

# **BioModels Database, a curated resource of annotated published models**

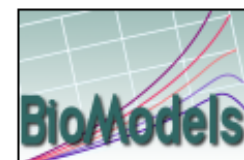
*Nicolas Le Novère, EMBL-EBI*





## BioModels Database - A Database of Annotated Published Models

BioModels Database is a data resource that allows biologists to store, search and retrieve published mathematical models of biological interests. Models present in BioModels Database are annotated and linked to relevant data resources, such as publications, databases of compounds and pathways, controlled vocabularies, etc.



Search models

[Advanced search](#)

[ [The list of curated models \(211\)](#) ]

[ [Browse curated models using GO tree](#) ]

[ [The list of non-curated models \(124\)](#) ]

[ [Model of Month](#) ]

[ [Simulate in JWS Online](#) ]

[ [Submit a new model](#) ]

[ [Web Services](#) ]

[ [BioModels on SourceForge](#) ]

### News

**25th March 2009 - Thirteenth Release!** [\[More\]](#) [\[Download All Models Under SBML Format\]](#)

**26th February 2009 - Mirror at Caltech** [\[http://biomodels.caltech.edu\]](http://biomodels.caltech.edu)

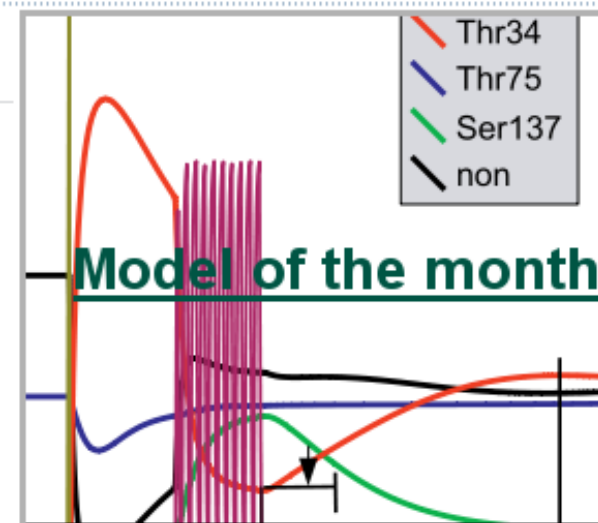
BioModels Database's has launched the first mirror site at Caltech.

**28th-30th March 2009 - BioModels meeting 2009** [\[More\]](#)

The Fourth BioModels Meeting will be held from March 28 to 30, 2009, at the [EBI](#) in Cambridge (United Kingdom).

**3rd December 2008 - Twelfth Release!** [\[More\]](#) [\[Download All Models Under SBML Format\]](#)

[more...](#)



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



- Store and serve **quantitative models** of **biomedical** interest
- Only models described in the **peer-reviewed** scientific literature.
- Models are **curated**: computer software check the **syntax**, while human curators check the **semantics**.
- Models are **simulated** to check the reference correspondence
- Model components are **annotated**, to improve identification and retrieval.
- BioModels DB native format is SBML but models are accepted in several formats, and served in several others.





## I) Individuals

- Authors (prior to grant application, before publication etc.)
- Members of the SBML community (developers+modellers)

## II) Existing model repositories

- SBML repository, JWS Online, The Virtual Cell, Database Of Quantitative Cell Signalling, CellML repository

## III) Journals (> 200 journals advise deposition, including all PloS journals, all BMC journals, Nature Molecular Systems Biology)

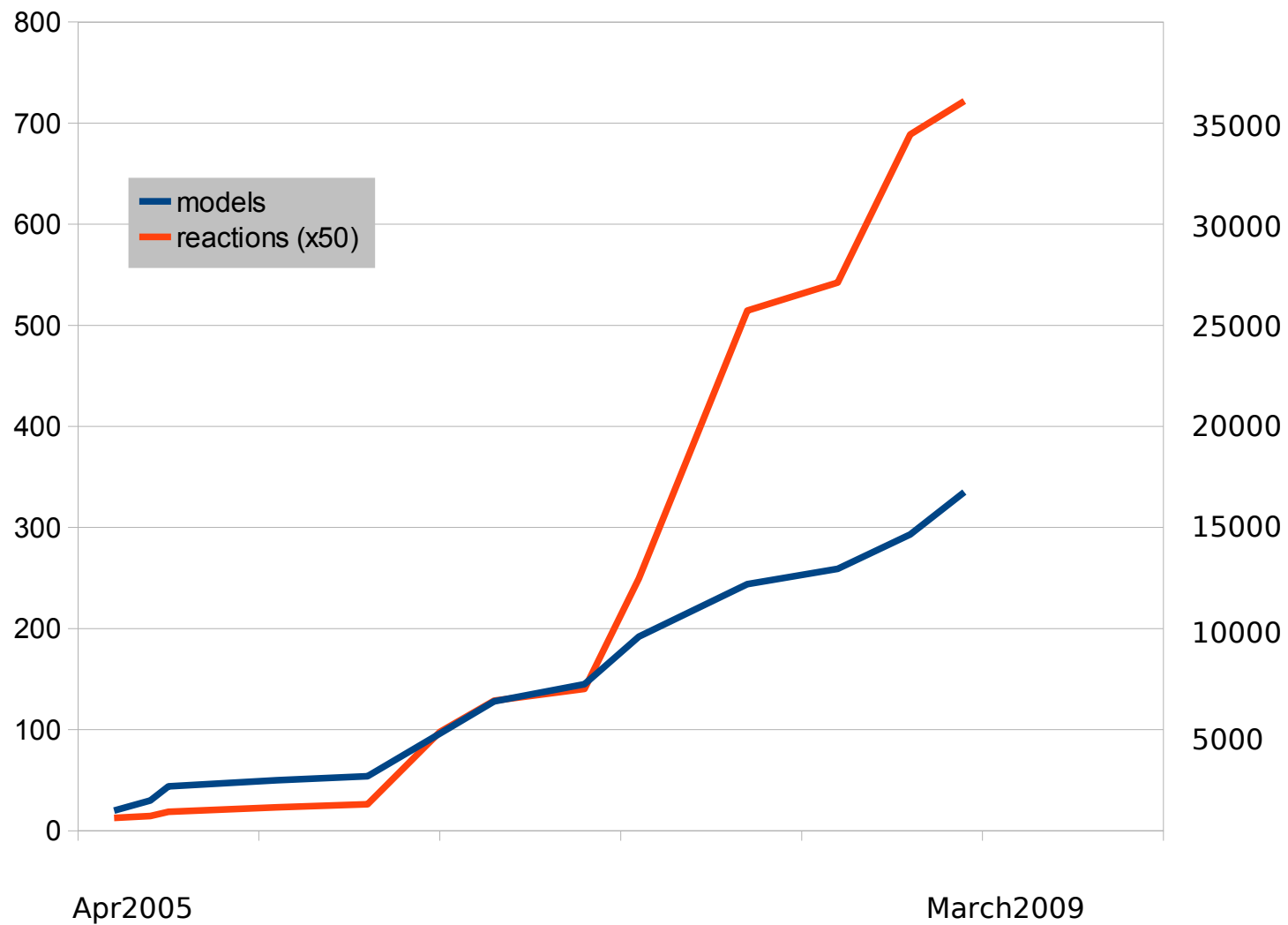
## IV) BioModels DB curators encode new models from literature





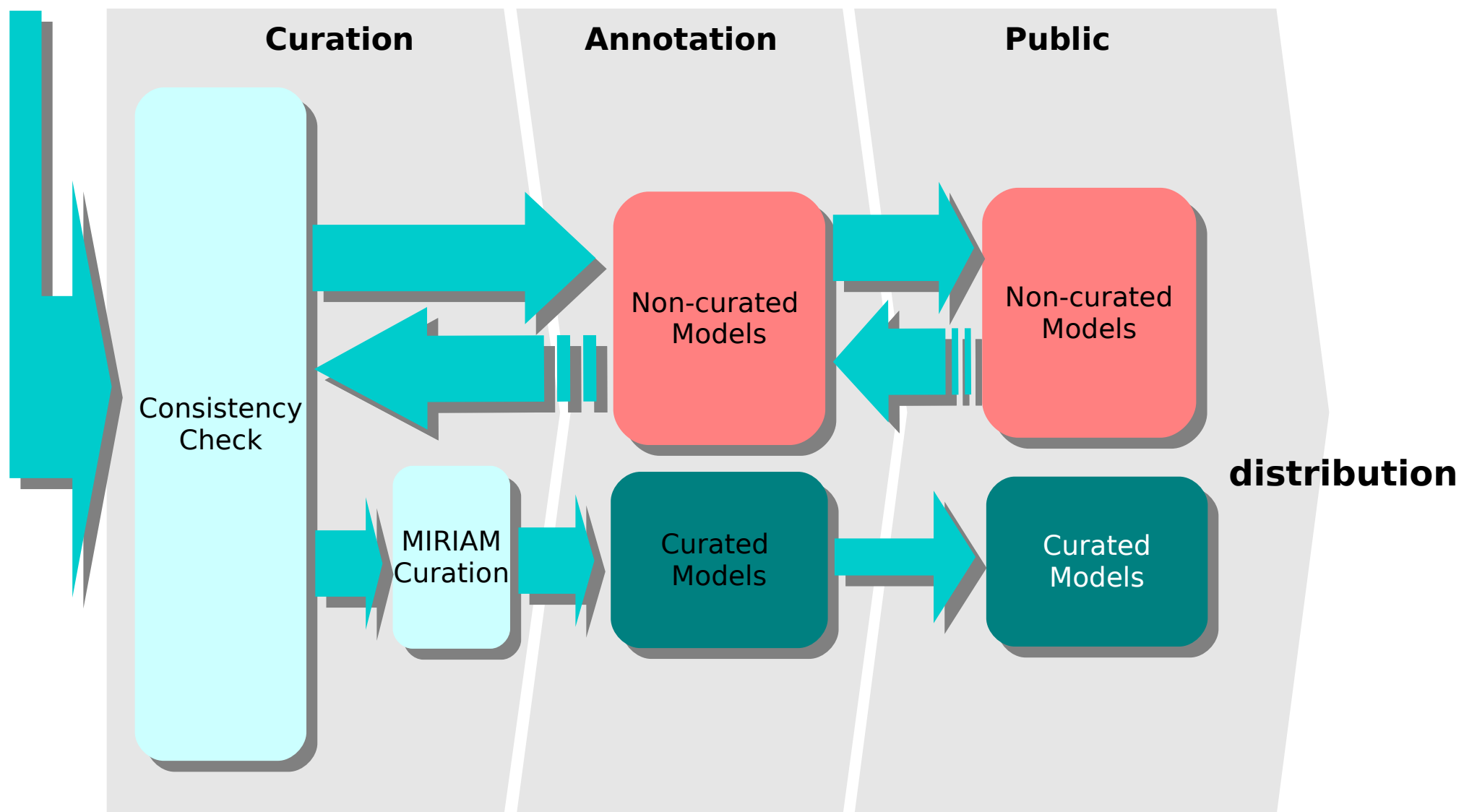
models

reactions



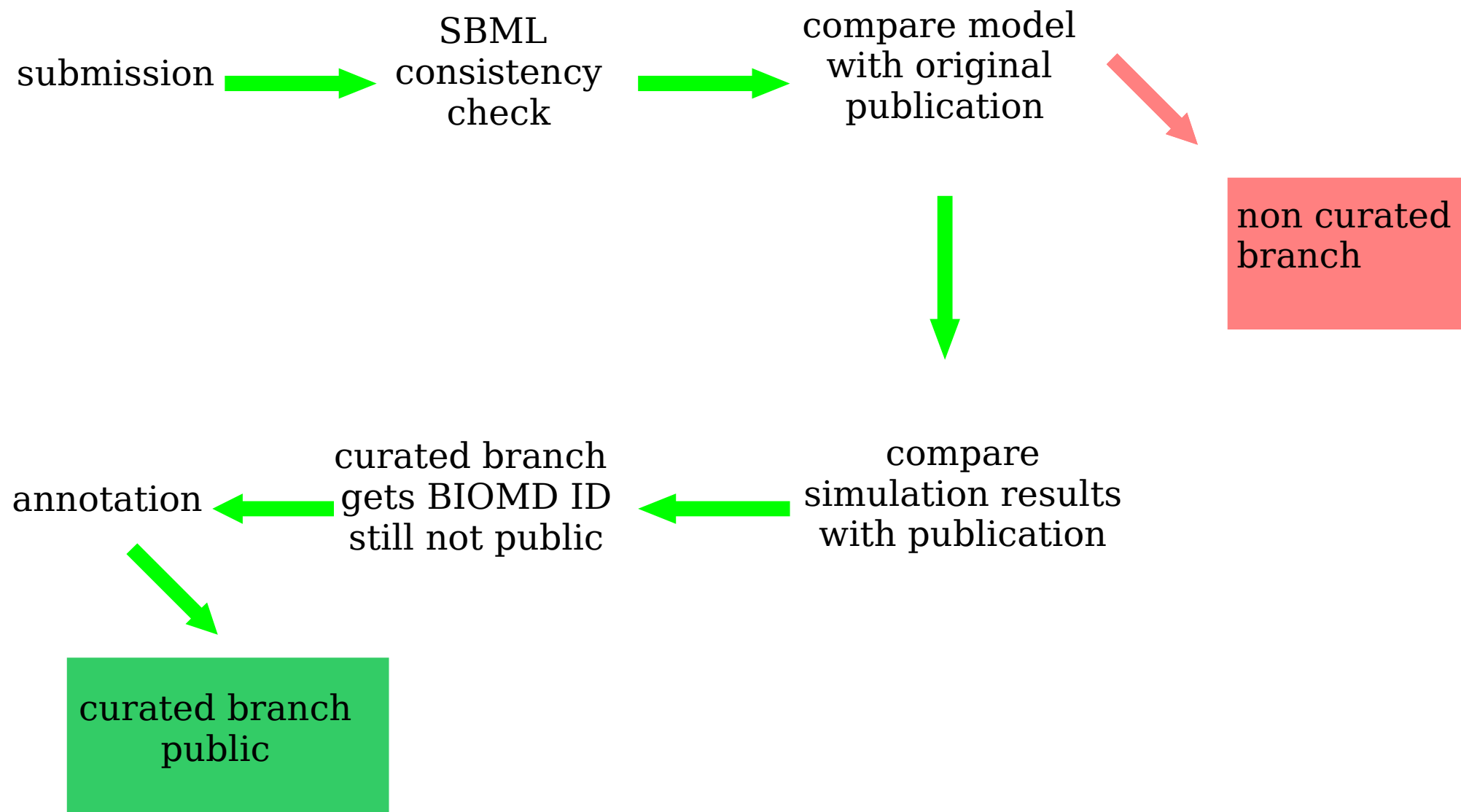


## Submission



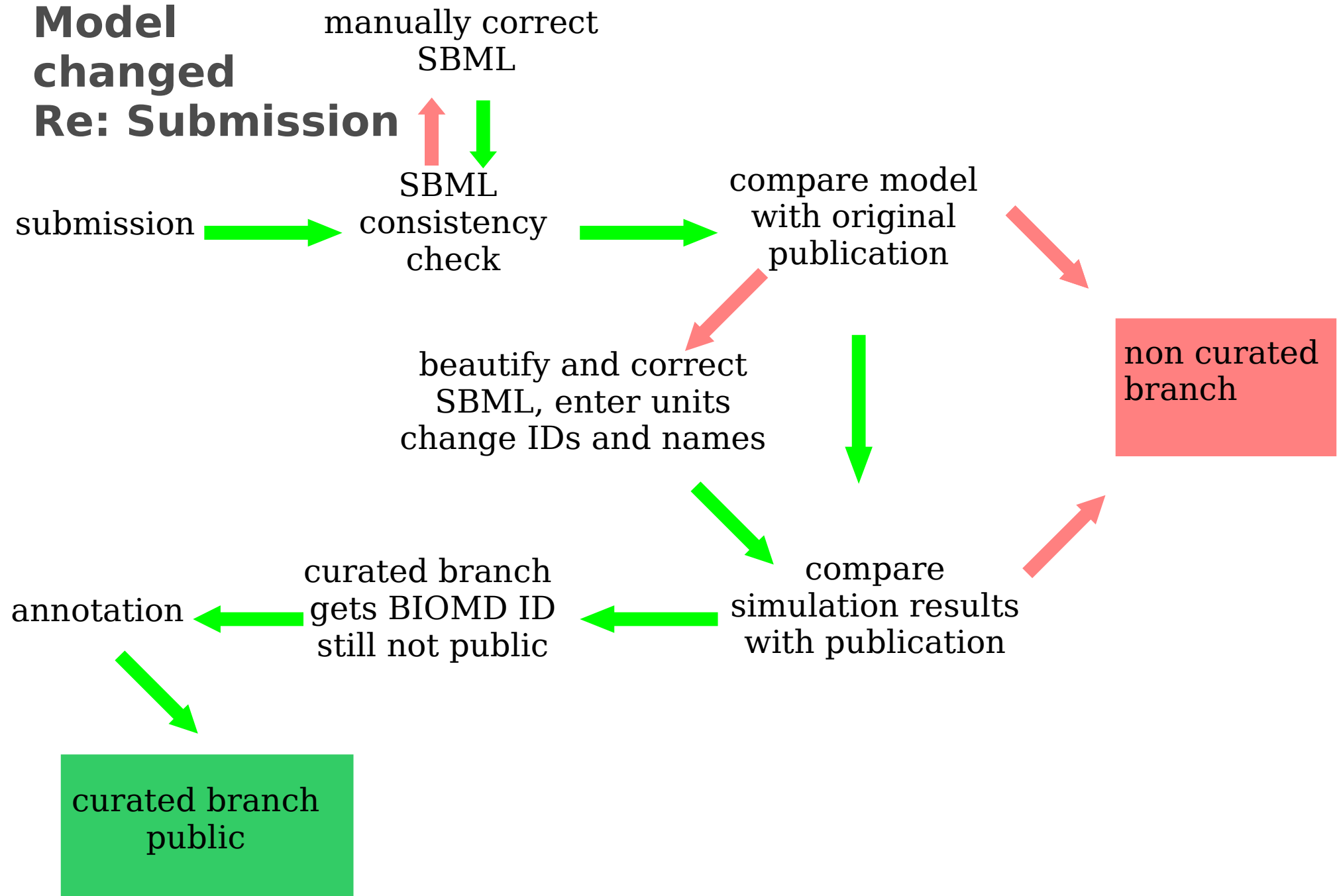


# Perfect pipeline: model unchanged



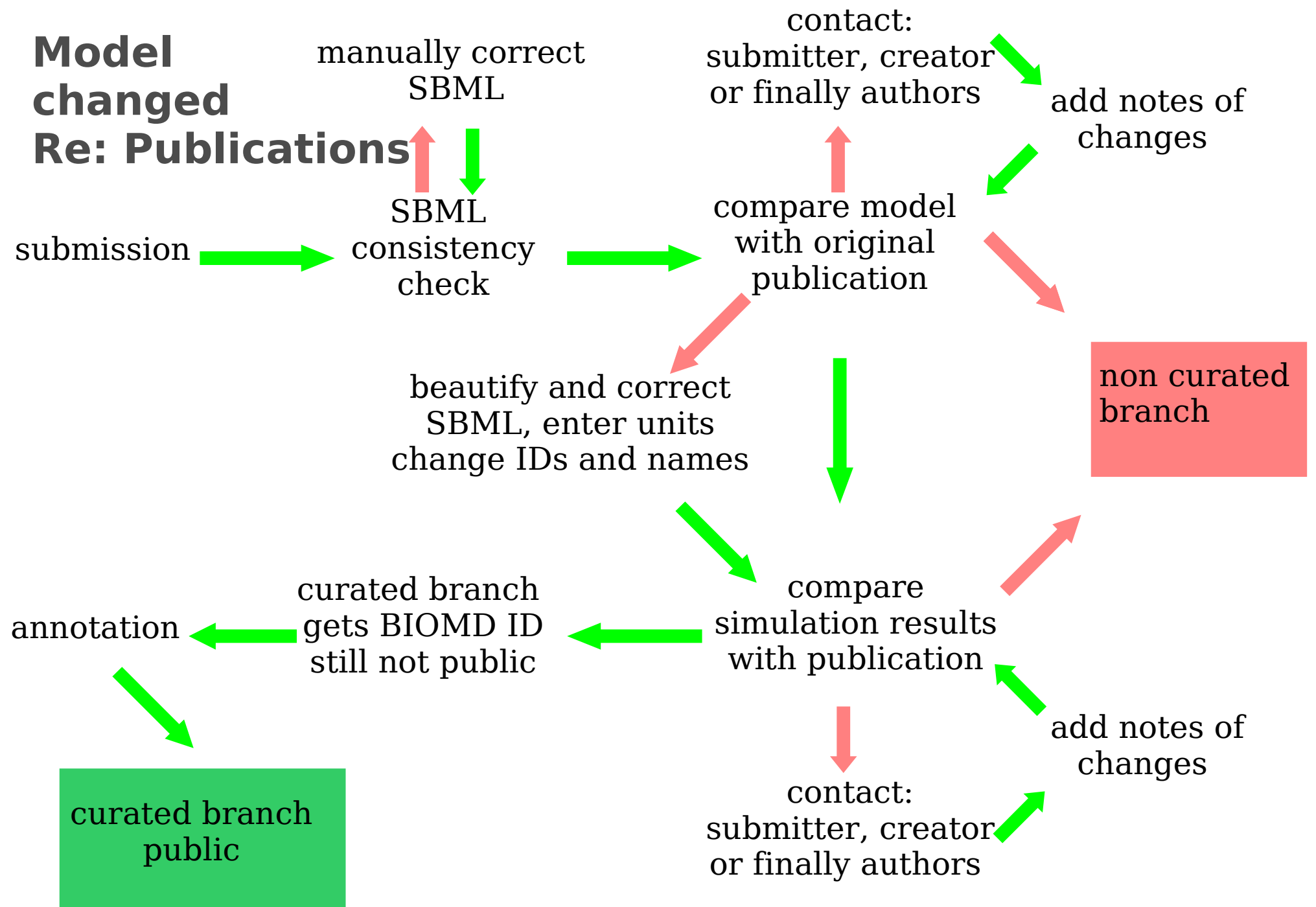


# Model changed Re: Submission

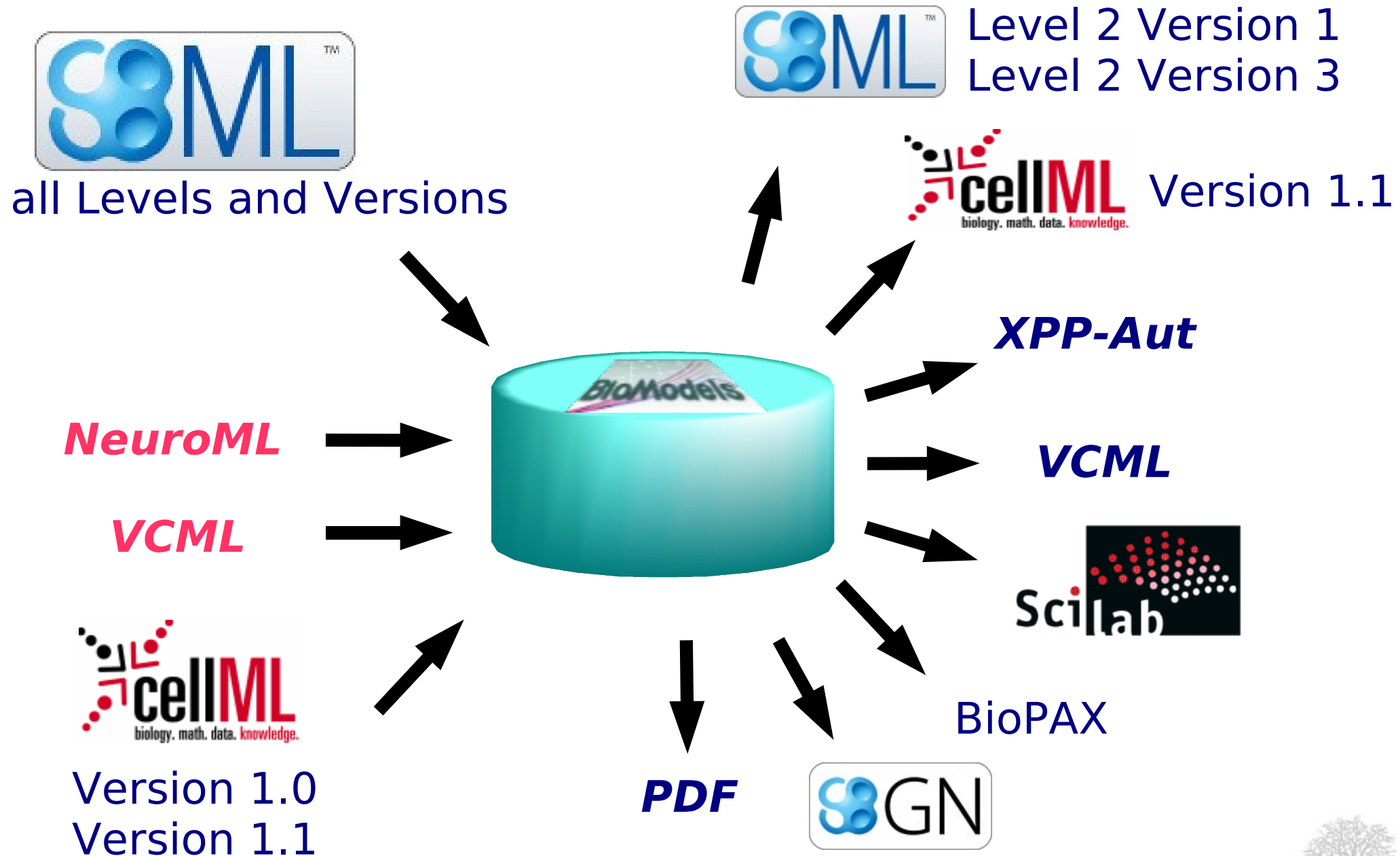




# Model changed Re: Publications









EMBL-EBI

EB-eye Search

All Databases

Enter Text Here

Go

Reset ?  
Advanced Search

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databases

Tools

EBI Groups


Training

Industry

About Us

Site Index

Help




- Curated Models
- Non-curated Models
- Search
- Simulate in JWS


- Submit Your Model

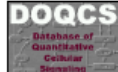
- Sign-in


- News
- Model of the Month
- Meetings
- Support
- Contact


BIO MODELS.NET














Related Software

The following software was developed for BioModels Database purposes. However, since it relates to [SBML](#), we feel it could be used by others. All our software is distributed under the [General Public License](#).

To edit the models, BioModels Database team uses the [SBML editor](#).

In order to provide a variety of export formats, we developed conversion tools. This software uses the [Extensible Stylesheet Language](#). We use them in conjunction with [Xalan Java](#). Because some of our XSL stylesheets use the extension [exsl](#), they could cause problems with other XSLT engines not supporting it.

SBML to XPP-Aut

[XPP-Aut](#) is a numerical analysis software. It permits to solve differential equations, difference equations, delay equations, functional equations, boundary value problems, and stochastic equations. Its graphical capabilities are quite user-friendly.

The conversion is performed in one XSLT pass, but using five stylesheets:

- [sbml\\_xpp16.xsl](#)
- [xpp\\_math16.xsl](#)
- [xpp\\_test16.xsl](#)
- [xpp\\_variable16.xsl](#)
- [bounds16.xsl](#)

To generate an XPP-Aut ode file from a SBML model, run:

```
Xalan MyModel_sbml.xml sbml_xpp16.xsl > MyModel.xpp
```

SBML to SciLab

[SciLab](#) is a scientific software package for numerical computations providing a powerful open computing environment for engineering and scientific applications.

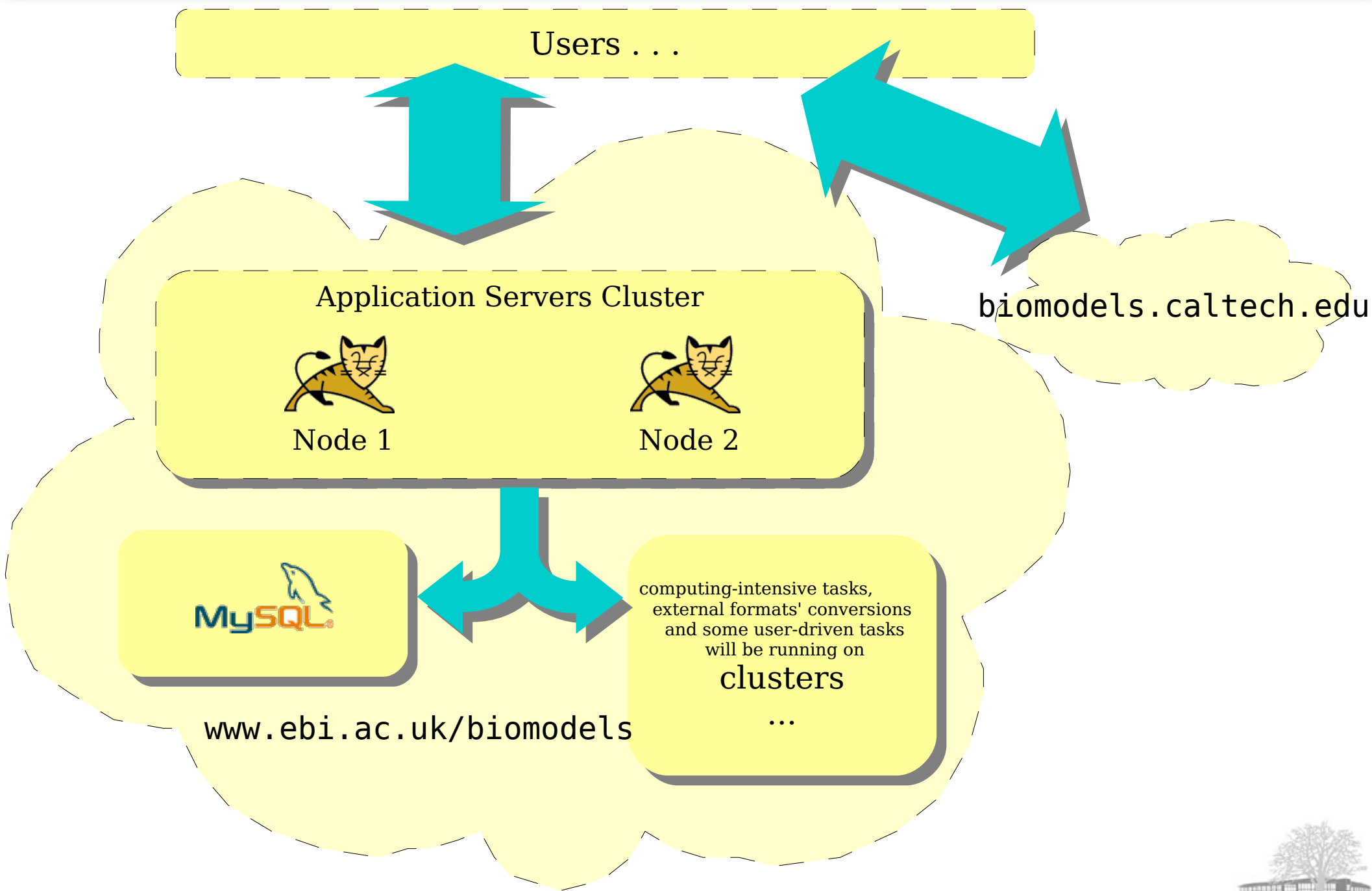
The conversion is performed in one XSLT pass, but using four stylesheets:

- [sbml\\_to\\_scilab.xsl](#)
- [scilab\\_math.xsl](#)
- [scilab\\_test.xsl](#)
- [scilab\\_variable.xsl](#)

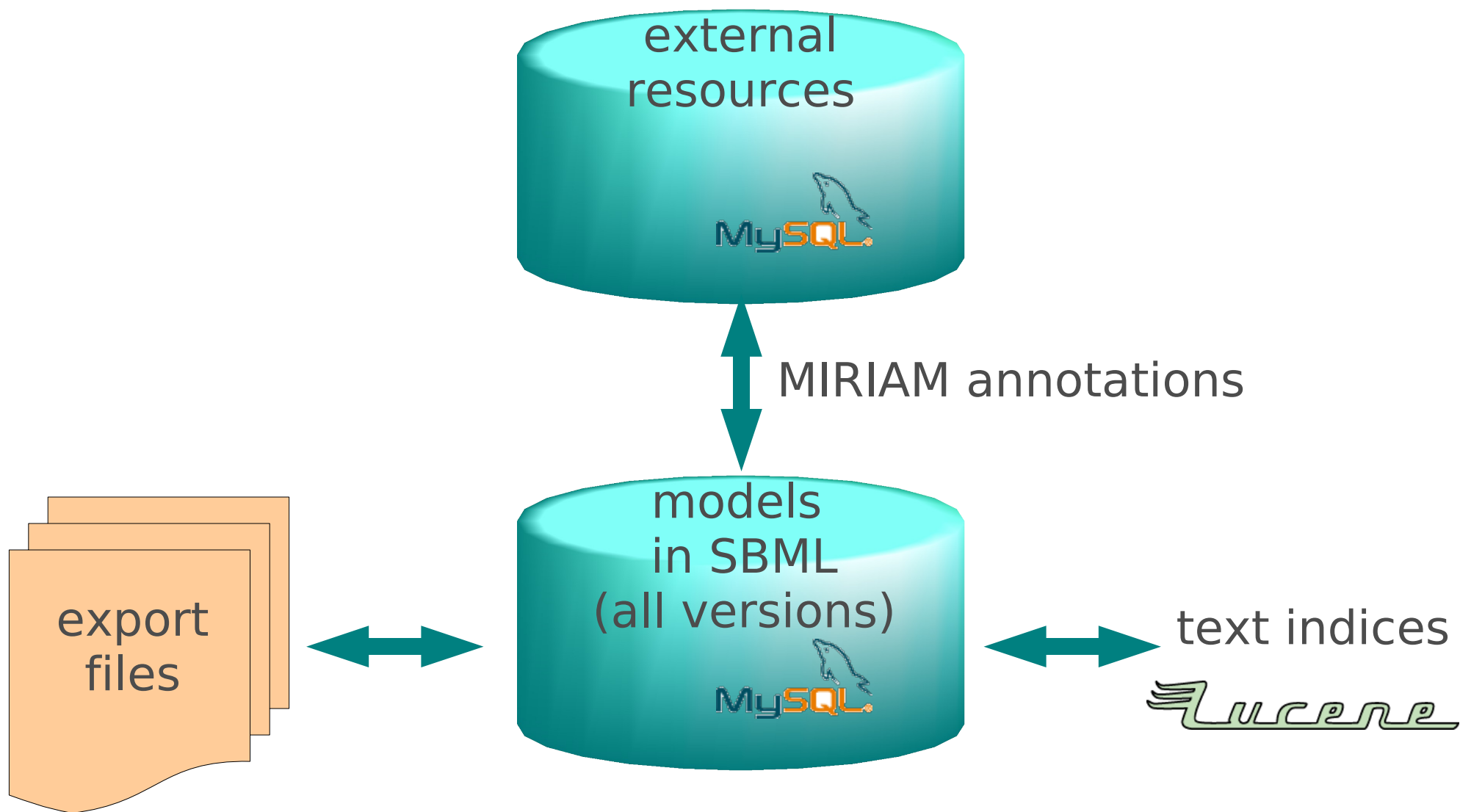
To generate an SciLab file from a SBML model, run:

Done











## Search - Models



### Text Search

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

- **BioModels ID** → 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.
- **Resource** → 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](#)).
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A part from the *BioModels ID*-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.

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**BioModels ID:**

**Person:**

**SBML Elements:**

☐ match the **exact phrase**

**Resource:**

**Resource:**

**Resource:**

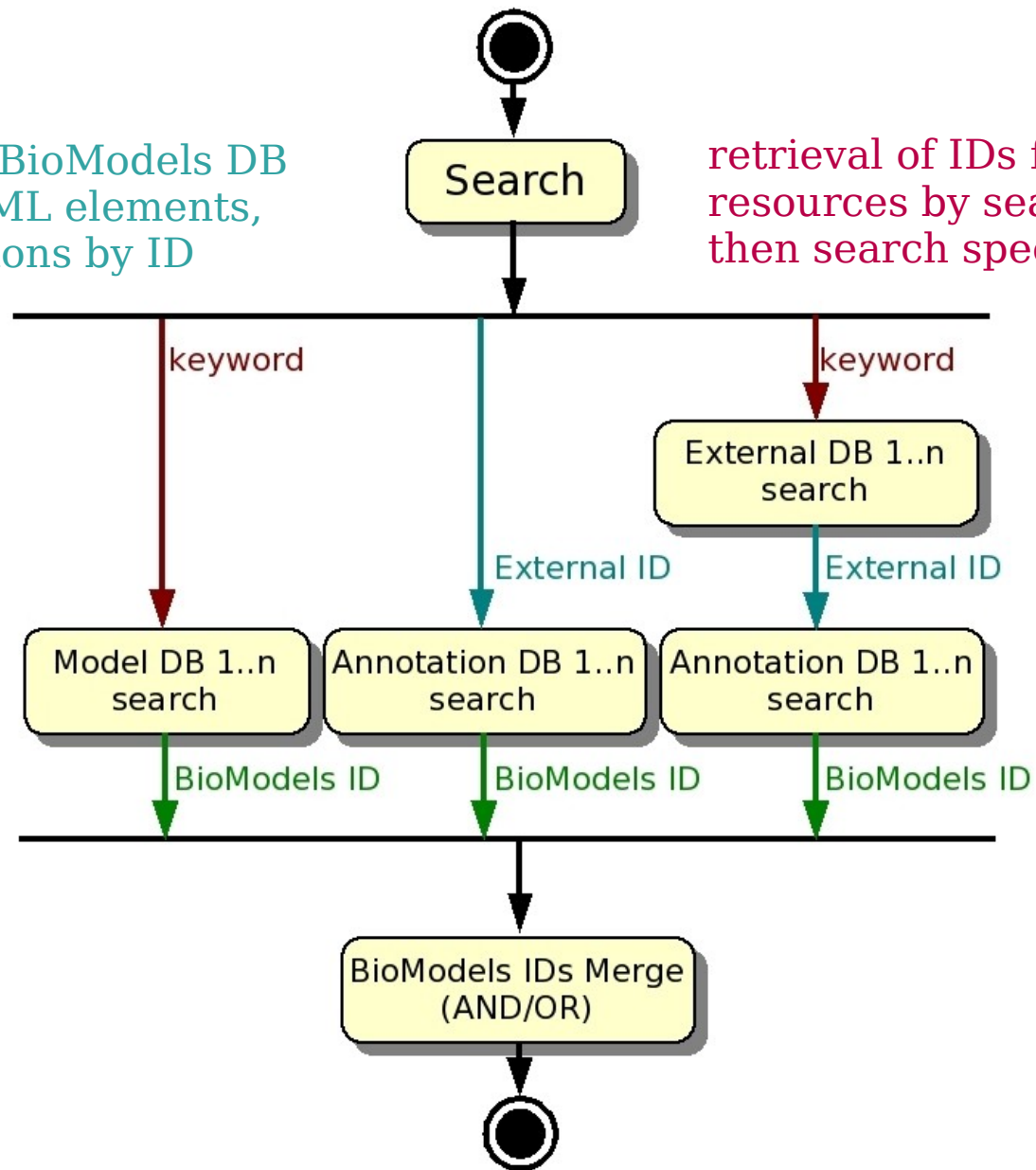
**Resource ID:**

**Resource ID:**

**Resource ID:**



direct search in BioModels DB  
eg. in notes, SBML elements,  
specific annotations by ID



retrieval of IDs from 3<sup>rd</sup> party  
resources by search terms →  
then search specific annotations



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**SBML Elements:**  ☐ match the **exact phrase**

**Resource:**

**Resource:**

**Resource:**

**Resource ID:**

**Resource ID:**

**Resource ID:**



## Search - Models



The search totally returned **24** models.

[← New Search](#)

24 Curated Models returned.

BioModels ID ▼	Name	Publication ID	Last Modified
<a href="#">BIOMD0000000009</a>	Huang1996_MAPK_ultrasens	<a href="#">8816754</a>	2008-08-21T11:34:49+00:00
<a href="#">BIOMD0000000010</a>	Kholodenko2000_MAPK_feedback	<a href="#">10712587</a>	2008-08-21T11:35:55+00:00
<a href="#">BIOMD0000000011</a>	Levchenko2000_MAPK_noScaffold	<a href="#">10823939</a>	2009-01-05T17:03:38+00:00
<a href="#">BIOMD0000000014</a>	Levchenko2000_MAPK_Scaffold	<a href="#">10823939</a>	2008-09-01T23:40:29+00:00
<a href="#">BIOMD0000000019</a>	Schoeberl2002_EGF_MAPK	<a href="#">11923843</a>	2008-08-21T11:44:44+00:00
<a href="#">BIOMD0000000026</a>	Markevich2004_MAPK_orderedElementary	<a href="#">14744999</a>	2008-08-21T11:47:39+00:00
<a href="#">BIOMD0000000027</a>	Markevich2004_MAPK_orderedMM	<a href="#">14744999</a>	2008-08-21T11:47:55+00:00
<a href="#">BIOMD0000000028</a>	Markevich2004_MAPK_phosphoRandomElementary	<a href="#">14744999</a>	2008-08-21T11:48:20+00:00
<a href="#">BIOMD0000000029</a>	Markevich2004_MAPK_phosphoRandomMM	<a href="#">14744999</a>	2008-08-21T11:48:42+00:00
<a href="#">BIOMD0000000030</a>	Markevich2004_MAPK_AIRandomElementary	<a href="#">14744999</a>	2009-01-30T14:08:33+00:00
<a href="#">BIOMD0000000031</a>	Markevich2004_MAPK_orderedMM2kinases	<a href="#">14744999</a>	2008-08-21T11:49:29+00:00
<a href="#">BIOMD0000000032</a>	Kofahl2004_pheromone	<a href="#">15300679</a>	2008-09-29T12:40:54+00:00
<a href="#">BIOMD0000000033</a>	Brown2004_NGF_EGF_signaling	<a href="#">14525003</a>	2008-08-21T11:50:24+00:00
<a href="#">BIOMD0000000049</a>	Sasagawa2005_MAPK	<a href="#">15793571</a>	2008-08-21T11:55:50+00:00
<a href="#">BIOMD0000000084</a>	Hornberg2005_ERKcascade	<a href="#">15634347</a>	2008-08-21T12:09:06+00:00
<a href="#">BIOMD0000000099</a>	Laub1998_SpontaneousOscillations	<a href="#">9843585</a>	2008-08-21T12:14:54+00:00



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<a href="#">BIOMD0000000049</a>	Sasagawa2005_MAPK	<a href="#">15793571</a>	2008-08-21T11:55:50+00:00
<a href="#">BIOMD0000000084</a>	Hornberg2005_ERKcascade	<a href="#">15634347</a>	2008-08-21T12:09:06+00:00
<a href="#">BIOMD0000000099</a>	Laub1998_SpontaneousOscillations	<a href="#">9843585</a>	2008-08-21T12:14:54+00:00



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[Text Search](#)

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**BioModels ID:**

**Person:**

**SBML Elements:**

☐ match the **exact phrase**

**Resource:** Taxonomy

**Resource:** Publication

**Resource:** ChEBI

**Resource:** Gene Ontology

**Resource:** Taxonomy

**Resource ID:** UniProt

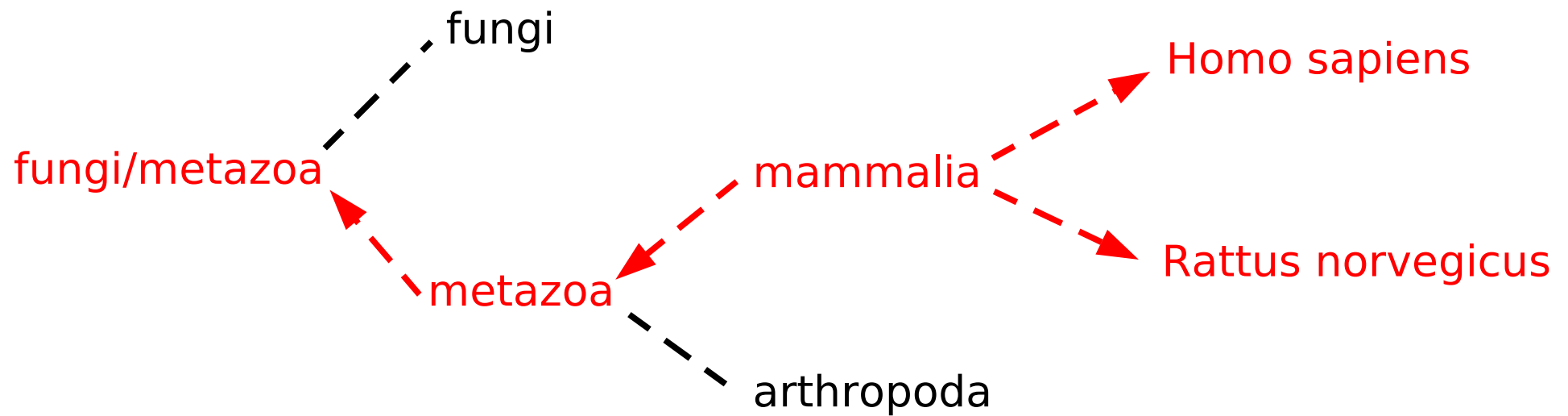
**Resource ID:** Enzyme Nomenclature

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**Resource ID:** Enzyme Nomenclature

**Resource ID:** Enzyme Nomenclature









## Search - Models

The search totally returned **85** models.

[← New Search](#)

85 Curated Models returned.

BioModels ID	Name	Publication ID	Last Modified
<a href="#">BIOMD0000000005</a>	Tyson1991_CellCycle_6var	<a href="#">1831179</a>	2009-02-25T14:58:48+00:00
<a href="#">BIOMD0000000006</a>	Tyson1991_CellCycle_2var	<a href="#">1831270</a>	2009-02-25T14:41:44+00:00
<a href="#">BIOMD0000000015</a>	Curto1998_purineMetabol	<a href="#">1564193</a>	2008-08-21T11:39:25+00:00
<a href="#">BIOMD0000000018</a>	Morrison1989_FolateCycle	<a href="#">2732237</a>	2008-08-21T11:44:21+00:00
<a href="#">BIOMD0000000019</a>	Schoeberl2002_EGF_MAPK	<a href="#">11923843</a>	2008-08-21T11:44:44+00:00
<a href="#">BIOMD0000000024</a>	Scheper1999_CircClock	<a href="#">9870936</a>	2008-08-21T11:46:43+00:00
<a href="#">BIOMD0000000041</a>	Kongas2001_creatine	<a href="#">10.1038/npre.2007.13...</a>	2008-08-21T11:53:00+00:00
<a href="#">BIOMD0000000043</a>	Borghans1997_CaOscillation_model1	<a href="#">17029867</a>	2008-08-21T11:53:37+00:00
<a href="#">BIOMD0000000044</a>	Borghans1997_CaOscillation_model2	<a href="#">17029867</a>	2008-08-21T11:53:55+00:00
<a href="#">BIOMD0000000045</a>	Borghans1997_CaOscillation_model3	<a href="#">17029867</a>	2008-08-21T11:54:12+00:00
<a href="#">BIOMD0000000047</a>	Oxhamre2005_Ca_oscillation	<a href="#">15596518</a>	2008-08-21T11:54:50+00:00
<a href="#">BIOMD0000000048</a>	Kholodenko1999_EGFRsignaling	<a href="#">1031407</a>	2008-08-21T11:55:14+00:00
<a href="#">BIOMD0000000049</a>	Sasagawa2005_MAPK	<a href="#">15793571</a>	2008-08-21T11:55:50+00:00
<a href="#">BIOMD0000000054</a>	Ataullahkhanov1996_Adenylate	<a href="#">8733433</a>	2008-08-21T11:57:42+00:00
<a href="#">BIOMD0000000057</a>	Sneyd2002_IP3_Receptor	<a href="#">11842185</a>	2008-08-21T11:58:43+00:00
<a href="#">BIOMD0000000059</a>	Fridlyand2003_Calcium_flux	<a href="#">12644446</a>	2008-10-01T17:23:42+00:00

fungi/metazoa

Homo sapiens

Rattus norvegicus





## Browse - Curated models

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

- GO:0008150 - biological\_process (204)
  - GO:0009987 - cellular process (196)
    - GO:0051641 - cellular localization (40)
    - GO:0007049 - cell cycle (26)
      - GO:0051726 - regulation of cell cycle (18)
        - GO:0000075 - cell cycle checkpoint (8)
          - GO:0007093 - mitotic cell cycle checkpoint (7)
            - GO:0007094 - mitotic cell cycle spindle assembly checkpoint
              - BIOMD0000000056 - Chen2004\_CellCycle
              - BIOMD0000000186 - Ibrahim2008\_Spindle\_Assembly\_Che
              - BIOMD0000000187 - Ibrahim2008\_Spindle\_Assembly\_Che
              - BIOMD0000000193 - Ibrahim2008\_MCC assembly model
              - BIOMD0000000194 - Ibrahim2008\_Cdc20 Sequestering Ter
            - GO:0031576 - G2/M transition checkpoint (1)
            - GO:0031575 - G1/S transition checkpoint (2)
            - GO:0031577 - spindle checkpoint (5)
            - GO:0031570 - DNA integrity checkpoint (1)
              - BIOMD0000000087 - Proctor2006\_telomere
              - BIOMD0000000110 - Qu2003\_CellCycle
          - GO:0000079 - regulation of cyclin-dependent protein kinase activi
          - GO:0007346 - regulation of mitotic cell cycle (10)
          - GO:0010564 - regulation of cell cycle process (5)
          - GO:0045786 - negative regulation of cell cycle (9)
          - GO:0045787 - positive regulation of cell cycle (8)
            - BIOMD0000000168 - Obeyesekere1999\_CellCycle
            - BIOMD0000000195 - Tyson2001\_Cell\_Cycle\_Regulation
          - GO:0000278 - mitotic cell cycle (23)

BioModels ID: *Unspecified*

Name: *N/A*

Publication ID: *N/A*

Last Modified: *N/A*



# BIOMD0000000010 - Kholodenko2000\_MAPK\_feedback



SBML L2 V1 | Other formats | Actions | [Submit Model Comment/Bug](#)

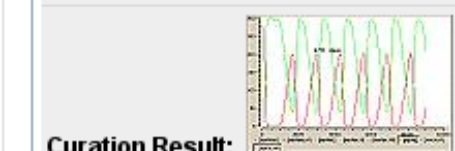
Model Overview Math Physical entities Parameters

## Reference Publication

**Publication ID:** [10712587](#)  
 Eur J Biochem 2000 Mar;267(6):1583-8.  
 Negative feedback and ultrasensitivity can bring about oscillations in the mitogen-activated protein kinase cascades.  
 Kholodenko BN.  
 Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA 19107, USA.  
 Boris.Kholodenko@mail.tju.edu [\[more\]](#)

## Model

<b>Original Model:</b> <i>Unspecified</i>	set #1 bqbiol:is <a href="#">Taxonomy</a> <a href="#">Xenopus laevis</a>
<b>Submitter:</b> <a href="#">Nicolas Le Novère</a>	set #2 bqbiol:isVersionOf <a href="#">Gene Ontology</a> <a href="#">MAPKKK cascade</a>
<b>Submission Date:</b> 2005-09-13T12:39:02+00:00	set #3 bqbiol:isHomologTo <a href="#">Reactome</a> <a href="#">REACT_634</a>
<b>Last Modification Date:</b> 2008-08-21T11:35:55+00:00	
<b>Creation Date:</b> 2005-02-12T00:18:12+00:00	
<b>Creators:</b> <a href="#">Herbert Sauro</a>	



## Notes

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 To cite BioModels Database, please use [Le Novère N., Bornstein B., Broicher A., Courtot M., Donizelli M., Dharuri H., Li L., Sauro H., Schilstra M., Shapiro B., Snoep J.L., Hucka](#)



# BIOMD0000000010 - Kholodenko2000\_MAPK\_feedback



SBML L2 V1 |  |  | [Submit Model Comment/Bug](#)

Model Overview **Math** Physical entities Parameters

## Reactions (10)

MAPKKK activation  $[MAPKKK] \rightarrow [MAPKKK-P]; \{MAPK-PP\}$

Math:

$$\frac{uVol \times V1 \times MKKK}{\left(1 + \left(\frac{MAPK\_PP}{K_i}\right)^n\right) \times (K1 + MKKK)}$$

[\(Detail\)](#)

Annotations:

set #1 bqbiol:isVersionOf [Enzyme Nomenclature 2.7.11.1](#)  
[Gene Ontology](#) activation of MAPKKK activity  
[Gene Ontology](#) MAP kinase kinase kinase kinase activity

set #2 bqbiol:isHomologTo [Reactome REACT\\_525](#)

MAPKKK inactivation  $[MAPKKK-P] \rightarrow [MAPKKK];$

phosphorylation of MAPKK  $[MAPKK] \rightarrow [MAPKK-P]; \{MAPKKK-P\}$

phosphorylation of MAPKK-P  $[MAPKK-P] \rightarrow [MAPKK-PP]; \{MAPKKK-P\}$

dephosphorylation of MAPKK-PP  $[MAPKK-PP] \rightarrow [MAPKK-P];$

dephosphorylation of MAPKK-P  $[MAPKK-P] \rightarrow [MAPKK];$

phosphorylation of MAPK  $[MAPK] \rightarrow [MAPK-P]; \{MAPKK-PP\}$

phosphorylation of MAPK-P  $[MAPK-P] \rightarrow [MAPK-PP]; \{MAPKK-PP\}$

dephosphorylation of MAPK-PP  $[MAPK-PP] \rightarrow [MAPK-P];$

dephosphorylation of MAPK-P  $[MAPK-P] \rightarrow [MAPK];$





# BIOMD0000000010 - Kholodenko2000\_MAPK\_feedback

SBML L2 V1 |  |  | [Submit Model Comment/Bug](#)

Model Overview Math **Physical entities** Parameters

<b>uVol</b>	Spatial dimensions: 3 Compartment size: 1.0
<input type="checkbox"/> <b>MAPKKK</b>	Initial concentration: 90.0
Compartment: uVol	
Annotations:	set #1 bqbiol:isVersionOf <a href="#">UniProt RAF1_XENLA</a>
<input checked="" type="checkbox"/> <b>MAPKKK-P</b>	Initial concentration: 10.0
Compartment: uVol	
<input type="checkbox"/> <b>MAPKK</b>	Initial concentration: 280.0
Compartment: uVol	
Annotations:	set #1 bqbiol:isVersionOf <a href="#">UniProt MP2K1_XENLA</a>
<input checked="" type="checkbox"/> <b>MAPKK-P</b>	Initial concentration: 10.0
Compartment: uVol	
<input checked="" type="checkbox"/> <b>MAPKK-PP</b>	Initial concentration: 10.0
Compartment: uVol	
<input type="checkbox"/> <b>MAPK</b>	Initial concentration: 280.0
Compartment: uVol	
Annotations:	set #1 bqbiol:isVersionOf <a href="#">UniProt MK01_XENLA</a>
<input checked="" type="checkbox"/> <b>MAPK-P</b>	Initial concentration: 10.0
Compartment: uVol	

2

4

1:3

Auck

d



# BIOMD0000000010 - Kholodenko2000\_MAPK\_feedback



SBML L2 V1 | Other formats | Actions | [Submit Model Comment/Bug](#)

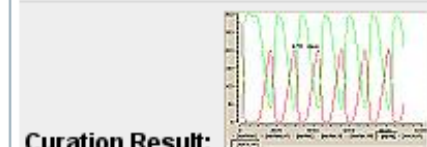
Mod	Other formats	Math	Physical entities	Parameters
	CellML			
	SciLab			
	XPP			
	BioPAX			
Publication ID:	VCell	Reference Publication	<p>Eur J Biochem 2000 Mar;267(6):1583-8.                  Negative feedback and ultrasensitivity can bring about oscillations in the mitogen-activated protein kinase cascades.                  Kholodenko BN.                  Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA 19107, USA.                  Boris.Kholodenko@mail.tju.edu <a href="#">[more]</a></p>	
	PDF			

Model		
Original Model: <i>Unspecified</i>	set #1	bqbiol:is <a href="#">Taxonomy</a> <a href="#">Xenopus laevis</a>
Submitter: <a href="#">Nicolas Le Novère</a>	set #2	bqbiol:isVersionOf <a href="#">Gene Ontology</a> <a href="#">MAPKKK cascade</a>
Submission Date: 2005-09-13T12:39:02+00:00	set #3	bqbiol:isHomologTo <a href="#">Reactome</a> <a href="#">REACT_634</a>

Last Modification Date: 2008-08-21T11:35:55+00:00

Creation Date: 2005-02-12T00:18:12+00:00

Creators: [Herbert Sauro](#)



Curation Result:

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# BIOMD0000000010 - Kholodenko2000\_MAPK\_feedback



SBML L2 V1 | Other formats | Actions | [Submit Model Comment/Bug](#)

Model

Overview

Physical entities

Parameters

Publication

3-8.

ty can bring about oscillations in the mitogen-activated protein kinase cascades.

Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA 19107, USA.

[Boris.Kholodenko@mail.tju.edu](mailto:Boris.Kholodenko@mail.tju.edu) [\[more\]](#)

Model

**Original Model:** *Unspecified*

**Submitter:** [Nicolas Le Novère](#)

**Submission Date:** 2005-09-13T12:39:02+00:00

**Last Modification Date:** 2008-08-21T11:35:55+00:00

**Creation Date:** 2005-02-12T00:18:12+00:00

**Creators:** [Herbert Sauro](#)

set #1 bqbiol:is [Taxonomy](#) [Xenopus laevis](#)

set #2 bqbiol:isVersionOf [Gene Ontology](#) [MAPKKK cascade](#)

set #3 bqbiol:isHomologTo [Reactome](#) [REACT\\_634](#)

**Curation Result:**

## Notes

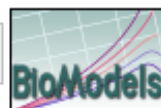
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## Model - Simulation



For doing an online simulation, please select the species below. After specifying the *simulation time* and *print step*, and then click *Submit* to submit simulation job to our research cluster.

Click *Cancel* to close the window.

Cancel

☐ Species

- |                                   |                                   |                                 |   |
|-----------------------------------|-----------------------------------|---------------------------------|---|
| <input type="checkbox"/> MAPKKK   | <input type="checkbox"/> MAPKKK-P | <input type="checkbox"/> MAPKK  | <input type="checkbox"/> MAPKK-P            |
| <input type="checkbox"/> MAPKK-PP | <input type="checkbox"/> MAPK     | <input type="checkbox"/> MAPK-P | <input checked="" type="checkbox"/> MAPK-PP |

Simulation Time (use scientific notation e.g. 1e7 for 10000000): 1000

Print step: 1000

Submit

Done

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Parameters

at oscillations in the mitogen-activated protein kinase cascades.

Thomas Jefferson University, Philadelphia, PA 19107, USA.

[cascade](#)

Done



## Model - Simulation

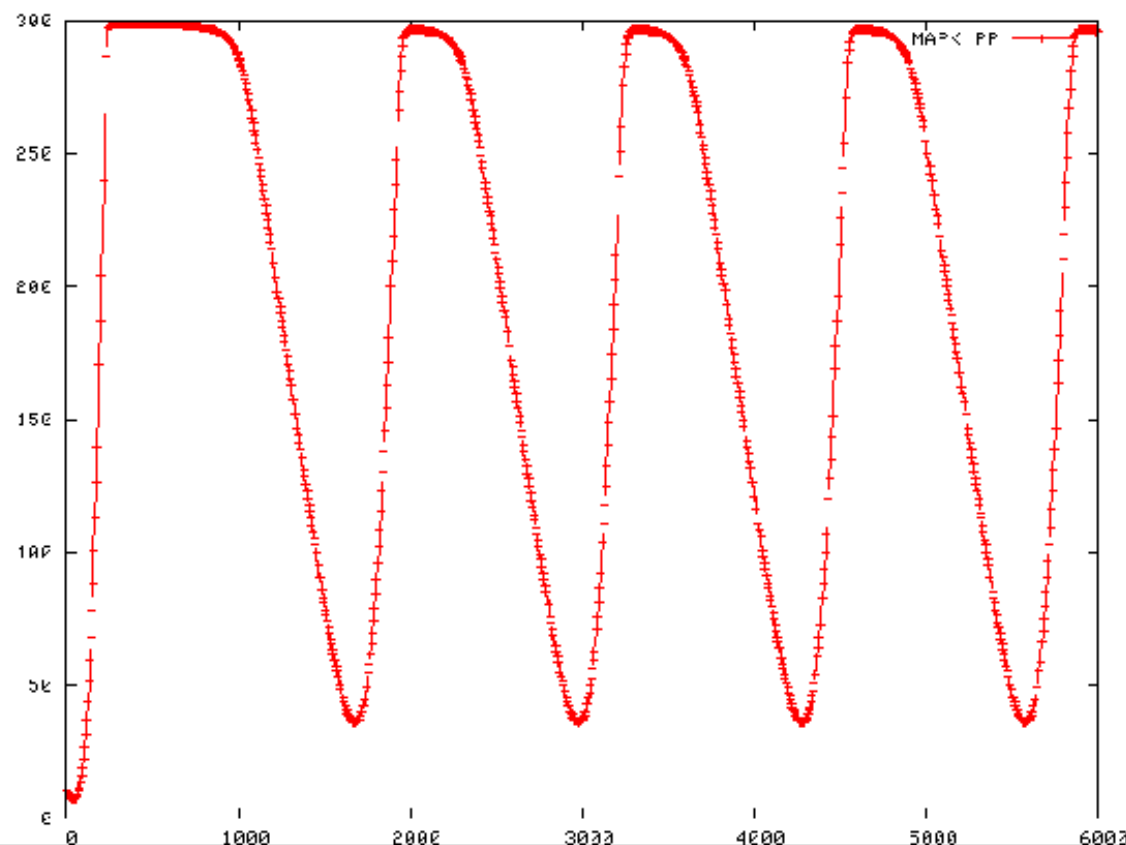


The simulation request has been submitted to the queue of our server cluster.

You could save following links and retrieve your simulation result later.

### Link of simulation result:

<http://www.ebi.ac.uk/biomodels-main/publ-model.do?cmd=SIMU:RETRIEVE&simuid=SIMU1238964>



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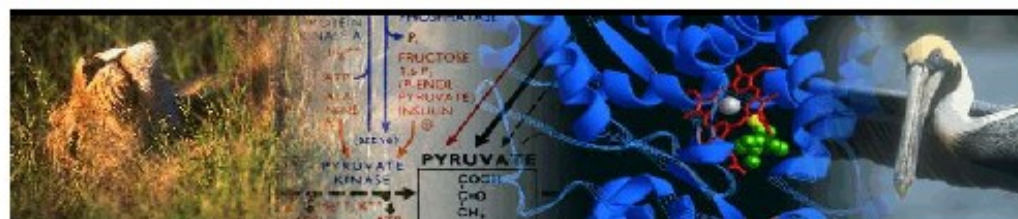
Parameters

at oscillations in the mitogen-activated protein kinase cascades.

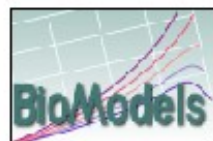
Thomas Jefferson University, Philadelphia, PA 19107, USA.

[cascade](#)





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



**BioModels: BIOMD0000000010  
noname10**

Powered by JWS Online



JWSApplet - ver 5.0.3 noname10

	Parameter	Value
P1_v1	uVol	1
P2_v1	V1	2.5
P3_v1	Ki	1
P4_v1	n	1
P5_v1	K1	10
P6_v1	V2	0.25
P7_v1	KK2	8
P8_v1	k3	0.025
P9_v1	KK3	15
P10_v1	k4	0.025
P11_v1	KK4	15
P12_v1	V5	0.75
P13_v1	KK5	15
P14_v1	V6	0.75
P15_v1	KK6	15
P16_v1	k7	0.025
P17_v1	KK7	15
P18_v1	k8	0.025
P19_v1	KK8	15
P20_v1	V9	0.5

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Reset

Evaluate Model

Sim State

StartTime EndTime

0 2500

☐ Rates ☒ Metabolites

Type	Output	Plot
M1	MAPK	<input checked="" type="checkbox"/>
M2	MAPKP	<input checked="" type="checkbox"/>
M3	MKK	<input checked="" type="checkbox"/>
M4	MKKK	<input checked="" type="checkbox"/>
M5	MKKP	<input checked="" type="checkbox"/>
M6	MAPK...	<input checked="" type="checkbox"/>
M7	MKKKP	<input checked="" type="checkbox"/>
M8	MKKPP	<input checked="" type="checkbox"/>
F1	v[J0]	<input checked="" type="checkbox"/>
F2	v[J1]	<input checked="" type="checkbox"/>
F3	v[J2]	<input checked="" type="checkbox"/>
F4	v[J3]	<input checked="" type="checkbox"/>
F5	v[J4]	<input checked="" type="checkbox"/>
F6	v[J5]	<input checked="" type="checkbox"/>

0 Search

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[Model Comment/Bug](#)

ties Parameters

g about oscillations in the mitogen-activated protein kinase cascades.

logy, Thomas Jefferson University, Philadelphia, PA 19107, USA.

[KKK cascade](#)

[T 634](#)

Applet jjjApplet started

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# Different views of a model

Biomodels Home Index JWS Online

Biomodels: BIOMD0000000010 noname8  
Powered by JWS Online

JWSApplet - ver 4.1.1 noname8

Parameter	Value
P1_v1	uVol
P2_v1	J0V1
P3_v1	J0K1
P4_v1	J0n
P5_v1	J0K1
P6_v1	J1V2
P7_v1	J1KK2
P8_v1	J2K3
P9_v1	J2KK3
P10_v1	J3K4
P11_v1	J3KK4
P12_v1	J4V5
P13_v1	J4KK5
P14_v1	J5V6
P15_v1	J5KK6
P16_v1	J6K7
P17_v1	J6KK7
P18_v1	J7K8
P19_v1	J7KK8
P20_v1	J8V9

Evaluate Model

Sim State MCA

Start Time End Time

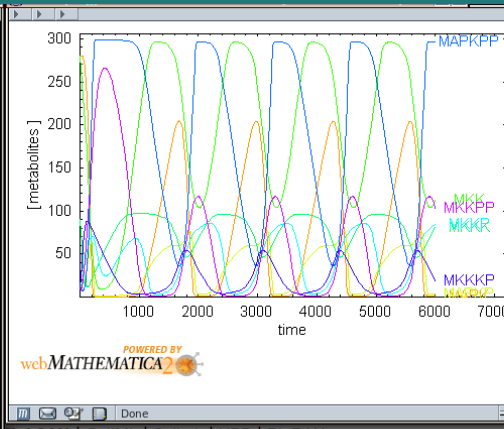
0 6000

Rates Metabolites

Type	Output	Plot
M1	MAPK	<input checked="" type="checkbox"/>
M2	MAPK-P	<input checked="" type="checkbox"/>
M3	MAPK-PP	<input checked="" type="checkbox"/>
M4	MAPK-K	<input checked="" type="checkbox"/>
M5	MAPK-K-P	<input checked="" type="checkbox"/>
M6	MAPK-K-PP	<input checked="" type="checkbox"/>
M7	MAPK-K-K	<input checked="" type="checkbox"/>
M8	MAPK-K-K-P	<input checked="" type="checkbox"/>
F1	V[J0]	<input checked="" type="checkbox"/>
F2	V[J1]	<input checked="" type="checkbox"/>
F3	V[J2]	<input checked="" type="checkbox"/>
F4	V[J3]	<input checked="" type="checkbox"/>
F5	V[J4]	<input checked="" type="checkbox"/>
F6	V[J5]	<input checked="" type="checkbox"/>

webMATHEMATICA2

Applet started



Reference Publication

Eur J Biochem 2000 Mar;267(6):1583-8.  
Negative feedback and ultrasensitivity can bring about oscillations  
Kholodenko BN.  
Department of Pathology, Anatomy and Cell Biology, University of  
Boris.Kholodenko@mail.tju.edu [more]

Model ID: 10712587

Model

Compartments (1)

Species (8)

Rules (0)

Reactions (10)

activation

MAPKKK

MAPKKK-P

MAPK-PP

as: J0

inactivation

MAPKKK-P

MAPKKK

as: J1

activation of MAPK

MAPK

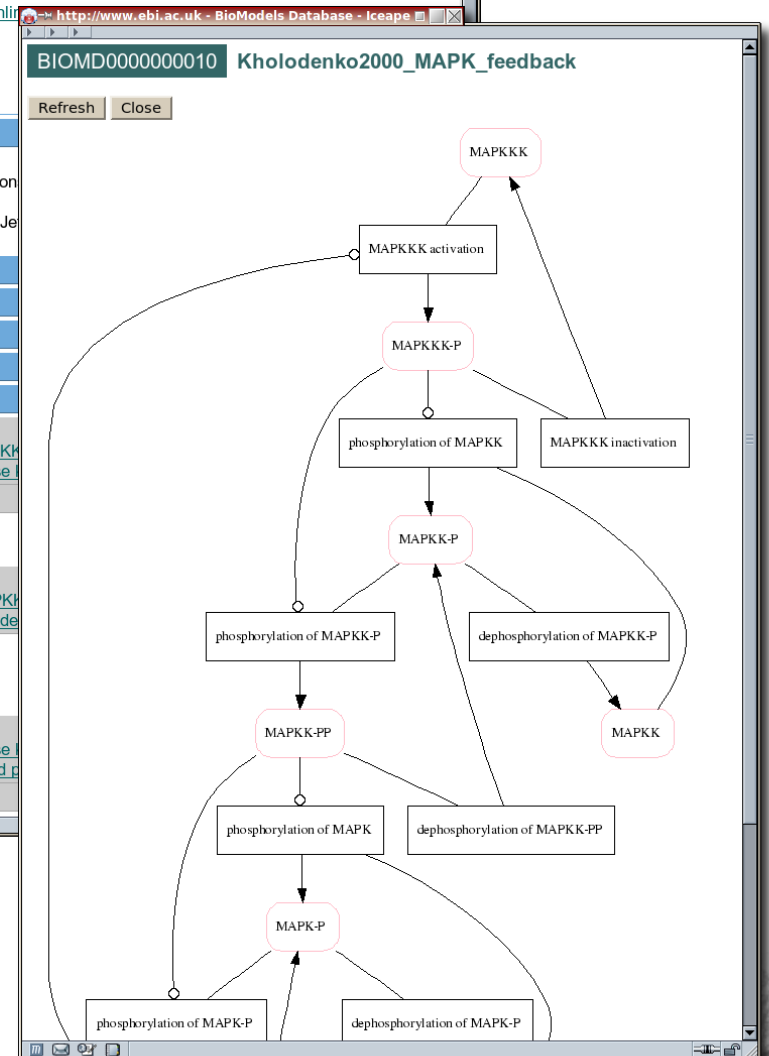
MAPK-P

MAPK-PP

MAPK-K

MAPK-K-P

MAPK-K-PP



Reaction:

MAPKKK activation

rate law:

$$uVol * V1 * MAPKKK / ((1 + pow(MAPK-PP / Ki, n)) * (K1 + MAPKKK))$$

Compartment

Name	Size
uVol	1.0

Species

Name	Compartment	Initial Amount	Initial Concentration
MAPKKK	uVol		90.0
MAPK-PP	uVol		10.0

Parameters

Name	Value
V1	2.5
Ki	9.0
n	1.0
K1	10.0

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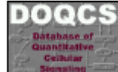


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Meetings

Support

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"Complete Dataset"

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  - b. Contact BioModels team to include your modifications in the standard version of the model.
  - c. Rename the modified model, and remove both the BioModels Database identifier and any mention of the model creators.

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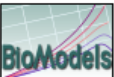
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BioModels Web Services

Available features

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

Following are the currently available features in BioModels Web Services. In order to make using data in BioModels Database more conveniently, we will consider all requirements about new features.

- String helloBioModels()
- String[] getAllModelIds()
- String getModelById(String id)
- String getModelNameById(String id)
- String[] getModelIdsByName(String modelName)
- String[] getModelIdsByPublication(String publicationIdOrText)
- String[] getModelIdsByPerson(String personName)

For more detail, please see [javadoc](#) or [WSDL](#).

Download


According to different cases, we provide two kinds of libraries for using BioModels Web Services. For downloading, please right click on the link and "Save Target As" or "Save Link As".

Name	Description	Size	Link
biomodelswslib-standalone.jar	standalone and includes all external dependencies and ready for use;	1.8M	<a href="http://www.ebi.ac.uk/compneur-srv/biomodels/software/biomodelswslib-standalone.jar">http://www.ebi.ac.uk/compneur-srv/biomodels/software/biomodelswslib-standalone.jar</a>
biomodelswslib.jar	light-weight, but needs other dependencies to work together.	2.1K	<a href="http://www.ebi.ac.uk/compneur-srv/biomodels/software/biomodelswslib.jar">http://www.ebi.ac.uk/compneur-srv/biomodels/software/biomodelswslib.jar</a>

These are the dependencies only needed by light-weight library.

- [axis.jar](#)
- [jaxrpc.jar](#)
- [commons-logging-1.1.jar](#)
- [commons-discovery-0.2.jar](#)
- [saaj.jar](#)
- [wsdl4j-1.5.1.jar](#)





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- Non-curated Models
- Search
- Simulate in JWS

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- Submit Your Model

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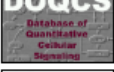


- Sign-in

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- News
- Model of the Month
- Meetings
- Support
- Contact

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### Model of the month

---

- June 2007 - BIOMD0000000026-31: **Markevich et al. (2004), MAPK** by *Lu Li* [\[More\]](#)
- May 2007 - BIOMD0000000017: **Hoefnagel et al. (2002), Metabolic Control Analysis** by *Dominic P. Tolle* [\[More\]](#)
- April 2007 - BIOMD0000000058: **Bindschadler and Sneyd (2001), Coupled Calcium Oscillators** by *Melanie Stefan* [\[More\]](#)
- March 2007 - BIOMD0000000001: **Edelstein (1996), Nicotinic Receptor** by *Nicolas Le Novère* [\[More\]](#)
- February 2007 - BIOMD0000000049: **Sasagawa (2005), MAPK** by *Lu Li* [\[More\]](#)
- January 2007 - BIOMD0000000064: **Teusink (2000), Glycolysis** by *Dominic P. Tolle* [\[More\]](#)
- December 2006 - BIOMD0000000065: **Yildirim (2003), lac Operon** by *Melanie Stefan* [\[More\]](#)
- November 2006 - BIOMD0000000025: **Smolen (2002), Circadian Oscillator** by *Enuo He* [\[More\]](#)
- October 2006 - BIOMD0000000005: **Tyson (1991), Modelling Cell Division** by *Nicolas Le Novère* [\[More\]](#)
- September 2006 - BIOMD0000000020: **Hodgkin and Huxley (1952), Membrane Current in the Giant Squid Axon** by *Melanie Stefan* [\[More\]](#)
- August 2006 - BIOMD0000000048: **Kholodenko (1999), Epidermal Growth Factor Receptor signalling** by *Renaud Schiappa* [\[More\]](#)
- July 2006 - BIOMD0000000012: **Elowitz and Leibler (2000), The Repressilator** by *Dominic P. Tolle* [\[More\]](#)
- June 2006 - BIOMD0000000009: **Huang and Ferrell (1996), MAPK ultrasensitivity** by *Nicolas Le Novère* [\[More\]](#)

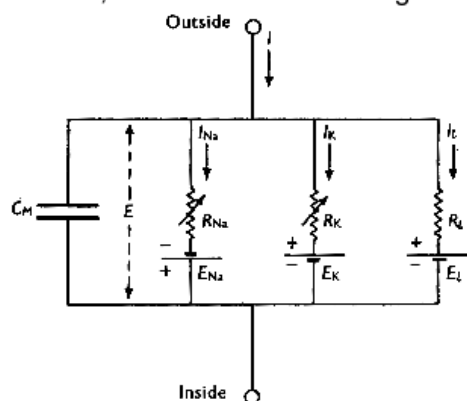


## BIOMD0000000020 - Hodgkin and Huxley (1952), Membrane Current in the Giant Squid Axon

*by Melanie Stefan*

The mechanisms and rules that govern nervous impulses have been the focus of research and speculation throughout the centuries [1]. In the 1930, Alan Hodgkin and Andrew Huxley started a series of experiments and modelling to elucidate the flow of electric current through an axonal membrane. This led to the formulation of the Hodgkin-Huxley model in 1952 [2], which has had a lasting influence on our understanding of neuronal function. Both were awarded the Nobel Prize in Physiology or Medicine in 1963.

Hodgkin and Huxley chose the giant squid axon as a model system for their experiments, since it is unusually large (around 0.5 mm in diameter) and therefore quite suitable for electrophysiological experiments [1]. In particular, it was possible to insert a micropipette into the axon and perform voltage-clamp experiments, a technique that had been devised in the 1930s by Cole and Curtis [3]. The experiments were combined with detailed quantitative modelling, which involved a considerable amount of work: Since the university computer in Cambridge was on a six-month downtime in 1951, the calculations were performed on a hand-operated machine [4]. The outcome was a sound mathematical description of the system's behaviour, now known as the Hodgkin-Huxley equations [2].



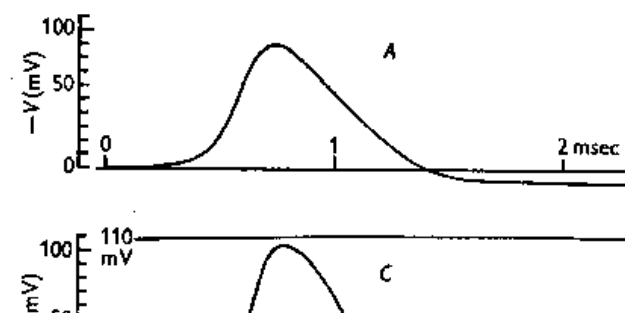
In the Hodgkin-Huxley model, the membrane can be represented as an electrical circuit, as shown in figure 1. Ionic current through the membrane can be divided into three components: potassium current ( $I_K$ ), sodium current ( $I_{Na}$ ), and a small leakage current ( $I_l$ ) caused by other ions [2]. Each component can be expressed in terms of the cell's resting potential ( $E$ ), the respective equilibrium potential for each component ( $E_K$ ,  $E_{Na}$ , and  $E_l$ ), constants reflecting the conductance of each component ( $G_K$ ,  $G_{Na}$ , and  $G_l$ ) and additional variables representing the activation of potassium transport ( $n$ ), or the activation ( $m$ ) or non-inhibition ( $h$ ) of sodium transport. The equation for the total ionic current thus reads:

$$I = G_K n^4 (E - E_K) + G_{Na} m^3 h (E - E_{Na}) + G_I (E - E_I)$$

Figure 1: The membrane as an electrical circuit (from [2])

The model thus related changes in membrane potentials to conductance changes. It proved to be very powerful in describing, amongst other things, the form and amplitude of propagated action potentials, the total inward movement of sodium ions and the total outward movement of potassium ions associated with an impulse, the threshold and response during the refractory period following an axon potential and the form of subthreshold responses [2].

An example for the fit between calculated and observed action potentials is shown in figure





**Model of Month - Thunderbird**

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Fernandez et al. (2006), Integration of glutamate and dopamine signals	Model of Month	01/01/09 00:00
Proctor et al. (2007), Ubiquitin-Proteasome System	Model of Month	01/12/08 00:00
Bakker et al. (2001), Glycolysis in Trypanosoma	Model of Month	01/11/08 00:00
Fung et al. (2005), Metabolator	Model of Month	01/10/08 00:00
Vilar et al. (2006), TGF- $\beta$	Model of Month	01/09/08 00:00
Yang et al. (2007), Arachidonic Acid	Model of Month	01/08/08 00:00
Marhl et al. (2000), Calcium Oscillations	Model of Month	01/07/08 00:00
Legewie et al. (2006), Apoptosis	Model of Month	01/06/08 00:00
Maurva et al. (2005), GTPase-Cycle Module	Model of Month	01/05/08 00:00

**Subject: Fernandez et al. (2006), Integration of glutamate and dopamine signals**

From: [Model of Month](#)

Date: 01/01/09 00:00

Website: [http://www.ebi.ac.uk/biomodels-main/static-pages.do?page=ModelMonth%252FJanuary2009%252FBIOMD0000000152\\_MM](http://www.ebi.ac.uk/biomodels-main/static-pages.do?page=ModelMonth%252FJanuary2009%252FBIOMD0000000152_MM)

**BIOMD0000000152, Fernandez et al. (2006), Integration of glutamate and dopamine signals**

by Michele Mattioni

The integration of different signals is one of the most complex and interesting features of the brain. In [BIOMD0000000152](#) Fernandez et al [1] elucidate in which way DARPP-32, a protein present in the spine of the Medium Spiny Neuron, is able to integrate the different stimuli provided by the release of glutamate and dopamine.

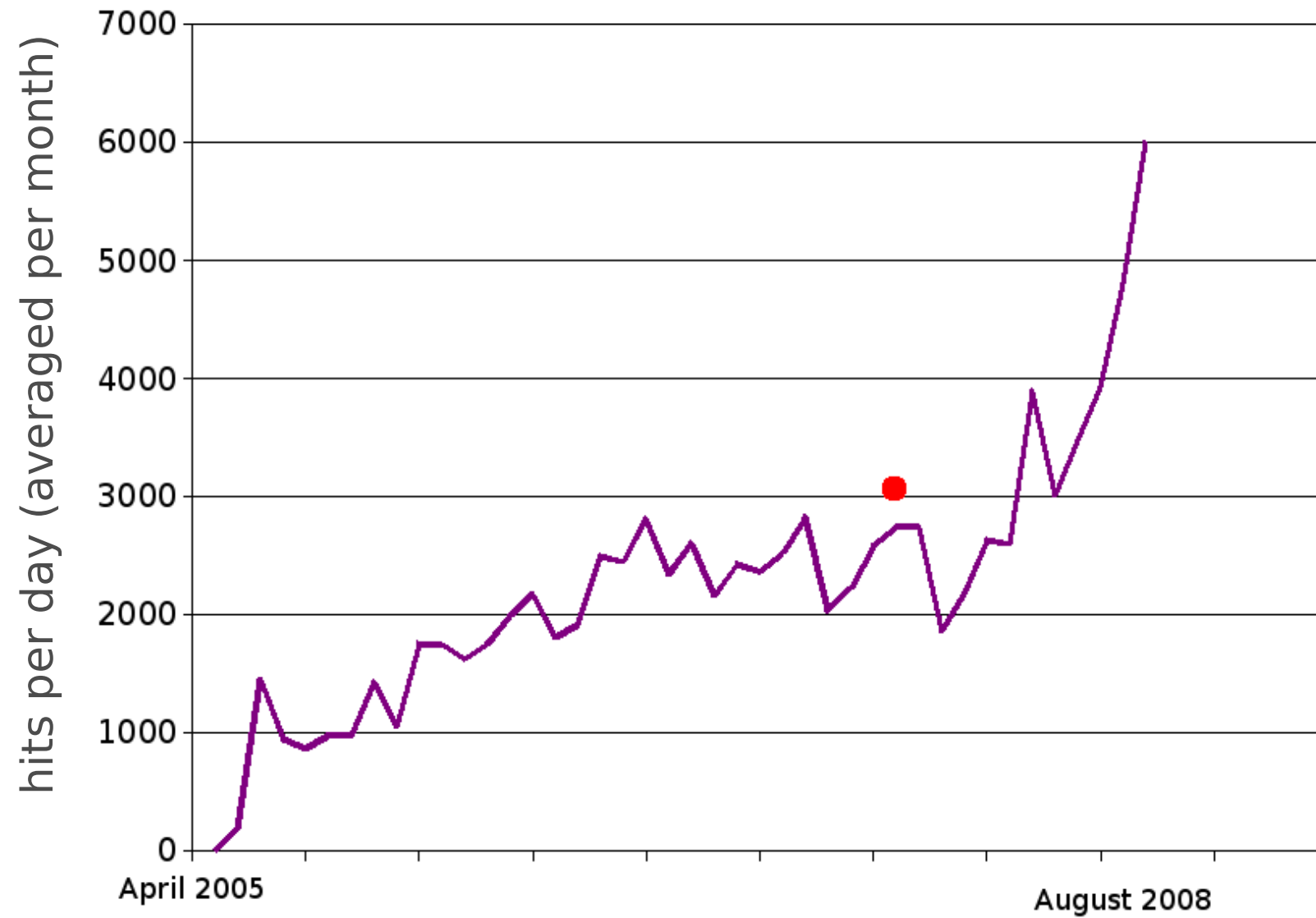
The peculiar ability of a synapse to change its own strength according to the series of inputs that it receives from other neurons plays a key role in the learning ability of the brain. Learning, in the basal ganglia, is often connected with reward. Two kinds of responses are able to encode this information: An activity-dependent increase in synapse strength, known as [Long Term Potentiation \(LTP\)](#) and an activity-dependent weakening of the synapse, known as [Long Term Depression \(LTD\)](#).

The capacity of a medium spiny neuron to encode long term memory (LTM) is given by the ability to change its state between those two. The model shows how DARPP-32 is a key player in this delicate equilibrium between these two forms of excitability.

The reactions involving DARPP-32 are depicted in figure 1. Model A features the biochemical network and the receptors present in the nigro-striatal medium spiny neuron, while model B represents a nigro-pallidal medium spiny neuron, which differs slightly in the types of dopamine receptors present (D2 instead of D1) and the corresponding biochemical cascades.

Unread: 31 Total: 32









Nicolas Le Novère  
PI



Chen Li  
developer



Lukas Endler  
curator



Melanie Stefan  
(model of the month)



Nicolas Rodriguez  
developer  
(50%)



Vijayalakshmi  
Chelliah  
curator



Camille Laibe  
developer  
(MIRIAM,  
SBO)



Michael Hucka  
PI



Nick Juty  
curator  
(MIRIAM,  
SBO)

