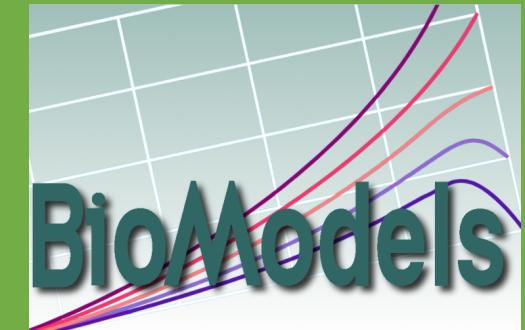


BioModels Database

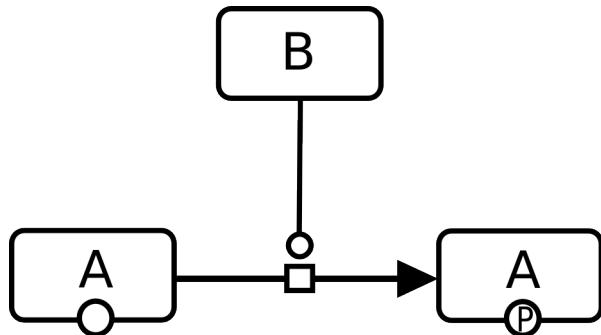
Camille Laibe



COMBINE 2012, 15-19th August 2012, Toronto



EBI is an Outstation of the European Molecular Biology Laboratory.

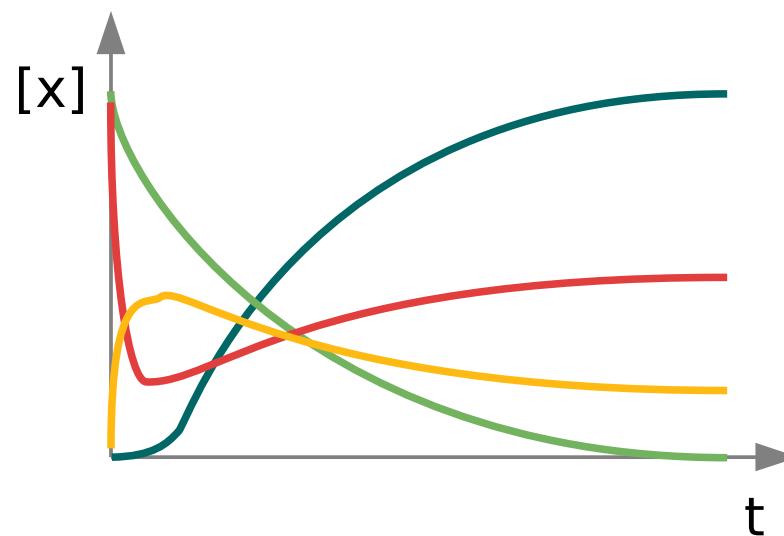


$$\frac{d[A]}{dt} = -k_1[B][A] + k_2[A_B]$$

$$\frac{d[Ap]}{dt} = +k_3[A_B]$$

$$\frac{d[B]}{dt} = -k_1[B][A] + k_2[A_B] + k_3[A_B]$$

$$\frac{d[A_B]}{dt} = +k_1[B][A] - k_2[A_B] - k_3[A_B]$$



- quantitative / dynamic understanding of biological systems
 - integration of data from various scales
 - make clear the current state of knowledge
 - effective way of highlighting gaps in the knowledge
- prediction of the behaviour of systems under certain conditions
 - sometimes the only tool available
- design novel experiments
- ...

Models are significant tools in Systems Biology



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](#).

[Search](#) [Go to model](#)

[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

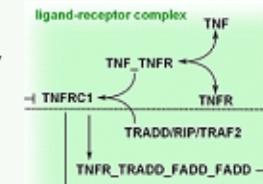
- [Main instance at EMBL-EBI, UK](#)
- [Mirror at Caltech, USA](#)
- [Project on SourceForge](#)
- [Web Services](#)
- [Download archived models](#)

<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
It is now possible 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](#)

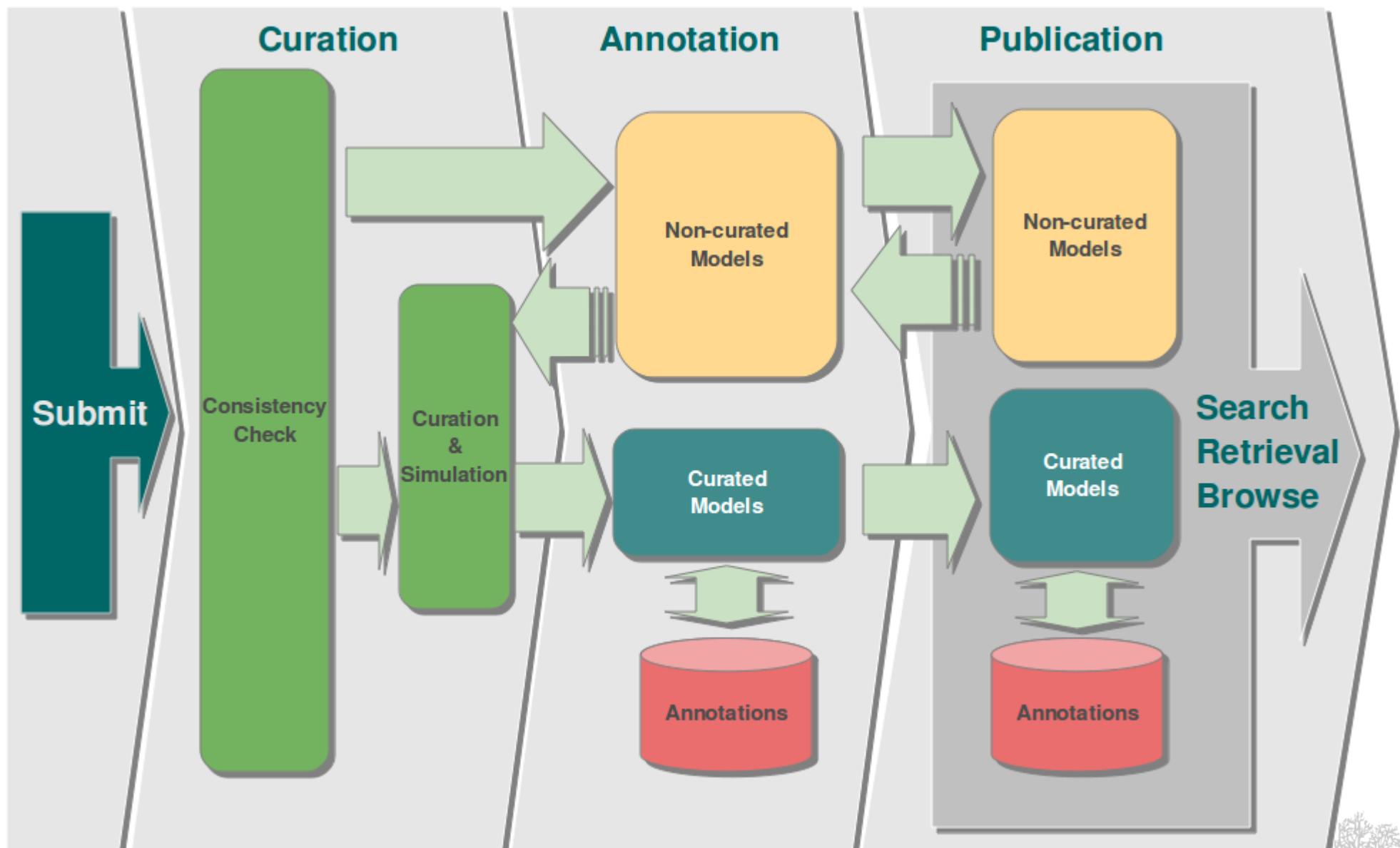
No Copyright



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.





Model submission (step 1)



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](#)



Model submission (step 2)

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

First name:

Last name:

Organisation:

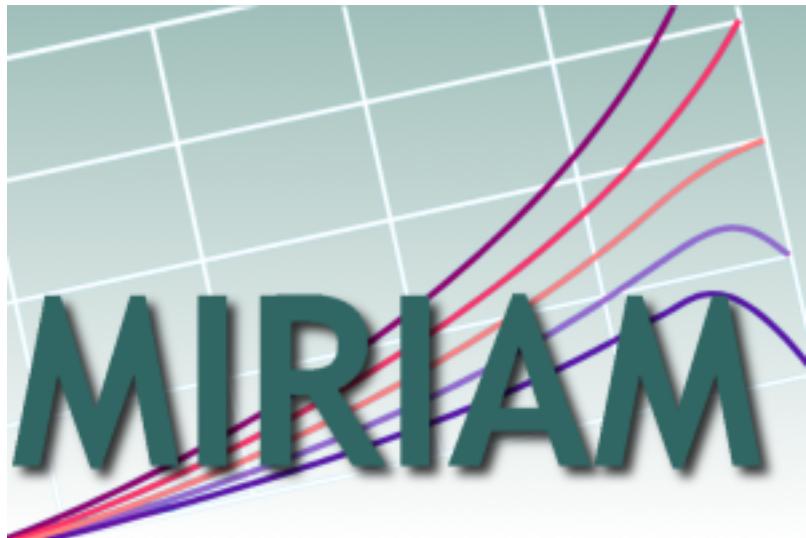
Email:

Comment:

Original model:

Model file:

 [Browse...](#)



- **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



Models **must** (among other things):

- be encoded in a **public machine-readable format**
- be clearly linked to a single **publication**
- reflect the structure of the **biological processes** described in the reference paper (list of reactions, ...)
- be instantiable in a **simulation** (possess initial conditions, ...)
- be able to **reproduce the results** given in the reference paper
- contain **creator's contact details**
- annotated: **each model constituent must be unambiguously identified**



Annotations, and generally **metadata**, are essential for:

- **understanding** data
- **reusing** data
- **comparing** data
- **integrating** data
- **converting** data
- providing efficient **search** strategies
- ...



Annotations, and generally **metadata**, are essential for:

- **understanding** data
- **reusing** data
- **comparing** data
- **integrating** data
- **converting** data
- providing efficient **search** strategies
- ...

→ *true for any kind of data!*



MIRIAM Registry

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

Identifiers.org

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



Human calmodulin: P62158 in UniProt

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

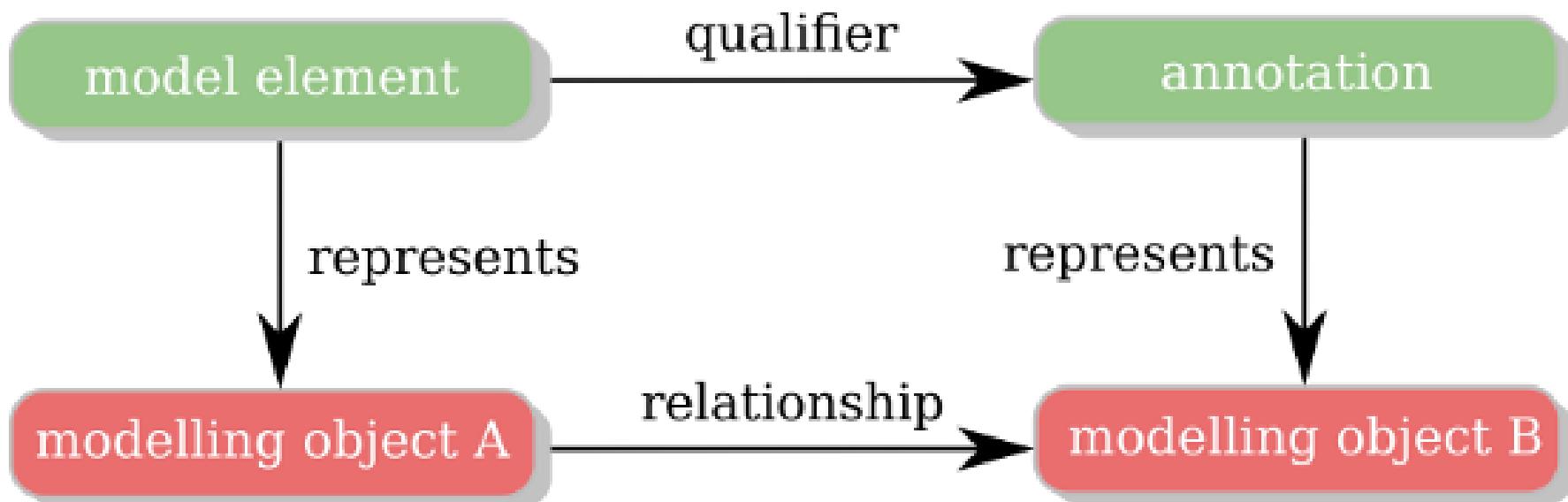
Alcohol dehydrogenase: 1.1.1.1 in Enzyme Nomenclature

➡ <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>





- bqmodel:is
- bqmodel:isDerivedFrom
- bqmodel:isDescribedBy

- bqbiol:is
- bqbiol:isDescribedBy
- bqbiol:hasPart
- bqbiol:hasProperty
- bqbiol:isPartOf

- bqbiol:isPropertyOf
- bqbiol:isVersionOf
- bqbiol:hasVersion
- bqbiol:isHomologTo
- bqbiol:isDescribedBy
- bqbiol:encodes
- bqbiol:isEncodedBy
- bqbiol:occursIn
- [...]

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



```
[...]
<species metaid="metaid_0000006"
          id="L_EGFR"
          compartment="compartment"
          initialConcentration="0">
  <annotation>
    <rdf:RDF xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntaxns#"
               xmlns:bqbiol="http://biomodels.net/biologyqualifiers/">
      <rdf:Description rdf:about="#metaid_0000006">
        <bqbiol:hasPart>
          <rdf:Bag>
            <rdf:li rdf:resource="http://identifiers.org/uniprot/P07522" />
            <rdf:li rdf:resource="http://identifiers.org/uniprot/Q9QX70" />
          </rdf:Bag>
        </bqbiol:hasPart>
      </rdf:Description>
    </rdf:RDF>
  </annotation>
</species>
[...]
```



Browse - Curated models

□ The following fields are used to describe a model:

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

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

◀ 1 2 3 4 5 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 ➡

[10](#) | [50](#) | [100](#) | [All](#)

BioModels ID	Name	Publication ID	Last Modified
BIOMD0000000279	Komarova2005_PTHaction_OsteoclastOsteoblastCoupling	15860557	2011-12-20T15:45:46+00:00
BIOMD0000000403	Ayati2010_BoneRemodelingDynamics_WithTumour+DrugTreatment	20406449	2011-12-20T14:45:58+00:00
BIOMD0000000402	Ayati2010_BoneRemodelingDynamics_WithTumour	20406449	2011-12-20T14:43:23+00:00
BIOMD0000000401	Ayati2010_BoneRemodelingDynamics_NormalCondition	20406449	2011-12-20T14:40:44+00:00
BIOMD0000000305	Kolomeisky2003_MyosinV_Processivity	12609867	2011-11-04T14:34:07+00:00
BIOMD0000000356	Nyman2011_M3Hierarchical_InsulinGlucosedynamics	21572040	2011-11-01T17:27:21+00:00
BIOMD0000000137	Sedaghat2002_InsulinSignalling_noFeedback	12376338	2011-11-01T17:19:19+00:00
BIOMD0000000343	Brannmark2010_InsulinSignalling_Mifamodel	20421297	2011-11-01T17:18:37+00:00
BIOMD0000000379	DallaMan2007_MealModel_GlucoseInsulinSystem	17926672	2011-11-01T13:42:58+00:00
BIOMD0000000362	Bulmer2004_BloodCoagulation	15039440	2011-09-02T10:16:08+00:00

Model browsing: basic list

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](#) ([BIOMD0000000169](#))
- [Bai2003_G1phaseRegulation](#) ([BIOMD0000000242](#))
- [Borisov2009_EGF_Insulin_Crosstalk](#) ([BIOMD0000000223](#))
- [Calzone2007_CellCycle](#) ([BIOMD0000000144](#))
- [Chen2004_CellCycle](#) ([BIOMD0000000056](#))
- [Ciliberto2003_Morphogenesis_Checkpoint](#) ([BIOMD0000000297](#))
- [Conradie2010_RPCControl_CellCycle](#) ([BIOMD0000000265](#))
- [Deineko2003_CellCycle](#) ([BIOMD0000000208](#))
- [Haberichter2007_cellcycle](#) ([BIOMD0000000109](#))
- [Ibrahim2008_Cdc20_Sequestring_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

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.

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- [Chen2004_CellCycle](#) ([BIOMD0000000056](#))
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- [Conradie2010_RPCControl_CellCycle](#) ([BIOMD0000000265](#))
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- [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](#)

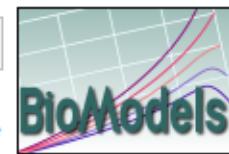
[Amphibia](#)
[Armoracia rusticana](#)
[Bordetella pertussis](#)
[Chlamydomonas reinhardtii](#)
[Dictyostelium discoideum](#)
[Escherichia coli](#)
[Homo sapiens](#)
[Mammalia](#)
[Mus musculus](#)
[Nicotiana tabacum](#)
[Ostreococcus tauri](#)
[Rattus rattus](#)
[Schizosaccharomyces pombe](#)
[Trypanosoma 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](#)
[Viriplantae](#)

Model browsing via Taxonomy

BioModels Database - A Database of Annotated Published Models



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[Search](#)
[Go to model](#)

[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

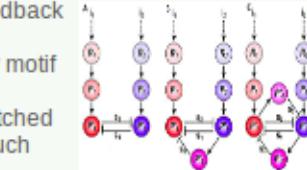
- [Main instance at EMBL-EBI, UK](#)
- [Mirror at Caltech, USA](#)
- [Project on SourceForge](#)
- [Web Services](#)
- [Download archived models](#)

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

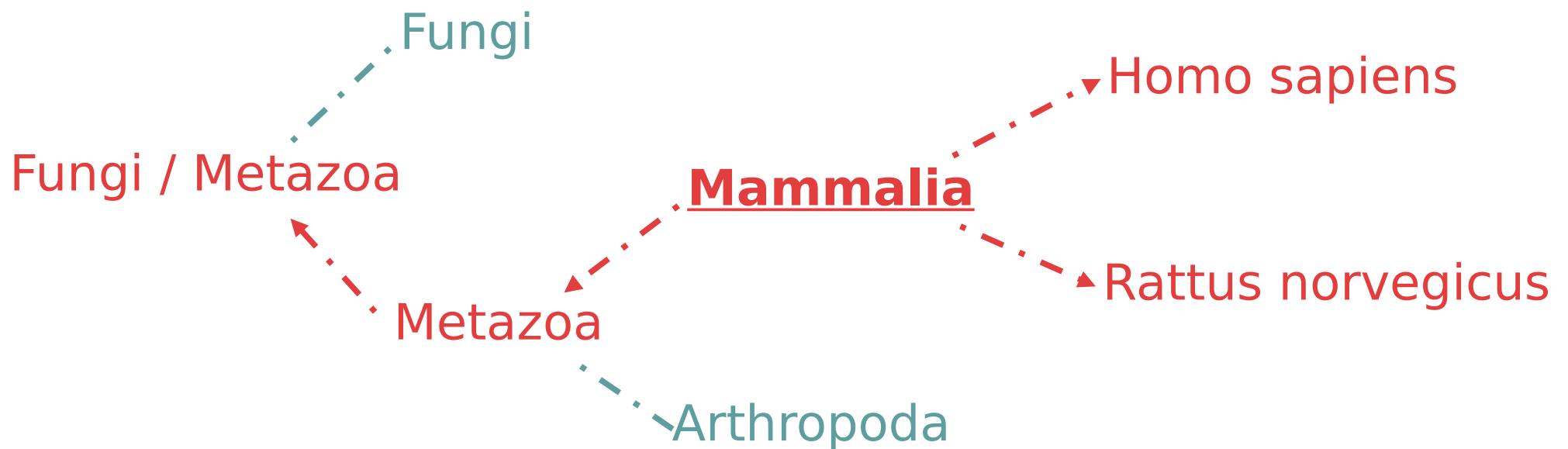
Annotation (identifier): KEGG Reaction

Annotation (identifier): Enzyme Nomenclature

Compose by: and or

Advanced model search

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



55 Curated Models returned.

<u>BioModels ID</u> ▾	<u>Name</u>	<u>Publication ID</u>	<u>Last Modified</u>
BIOMD00000000005	Tyson1991_CellCycle_6var	1831270	2008-04-22T21:31:27+00:00
BIOMD00000000006	Tyson1991_CellCycle_2var	1831270	2007-10-05T17:34:05+00:00
BIOMD00000000015	Curto1998_purineMetabol	9664759	2008-06-02T13:14:28+00:00
BIOMD00000000018	Morrison1989_FolateCycle	2732237	2007-09-25T09:31:06+00:00
BIOMD00000000024	Scheper1999_CircClock	9870936	2007-09-25T09:33:32+00:00
BIOMD00000000041	Kongas2001_creatine	10.1038/npre.2007.13...	2008-02-05T14:03:10+00:00
BIOMD00000000043	Borghans1997_CaOscillation_model1	17029867	2007-09-25T09:46:49+00:00
BIOMD00000000044	Borghans1997_CaOscillation_model2	17029867	2007-09-25T09:47:07+00:00
BIOMD00000000045	Borghans1997_CaOscillation_model3	17029867	2007-09-25T09:47:26+00:00
BIOMD00000000047	Oxhamre2005_Ca_oscillation	15596518	2007-09-25T09:48:07+00:00
BIOMD00000000048	Kholodenko1999_EGFRsignaling	1614507	2008-02-05T14:27:44+00:00
BIOMD00000000049	Sasagawa2005_MAPK	15793571	2007-09-25T09:48:55+00:00
BIOMD00000000054	Ataullahkhanov1996_Adenylate	8733433	2008-01-18T08:48:23+00:00
BIOMD00000000057	Sneyd2002_IP3_Receptor	11842185	2007-09-25T09:51:51+00:00
BIOMD00000000059	Fridlyand2003_Calcium_flux	12644446	2008-02-19T07:45:51+00:00
BIOMD00000000069	Fuss2006_MitoticActivation	16873466	2007-09-25T09:58:26+00:00
BIOMD00000000070	Holzhtutter2004_Erythrocyte_Metabolism	15233787	2007-09-25T09:58:55+00:00
BIOMD00000000073	Leloup2003_CircClock_DD	12775757	2007-09-25T10:00:03+00:00
BIOMD00000000081	Suh2004_KCNQ_Regulation	15173220	2007-09-25T10:03:07+00:00
BIOMD00000000088	Maeda2006_MyosinPhosphorylation	16923126	2007-09-25T10:05:59+00:00
BIOMD00000000093	Yamada2003_JAK_STAT_pathway	12527385	2007-09-25T10:08:21+00:00

BIOMD0000000003 - Goldbeter1991_MinMitOscil[Download SBML](#)[Other formats \(auto-generated\)](#)[Actions](#)[Submit Model Comment/Bug](#)[Model](#)[Overview](#)[Math](#)[Physical entities](#)[Parameters](#)[Curation](#)**Reference Publication**

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](#)set #1 bqbiol:occursIn [Taxonomy Amphibia](#)**Submitter:** [Nicolas Le Novère](#)set #2 bqbiol:isVersionOf [KEGG Pathway hsa04110](#)**Submission ID:** MODEL6614271263

Gene Ontology mitotic cell cycle

Submission Date: 13 Sep 2005 12:24:56 UTCbqbiol:isHomologTo [Reactome REACT_152](#)**Last Modification Date:** 17 Mar 2010 00:25:38 UTC**Creation Date:** 06 Feb 2005 23:39:40 UTC**Encoders:** [Bruce Shapiro](#)
[Vijayalakshmi Chelliah](#)**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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Reference Publication

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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](#)set #1 bqbiol:occursIn [Taxonomy Amphibia](#)Submitter: [Nicolas Le Novère](#)set #2 bqbiol:isVersionOf [KEGG Pathway hsa04110](#)

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BIOMD0000000003 - Goldbeter1991_MinMitOscil



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Reference / Publication

Publication ID: [1833774](#)

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

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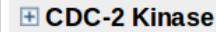
This a model from the article:

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BIOMD0000000003 - Goldbeter1991_MinMitOscil[Download SBML](#)[Other formats \(auto-generated\)](#)[Actions](#)[Submit Model Comment/Bug](#)[Model](#)[Overview](#)[Math](#)**Physical entities**[Parameters](#)[Curation](#)**cell** Spatial dimensions: 3 Compartment size: 1.0 (*Units: volume*)**Cyclin** Initial concentration: 0.01 (*Units: substance*)

Compartment: cell

Annotations:
(SBO: [polypeptide chain](#))set #1 bqbiol:isVersionOf [UniProt CCNC_XENLA](#)
[InterPro IPR006670](#)**CDC-2 Kinase** Initial concentration: 0.01 (*Units: substance*)

Compartment: cell

**Cyclin Protease** Initial concentration: 0.01 (*Units: substance*)

Compartment: cell



BIOMD0000000003 - Goldbeter1991_MinMitOscil[Download SBML](#)[Other formats \(auto-generated\)](#)[Actions](#)[Submit Model Comment/Bug](#)[Model](#)[Overview](#)[Math](#)**Physical entities**[Parameters](#)[Curation](#)**+ cell**

Spatial dimensions: 3 Compartment size: 1.0 (Units: volume)

Cyclin

Compartment: cell

Annotations:
(SBO: [polypeptide chain](#))[UniProt CCNC_XENLA](#)
InterPro IDP0000070

- [Browse](#)
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Term: SBO:0000252**Name****polypeptide chain****Definition**

Naturally occurring macromolecule formed by the ribosome. CHEBI:16541

Comment

Name changed on January 10 2007 by Nicolas Le Novere.

Miscellaneous

Date of creation:

10 November 2006, 15:38

Date of last modification:

10 January 2007, 13:49

Parent(s)[SBO:0000246](#) information macromolecule (is a)**Children**[UniProt CCNC_XENLA](#)
InterPro IDP0000070[UniProt](#) > UniProtKB[Search](#)[Blast *](#)[Align](#)[Retrieve](#)[ID](#)**Search in**

Protein Knowledgebase (UniProtKB) ▾

Q4KLA0 (CCNC_XENLA) ★ Reviewed, UniProtKB/Swiss-ProtLast modified November 16, 2011. Version 37. [History...](#)[Clusters with 100%, 90%, 50% identity](#) | [Documents \(1\)](#) | [Third-party](#)[Names](#) · [Attributes](#) · [General annotation](#) · [Ontologies](#) · [Sequence](#)
[Documents](#) · [Customize order](#)**Names and origin**

Protein names

Recommended name:
Cyclin-C

Gene names

Name:**ccnc**

Organism

Xenopus laevis (African clawed frog)

Taxonomic identifier

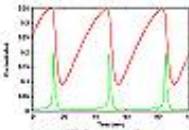
8355 [NCBI]

Taxonomic lineage

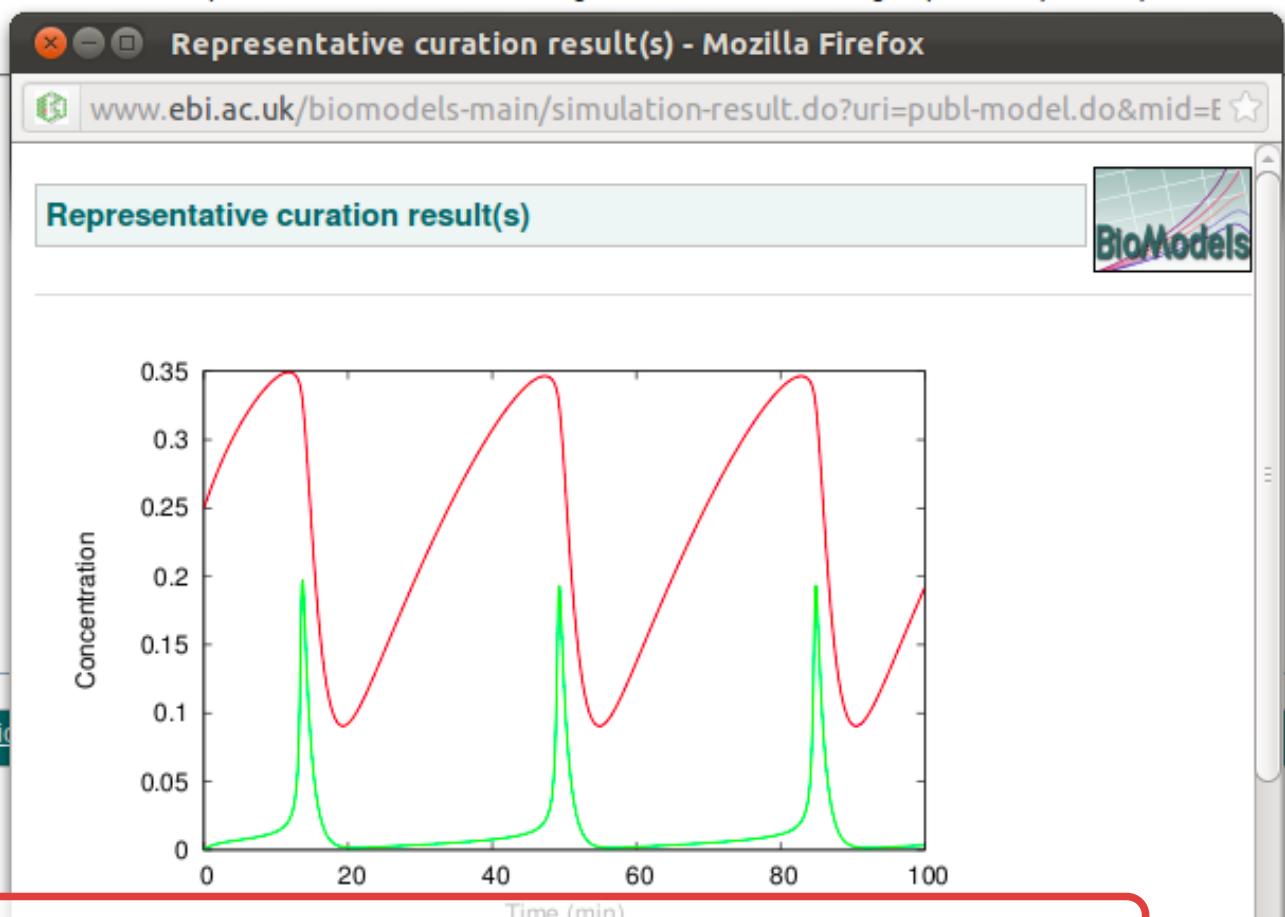
Eukaryota > Metazoa > Chordata > Craniata > Vertebrata > Mesobatrachia > Pipoidea > Pipidae > Xenopoda

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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).

[Computational Systems Neurobiology Group, European Bio](#)

Curation information

[Download SBML](#)[Other formats \(auto-generated\)](#)[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)

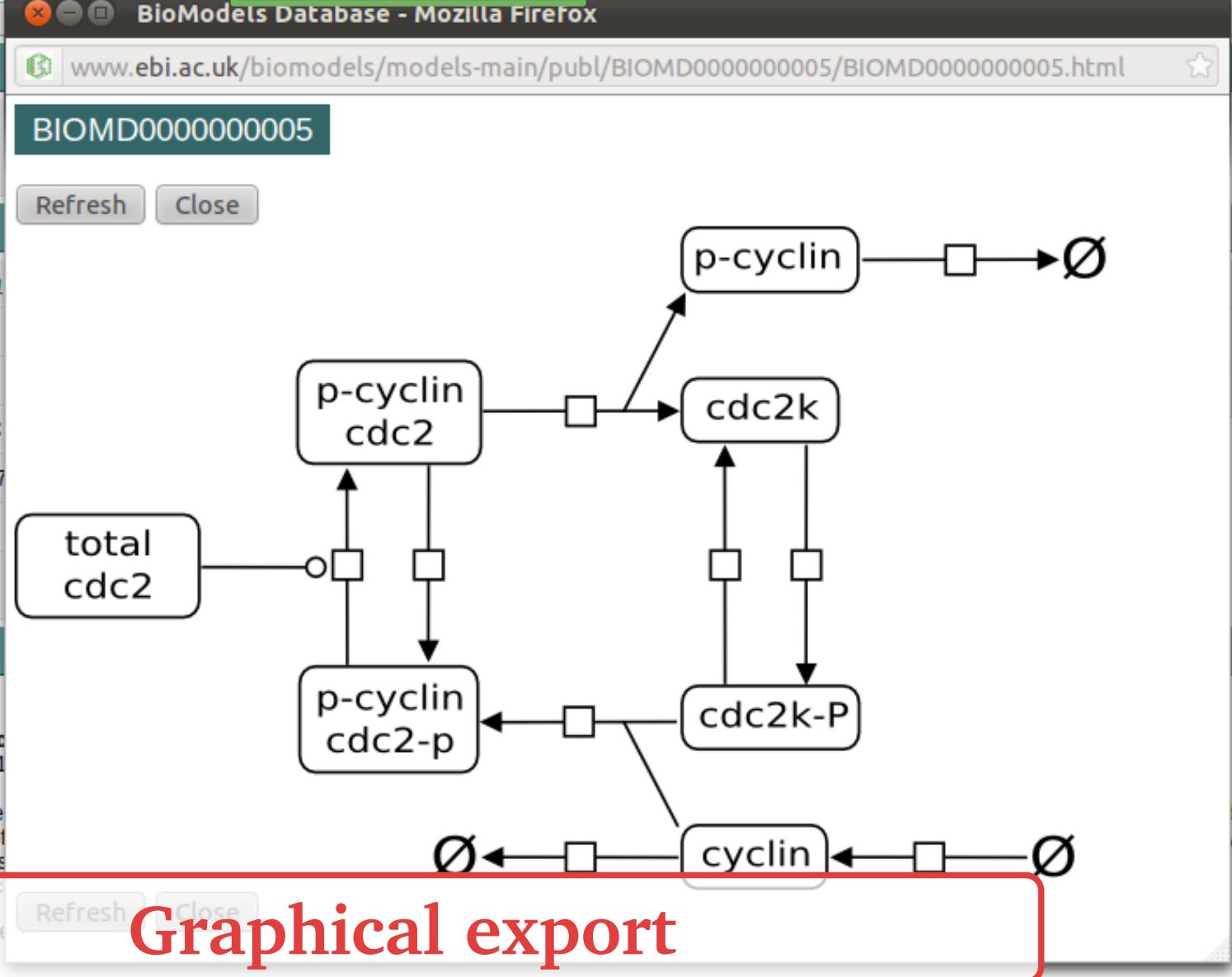
Abstract:

The proteins cdc2 and cyclin form a heterodimer. When cdc2 is bound to cyclin it is called cdc2k. When cdc2 is bound to p-cyclin it is called cdc2-p. When cdc2k is bound to p-cyclin it is called cdc2k-P. The cyclin protein is a monomer. The total amount of cdc2 protein is constant. The total cdc2 protein is converted to cdc2k by the addition of p-cyclin. The cdc2k protein is converted to cdc2-p by the removal of p-cyclin. The cdc2-p protein is converted to cdc2k-P by the addition of p-cyclin. The cdc2k-P protein is converted to cdc2 by the removal of p-cyclin. The cdc2 protein is converted to cdc2k by the addition of cyclin. The cdc2k protein is converted to cdc2 by the removal of cyclin.

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 L, Chelliah V, Li T, He F, Henry A, Stefan MI, Snoep JL, Hucka M, Le Novère N, Leibler S, Kholodenko DM, Sauro HM, Schmid J, Eisinger R, Lohof H, Ginkel M, Kremling A, Lévy M, and Schuster S (2009) BioModels Database: a free, central repository for quantitative kinetic models in systems biology. Nucleic Acids Res. 37: D621-D626.



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[Publication ID: 1831270](#)

Tyson JJ.

Modeling the cell cycle

Proc Natl Acad Sci U S A

[JWS Online Simulation](#)
[BioModels Online Simulation](#)

 Department of Biology, Virginia Polytechnic Institute and State University, Blacksburg 24061. [\[more\]](#)

Model

Original Model: [BIOMD0000000005.xml.origin](#)
Submitter: [Nicolas Le Novère](#)
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Submission Date: 13 Sep 2005 12:31:08 UTC

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

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

Notes

This a model from the article:

Modeling the cell division cycle: cdc2 and cyclin interactions.

Tyson JJ Proc. Natl. Acad. Sci. U.S.A.1991; 88(16); 7328-32 [1831270](#),

Abstract:

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

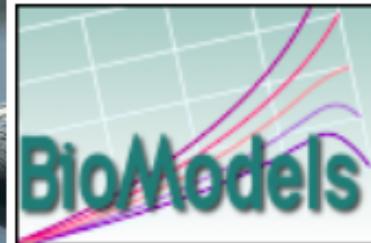
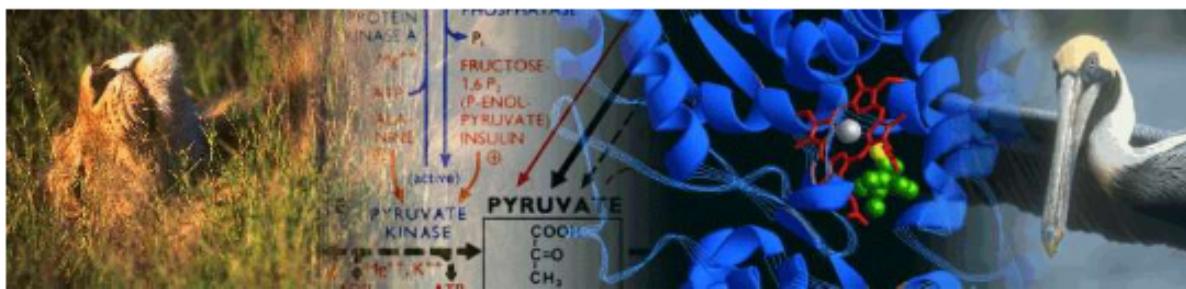
This model originates from BioModels Database: A Database of Annotated Published Models (<http://www.ebi.ac.uk/biomodels/>). It is copyright (c) 2005-2011 The BioModels.net Team.

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To cite BioModels Database:

Online simulation

N. Le Novère N. Le Novère C.



S3ML

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Biomodels: BIOMD0000000005 Tyson1991

Param...	Value
cell	1.0
k6	1.0
k8notP	10000.0
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

Y
pM
C2
CP
M
pM

R1, R2, R3, R4, R5, R6, R7, R8, R9

JWS Online

Applet started.

BIOMD0000000003 - Goldbeter1991_MinMitOscil



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Physical entities

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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

<input checked="" type="checkbox"/> creation of cyclin	<input type="checkbox"/> default degradation of cyclin	<input type="checkbox"/> cdc2 kinase triggered degration of cyclin	<input type="checkbox"/> activation of cdc2 kinase
<input type="checkbox"/> deactivation of cdc2 kinase	<input type="checkbox"/> activation of cyclin protease	<input type="checkbox"/> 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](#)

Sub-model creation

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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](#)

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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 degration 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](#)

Sub-model creation



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Other formats (auto-generated)

Actions

Submit Model Comment/Bug

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 $v_1 = C * VM1 * \text{pow}(C + Kc, -1)$ + Assignment Rule $v_3 = M * VM3$



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Other formats (auto-generated)

Actions

Submit Model Comment/Bug

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 Compartment: cell Initial concentration: 0.01 (Units: substance)

+ CDC-2 Kinase Compartment: cell Initial concentration: 0.01 (Units: substance)

Rules (2)

+ Assignment Rule $v_1 = C * VM1 * \text{pow}(C + Kc, -1)$ + Assignment Rule $v_3 = M * VM3$

Kim et al., (2007). Interlinked mutual inhibitory positive feedbacks induce robust cellular memory effects.

May 2012, model of the month by Vladimir Kiselev

Original model: [BIOMD0000000179](#), [BIOMD0000000180](#)

Biological systems often need to remember their current state to produce reasonable responses for future decisions. To achieve this, a capability of maintaining transited states caused by transient stimuli is required. One of the mechanisms that can create such an effect is a feedback loop.

Feedback loops are processes that connects the output signal of the system back to their input signal. The concept and mechanism of feedback loops have been extensively investigated in various model and experimental systems, such as Turing's model of pattern formation; as well as investigations of metabolic endproduct inhibition, metabolic oscillations, and transcriptional self-repression [1]. It has also been proved that the feedback loops may be useful as a framework for understanding intracellular signalling systems.

There are two main types of feedback loops: negative and positive (Figure 1). Negative feedback loops appear in almost all biological signalling pathways. They are typical characteristics of systems, where the inverted output signal is fed back to the input. Depending on its characteristics and initial conditions, a single negative feedback loop can create four distinct signalling functions: basal homeostat, output limiter, adaptation, and transient generator [1]. In contrary, a positive feedback loop is a major characteristic of a system, where the input is fed by the forward output signal. Positive feedback can amplify signalling responses, alter kinetics, or create bistable switches [1].

A single positive feedback loop between two molecules A and B can be subcategorized into mutual activation (A activates B and B activates A) and mutual inhibition (A inhibits B and B inhibits A). Despite the same nature of these two feedbacks, their steady-state characteristics are however different. In a positive feedback formed by a mutual activation, two molecules A and B show the same expression states (both A and B are on or off). On the other hand, in a mutual inhibitory positive feedback (MIPF), two molecules A and B show different expression states (one is on while the other is off). Such MIPFs can be found in biological processes where transitions between two different stable states are necessary.

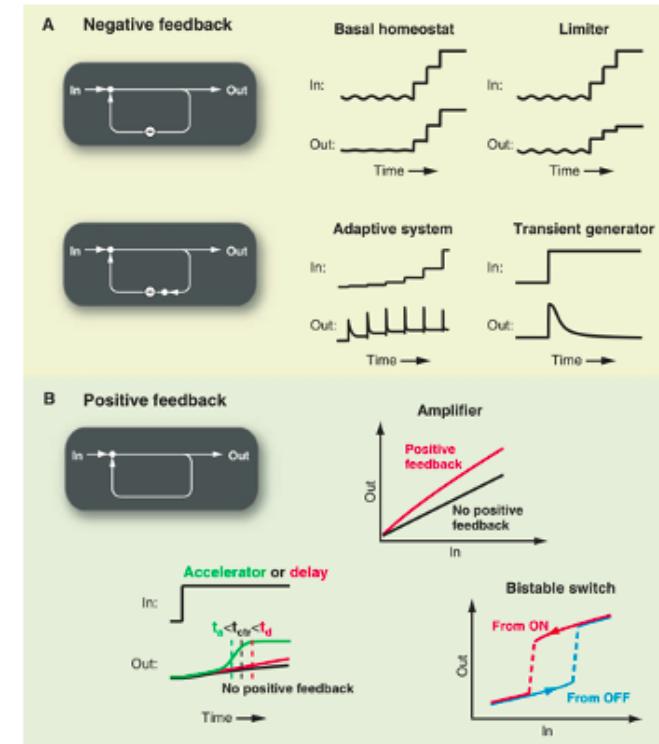
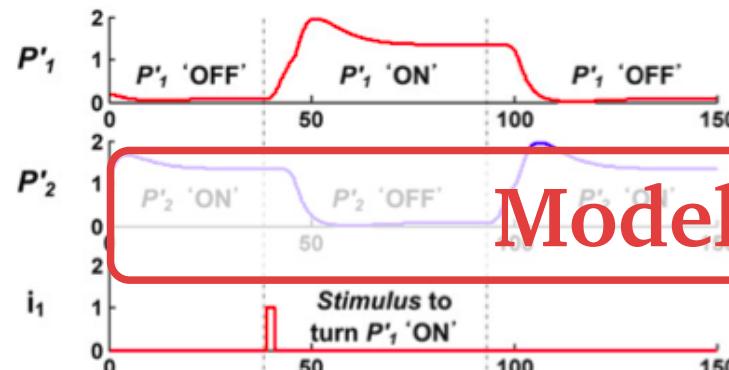


Figure 1 (adapted from [1]). Feedback motifs have important functions in signalling systems. (A) Negative feedback can stabilize basal signalling levels, limit maximal signalling output, enable adaptive responses, or create transient signal responses. (B) Positive feedback can amplify signalling responses, alter kinetics, or create bistable switches.



BIOMD000000049 - 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, Japan

Original Model: [BIOMD000000049.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 MAPKK cascade
	bqbiol:occursIn	Taxonomy Rattus

This 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:**

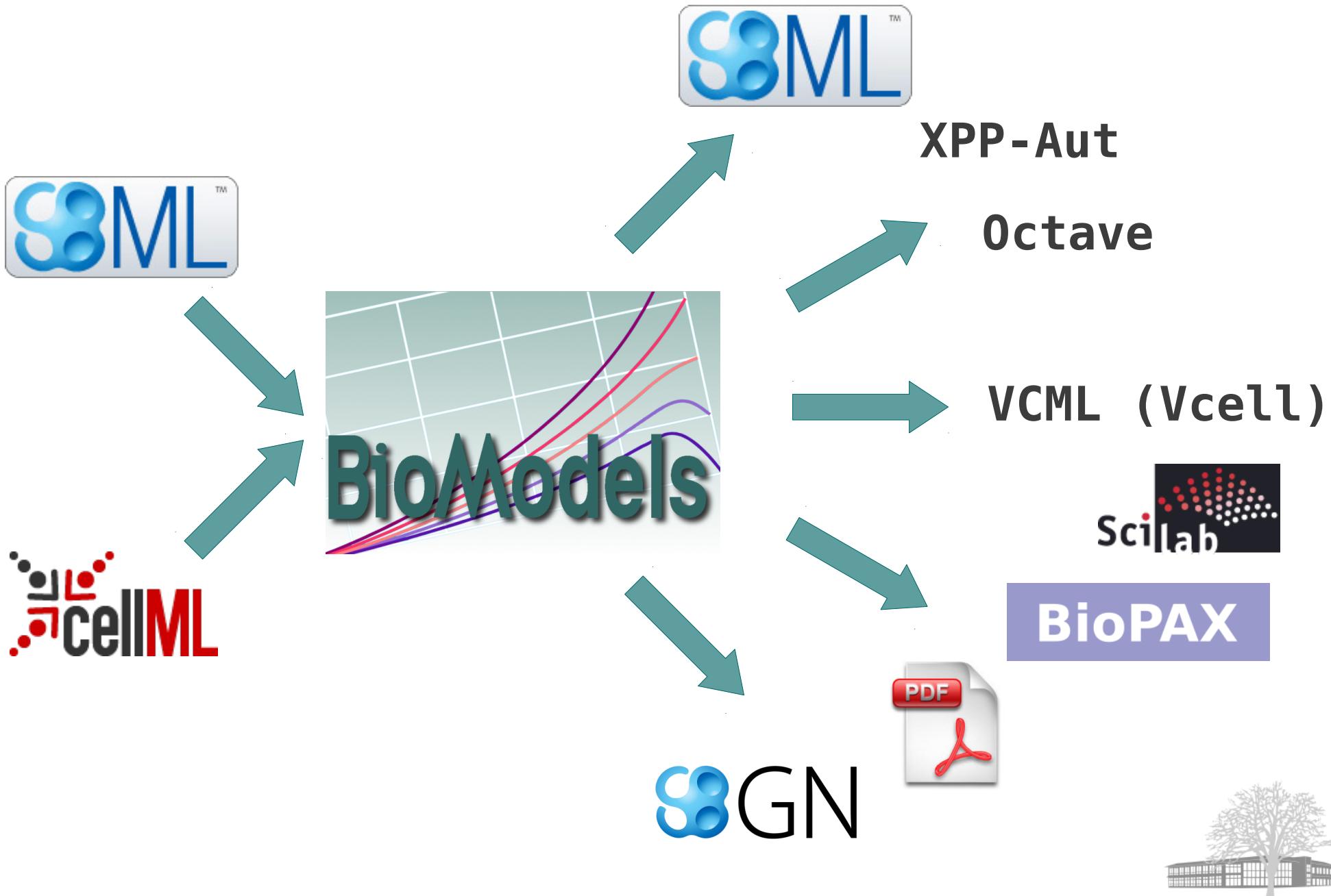
To elucidate the hidden dynamics of extracellular-signal-regulated kinase (ERK) signalling networks, we developed a simulation model of ERK signalling networks by constraining in silico models to experimental observations. Our results show that transient ERK activation depends on the final concentration of NGF, whereas sustained ERK activation depends on the temporal rate of increase of NGF. These ERK dynamics depend on different physical properties of the components, and encode these distinct physical properties into transient and sustained ERK activation, respectively.

Dynamics of active Ras, active Rap1 and phosphorylated ERK were obtained from our simulations.

Report issues

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 I, Chelliah V, Li L, He F, Henry A, Stefan MI, Snoep JL, Hucka M, Le Novère N, Laibe C (2011).



- **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.

Web Services

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.bioma...
```

- **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 form 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](#)

Path2Models

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



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Browsing



Path2Models

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- [whole genome metabolism models](#)

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Path2Models: non-metabolic



Here are all the different types of models from the category ***non-metabolic***:

- [ABC transporters](#)
- [Acute myeloid leukemia](#)
- [Adherens junction](#)
- [Adipocytokine signaling pathway](#)
- [African trypanosomiasis](#)
- [Aldosterone-regulated sodium reabsorption](#)
- [Allograft rejection](#)
- [Alzheimer's disease](#)
- [Amoebiasis](#)
- [Amyotrophic lateral sclerosis \(ALS\)](#)
- [Amyotrophic lateral sclerosis \(ALS\) \(Homo sapiens \(human\)\)](#)
- [Antigen processing and presentation](#)
- [Apoptosis](#)
- [Apoptosis \(Homo sapiens \(human\)\)](#)
- [Arrhythmogenic right ventricular cardiomyopathy \(ARVC\)](#)
- [Asthma](#)
- [Autoimmune thyroid disease](#)
- [Axon guidance](#)
- [B cell receptor signaling pathway](#)
- [Bacterial chemotaxis](#)
- [Bacterial invasion of epithelial cells](#)
- [Bacterial secretion system](#)
- [Basal cell carcinoma](#)
- [Basal transcription factors](#)
- [Base excision repair](#)
- [Bile secretion](#)
- [Bladder cancer](#)
- [Bladder cancer \(Homo sapiens \(human\)\)](#)
- [Calcium signaling pathway](#)
- [Carbohydrate digestion and absorption](#)
- [Cardiac muscle contraction](#)



Path2Models: non-metabolic



Here are all the different types of models from the category ***non-metabolic***:

- [ABC transporters](#)
- [Acute myeloid leukemia](#)
- [Adheren](#) • [Cell adhesion molecules \(CAMs\)](#)
- [Adipocyt](#) • [Cell cycle](#)
- [African tr](#) • [Cell cycle \(f](#)
- [Aldosteron](#) • [Cell cycle - c](#)
- [Allograft](#) • [Cell cycle - v](#)
- [Alzheimer](#) • [Chagas disease](#)
- [Amoebia](#) • [Chemokine](#)
- [Amyotro](#) • [Cholinergic](#)
- [Amyotro](#) • [Chronic mye](#)
- [Antigen](#) • [Chronic mye](#)
- [Apoptosi](#) • [Circadian rhy](#)
- [Apoptosi](#) • [Circadian rhy](#)
- [Arrhythm](#) • [Circadian rhy](#)
- [Asthma](#) • [Collecting d](#)
- [Autoimm](#) • [Colorectal c](#)
- [Axon gui](#) • [Colorectal c](#)
- [B cell rec](#) • [Complemer](#)
- [Bacterial](#) • [Cytokine-cy](#)
- [Bacterial](#) • [Cytosolic DI](#)
- [Bacterial](#) • [Dilated card](#)
- [Basal ce](#) • [DNA replica](#)
- [Basal tra](#) • [Dorso-ventr](#)
- [Base exc](#) • [ECM-recept](#)
- [Bile secr](#) • [Endocrine a](#)
- [Bladder](#) • [Endocytosis](#)
- [Bladder](#) • [Endometrial](#)
- [Calcium](#) • [Epithelial ce](#)
- [Carbohy](#) • [ErbB signali](#)
- [Cardiac](#) • [Fat digestio](#)
- [Cell adhesi](#) • [Glutamaterg](#)
- [Cell cycle \(f](#) • [GnRH signaling](#)
- [Cell cycle - c](#) • [Graft-versus-ho](#)
- [Cell cycle - v](#) • [Hedgehog signaling](#)
- [Chagas dise](#) • [Hematopoietic](#)
- [Chemokine](#) • [Hepatitis C](#)
- [Cholinergic](#) • [Hepatitis C \(Ho](#)
- [Chronic mye](#) • [Homologous re](#)
- [Chronic mye](#) • [Huntington's di](#)
- [Circadian rhy](#) • [Huntington's di](#)
- [Circadian rhy](#) • [Hypertrophic car](#)
- [Circadian rhy](#) • [Influenza A](#)
- [Collecting d](#) • [Insulin signaling](#)
- [Colorectal c](#) • [Intestinal immune](#)
- [Colorectal c](#) • [Jak-STAT signa](#)
- [Complemer](#) • [Leishmaniasis](#)
- [Cytokine-cy](#) • [Leukocyte transendo](#)
- [Cytosolic DI](#) • [Long-term depressi](#)
- [Dilated card](#) • [Long-term potenti](#)
- [DNA replica](#) • [Lysosome](#)
- [Dorso-ventr](#) • [Malaria](#)
- [ECM-recept](#) • [MAPK signaling pa](#)
- [Endocrine a](#) • [MAPK signaling pa](#)
- [Endocytosis](#) • [MAPK signaling pa](#)
- [Endometrial](#) • [Maturity onset dia](#)
- [Epithelial ce](#) • [Measles](#)
- [ErbB signali](#) • [Meiosis - yeast](#)
- [Fat digestio](#) • [Melanogenesis](#)
- [Glutamaterg](#) • [Melanoma](#)



Path2Models: non-metabolic



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- [Amoebia](#) • [Chemokine](#)
- [Amyotro](#) • [Cholinergic](#)
- [Amyotro](#) • [Chronic mye](#)
- [Antigen](#) • [Chronic mye](#)
- [Apoptosi](#) • [Circadian rhy](#)
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- [Bacterial](#) • [Cytokine-cy](#)
- [Bacterial](#) • [Cytosolic DI](#)
- [Bacterial](#) • [Dilated card](#)
- [Basal ce](#) • [DNA rep/c](#)
- [Basal tra](#) • [Dorsal-ventr](#)
- [Base exc](#) • [ECM-recept](#)
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- [Collecting d](#) • [Insulin signaling](#)
- [Colorectal c](#) • [Intestinal immune](#)
- [Colorectal c](#) • [Jak-STAT signaling](#)
- [Complemer](#) • [Leishmaniasis](#)
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- [Cytosolic DI](#) • [Long-term depressi](#)
- [Dilated card](#) • [Long-term potenti](#)
- [DNA rep/c](#) • [Lysosome](#)
- [Dorsal-ventr](#) • [Malaria](#)
- [ECM-recept](#) • [MAPK signaling pa](#)
- [Endocrine a](#) • [MAPK signaling pa](#)
- [Endocytosis](#) • [MAPK signaling pa](#)
- [Endometrial](#) • [Maturity onset diab](#)
- [Epithelial ce](#) • [Measles](#)
- [ErbB signali](#) • [Meiosis - yeast](#)
- [Fat digestio](#) • [Melanogenesis](#)
- [Glutamaterg](#) • [Melanoma](#)



Path2Models: Malaria



Here are all the organisms which have a model about **Malaria**:

- [Ailuropoda melanoleuca](#)
- [Bos taurus](#)
- [Canis familiaris](#)
- [Equus caballus](#)
- [Homo sapiens](#)
- [Macaca mulatta](#)
- [Monodelphis domestica](#)
- [Mus musculus](#)
- [Ornithorhynchus anatinus](#)
- [Pan troglodytes](#)
- [Plasmodium berghei \(strain Anka\)](#)
- [Plasmodium chabaudi chabaudi](#)
- [Plasmodium falciparum \(isolate 3D7\)](#)
- [Plasmodium falciparum \(isolate Dd2\)](#)
- [Plasmodium falciparum \(isolate HB3\)](#)
- [Plasmodium knowlesi \(strain H\)](#)
- [Plasmodium vivax \(strain Salvador I\)](#)
- [Plasmodium yoelii yoelii 17XNL](#)
- [Pongo abelii](#)
- [Rattus norvegicus](#)
- [Sus scrofa](#)



Path2Models: Malaria



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- [Pan troglodytes](#)
- [Plasmodium berghei \(strain Anka\)](#)
- [Plasmodium chabaudi chabaudi](#)
- [Plasmodium falciparum \(isolate 3D7\)](#)
- [Plasmodium falciparum \(isolate Dd2\)](#)
- [Plasmodium falciparum \(isolate HB3\)](#)
- [Plasmodium knowlesi \(strain H\)](#)
- [Plasmodium vivax \(strain Salvador I\)](#)
- [Plasmodium yoelii yoelii 17XNL](#)
- [Pongo abelii](#)
- [Rattus norvegicus](#)
- [Sus scrofa](#)



Malaria - Homo sapiens

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

Model information

Identifier: [BMID000000017795](#)**Format:** SBML L3 V1 (Layout, Qualitative Models)**Project:** [path2models](#)**Categories:** [non-metabolic](#)**Submission:** 17 May 2012 16:59:53 UTC**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:



Search

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.
- 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)

Search





Path2Models: search

Here are the 147 models from the [Path2Models project](#) returned by a search for **malaria**:

Model name	Organism	Last modified
Malaria	Plasmodium chabaudi chabaudi	17 May 2012 15:03:31 UTC
Malaria	Plasmodium yoelii yoelii 17XNL	17 May 2012 16:06:58 UTC
Malaria	Plasmodium berghei (strain Anka)	17 May 2012 16:56:27 UTC
Malaria	Plasmodium falciparum (isolate Dd2)	17 May 2012 15:43:10 UTC
Malaria	Plasmodium falciparum (isolate HB3)	17 May 2012 17:19:05 UTC
Malaria	Plasmodium knowlesi (strain H)	17 May 2012 15:57:52 UTC
Malaria	Plasmodium vivax (strain Salvador I)	17 May 2012 14:05:16 UTC
Malaria	Ornithorhynchus anatinus	17 May 2012 17:58:46 UTC
Malaria	Monodelphis domestica	17 May 2012 16:31:48 UTC
Malaria	Plasmodium falciparum (isolate 3D7)	17 May 2012 16:56:58 UTC
Malaria	Ailuropoda melanoleuca	17 May 2012 14:41:36 UTC
Malaria	Sus scrofa	17 May 2012 18:37:23 UTC
Malaria	Equus caballus	17 May 2012 17:01:34 UTC
Malaria	Pongo abelii	17 May 2012 16:46:55 UTC
Malaria	Homo sapiens	17 May 2012 16:59:53 UTC
Malaria	Mus musculus	17 May 2012 14:21:12 UTC
Malaria	Canis familiaris	17 May 2012 15:22:16 UTC
Malaria	Macaca mulatta	17 May 2012 14:46:24 UTC

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
Models	112,898	27,306	1,846	142,050
Species	32,594,642	844,098	6,356,779	39,795,519
Relations	5,591,318	1,926	4,954,345	10,547,589
Annotations	404,248,120	16,914,269	22,861,664	444,024,053



EBI

Finja Büchel (*)

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