD00000000193)
- [Ibrahim2008_Spindle_Assembly_Checkpoint_convey](#) (BIOMD00000000187)
- [Ibrahim2008_Spindle_Assembly_Checkpoint_dissociation](#) (BIOMD00000000186)
- [Novak1997_CellCycle](#) (BIOMD00000000007)
- [Novak2001_FissionYeast_CellCycle](#) (BIOMD00000000111)
- [Proctor2006_telomere](#) (BIOMD00000000087)
- [Qu2003_CellCycle](#) (BIOMD00000000110)
- [Swat2004_Mammalian_G1_S_Transition](#) (BIOMD00000000228)
- [Yao2008_Rb_E2F_Switch](#) (BIOMD00000000318)

Model browsing via GO terms

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 - GO:0023061 - signal release (14)

Model(s) annotated with the GO term [GO:0022402](#)  or one of its descendant(s):

- [Aguda1999_CellCycle](#) (BIOMD0000000169)
- [Bai2003_G1phaseRegulation](#) (BIOMD0000000242)
- [Borisov2009_EGF_Insulin_Crosstalk](#) (BIOMD0000000223)
- [Calzone2007_CellCycle](#) (BIOMD0000000144)
- [Chen2004_CellCycle](#) (BIOMD0000000056)
- [Ciliberto2003_Morphogenesis_Checkpoint](#) (BIOMD0000000297)
- [Conradie2010_RPControl_CellCycle](#) (BIOMD0000000265)
- [Deineko2003_CellCycle](#) (BIOMD0000000208)
- [Haberichter2007_cellcycle](#) (BIOMD0000000109)
- [Ibrahim2008_Cdc20_Sequestering_Template_Model](#) (BIOMD0000000194)
- [Ibrahim2008_MCC_assembly_model_KDM](#) (BIOMD0000000193)
- [Ibrahim2008_Spindle_Assembly_Checkpoint_convey](#) (BIOMD0000000187)
- [Ibrahim2008_Spindle_Assembly_Checkpoint_dissociation](#) (BIOMD0000000186)
- [Novak1997_CellCycle](#) (BIOMD0000000007)
- [Novak2001_FissionYeast_CellCycle](#) (BIOMD0000000111)
- [Proctor2006_telomere](#) (BIOMD0000000087)
- [Qu2003_CellCycle](#) (BIOMD0000000110)
- [Swat2004_Mammalian_G1_S_Transition](#) (BIOMD0000000228)
- [Yao2008_Rb_E2F_Switch](#) (BIOMD0000000318)

Model browsing via GO terms

Taxonomy cloud

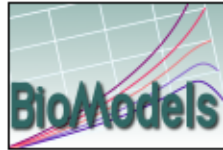


Here are all the taxonomic terms used to annotate the [curated models](#):

[Amniota](#)[Arabidopsis thaliana](#)[Balanus nubilis](#)[cellular organisms](#)[Dictyostelium](#)[Equus caballus](#)[Glycine max](#)[Macaca fascicularis](#)[Murinae](#)[Neurospora crassa](#)[Oryctolagus](#)[Rattus norvegicus](#)[Saccharum officinarum](#)[Torpedo californica](#)[Xenopus laevis](#)[Amphibia](#)[Armoracia rusticana](#)[Bordetella pertussis](#)[Chlamydomonas reinhardtii](#)[Dictyostelium discoideum](#)[Escherichia coli](#)[Homo sapiens](#)[Mammalia](#)[Mus musculus](#)[Nicotiana tabacum](#)[Ostreococcus tauri](#)[Rattus rattus](#)[Schizosaccharomyces pombe](#)[Trypanosoma brucei](#)[Aplysia](#)[Bacillus subtilis](#)[Bos taurus](#)[Chordata](#)[Drosophila](#)[Escherichia coli \(strain K12\)](#)[Lactococcus lactis](#)[Mesocricetus auratus](#)[Mustela vison](#)[Octodon degus](#)[Physarum polycephalum](#)[Rodentia](#)[Schizosaccharomycetaceae](#)[Vertebrata](#)[Arabidopsis](#)[Bacteria](#)[Cavia porcellus](#)[Cricetinae](#)[Drosophila melanogaster](#)[Eukaryota](#)[Loligo forbesi](#)[Metazoa](#)[Mycobacterium tuberculosis](#)[Opisthokonta](#)[Rattus](#)[Saccharomyces cerevisiae](#)[Strongylocentrotus purpuratus](#)[Viridiplantae](#)

Model browsing via Taxonomy

BioModels Database - A Database of Annotated Published Models



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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](#).

[Advanced Search](#)

Search

Go to model

Models published in the literature

- [Browse curated models](#)
- [Browse curated models using GO](#)
- [Browse curated models using Taxonomy](#)
- [Browse non-curated models](#)

Path2Models (new)

Submit a model

Links

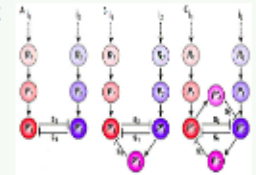
- [Main instance at EMBL-EBI, UK](#)
- [Mirror at Caltech, USA](#)
- [Project on SourceForge](#)
- [Web Services](#)
- [Download archived models](#)

Model search

Model of the month

May, 2012

Mutual inhibitory positive feedback (MIPF), or double-negative feedback, is a key regulatory motif of cellular memory with the capability of maintaining switched states for transient stimuli. Such MIPFs are found in various biological systems where they are interlinked in many cases. Mathematical model to investigate the advantages of interlinked MIPF systems have been proposed by Kim et al. (2007). [Read more...](#)



News

20th May 2012 **Twenty-second Release of BioModels Database!**

This release sees the availability of the models generated by the Path2Models project, a change in the terms of use and several improvements and new features. Please [read more...](#)
[Download models archives](#)

30th April 2012 **Taxonomy cloud**

A [Taxonomy cloud](#) is now available which allows the retrieval of all curated models related to a given organism.

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...](#)

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

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

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

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

BioModels identifier:

Person:

SBML elements:

☐ match the exact phrase

Annotation (full text):

UniProt

Annotation (full text):

Publication

Annotation (full text):

Gene Ontology

Annotation (identifier):

PubChem-compound

Annotation (identifier):

KEGG Reaction

Annotation (identifier):

Enzyme Nomenclature

Compose by:

☒ and

☐ or

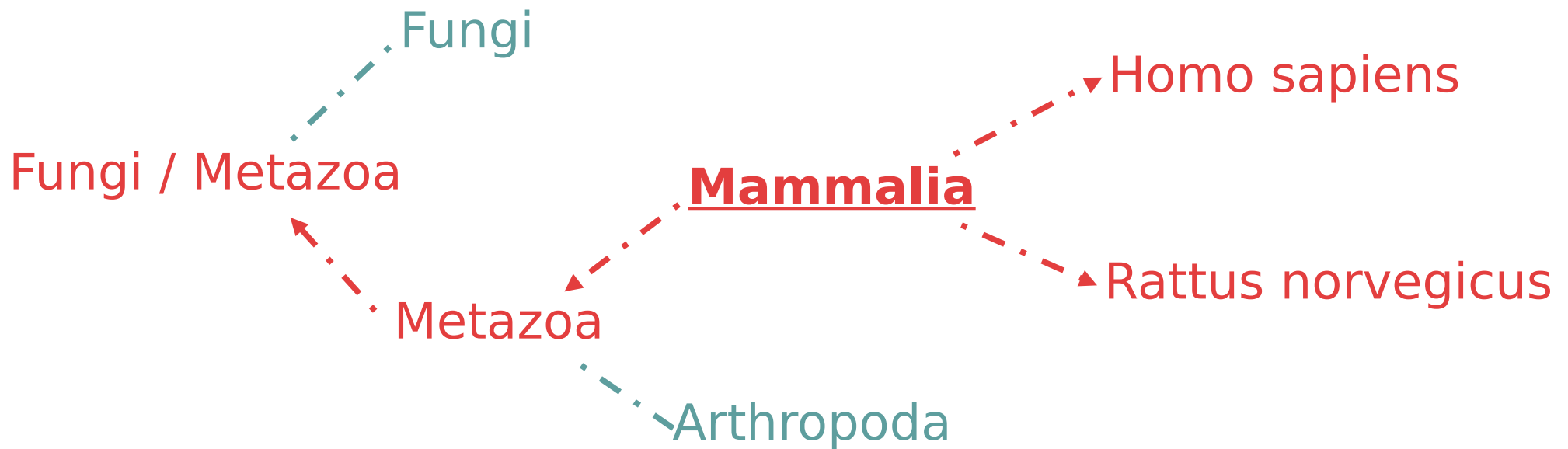
Search

Reset

Advanced model search



Searching for *mammalia* retrieves all models fitting mammals, both **up** and **down** the phylogenetic tree.





55 Curated Models returned.

BioModels_ID	Name	Publication_ID	Last Modified
BIOMD0000000005	Tyson1991_CellCycle_6var	1831270	2008-04-22T21:31:27+00:00
BIOMD0000000006	Tyson1991_CellCycle_2var	1831270	2007-10-05T17:34:05+00:00
BIOMD0000000015	Curto1998_purineMetabol	9664759	2008-06-02T13:14:28+00:00
BIOMD0000000018	Morrison1989_FolateCycle	2732237	2007-09-25T09:31:06+00:00
BIOMD0000000024	Scheper1999_CircClock	9870936	2007-09-25T09:33:32+00:00
BIOMD0000000041	Kongas2001_creatine	10.1038/npre.2007.13...	2008-02-05T14:03:10+00:00
BIOMD0000000043	Borghans1997_CaOscillation_model1	17029867	2007-09-25T09:46:49+00:00
BIOMD0000000044	Borghans1997_CaOscillation_model2	17029867	2007-09-25T09:47:07+00:00
BIOMD0000000045	Borghans1997_CaOscillation_model3	17029867	2007-09-25T09:47:26+00:00
BIOMD0000000047	Oxhamre2005_Ca_oscillation	15596518	2007-09-25T09:48:07+00:00
BIOMD0000000048	Kholodenko1999_EGFRsignaling	16914507	2008-02-05T14:27:44+00:00
BIOMD0000000049	Sasagawa2005_MAPK	15793571	2007-09-25T09:48:55+00:00
BIOMD0000000054	Ataullahkhanov1996_Adenylate	8733433	2008-01-18T08:48:23+00:00
BIOMD0000000057	Sneyd2002_IP3_Receptor	11842185	2007-09-25T09:51:51+00:00
BIOMD0000000059	Fridlyand2003_Calcium_flux	12644446	2008-02-19T07:45:51+00:00
BIOMD0000000069	Fuss2006_MitoticActivation	16873466	2007-09-25T09:58:26+00:00
BIOMD0000000070	Holzthutter2004_Erythrocyte_Metabolism	15233787	2007-09-25T09:58:55+00:00
BIOMD0000000073	Leloup2003_CircClock_DD	12775757	2007-09-25T10:00:03+00:00
BIOMD0000000081	Suh2004_KCNQ_Regulation	15173220	2007-09-25T10:03:07+00:00
BIOMD0000000088	Maeda2006_MyosinPhosphorylation	16923126	2007-09-25T10:05:59+00:00
BIOMD0000000093	Yamada2003_JAK_STAT_pathway	12527385	2007-09-25T10:08:21+00:00

Metazoa/Fungi

Homo sapiens

Rattus

Rattus norvegicus

Mammalia

BIOMD0000000003 - Goldbeter1991_MinMitOscil



Download SBML

Other formats (auto-generated)

Actions

Submit Model Comment/Bug

Model

Overview

Math

Physical entities

Parameters

Curation

Reference Publication

Publication ID: [1833774](#)

Goldbeter A.
A minimal cascade model for the mitotic oscillator involving cyclin and cdc2 kinase.
Proc Natl Acad Sci U S A 1991 Oct;88(20):9107-11.
Faculté des Sciences, Université Libre de Bruxelles, Belgium. [\[more\]](#)

Model

Original Model: [BIOMD0000000003.xml.origin](#)

Submitter: [Nicolas Le Novère](#)

Submission ID: MODEL6614271263

Submission Date: 13 Sep 2005 12:24:56 UTC

Last Modification Date: 17 Mar 2010 00:25:38 UTC

Creation Date: 06 Feb 2005 23:39:40 UTC

Encoders: [Bruce Shapiro](#)
[Vijayalakshmi Chelliah](#)

set #1 bqbiol:occursIn [Taxonomy Amphibia](#)

set #2 bqbiol:isVersionOf [KEGG Pathway hsa04110](#)
[Gene Ontology mitotic cell cycle](#)

bqbiol:isHomologTo [Reactome REACT_152](#)

Notes

This a model from the article:

A minimal cascade model for the mitotic oscillator involving cyclin and cdc2 kinase.

Goldbeter A *Proc. Natl. Acad. Sci. U.S.A.* 1991;88(20):9107-11 [1833774](#),

Abstract:

A minimal model for the mitotic oscillator is presented. The model, built on recent experimental advances, is based on the cascade of post-translational modification that modulates the activity of cdc2 kinase during the cell cycle. The model pertains to the situation encountered in early amphibian embryos, where the accumulation of cyclin suffices to trigger the onset of mitosis. In the first cycle of the bicyclic cascade model, cyclin promotes the activation of cdc2 kinase through reversible dephosphorylation, and in the second cycle, cdc2 kinase activates a cyclin protease by reversible phosphorylation. That cyclin activates cdc2 kinase while the kinase triggers the degradation of cyclin has suggested that oscillations may originate from such a negative feedback loop [Félix, M. A., Labbé, J. C., Dorée, M., Hunt, T. & Karsenti, E. (1990) *Nature* (London) 346, 379-382]. This conjecture is corroborated by the model, which indicates that sustained oscillations of the limit cycle type can arise in the cascade, provided that a threshold exists in the activation of cdc2 kinase by cyclin and in the activation of cyclin proteolysis by cdc2 kinase. The analysis shows how mitotic oscillations may readily arise from time lags associated with these thresholds and from the delayed negative feedback provided by cdc2-induced cyclin degradation. A mechanism for the origin of the thresholds is proposed in terms of the phenomenon of zero-order ultrasensitivity previously described for biochemical systems regulated by covalent modification.

BIOMD0000000003 - Goldbeter1991_MinMitOscil



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Actions

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Model

Overview

Math

Physical entities

Parameters

Curation

Reference Publication

Publication ID: [1833774](#)

Goldbeter A.

A minimal cascade model for the mitotic oscillator involving cyclin and cdc2 kinase.

Proc Natl Acad Sci U S A 1991 Oct;88(20):9107-11.

Faculté des Sciences, Université Libre de Bruxelles, Belgium. [\[more\]](#)

Model

Original Model: [BIOMD0000000003.xml.origin](#)

Submitter: [Nicolas Le Novère](#)

Submission ID: MODEL6614271263

Submission Date: 13 Sep 2005 12:24:56 UTC

Last Modification Date: 17 Mar 2010 00:25:38 UTC

Creation Date: 06 Feb 2005 23:39:40 UTC

Encoders: [Bruce Shapiro](#)

[Vijayalakshmi Chelliah](#)

set #1 bqbiol:occursIn [Taxonomy Amphibia](#)

set #2 bqbiol:isVersionOf [KEGG Pathway hsa04110](#)
[Gene Ontology mitotic cell cycle](#)

bqbiol:isHomologTo [Reactome REACT_152](#)

Notes

This a model from the article:

A minimal cascade model for the mitotic oscillator involving cyclin and cdc2 kinase.

Goldbeter A *Proc. Natl. Acad. Sci. U.S.A.* 1991;88(20):9107-11 [1833774](#),

Abstract:

A minimal model for the mitotic oscillator is presented. The model, built on recent experimental advances, is based on the cascade of post-translational modification that modulates the activity of cdc2 kinase during the cell cycle. The model pertains to the situation encountered in early amphibian embryos, where the accumulation of cyclin suffices to trigger the onset of mitosis. In the first cycle of the bicyclic cascade model, cyclin promotes the activation of cdc2 kinase through reversible dephosphorylation, and in the second cycle, cdc2 kinase activates a cyclin protease by reversible phosphorylation. That cyclin activates cdc2 kinase while the kinase triggers the degradation of cyclin has suggested that oscillations may originate from such a negative feedback loop [Félix, M. A., Labbé, J. C., Dorée, M., Hunt, T. & Karsenti, E. (1990) *Nature* (London) 346, 379-382]. This conjecture is corroborated by the model, which indicates that sustained oscillations of the limit cycle type can arise in the cascade, provided that a threshold exists in the activation of cdc2 kinase by cyclin and in the activation of cyclin proteolysis by cdc2 kinase. The analysis shows how mitotic oscillations may readily arise from time lags associated with these thresholds and from the delayed negative feedback provided by cdc2-induced cyclin degradation. A mechanism for the origin of the thresholds is proposed in terms of the phenomenon of zero-order ultrasensitivity previously described for biochemical systems regulated by covalent modification.

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[Vijayalakshmi Chelliah](#)

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[Gene Ontology mitotic cell cycle](#)

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BIOMD0000000003 - Goldbeter1991_MinMitOscil



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Actions

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Goldbeter A.
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Model

Original Model: [BIOMD0000000003.xml.origin](#)

Submitter: [Nicolas Le Novère](#)

Submission ID: MODEL6614271263

Submission Date: 13 Sep 2005 12:24:56 UTC

Last Modification Date: 17 Mar 2010 00:25:38 UTC

Creation Date: 06 Feb 2005 23:39:40 UTC

Encoders: [Bruce Shapiro](#)
[Vijayalakshmi Chelliah](#)

set #1 bqbiol:occursIn [Taxonomy Amphibia](#)

set #2 bqbiol:isVersionOf [KEGG Pathway hsa04110](#)
[Gene Ontology mitotic cell cycle](#)

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Abstract:

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Actions

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Model

Overview

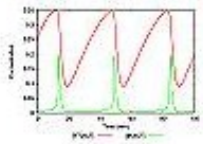
Math

Physical entities

Parameters

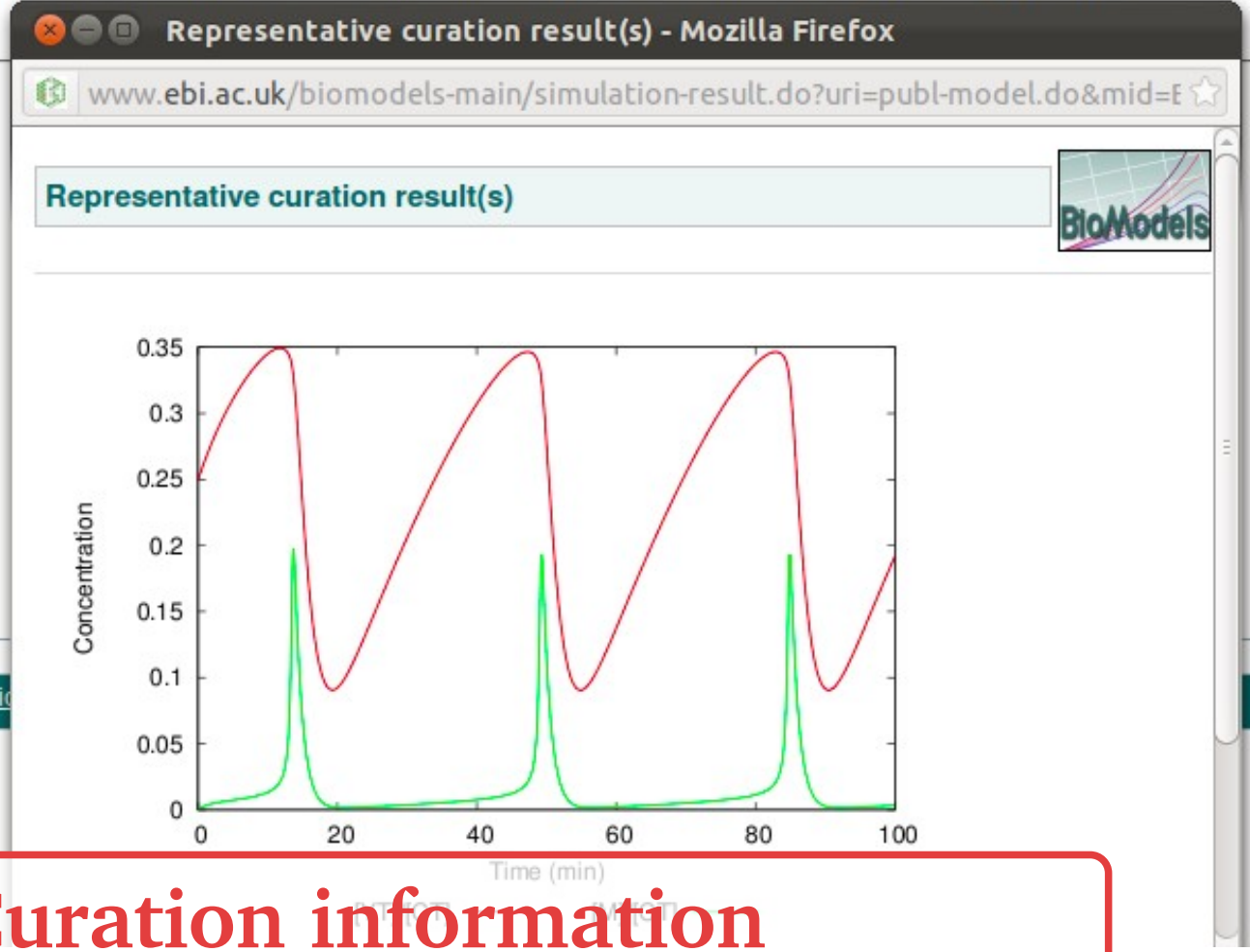
Curation

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).



Curation information

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Actions

Submit Model Comment/Bug

Model

Overview

Publication ID: [1831270](#)

Original Model: [BIOMD0000000005.xml.origin](#)

Submitter: [Nicolas Le Novère](#)

Submission ID: MODEL6614644188

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

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

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

Encoders: [Bruce Shapiro](#)
[Vijayalakshmi Chelliah](#)

This a model from the article:

Modeling the cell division cycle: cdc2 and cyclin
Tyson JJ *Proc. Natl. Acad. Sci. U.S.A.*1991; 88(1)

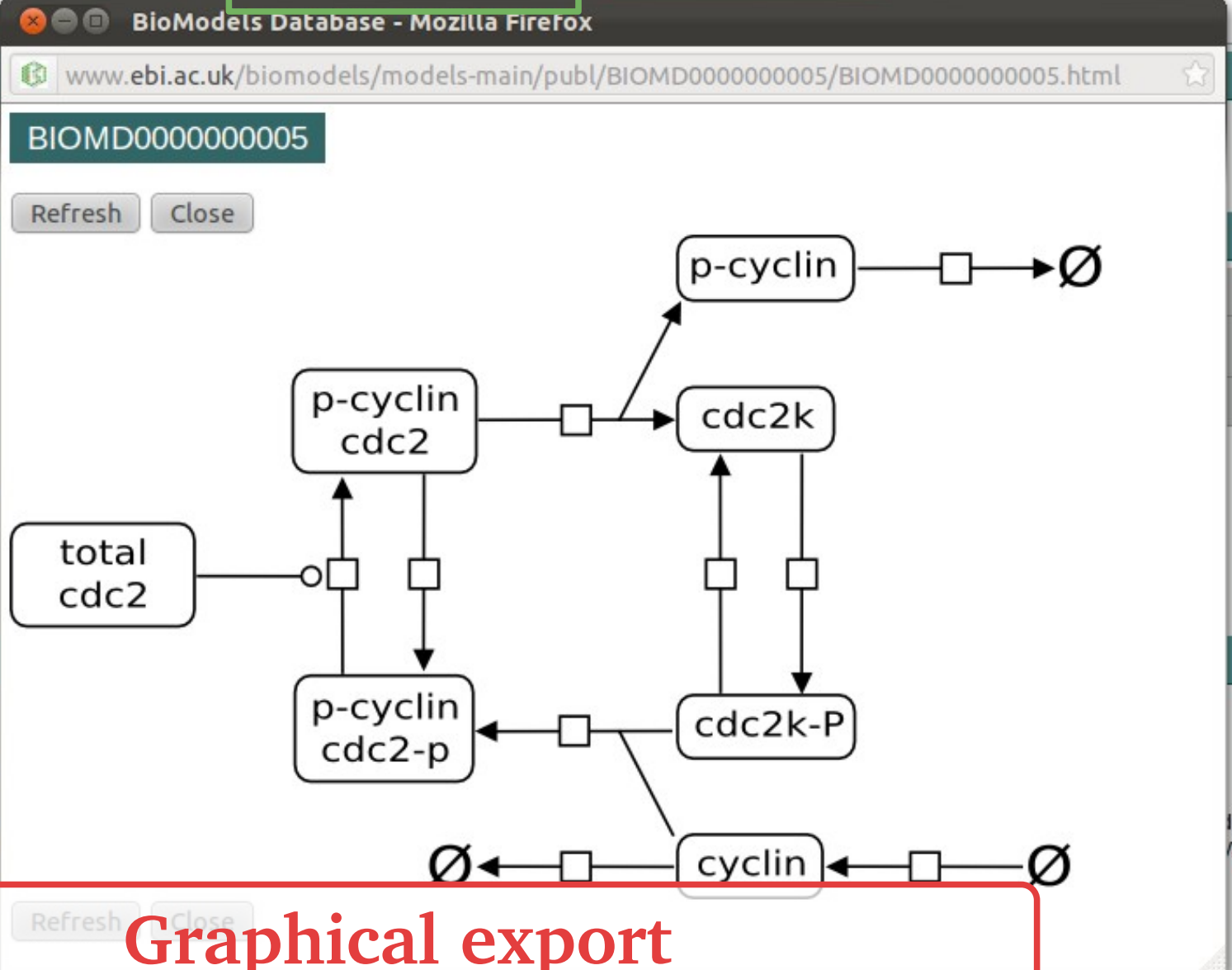
Abstract:

The proteins cdc2 and cyclin form a heterodimeric complex. Simulation and analysis of the model as a spontaneous oscillator, or as an excitable switch, and the excitable switch cycles in early embryos, and the excitable switch

This model originates from BioModels Database Team.

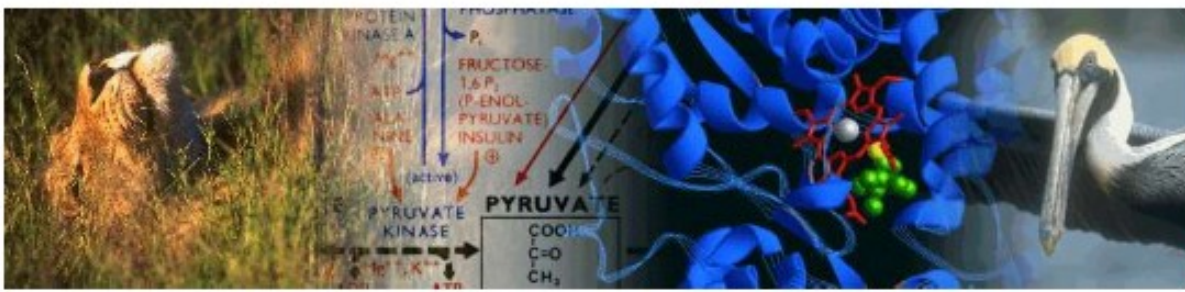
For more information see the [terms of use](#).

To cite BioModels Database, please use: Li C, Donizelli M, Rodriguez N, Dharuri H, Endler J, Chelliah V, Li L, He F, Henry A, Stefan MI, Snoen T, Hucka M, Le Novère N, Laihe C



To cite BioModels Database please use: F. J. Hermida et al., *Bioinformatics*, 2019, Vol. 34, No. 17, pp. i-ii. doi:10.1093/bioinformatics/btz186. [Full citation information](#)

Online simulation



[Biomodels Home](#) [Index](#) [JWS Online](#)

Biomodels: BIOMD0000000005 Tyson1991

Param...	Value
cell	1.0
k6	1.0
k8notP	10000...
k9	1000.0
k3	200.0
k5notP	0.0
k1aa	0.015
k2	0.0
k7	0.6
k4	180.0
k4prime	0.018
EmptyS...	0.0
C2[0]	0.0
CP[0]	1.0
Mvar[0]	0.0
Y[0]	0.0
YP[0]	0.0
pM[0]	0.3

Evaluate Model

Sim **State**

Start value

End value

Rates ☐

Metabolites ☒

Select values

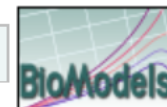
C2
CP
Mvar
Y
YP
pM

Param Reset

CDK2-P-Cyclin-P complex

JWS Online

BIOMD0000000003 - Goldbeter1991_MinMitOscil

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Model

Overview

Math

Physical entities

Parameters

Curation



Create a submodel with selected elements



Deselect All

ModelPublication ID: [1833774](#)

Submission Date: 13 Sep 2005 12:24:56 UTC

Last Modification Date: 17 Mar 2010 00:25:38 UTC

Creation Date: 06 Feb 2005 23:39:40 UTC

Mathematical expressions☐ Reactions[creation of cyclin](#)[default degradation of cyclin](#)[cdc2 kinase triggered degradation of cyclin](#)[activation of cdc2 kinase](#)[deactivation of cdc2 kinase](#)[activation of cyclin protease](#)[deactivation of cyclin protease](#)**Rules**[Assignment Rule \(variable: V1\)](#)[Assignment Rule \(variable: V3\)](#)**Physical entities**

Compartments



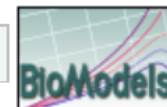
Species



cell

[Cyclin](#)[CDC-2 Kinase](#)[Cyclin Protease](#)**Global parameters**[V1](#)[V3](#)[VM1](#)[VM3](#)[Kc](#)

BIOMD0000000003 - Goldbeter1991_MinMitOscil

[Download SBML](#)[Other formats \(auto-generated\)](#)[Actions](#)[Submit Model Comment/Bug](#)

Model

Overview

Math

Physical entities

Parameters

Curation

[Create a submodel with selected elements](#)[Deselect All](#)**Model**Publication ID: [1833774](#)

Submission Date: 13 Sep 2005 12:24:56 UTC

Last Modification Date: 17 Mar 2010 00:25:38 UTC

Creation Date: 06 Feb 2005 23:39:40 UTC

Mathematical expressions☐ Reactions☒ [creation of cyclin](#)☐ [default degradation of cyclin](#)☐ [cdc2 kinase triggered degradation of cyclin](#)☐ [activation of cdc2 kinase](#)☒ [deactivation of cdc2 kinase](#)☐ [activation of cyclin protease](#)☐ [deactivation of cyclin protease](#)**Rules**[Assignment Rule \(variable: V1\)](#)[Assignment Rule \(variable: V3\)](#)**Physical entities**☐ Compartments ☐ Species☐ cell☐ [Cyclin](#)☐ [CDC-2 Kinase](#)☐ [Cyclin Protease](#)**Global parameters**[V1](#)[V3](#)[VM1](#)[VM3](#)[Kc](#)

BIOMD0000000003 - Goldbeter1991_MinMitOscil

[Download SBML](#)[Other formats \(auto-generated\)](#)[Actions](#)[Submit Model Comment/Bug](#)

Model

Overview

Math

Physical entities

Parameters

Curation



Create a submodel with selected elements



Deselect All

ModelPublication ID: [1833774](#)

Submission Date: 13 Sep 2005 12:24:56 UTC

Last Modification Date: 17 Mar 2010 00:25:38 UTC

Creation Date: 06 Feb 2005 23:39:40 UTC

Mathematical expressions☐ Reactions☒ [creation of cyclin](#)☐ [default degradation of cyclin](#)☐ [cdc2 kinase triggered degradation of cyclin](#)☐ [activation of cdc2 kinase](#)☒ [deactivation of cdc2 kinase](#)☐ [activation of cyclin protease](#)☐ [deactivation of cyclin protease](#)**Rules**[Assignment Rule \(variable: V1\)](#)[Assignment Rule \(variable: V3\)](#)**Physical entities**☐ Compartments ☐ Species☐ cell☐ [Cyclin](#)☐ [CDC-2 Kinase](#)☐ [Cyclin Protease](#)**Global parameters**[V1](#)[V3](#)[VM1](#)[VM3](#)[Kc](#)

BIOMD0000000003 - Goldbeter1991_MinMitOscil



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Actions

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Overview

Math

Physical entities

Parameters

Curation

Submodel1



View the submodel in SBML



Save as

Reactions (2)

+ creation of cyclin → [\[Cyclin\]](#);**+ deactivation of cdc2 kinase** [\[CDC-2 Kinase\]](#) → ;

Compartments (1)

cell

set #1 bqbiol:is [Gene Ontology cell](#)

Referred to as: cell

Species (2)

+ Cyclin

Initial concentration: 0.01 (Units: substance)

Compartment: cell

+ CDC-2 Kinase

Initial concentration: 0.01 (Units: substance)

Compartment: cell

Rules (2)

+ Assignment Rule[V1](#) = C * VM1 * pow(C + Kc, -1)**+ Assignment Rule**[V3](#) = M * VM3

Sub-model creation

BIOMD0000000049 - Sasagawa2005_MAPK

[Download SBML](#)[Other formats \(auto-generated\)](#)[Actions](#)[Send feedback](#)**Model**[Overview](#)[Math](#)[Physical entities](#)[Parameters](#)[Curation](#)**Publication ID:** [15793571](#)

Sasagawa S, Ozaki Y, Fujita K, Kuroda S.

Prediction and validation of the distinct dynamics of transient and sustained ERK activation.

Nat Cell Biol 2005 Apr;7(4):365-73.

Undergraduate Program for Bioinformatics and Systems Biology, Graduate School of Information Science and Technology, University of Tokyo

Original Model: [BIOMD0000000049.xml.origin](#)**Submitter:** [Shinya Kuroda](#)**Submission ID:** MODEL6624243033**Submission Date:** 12 Jan 2006 13:42:52 UTC**Last Modification Date:** 10 Jun 2011 18:18:14 UTC**Creation Date:** 21 Dec 2005 10:59:39 UTC**Encoders:** [Lu Li](#)[Shinya Kuroda](#)

set #1

bqbiol:isVersionOf

[Gene Ontology](#) epidermal growth factor receptor signaling pathway[Gene Ontology](#) Ras protein signal transduction[Gene Ontology](#) nerve growth factor receptor signaling pathway[Gene Ontology](#) MAPKKK cascade

bqbiol:occursIn

[Taxonomy](#) [Rattus](#)

This is a model from the article:

Prediction and validation of the distinct dynamics of transient and sustained ERK activation.Sasagawa S, Ozaki Y, Fujita K, Kuroda S *Nat. Cell Biol.*[2005 Apr; Volume: 7 (Issue: 4)]: 365-73 [15793571](#),**Abstract:**

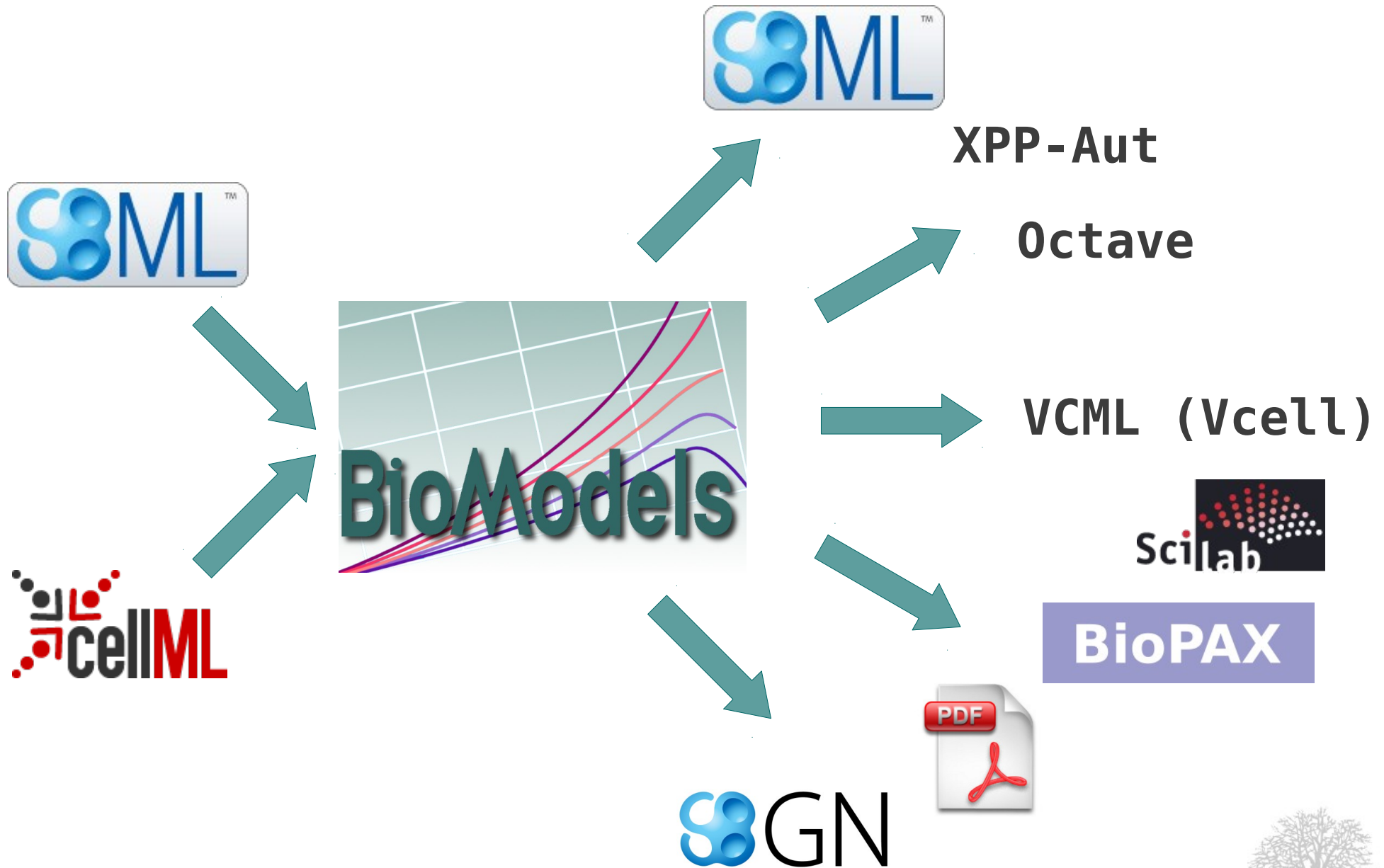
To elucidate the hidden dynamics of extracellular-signal-regulated kinase (ERK) signalling networks, we developed a simulation model of ERK signalling networks by constraining in silico not on their final concentrations, whereas sustained ERK activation depends on the final concentration of NGF but not on the temporal rate of increase. These ERK dynamics depend on the concentration of growth factors, and encode these distinct physical properties into transient and sustained ERK activation, respectively.

Dynamics of active Ras, active Rap1 and phosphorylated ERK were determined from cell with a high resolution

This model originates from BioModels Database: A Database of Annotated Published Models (<http://www.ebi.ac.uk/biomodels/>). It is copyright (c) 2005-2011 The BioModels.net Team.For more information see the [terms of use](#).

To cite BioModels Database, please use: Li C, Donizelli M, Rodriguez N, Dharuri H, Endler J, Chelliah V, Li L, He F, Henry A, Stefan MI, Snoen JJ, Hucka M, Le Novère N, Laibe C. (2011)

Report issues



- **System Biology Format Converter**
- generic framework that potentially allows any conversion between two formats
- aims to be easily extended
- currently supported: conversion from SBML to SBGN-ML, BioPAX Level 2 and Level 3, XPP, Octave, Dot, ...
- allows the combination of several existing converters (conversion pipeline)
- collaborative project developed in Java
- online conversion service:
 - <http://www.ebi.ac.uk/compneur-srv/converters/> (*beta*)

<http://sourceforge.net/projects/sbfc>



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.

Documentation

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

- [Java library documentation \(Javadoc\)](#)

Download

Two versions of the Java library for querying BioModels Database Web Services are provided. These are available for download from the [SourceForge project download page](#) (latest release: 1.21):

- [light version](#) (you need a couple of external jars to use it)
- [standalone version](#) (all the dependencies are already included in the jar)

These are the dependencies which are required by the light-weight library:

- [axis.jar](#) (version 1.4)
- [commons-discovery.jar](#) (version 0.4)
- [commons-logging.jar](#) (version 1.1.1)
- [jaxrpc.jar](#)
- [mail.jar](#) (version 1.4.3)
- [saaj.jar](#)
- [wsdl4j.jar](#) (version 1.6.2)

Note: you can find the latest version of each of these packages on their official web site.

Java 1.5 (or newer) is required in order to use the library.

How to use the library

First, download the provided library.

Assuming that you downloaded the biomodels-wslib_standalone.jar, let's write a simple [HelloBioModels.java](#) to test if it works in your environment.

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

Web Services

■ Models published in the literature

■ Curated models

MIRIAM compliant models

■ Non-curated models

- valid SBML but not curated or annotated
- not MIRIAM compliant models
 - cannot reproduce published results
 - different model structure
 - non kinetic model (FBA, stoichiometric maps, ...)
- MIRIAM compliant models
 - models contain kinetic that we cannot curate up to now
 - work in progress, will be curated in the near future

■ Models from projects (automatically) generating quantitative models

■ Path2Models



- large scale generation of quantitative models from pathways
- initial pathways coming from databases (KEGG, MetaCyc, ...)
- completed with information coming from other resources (BioCarta, ...)
- converted into SBML
- enriched with cross-references
- mathematical models are generated (using common modular rate law for the metabolic networks and logical models for the signalling pathways)
- whole genome metabolism models are reconstructed using flux balance constraint methods

<http://www.ebi.ac.uk/biomodels-main/path2models>



Path2Models

The [path2models](#) project aims at the large scale generation of quantitative models from pathways.

Browse models

Models from this project 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:

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
- Double quotes (") can be used to force the search engine to match a whole expression containing several words.
- The colon character (:) must be escaped in the queries; one can use a backslash for this purpose (\\:).

Download all models

- [Archives of all models \(from the latest release\)](#)

Path2Models



Path2Models

The [path2models](#) project aims at the large scale generation of quantitative models form pathways.

Browse models

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- [metabolic models](#)
- [non-metabolic models](#)
- [whole genome metabolism models](#)

One can also browse those models by organism:

- [list of all organisms](#)

Browsing



Malaria - Homo sapiens


[Download SBML](#)
[Additional file\(s\)](#)
[Send feedback](#)

Model information

Identifier: BMID000000017795

Project: [path2models](#)
Submission: 17 May 2012 16:59:53 UTC

Format: SBML L3 V1 (Layout, Qualitative Models)

Categories: [non-metabolic](#)
Last modified: 17 May 2012 16:59:53 UTC

Published: 19 May 2012 23:49:21 UTC

Annotations

occursIn

[Homo sapiens](#)
Taxonomy

isDescribedBy

[Malaria](#)
KEGG Pathway

Notes

Model of “Malaria” in “Homo sapiens (human)”

Plasmodium protozoa are parasites that account for malaria infection. Sporozoite forms of the parasite are injected by mosquito bites under the skin and are carried to the liver where they develop into the merozoite form. Sporozoite invasion of hepatocytes is mediated by parasite surface protein like CSP. Subsequent infection into red blood cells (RBCs) by merozoites causes malaria disease via aberrant cytokine production and sequestration of parasite-infected red blood cells (pRBCs) to host endothelium. Microvasculature sequestration in the brain brings about cerebral malaria that can result in death or persisting neurological impairment. PfEMP1 has been suggested as the key adhesive molecule of pRBCs.

[Graphical representation of 'Malaria'](#) (PNG image hosted by the Kyoto Encyclopedia of Genes and Genomes, KEGG)

[Original pathway](#) (from the KEGG PATHWAY Database)

This model has been generated by the [path2models](#) project and is currently hosted on [BioModels Database](#) and identified by: [BMID000000017795](#).

To the extent possible under law, all copyright and related neighbouring rights to this encoded model have been dedicated to the public domain worldwide. Please refer to [CC0 Public Domain Dedication](#) for more information.

Model display

Search models

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

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.
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Download all models






- [Archives of all models](#) (from the latest release)

Search



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

[Download all models](#)



■ Models published in the literature:

- Models: 867
- Species: 133,559
- Relations: 154,456
- Annotations: 108,345

■ Path2Models:

	Metabolic	Non-metabolic	Whole genome metabolism	Total
<i>Models</i>	112,898	27,306	1,846	142,050
<i>Species</i>	32,594,642	844,098	6,356,779	39,795,519
<i>Relations</i>	5,591,318	1,926	4,954,345	10,547,589
<i>Annotations</i>	404,248,120	16,914,269	22,861,664	444,024,053



EBI

Finja Büchel (*)

Mihai Glont

Sarah Keating

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