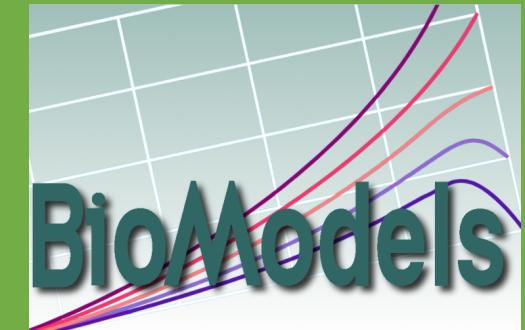


# BioModels Database

Camille Laibe



HARMONY 2012, 21-25th May 2012, Maastricht

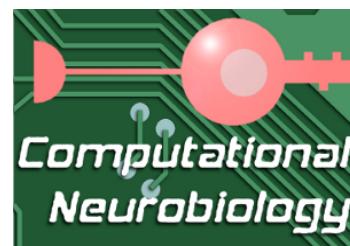
EBI is an Outstation of the European Molecular Biology Laboratory.

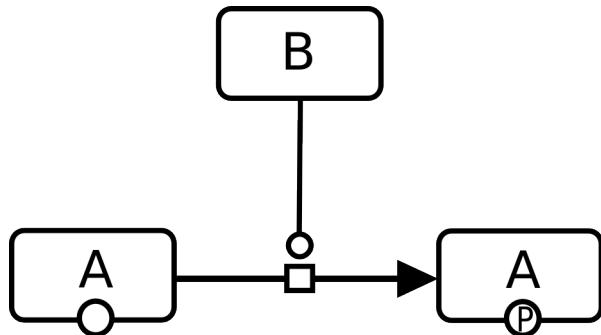


## ■ BioModels.net team

Technology part of the *Computational Systems Neurobiology* group  
(Nicolas Le Novère) at EMBL-EBI

- **Standards:** Minimal Information Required In the Annotation of Models (MIRIAM), Minimal Information About a Simulation Experiment (MIASE), Systems Biology Graphical Notation (SBGN), ...
- **Formats:** Systems Biology Markup Language (SBML), Simulation Experiment Description Markup Language (SED-ML), ...
- **Ontologies:** Systems Biology Ontology (SBO), Kinetic Simulation Algorithm Ontology (KiSAO), TErminology for the Description of DYnamics (TEDDY), ...
- **Services:** **BioModels Database**, MIRIAM Registry, Identifiers.org, ...
- **Tools:** libSBML, JSBML, SBFC, SBMLEditor, ...



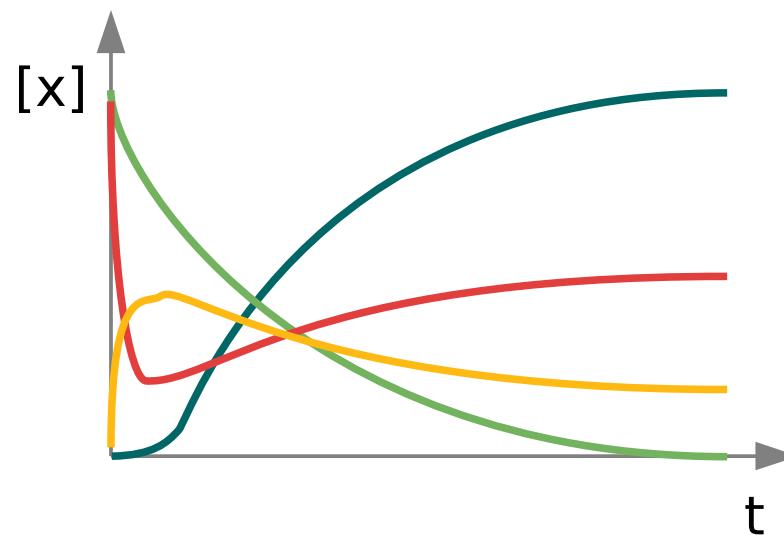


$$\frac{d[A]}{dt} = -k_1[B][A] + k_2[A\_B]$$

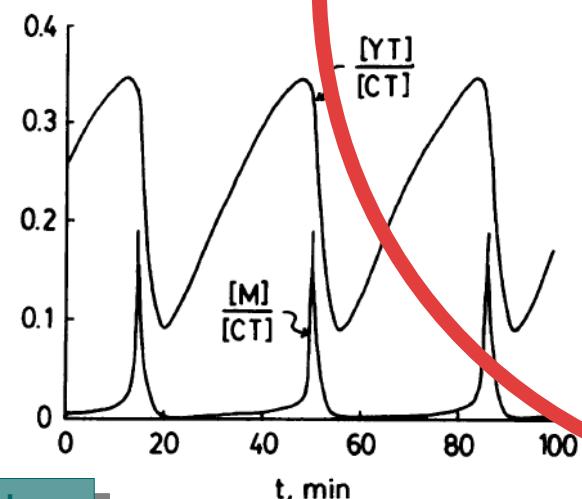
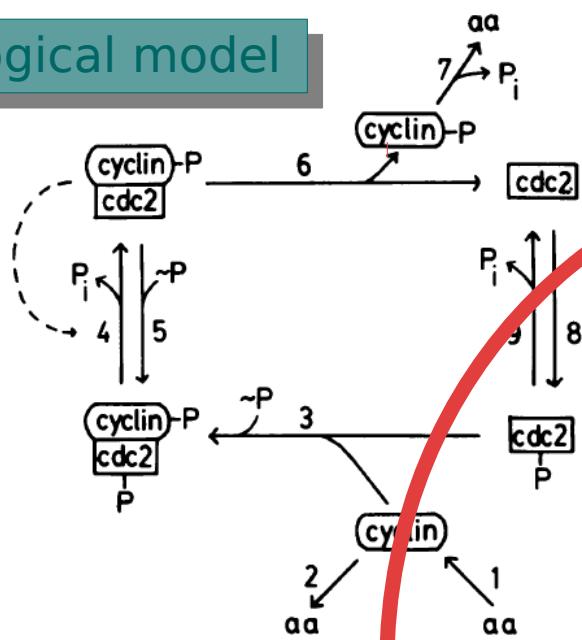
$$\frac{d[Ap]}{dt} = +k_3[A\_B]$$

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

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



## biological model



## simulation

## mathematical model

$$\begin{aligned}
 \frac{d[C2]}{dt} &= k_6[M] - k_8[\sim P][C2] + k_9[CP] \\
 \frac{d[CP]}{dt} &= -k_3[CP][Y] + k_8[\sim P][C2] - k_9[CP] \\
 \frac{d[pM]}{dt} &= k_3[CP][Y] - [pM]F([M]) + k_5[\sim P][M] \\
 \frac{d[M]}{dt} &= [pM]F([M]) - k_5[\sim P][M] - k_6[M] \\
 \frac{d[Y]}{dt} &= k_1[aa] - k_2[Y] - k_3[CP][Y] \\
 \frac{d[YP]}{dt} &= k_6[M] - k_8[YP]
 \end{aligned}$$

Parameter	Value	Notes
$k_1[aa]/[CT]$	$0.015 \text{ min}^{-1}$	*
$k_2$	0	†
$k_3[CT]$	$200 \text{ min}^{-1}$	*
$k_4$	$10-1000 \text{ min}^{-1}$ (adjustable)	
$k_4'$	$0.018 \text{ min}^{-1}$	
$k_5[\sim P]$	0	‡
$k_6$	$0.1-10 \text{ min}^{-1}$ (adjustable)	
$k_7$	$0.6 \text{ min}^{-1}$	†
$k_8[\sim P]$	$>>k_9$	§
$k_9$	$>>k_6$	§

## computational model



- 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:

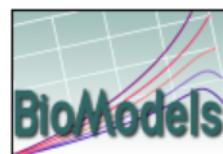
- **find**
- **understand**
- **reuse**
- **combine**

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](#).



[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](#)

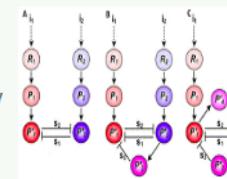
<http://www.ebi.ac.uk/biomodels/>

### Model of the month

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...](#)

8th February 2012 **Twenty-first Release of BioModels Database!**

- 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
- ...



■ signal transduction (GO:0007165)

■ metabolic process (GO:0008152)

■ multicellular organismal\_process (GO:0032501)

■ rhythmic process (GO:0048511)

■ cell cycle (GO:0007049)

■ homeostatic process (GO:0042592)

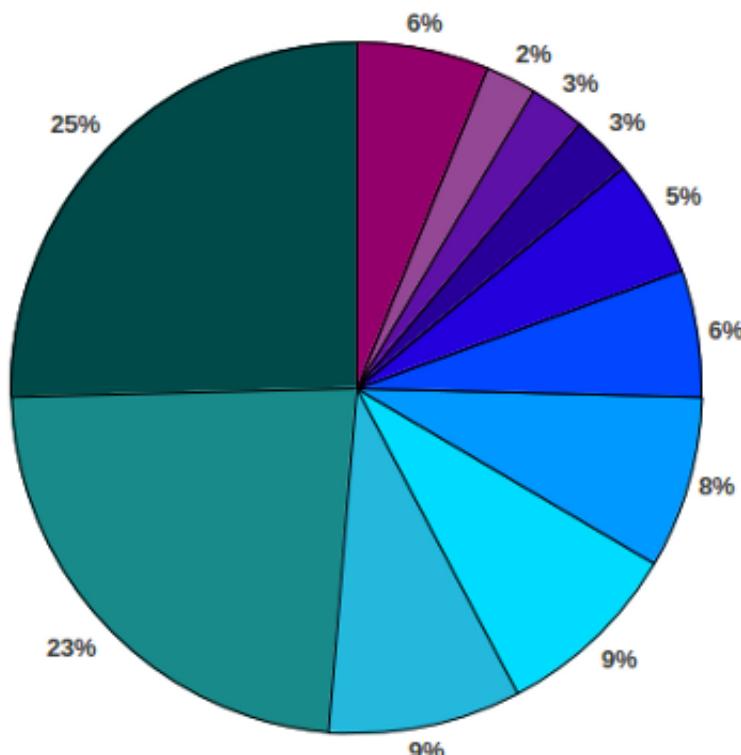
■ response to stimulus (GO:0050896)

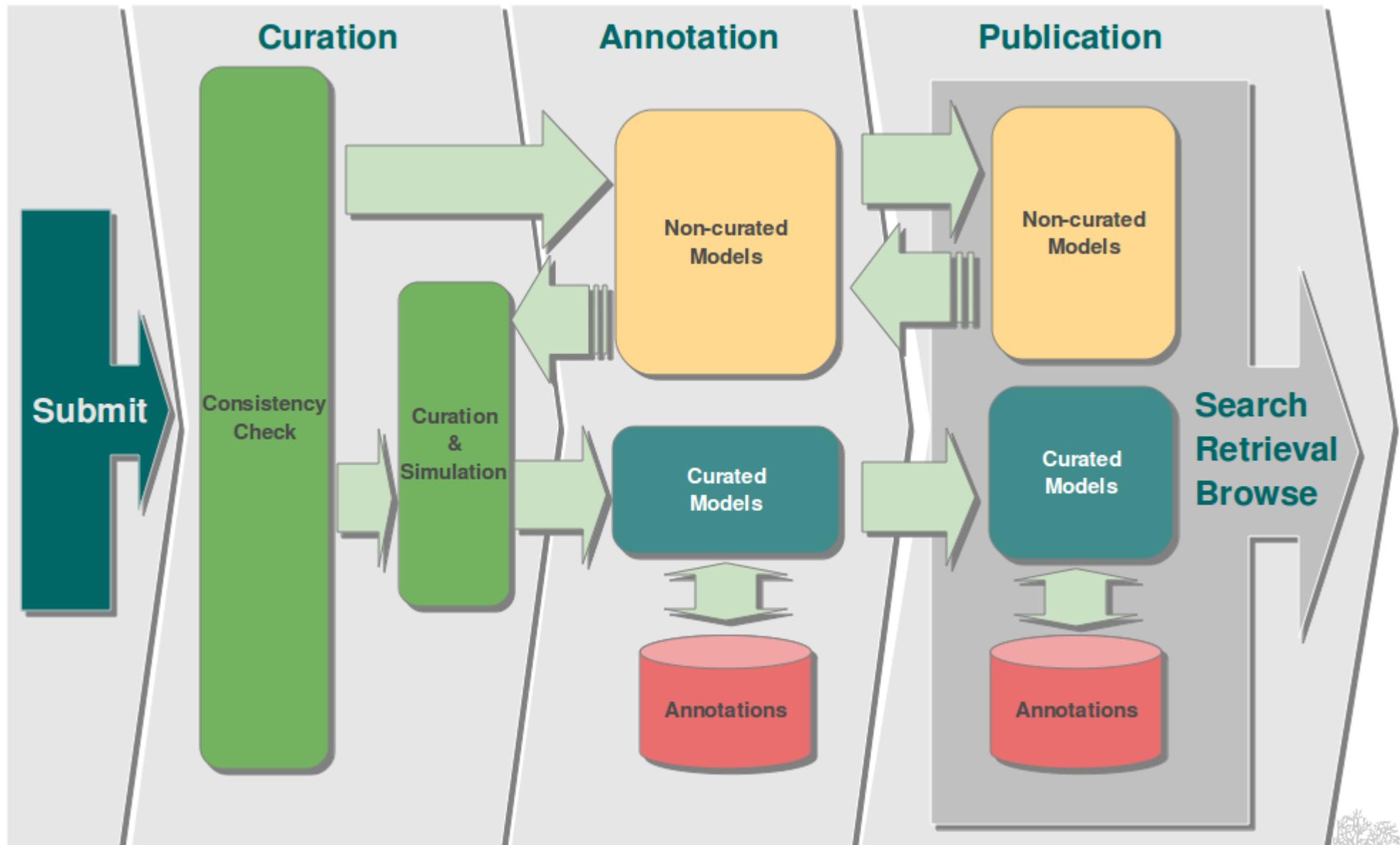
■ cell death (GO:0008219)

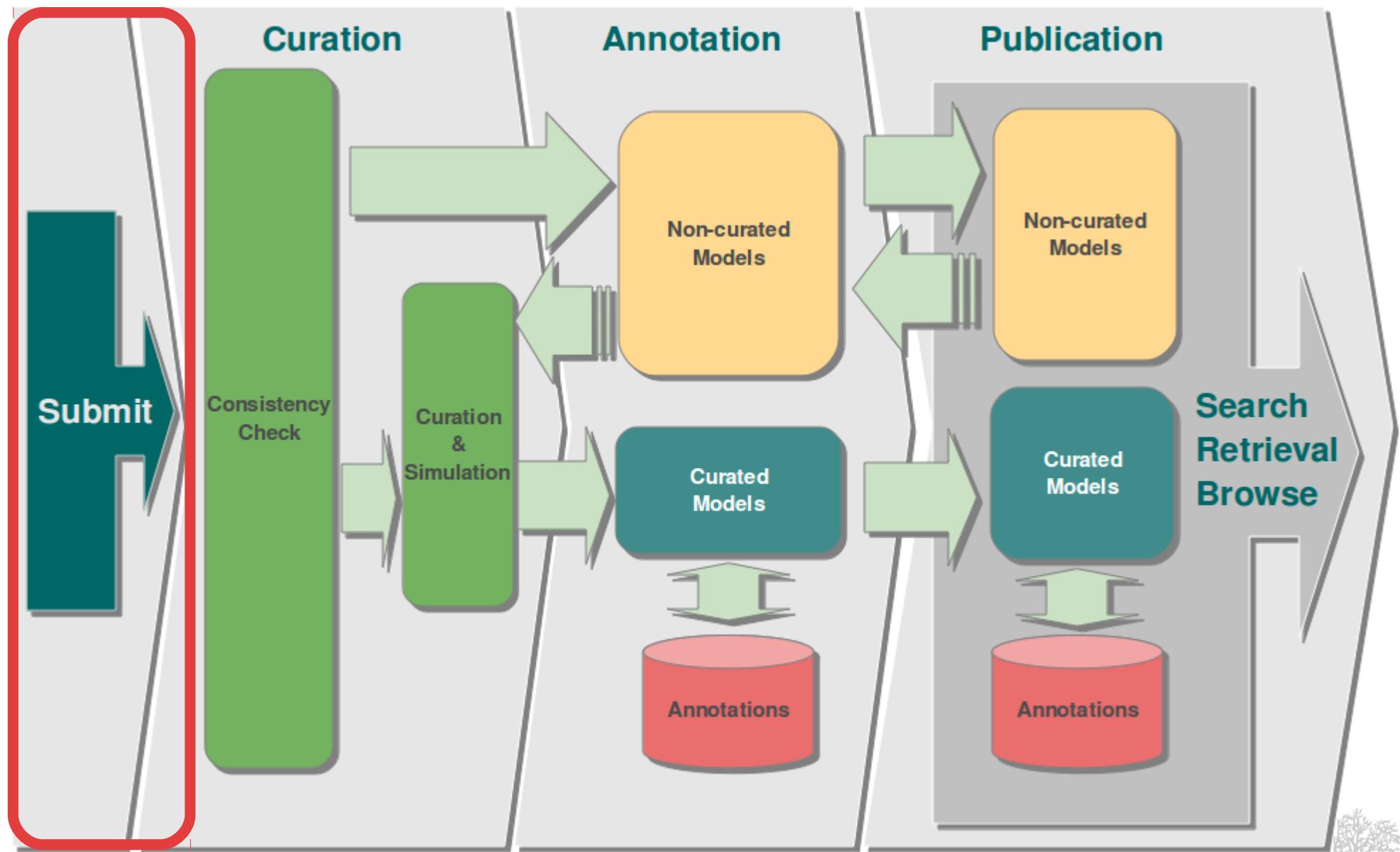
■ localization (GO:0051179)

■ channel activity (GO:0015267)

■ others (notably includes cellular developmental process (GO:0048869); catalytic activity (GO:0003824) and entry into host cell (GO:0030260) among few others)







- From **authors** prior to publication

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

- Molecular Systems Biology
- All PLoS journals
- All BioMedCentral journals
- ...

- Submitted by **curators**

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

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

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



# 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:**

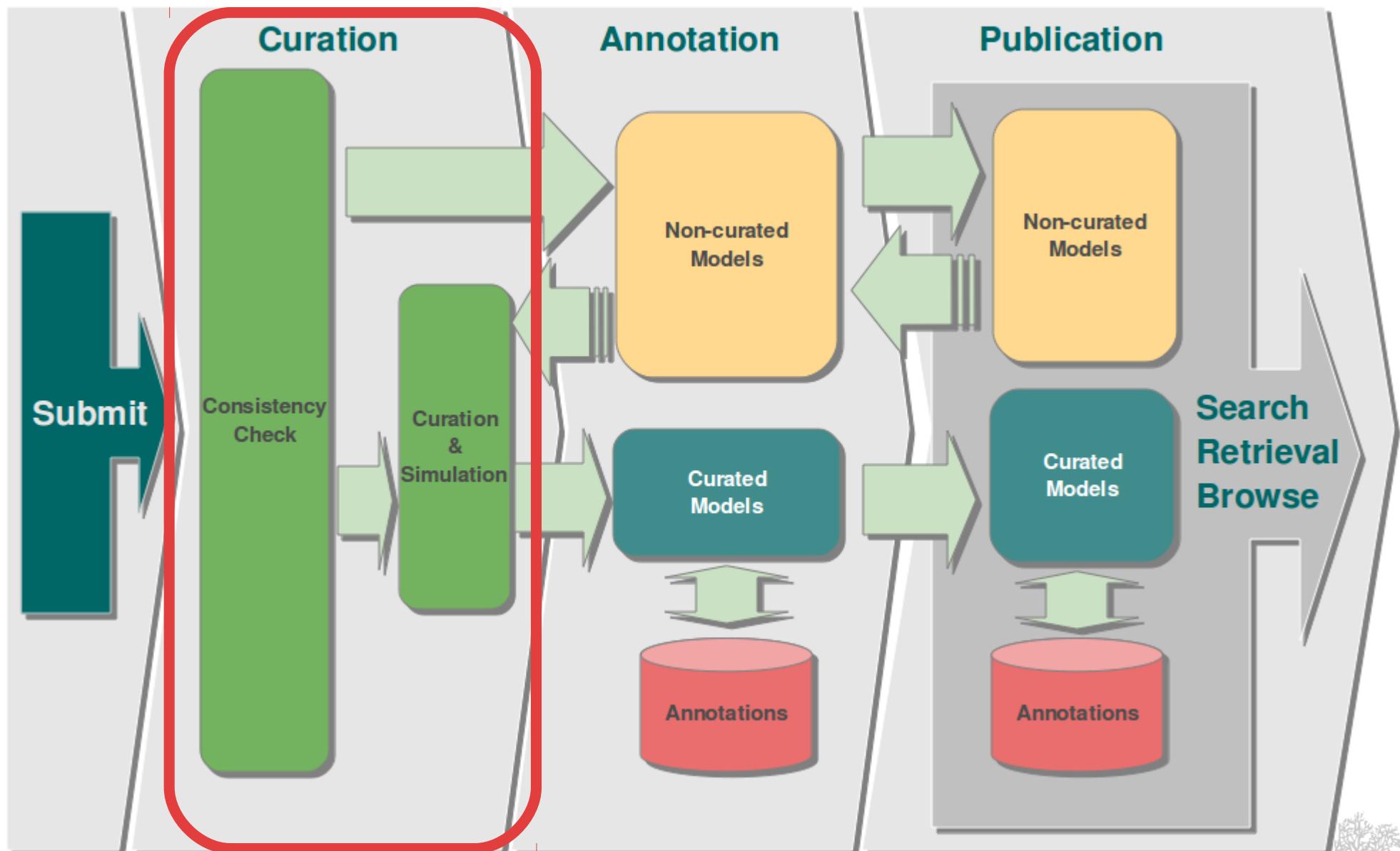
**Email:**

**Comment:**

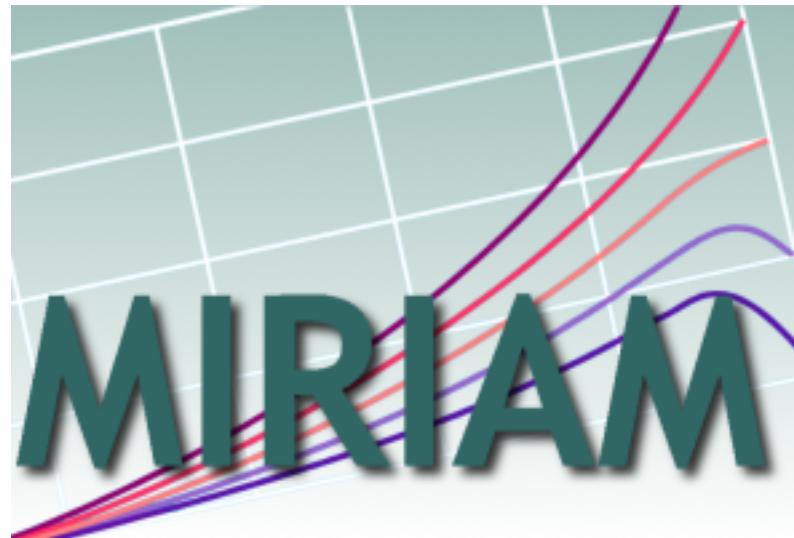
**Original model:**

**Model file:**

 [Browse...](#)



# The Minimum Information Required In the Annotation of a Model



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



 **PERSPECTIVE**

## Minimum information requested in the annotation of biochemical models (MIRIAM)

Nicolas Le Novère<sup>1,15</sup>, Andrew Finney<sup>2,15</sup>, Michael Hucka<sup>3</sup>, Upinder S Bhalla<sup>4</sup>, Fabien Campagne<sup>5</sup>, Julio Collado-Vides<sup>6</sup>, Edmund J Crampin<sup>7</sup>, Matt Halstead<sup>7</sup>, Edda Klipp<sup>8</sup>, Pedro Mendes<sup>9</sup>, Poul Nielsen<sup>7</sup>, Herbert Sauro<sup>10</sup>, Bruce Shapiro<sup>11</sup>, Jacky L Snoep<sup>12</sup>, Hugh D Spence<sup>13</sup> & Barry L Wanner<sup>14</sup>

Most of the published quantitative models in biology are lost for the community because they are either not made available or they are insufficiently characterized to allow them to be reused. The lack of a standard description format, lack of stringent reviewing and authors' carelessness are the main causes for incomplete model descriptions. With today's increased interest in detailed biochemical models, it is necessary to define a minimum quality standard for the encoding of those models. We propose a set of rules for curating quantitative models of biological systems. These rules define procedures for encoding and annotating models represented in machine-readable form. We believe their application will enable users to (i) have confidence that curated models are an accurate reflection of their associated reference descriptions, (ii) search collections of curated models with precision, (iii) quickly identify the biological phenomena that a given curated model or model constituent represents and (iv) facilitate model reuse and composition into large subcellular models.

**Box 1 Glossary**

Some terms are used in a very specific way throughout the article. We provide here a precise definition of each one.

**Quantitative biochemical model.** A formal model of a biological system, based on the mathematical description of its molecular and cellular components, and the interactions between those components.

**Encoded model.** A mathematical model written in a formal machine-readable language, such that it can be systematically parsed and employed by simulation and analysis software without further human translation.

**MIRIAM-compliant model.** A model that passes all the tests and fulfills all the conditions listed in MIRIAM.

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

**Curation process.** The process by which the compliance of an encoded model with MIRIAM is achieved and/or verified. The curation process may encompass some or all of the following tasks: encoding of the model, verification of the reference correspondence and annotation of the model.

**Reference correspondence.** The fact that the structure of a model and the results of a simulation or an analysis match the information present in the reference description.

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Published online 6 December 2005; doi:10.1038/nbt1156

NATURE BIOTECHNOLOGY VOLUME 23 NUMBER 12 DECEMBER 2005

1509

- set of guidelines for the curation and annotation of quantitative models
- about encoding and annotation
- applicable to **any structured model format**

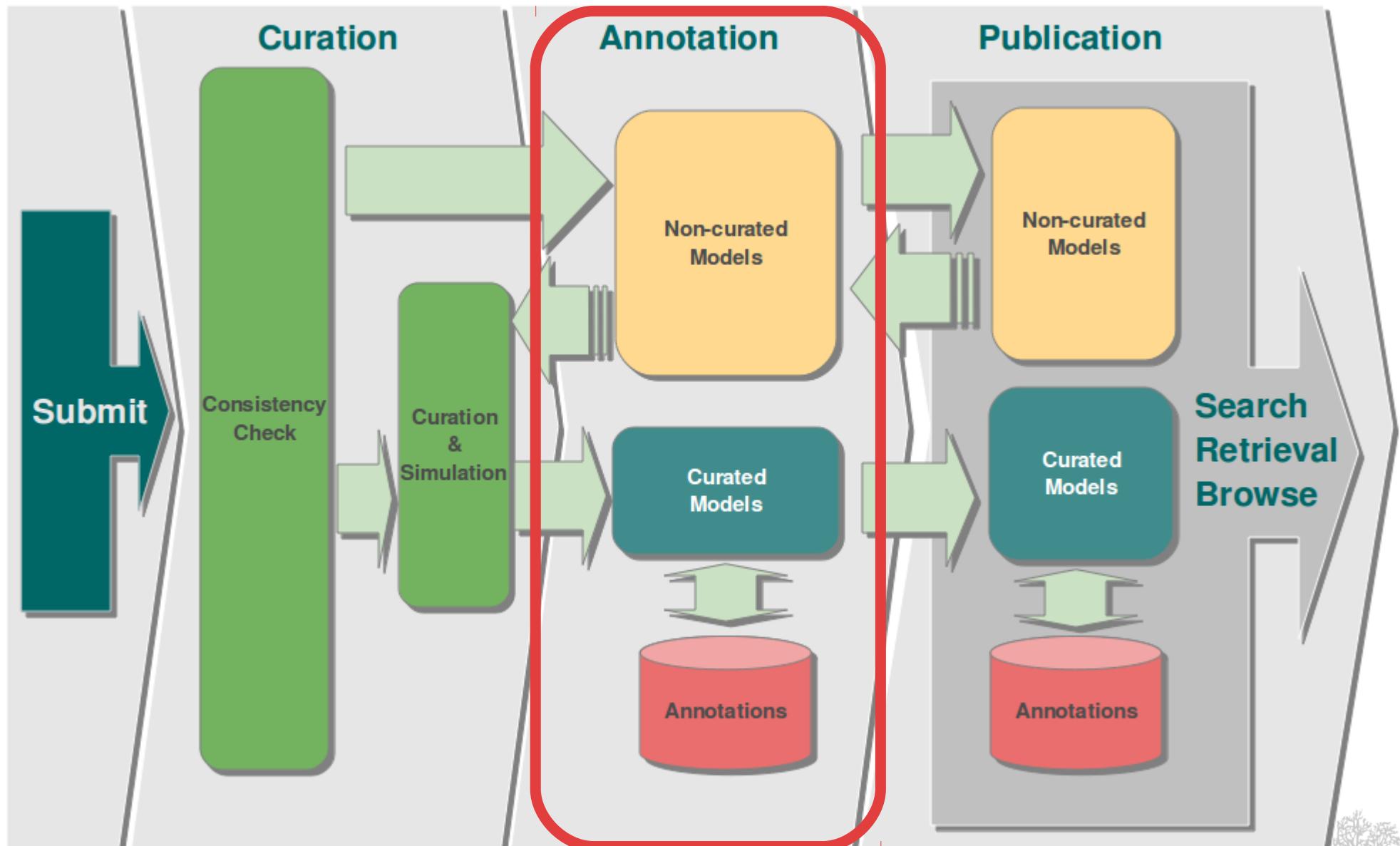
cf. Nicolas Le Novère *et al.* Minimum Information Requested in the Annotation of biochemical Models (MIRIAM). *Nature Biotechnology*, 2005



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**





- **Curated branch**

MIRIAM compliant models

- **Non-curated branch**

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 moved to curated branch in the near future



**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!*



- **Unique and unambiguous**

an identifier must never be assigned to two different objects

- **Perennial**

the identifier is constant and its lifetime is permanent

- **Standards compliant**

must conform on existing *standards*, such as URI

- **Resolvable**

identifiers must be able to be transformed into locations of online resources storing the object or information about the object

- **Free of use**

everybody should be able to use and create identifiers, freely and at no cost



## Namespace

Identifies a  
data collection

from a shared list of  
*namespaces*

## Entity identifier

Identifies a data  
entry within the  
data collection

provided by the  
data collection

unique within the  
data collection

format defined by  
the data collection



## ■ MIRIAM Registry

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

Human calmodulin: P62158 in UniProt

➡ urn:miriam:uniprot:P62158

Alcohol dehydrogenase: 1.1.1.1 in Enzyme Nomenclature

➡ urn:miriam:ec-code:1.1.1.1

Activation of MAPKK activity: GO:0000186 in Gene Ontology

➡ urn:miriam:obo.go:GO%3A0000186



## 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>

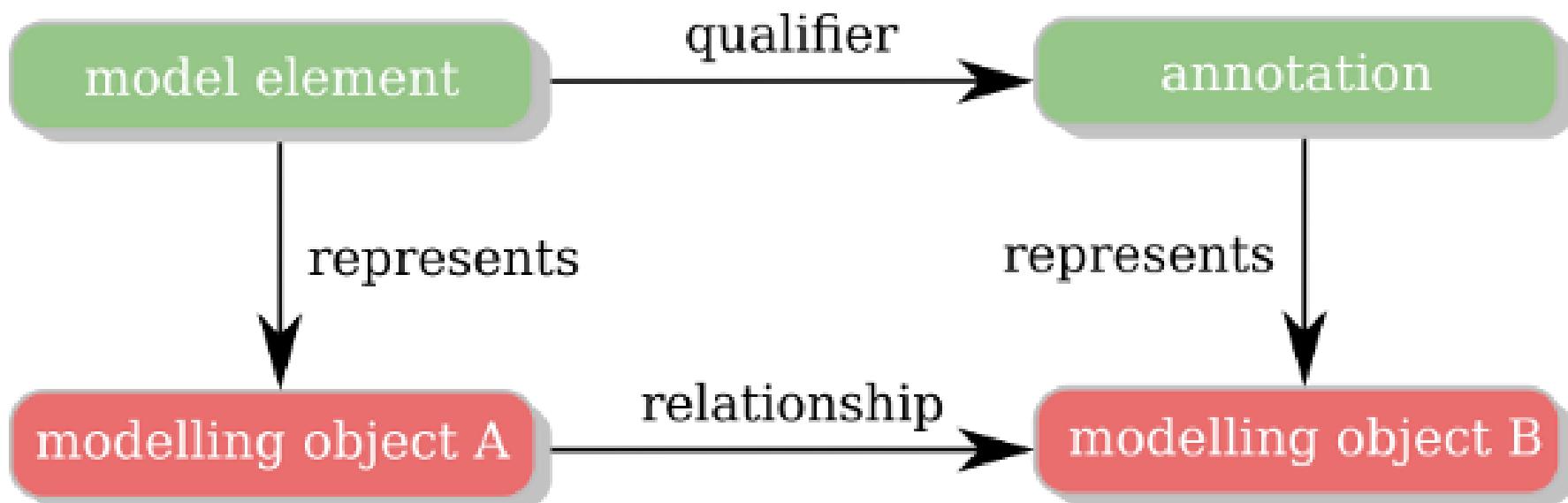
Alcohol dehydrogenase: 1.1.1.1 in Enzyme Nomenclature

→ <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>





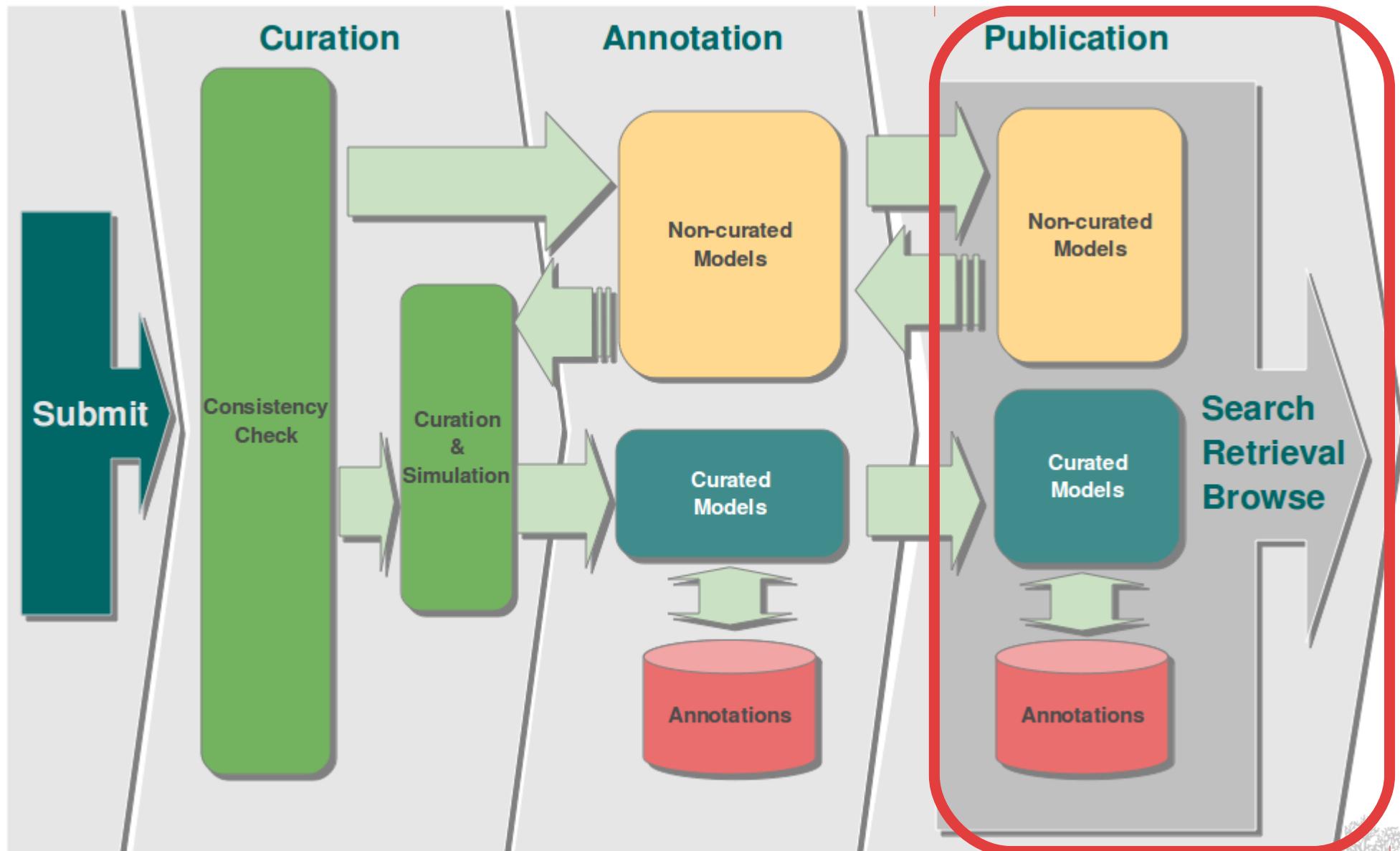
- bqmodel:is
- bqmodel:isDerivedFrom
- bqmodel:isDescribedBy
  
- bqbiol:is
- bqbiol:isDescribedBy
- bqbiol:hasPart
- bqbiol:hasProperty
- bqbiol:isPartOf
  
- bqbiol:isPropertyOf
- bqbiol:isVersionOf
- bqbiol:hasVersion
- bqbiol:isHomologTo
- bqbiol:isDescribedBy
- bqbiol:encodes
- bqbiol:isEncodedBy
- 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](#)

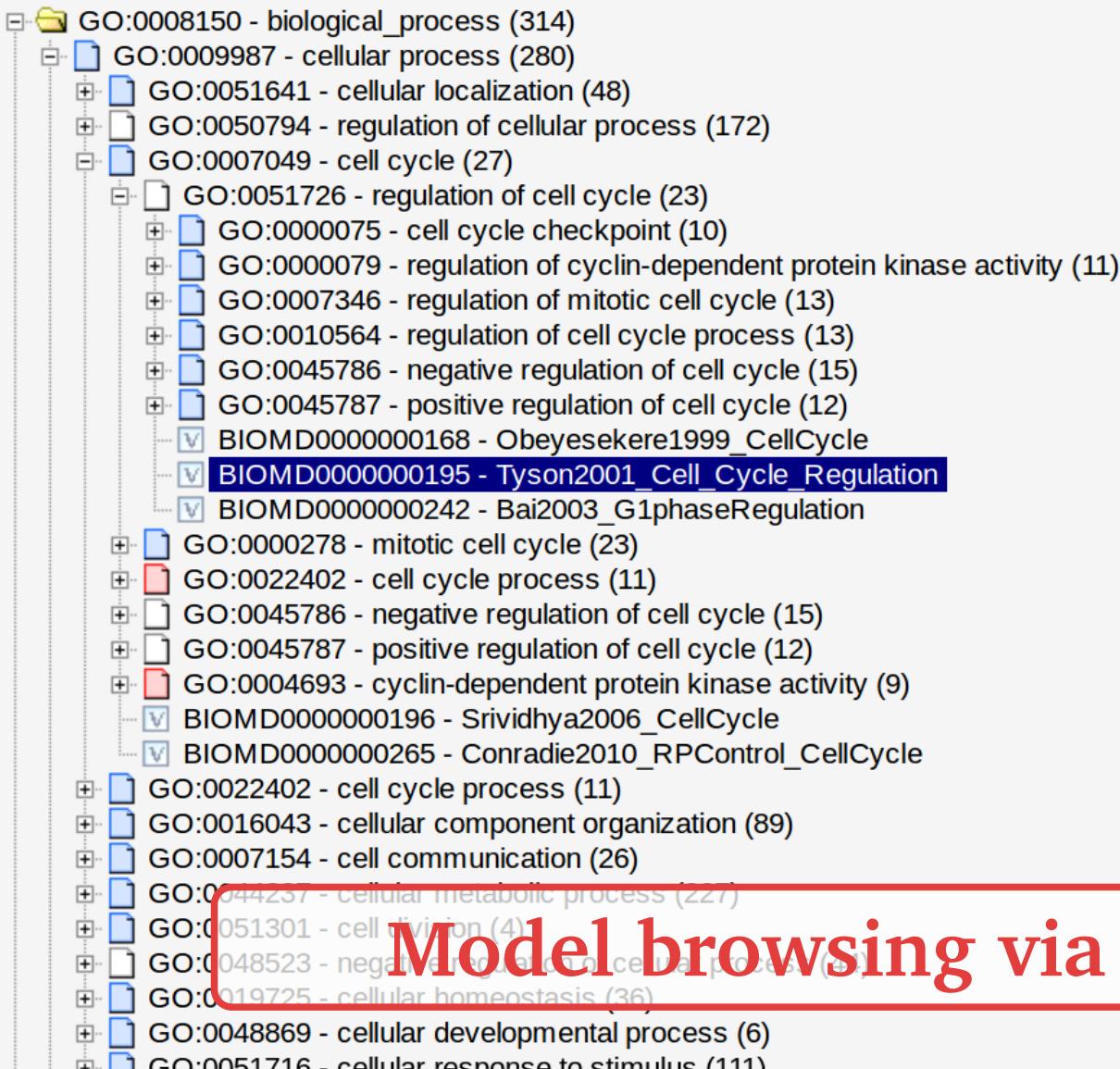
BioModels ID	Name	Publication ID	Last Modified
<a href="#">BIOMD0000000279</a>	Komarova2005_PTHaction_OsteoclastOsteoblastCoupling	<a href="#">15860557</a>	2011-12-20T15:45:46+00:00
<a href="#">BIOMD0000000403</a>	Ayati2010_BoneRemodelingDynamics_WithTumour+DrugTreatment	<a href="#">20406449</a>	2011-12-20T14:45:58+00:00
<a href="#">BIOMD0000000402</a>	Ayati2010_BoneRemodelingDynamics_WithTumour	<a href="#">20406449</a>	2011-12-20T14:43:23+00:00
<a href="#">BIOMD0000000401</a>	Ayati2010_BoneRemodelingDynamics_NormalCondition	<a href="#">20406449</a>	2011-12-20T14:40:44+00:00
<a href="#">BIOMD0000000305</a>	Kolomeisky2003_MyosinV_Processivity	<a href="#">12609867</a>	2011-11-04T14:34:07+00:00
<a href="#">BIOMD0000000356</a>	Nyman2011_M3Hierarchical_InsulinGlucosedynamics	<a href="#">21572040</a>	2011-11-01T17:27:21+00:00
<a href="#">BIOMD0000000137</a>	Sedaghat2002_InsulinSignalling_noFeedback	<a href="#">12376338</a>	2011-11-01T17:19:19+00:00
<a href="#">BIOMD0000000343</a>	Brannmark2010_InsulinSignalling_Mifamodel	<a href="#">20421297</a>	2011-11-01T17:18:37+00:00
<a href="#">BIOMD0000000379</a>	DallaMan2007_MealModel_GlucoseInsulinSystem	<a href="#">17926672</a>	2011-11-01T13:42:58+00:00
<a href="#">BIOMD0000000362</a>	Bulmeras2004_BloodCoagulation	<a href="#">15039440</a>	2011-09-02T10:16:08+00:00

# List of models

## Browse - Curated models



This is a tree view of the models in BioModels Database based on [Gene Ontology](#). To browse the models, please click to expand the branch, or click to collapse the branch. By double clicking the Gene Ontology term, the detail of the term will be displayed in a new window. By double clicking the BioModels Model ID, this page will be forwarded to the detail of selected model.



BioModels ID: [BIOMD0000000195](#)

Name: Tyson2001\_Cell\_Cycle\_Regulation

Publication ID: [11371178](#)

Last Modified: 2009-03-16T14:37:30+00:00

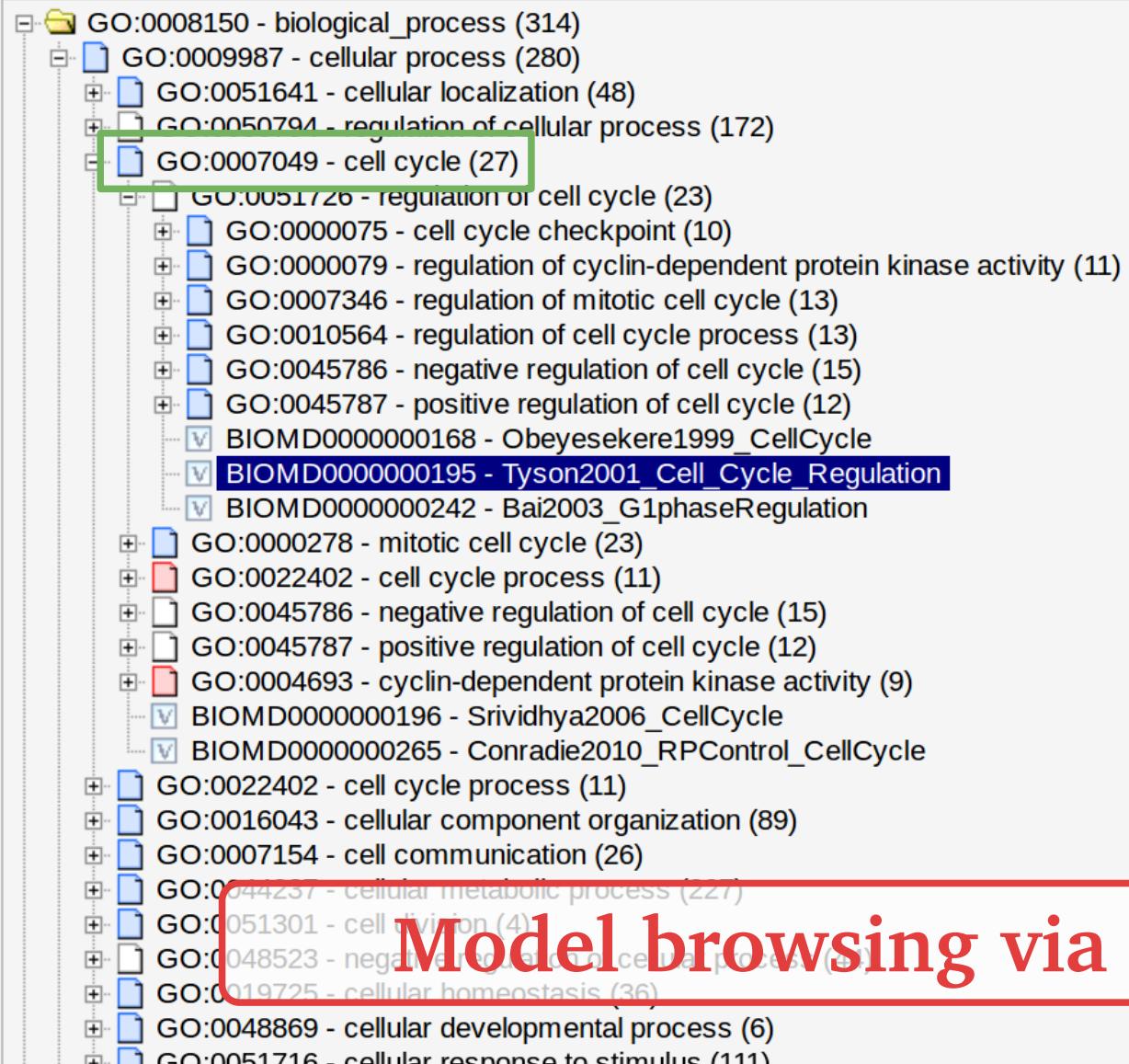
[SBML L2 V3](#)

Model browsing via GO terms

## Browse - Curated models



This is a tree view of the models in BioModels Database based on [Gene Ontology](#). To browse the models, please click to expand the branch, or click to collapse the branch. By double clicking the Gene Ontology term, the detail of the term will be displayed in a new window. By double clicking the BioModels Model ID, this page will be forwarded to the detail of selected model.



BioModels ID: [BIOMD0000000195](#)

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Publication ID: [11371178](#)

Last Modified: 2009-03-16T14:37:30+00:00

[SBML L2 V3](#)

## Model browsing via GO terms

## Taxonomy cloud

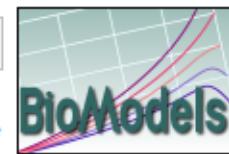


Here are all the taxonomic terms used to annotate the [curated models](#):

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

# Model browsing via Taxonomy

## 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](#).

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### Models published in the literature

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- [Browse curated models using GO](#)
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**Path2Models**    (*new*)

**Submit a model**

### Links

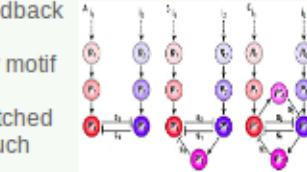
- [Main instance at EMBL-EBI, UK](#)
- [Mirror at Caltech, USA](#)
- [Project on SourceForge](#)
- [Web Services](#)
- [Download archived models](#)

## 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

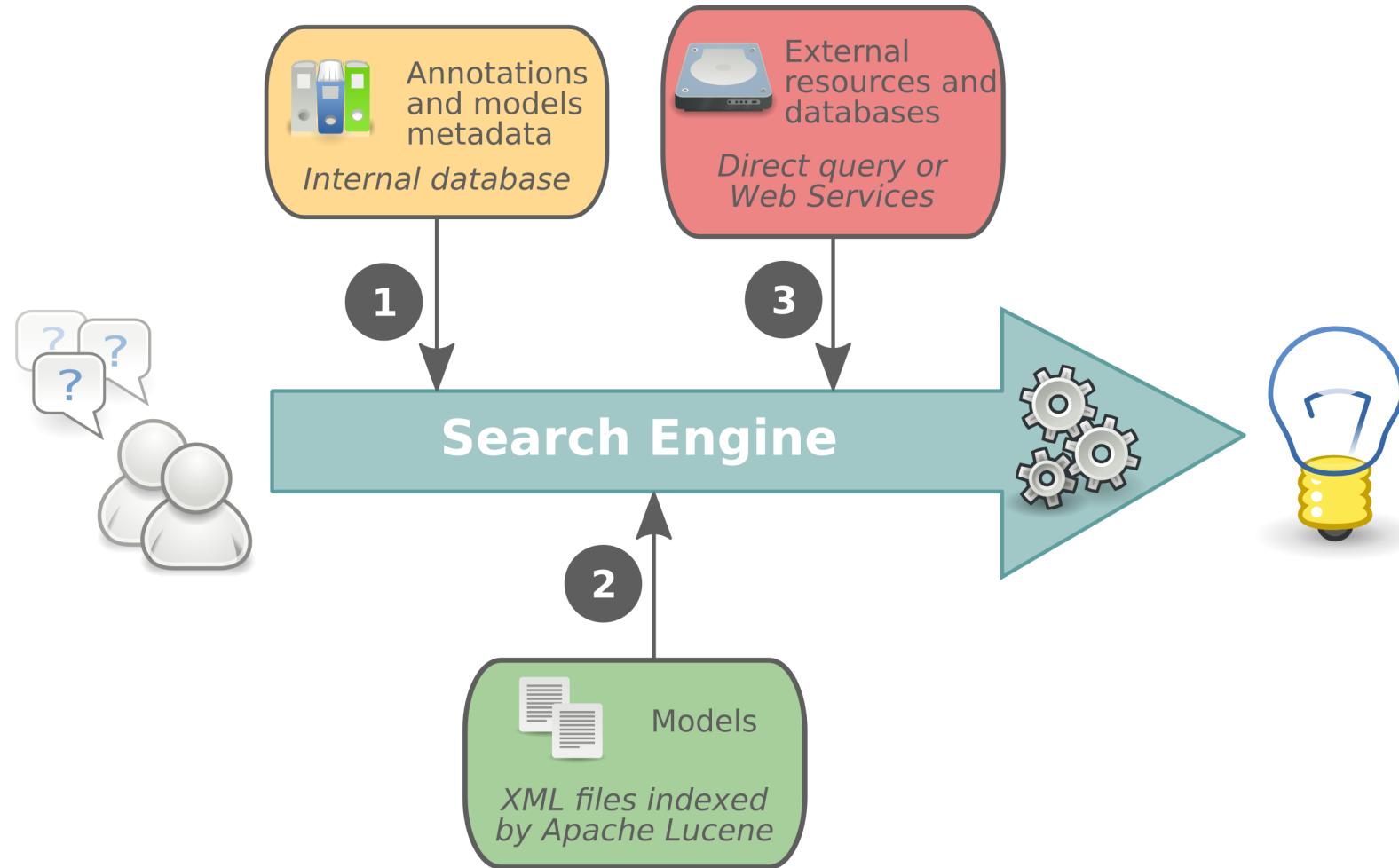
Annotation (identifier): PubChem-compound

Annotation (identifier): KEGG Reaction

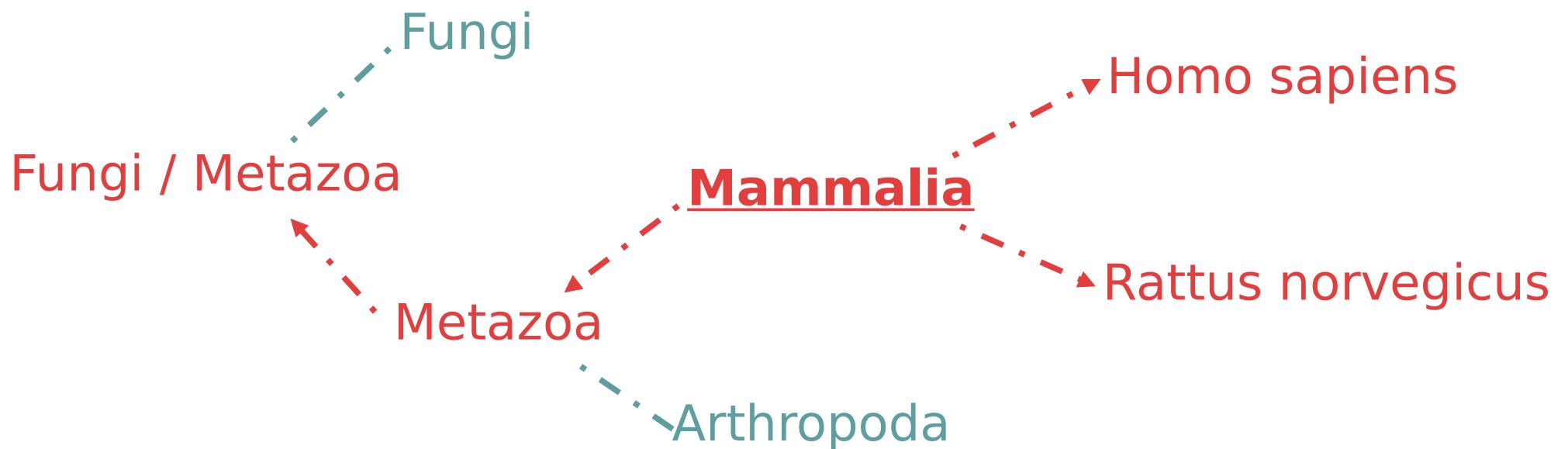
Annotation (identifier): Enzyme Nomenclature

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>
<a href="#">BIOMD0000000005</a>	Tyson1991_CellCycle_6var	<a href="#">1831270</a>	2008-04-22T21:31:27+00:00
<a href="#">BIOMD0000000006</a>	Tyson1991_CellCycle_2var	<a href="#">1831270</a>	2007-10-05T17:34:05+00:00
<a href="#">BIOMD0000000015</a>	Curto1998_purineMetabol	<a href="#">9664759</a>	2008-06-02T13:14:28+00:00
<a href="#">BIOMD0000000018</a>	Morrison1989_FolateCycle	<a href="#">2732237</a>	2007-09-25T09:31:06+00:00
<a href="#">BIOMD0000000024</a>	Scheper1999_CircClock	<a href="#">9870936</a>	2007-09-25T09:33:32+00:00
<a href="#">BIOMD0000000041</a>	Kongas2001_creatine	<a href="#">10.1038/npre.2007.13...</a>	2008-02-05T14:03:10+00:00
<a href="#">BIOMD0000000043</a>	Borghans1997_CaOscillation_model1	<a href="#">17029867</a>	2007-09-25T09:46:49+00:00
<a href="#">BIOMD0000000044</a>	Borghans1997_CaOscillation_model2	<a href="#">17029867</a>	2007-09-25T09:47:07+00:00
<a href="#">BIOMD0000000045</a>	Borghans1997_CaOscillation_model3	<a href="#">17029867</a>	2007-09-25T09:47:26+00:00
<a href="#">BIOMD0000000047</a>	Oxhamre2005_Ca_oscillation	<a href="#">15596518</a>	2007-09-25T09:48:07+00:00
<a href="#">BIOMD0000000048</a>	Kholodenko1999_EGFRsignaling	<a href="#">15514507</a>	2008-02-05T14:27:44+00:00
<a href="#">BIOMD0000000049</a>	Sasagawa2005_MAPK	<a href="#">15793571</a>	2007-09-25T09:48:55+00:00
<a href="#">BIOMD0000000054</a>	Ataullahkhanov1996_Adenylate	<a href="#">8733433</a>	2008-01-18T08:48:23+00:00
<a href="#">BIOMD0000000057</a>	Sneyd2002_IP3_Receptor	<a href="#">11842185</a>	2007-09-25T09:51:51+00:00
<a href="#">BIOMD0000000059</a>	Fridlyand2003_Calcium_flux	<a href="#">12644446</a>	2008-02-19T07:45:51+00:00
<a href="#">BIOMD0000000069</a>	Fuss2006_MitoticActivation	<a href="#">16873466</a>	2007-09-25T09:58:26+00:00
<a href="#">BIOMD0000000070</a>	Holzhtutter2004_Erythrocyte_Metabolism	<a href="#">15233787</a>	2007-09-25T09:58:55+00:00
<a href="#">BIOMD0000000073</a>	Leloup2003_CircClock_DD	<a href="#">12775757</a>	2007-09-25T10:00:03+00:00
<a href="#">BIOMD0000000081</a>	Suh2004_KCNQ_Regulation	<a href="#">15173220</a>	2007-09-25T10:03:07+00:00
<a href="#">BIOMD0000000088</a>	Maeda2006_MyosinPhosphorylation	<a href="#">16923126</a>	2007-09-25T10:05:59+00:00
<a href="#">BIOMD0000000093</a>	Yamada2003_JAK_STAT_pathway	<a href="#">12527385</a>	2007-09-25T10:08:21+00:00

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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

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 UTC

bqbiol:isHomologTo [Reactome REACT\\_152](#)

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

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

## Notes

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Goldbeter A.

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

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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**

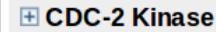
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Compartment: cell

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

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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

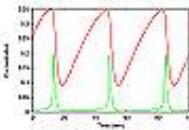
8355 [NCBI]

Taxonomic lineage

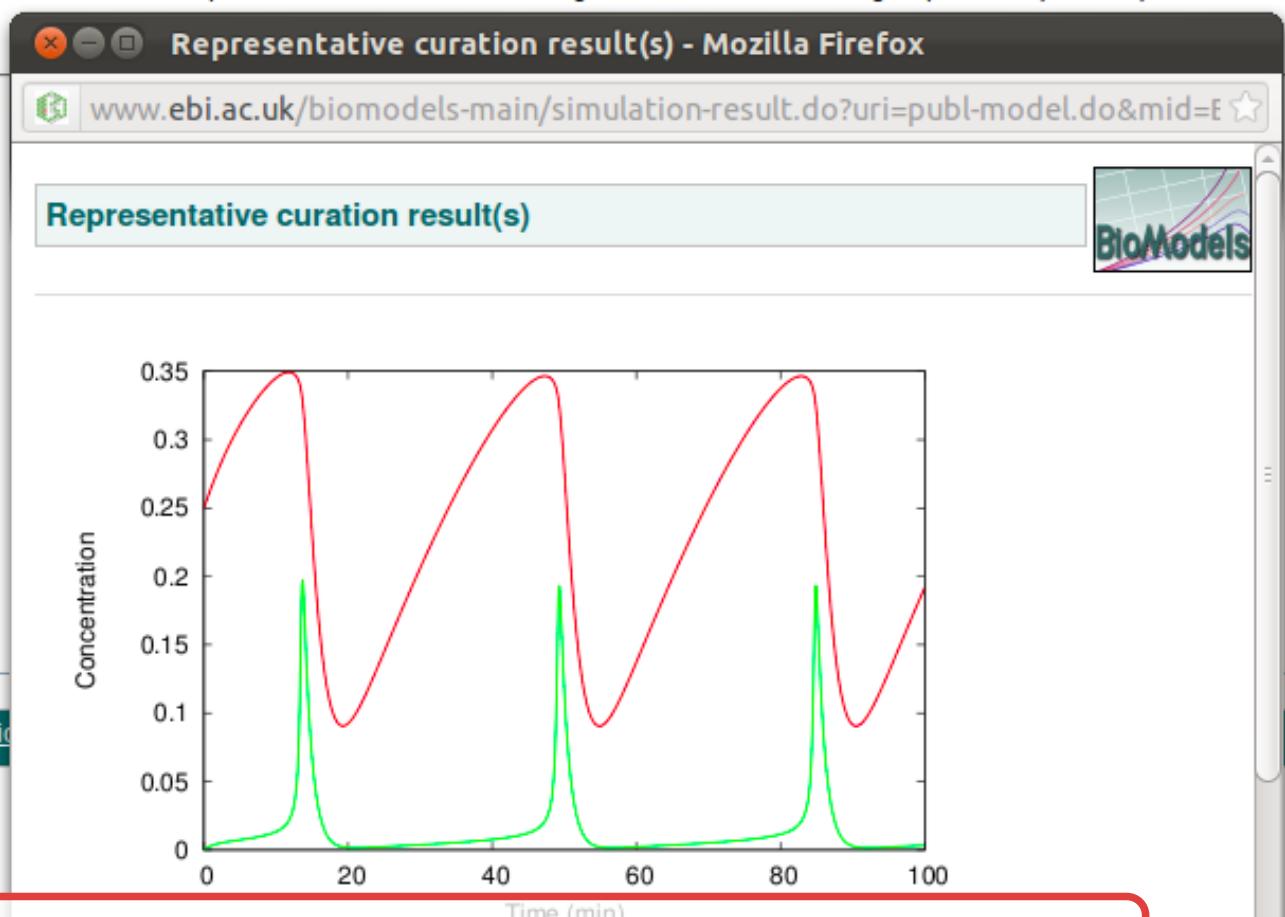
Eukaryota &gt; Metazoa &gt; Chordata &gt; Craniata &gt; Vertebrata &gt; Mesobatrachia &gt; Pipoidea &gt; Pipidae &gt; Xenopoda

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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).



## 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)

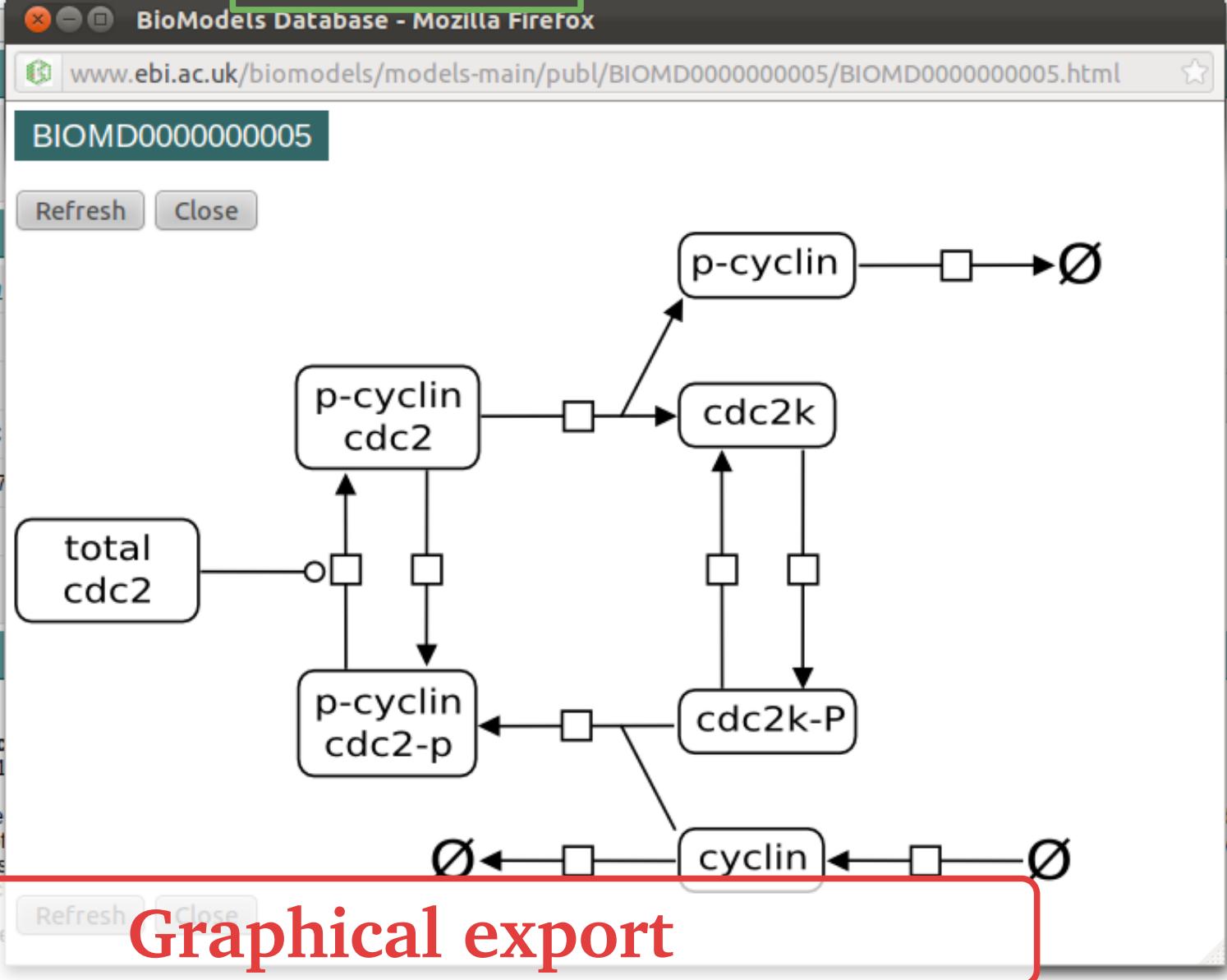
**Abstract:**

The proteins cdc2 and cyclin form a heterodimer. When cdc2 is bound to cyclin it is active. When cyclin is removed, cdc2 becomes inactive. When cdc2 is bound to p-cyclin it is inactive. When p-cyclin is removed, cdc2 becomes active. This model shows how a dimer of cdc2 and cyclin can act as a spontaneous oscillator, or as an excitable switch. It also shows how oscillations in cdc2 activity drive oscillations in cyclin levels. The model was used to predict oscillations in cdc2 activity and cyclin levels in early embryos, and the excitability switch behavior in response to external stimuli.

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

Department of Biology, Virginia Polytechnic Institute and State University, Blacksburg 24061.

[\[more\]](#)
[JWS Online Simulation](#)
[BioModels Online Simulation](#)
**Original Model:** [BIOMD0000000005.xml.origin](#)
**Submitter:** [Nicolas Le Novère](#)
**Submission ID:** MODEL6614644188

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

	bqbiol:occursIn	<a href="#">Taxonomy Opisthokonta</a>
set #1	bqbiol:isVersionOf	<a href="#">KEGG Pathway sce04111</a> <a href="#">Gene Ontology mitotic cell cycle</a>
	bqbiol:hasVersion	<a href="#">Reactome REACT_152</a>

## Model

## 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.

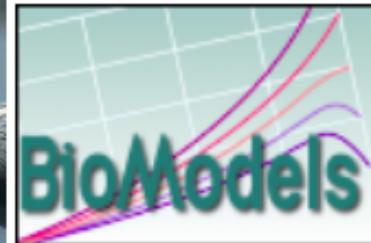
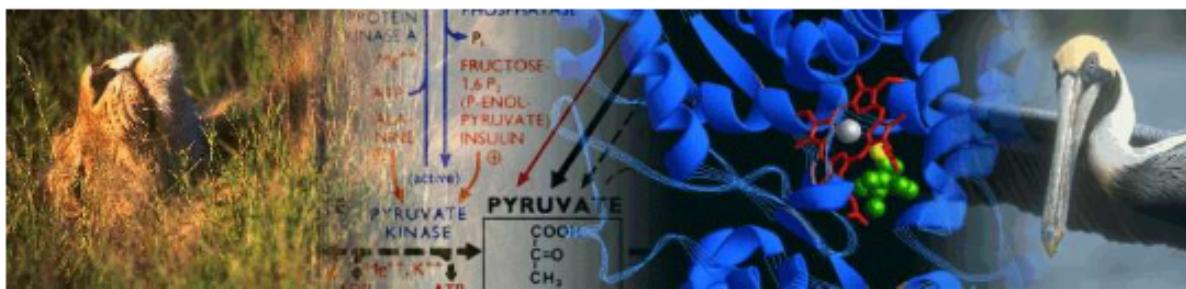
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To cite BioModels Database:

# Online simulation

N. Le Novère N. Le Novère C.



# S3ML

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

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

## JWS Online

Applet started.

## 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 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

## BIOMD0000000003 - Goldbeter1991\_MinMitOscil



Download SBML

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| Actions

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## BIOMD0000000003 - Goldbeter1991\_MinMitOscil



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## Global parameters

[V1](#)[V3](#)[VM1](#)[VM3](#)[Kc](#)

# Sub-model creation



Download SBML

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  $v_3 = M * VM3$



Download SBML

Other formats (auto-generated)

Actions

Submit Model Comment/Bug

Overview

Math

Physical entities

Parameters

Curation

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[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

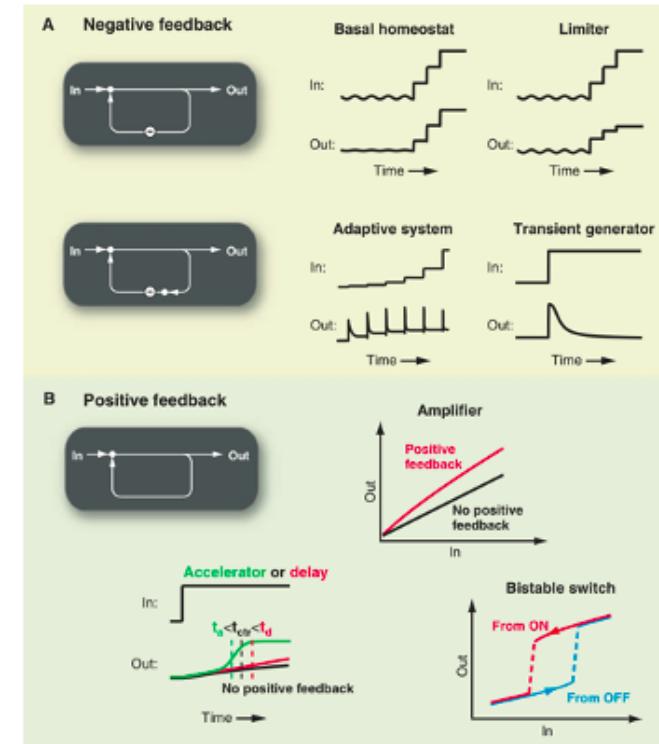
Original model: [BIOMD0000000179](#), [BIOMD0000000180](#)

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.

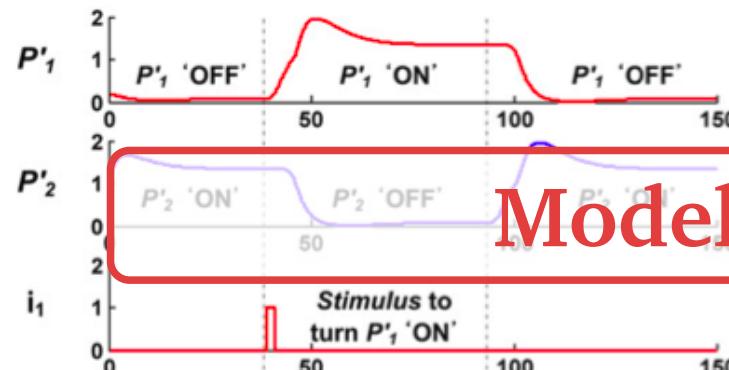
Feedback loops are processes that connects the output signal of the system back to their input signal. The concept and mechanism of feedback loops have been extensively investigated in various model and experimental systems, such as Turing's model of pattern formation; as well as investigations of metabolic 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].

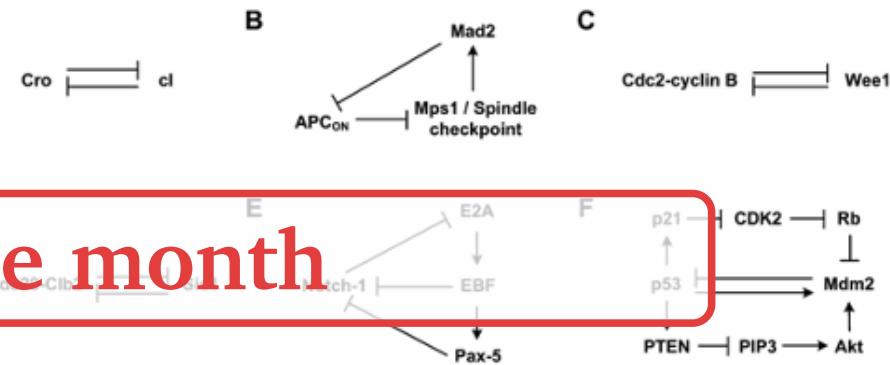
A single positive feedback loop between two molecules A and B can be subcategorized into mutual activation (A activates B and B activates A) and mutual inhibition (A inhibits B and B inhibits A). Despite the same nature of these two feedbacks, their steady-state characteristics are however different. 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.



# Model of the month



**BIOMD0000000049 - Sasagawa2005\_MAPK**[Download SBML](#)[Other formats \(auto-generated\)](#)[Actions](#)[Submit Model Comment/Bug](#)**Model**[Overview](#)[Math](#)[Physical entities](#)[Parameters](#)[Curation](#)

R

**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

**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	<a href="#">Gene Ontology epidermal growth factor receptor signaling pathway</a> <a href="#">Gene Ontology Ras protein signal transduction</a> <a href="#">Gene Ontology nerve growth factor receptor signaling pathway</a> <a href="#">Gene Ontology MAPKK cascade</a>
	bqbiol:occursIn	<a href="#">Taxonomy Rattus</a>

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 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 obtained from our in silico model.

## Report issues

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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).

## 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.

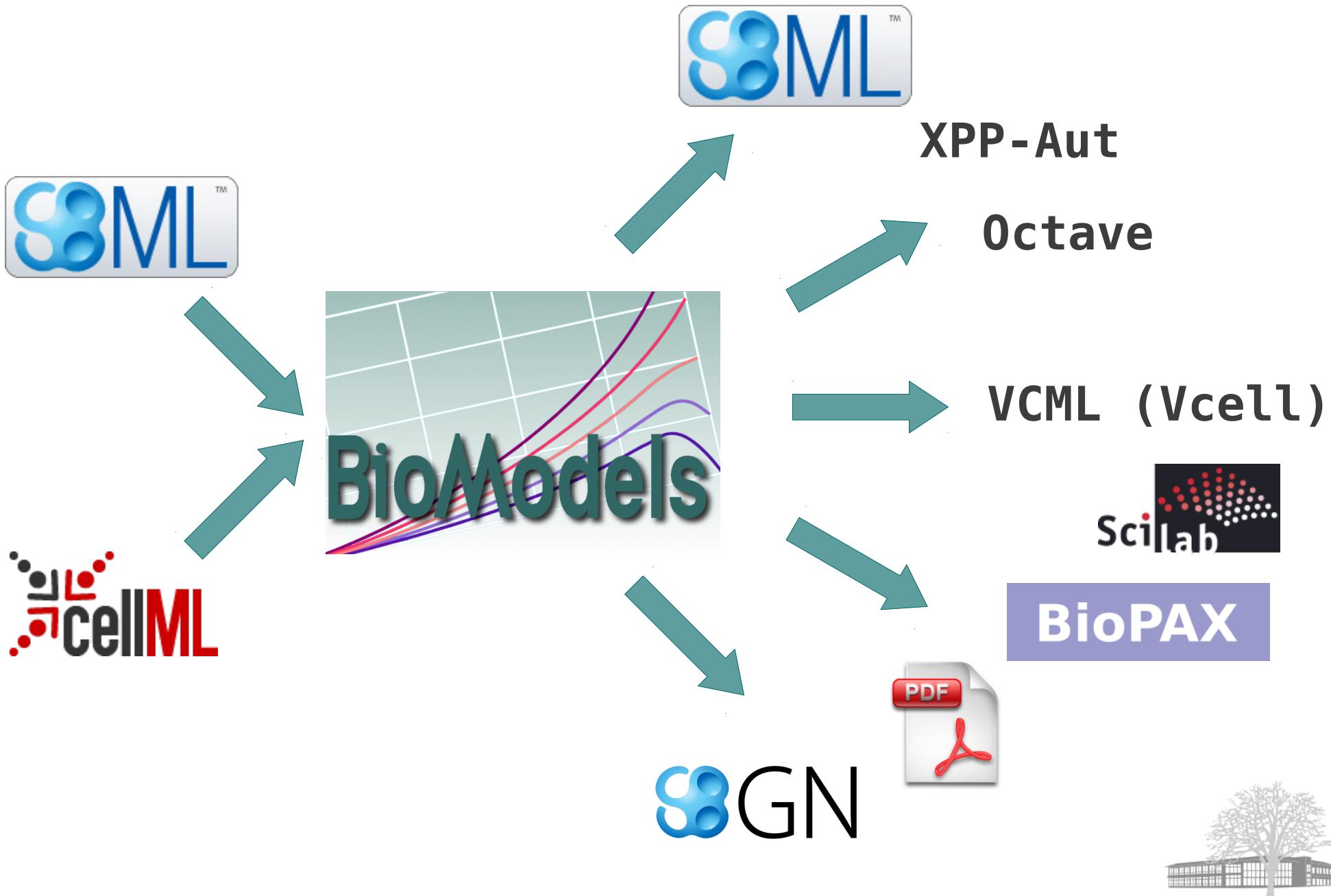
### How to use the library

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...
```



- **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>**



- **large scale generation of quantitative models form pathways**
- initial pathways coming from databases (such as KEGG)
- completed with information coming from other resources (BioCarta, MetaCyc, ...)
- 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:

*Coming very soon...*

### Download all models

*Coming very soon...*

# 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](#)

**Path2Models: browsing**

## Alzheimer's disease - Homo sapiens

[Download SBML](#)[Additional file\(s\)](#)[Submit Model Comment/Bug](#)

## Model information

**Identifier:** BMID000000017738**Format:** SBML L3 V1 (Layout, Qualitative Models)**Project:** [path2models](#)**Categories:** [non-metabolic](#)**Submission:** 17 May 2012 16:59:10 UTC**Last modified:** 17 May 2012 16:59:10 UTC**Published:** 19 May 2012 23:49:21 UTC

## Annotations

occursIn[Homo sapiens](#)*Taxonomy*isDescribedBy[Alzheimer's disease](#)*KEGG Pathway*

## Notes

**Model of "Alzheimer's disease" in "Homo sapiens (human)"**

Alzheimer's disease (AD) is a chronic disorder that slowly destroys neurons and causes serious cognitive disability. AD is associated with senile plaques and neurofibrillary tangles (NFTs). Amyloid-beta (Abeta), a major component of senile plaques, has various pathological effects on cell and organelle function. The extracellular Abeta oligomers may activate caspases through activation of cell surface death receptors. Alternatively, intracellular Abeta may contribute to pathology by facilitating tau hyper-phosphorylation, disrupting mitochondria function, and triggering calcium dysfunction. To date genetic studies have revealed four genes that may be linked to autosomal dominant or familial early onset AD (FAD). These four genes include: amyloid precursor protein (APP), presenilin 1 (PS1), presenilin 2 (PS2) and apolipoprotein E (ApoE). All mutations associated with APP and PS proteins can lead to an increase in the production of Abeta peptides, specifically the more amyloidogenic form, Abeta42. FAD-linked PS1 mutation downregulates the unfolded protein response and leads to vulnerability to ER stress.

[Graphical representation of 'Alzheimer's disease'](#) (PNG image hosted by the Kyoto Encyclopedia of Genes and Genomes, KEGG)[Original pathway](#) (from the KEGG PATHWAY Database)

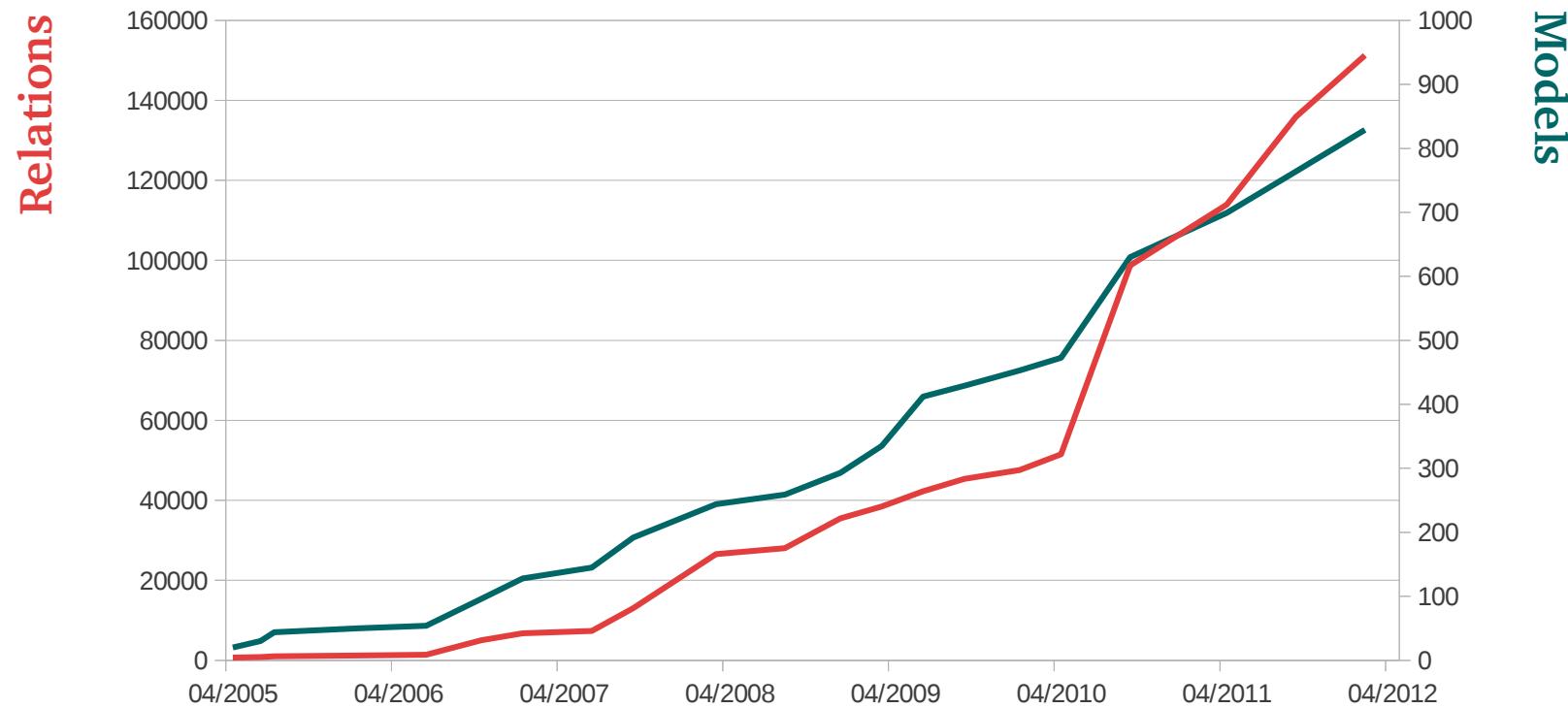
This model has been generated by the [path2models](#) project and is currently hosted on [BioModels Database](#) and identified by: [BMID000000017738](#).

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

# Path2Models: display

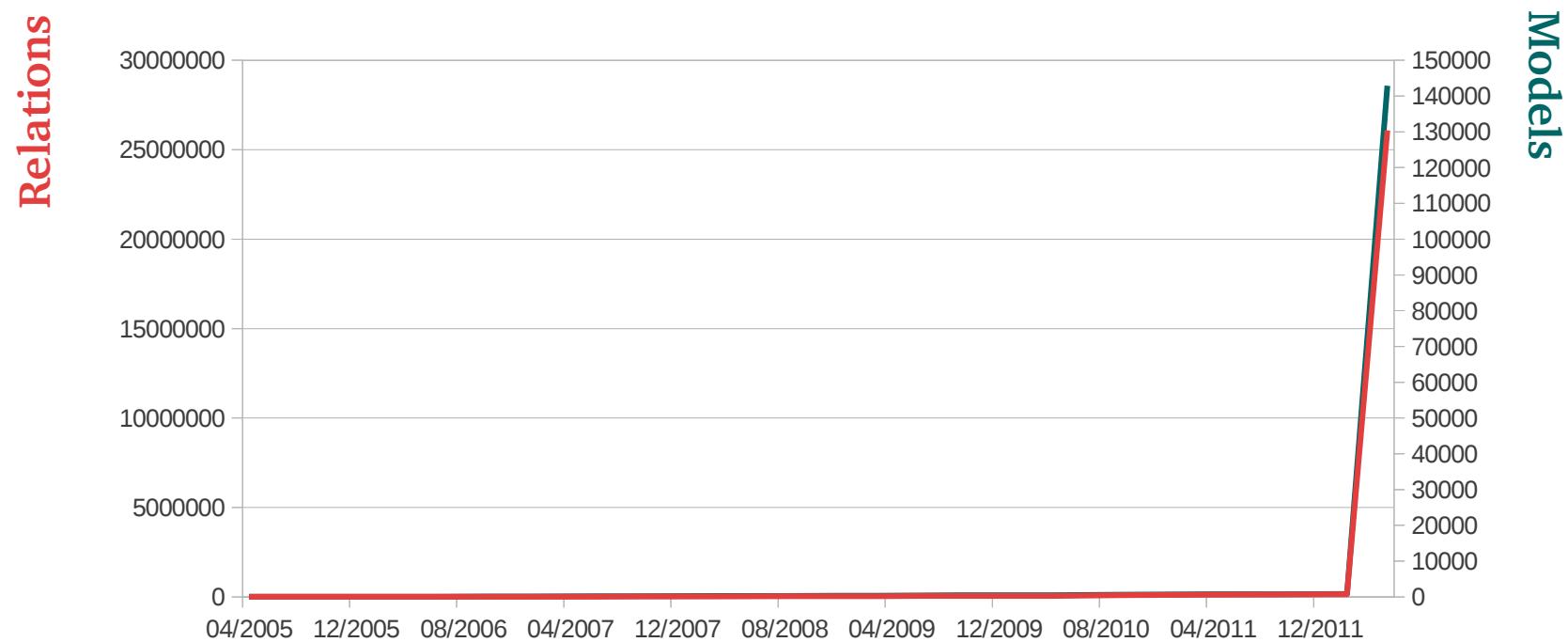
- Finja Büchel
- Andreas Dräger
- Camille Laibe
- Nicolas Le Novère
- Florian Mittag
- Nicolas Rodriguez
- Michael Schubert
- Niel Swainston
- Clemens Wrzodek
- Claudine Chaouiya
- Sarah Keating
- Julio Saez-Rodriguez
- Martijn Van Iersel
- Tobias Czauderna
- Michael Hucka
- Roland Keller
- Falk Schreiber





*Evolution of the content of BioModels Database*





*Evolution of the content of BioModels Database*



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[Disclaimer](#)

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## ■ Features

- format independent
- full model versioning
- ranked search results (making full use of annotations)
- private secured access to the pipeline for the models you submitted
- collaboration: model sharing and development
- standard access for reviewers (before model publication)

## ■ Software

- easy deployment and reuse (independent of EBI infrastructure)
- easy to extend (usage of plugins)
- improved performance (more and larger models)
- improved security
- customisable theme
- ...



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jummp / jummp  
Just a Model Management Platform

Clone this repository (size: 208.3 KB): HTTPS / SSH  
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Home New Edit History Wiki Markup hg clone <https://perkeo@bitbucket.org/jummp/jummp/wiki>

## JUMMP

Just a Model Management Platform (JUMMP) will be a modular software infrastructure for the collaborative development and management of biochemical models.

**<https://bitbucket.org/jummp/jummp/>**

News

- 2011-02-04: official announce at EBI and DKFZ
- 2010-12-22: starting work on a first testing prototype
- 2010-12-07: project created on Bitbucket

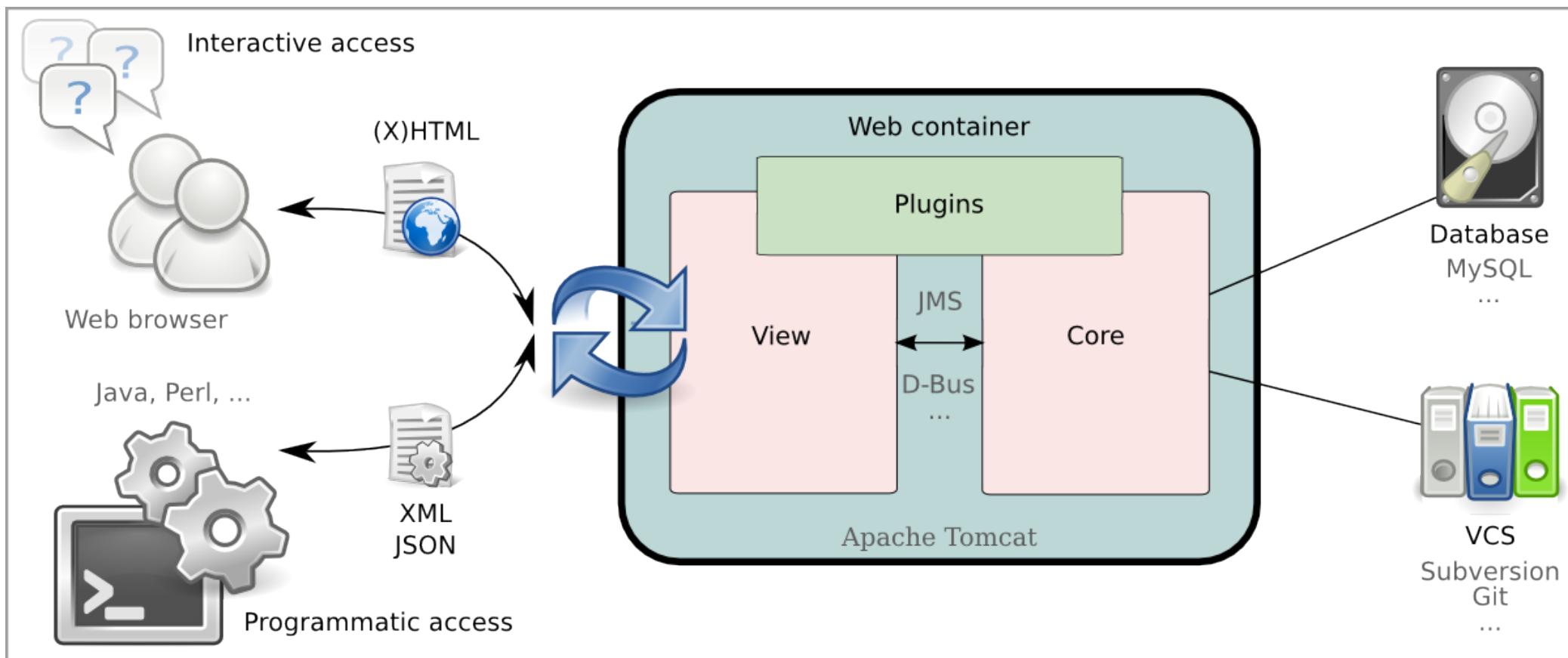
## Documentation

**WARNING: all documents are currently under active development!**

- Introduction
- Use Jummp
- Roadmap
- Announcement
- Contribute to the development of Jummp
- Use Cases

Documentation





- Groovy
- Grails (Spring, Hibernate, ...)
- Spring Security
- Hibernate Search
- Apache ActiveMQ / D-Bus
- jQuery, jQuery UI
- JSBML
- Subversion / Git
- ...



- new application focused on **security**, **performance** and **flexibility**
- multiple instances running in various institutes (various projects using the software to run their infrastructure)
- EBI (and its mirrors) remains the location where models are **publicly** available
- **community** developed project
  - initially undertaken by:
    - European Bioinformatics Institute (EBI)
    - German Cancer Research Center (DKFZ)





- Jürgen Eils
- Martin Gräßlin
- Jochen Schramm
- Michael Hoehl



## BioModels.net Team:

- Viji Chelliah
- Mihai Glont
- Nick Juty
- Sarah Keating
- Camille Laibe
- Nicolas Le Novère
- Stuart Moodie
- Nicolas Rodriguez
- Maciej Swat
- Yangyang Zhao



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