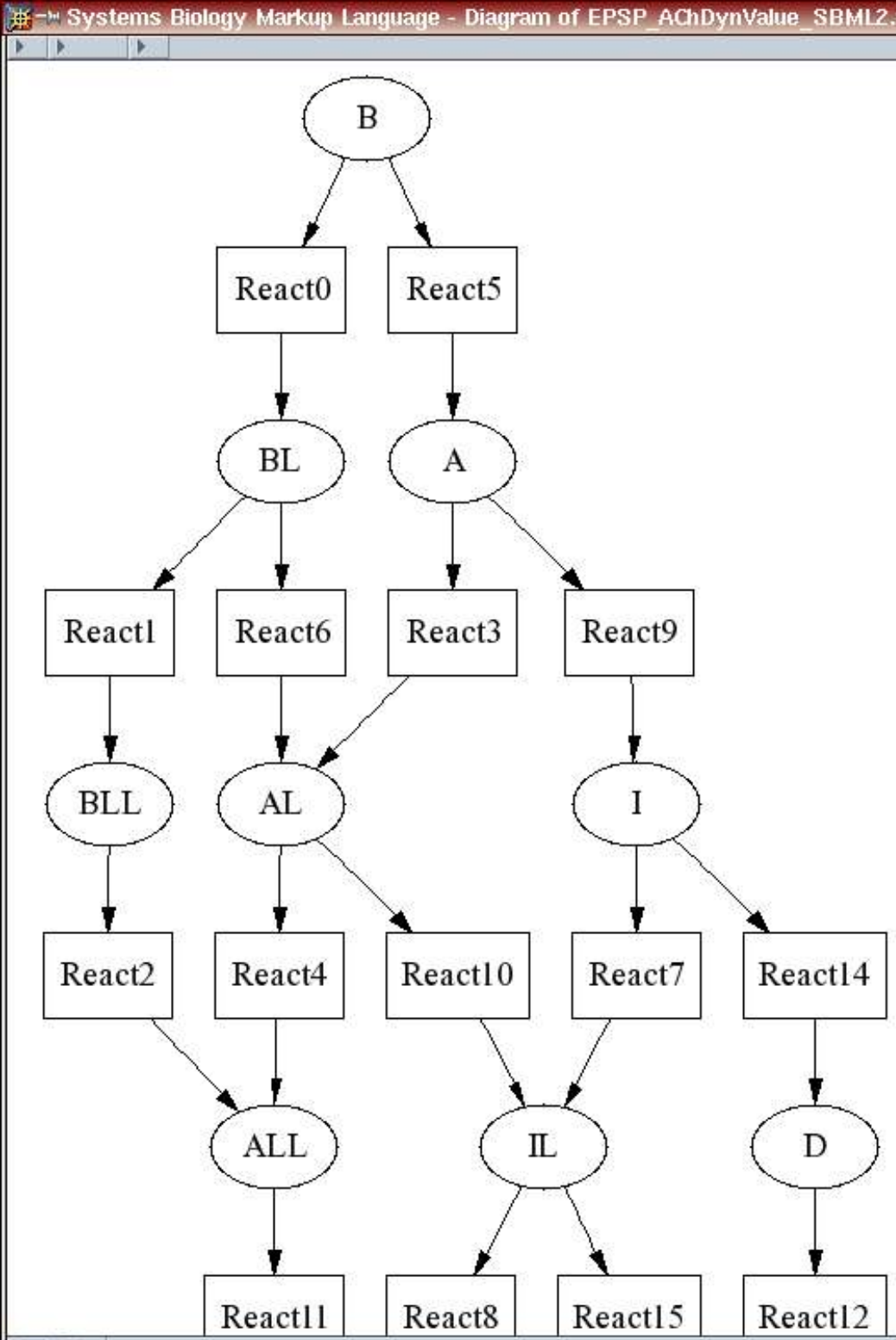
Curation and exchange of kinetic models of biochemical pathways

Nicolas Le Novère
EMBL-EBI, United-Kingdom

BioPAX F2F meeting, Tokyo, November 18th 2005

Is SBML sufficient?


Systems Biology Markup Language - Diagram of EPSP_AChDynValue_SBML2.xml - Mozilla
B
React0
React5
BL
A
React1
React6
React3
React9
BLL
AL
I
React2
React4
React10
React7
React14
ALL
IL
D
React11
React8
React15
React12
http://sbml.org/documents

No, it isn't!

BIOMODELS.NET

The Next Step After Standard Formats

For computational modeling to become more widely used in biological research, researchers must be able to exchange and share their results. The development and broad acceptance of common model representation formats such as **SBML** is a crucial step in that direction, allowing researchers to exchange and build upon each other's work with greater ease and accuracy.

The BioModels.net project is another step: an international effort to (1) define agreed-upon standards for model curation, (2) define agreed-upon vocabularies for annotating models with connections to biological data resources, and (3) provide a free, centralized, publicly-accessible database of annotated, computational models in SBML and other structured formats.

Helping to Define Community Standards

To facilitate assembling useful collections of quantitative models of biological phenomena, it is crucial to establish standards for the vocabularies used in model annotations as well as criteria for minimum quality levels of those models. The BioModels.net project aims to bring together a community of interested researchers to address these issues. We are working towards defining these standards through white papers and process definitions. All of the products of our efforts are open and freely available through this site.

Standards and Processes Developed Hand-in-Hand with a New Database

The database component of BioModels.net is especially designed for working with *annotated* computational models: each model is carefully reviewed and augmented by human annotators on the BioModels.net team to add metadata linking the model elements to other biological databases and resources. The **BioModels database at the EBI** system goes far beyond other collections of models by being a *true* database, featuring browsing, cross-referencing, searching, and (coming soon) facilities for visualization, exporting models in different formats, and remote API access.

Minimum Information Requested In the Annotation of biochemical Models (MIRIAM)

Le Novère N.*, Finney A.*, Hucka M., Bhalla U., Campagne F., Collado-Vides J., Crampin E., Halstead M., Klipp E., Mendes P., Nielsen P., Sauro H., Shapiro B., Snoep J.L., Spence H.D., Wanner B.L.

Nature Biotechnology **(2005), 23: in the press**

Reference correspondence

- The model must be encoded in a public, standardized, machine-readable format (SBML, CellML, GENESIS ...)
- The model must comply with the standard in which it is encoded!
- The model must be clearly related to a single reference description. If a model is composed from different parts, there should still be a description of the derived/combined model.
- The encoded model structure must reflect the biological processes listed in the reference description.
- The model must be instantiated in a simulation: All quantitative attributes have to be defined, including initial conditions.
- When instantiated, the model must be able to reproduce all results given in the reference description within an epsilon (algorithms, round-up errors)

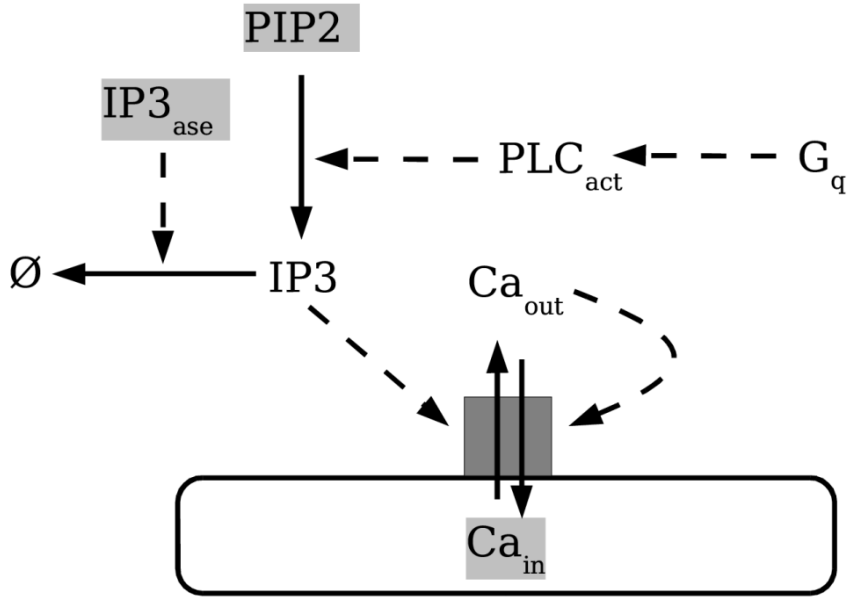
Attribution annotation

- The model has to be named.
- A citation of the reference description must be joined (complete citation, unique identifier, unambigous URL). The citation should permit to identify the *authors* of the model.
- The name and contact of model *creators* must be joined.
- The date and time of creation and last modification should be specified. An history is useful but not required.
- The model should be linked to a precise statement about the terms of distribution. MIRIAM does not require “freedom of use” or “no cost”.

External resource annotation

- The annotation must permit to unambiguously relate a piece of knowledge to a model constituent.
- The referenced information should be described using a triplet {data-type, identifier, qualifier}
  - The data-type should be written as a Unique Resource Identifier (URI). Either a URL (webpage) or a URN (e.g. LSID). Not necessarily a physical location.
  - The identifier is analysed by the software within the framework of the data-type.
  - Data-type and Identifier can be combined in a single URI
    http://www.myResource.org/#myIdentifier
    urn:lsid:myResource.org:myIdentifier
  - Qualifiers (optional) should refine the link between the model constitutent and the piece of knowledge: “has a”, “is version of”, “is homolog to” etc.
- The community will have to agree on a set of standard valid URIs.

Model example



$$k_1 = k_2 = k_3 = 1\ s^{-1}$$

$$Km_1 = 10^{-7}\ M, Km_2 = 10^{-8}, Km_3 = 2.10^{-6}\ M$$

$$K_A = 10^{-11}, m = 4, n = 3, \alpha = 0.001$$

$$[Ca_{in}] = [IP3R] = [PLC_{tot}] = [PIP2] = [IP3_{ase}] = 0.001\ M$$

$$[G_q] = 0.01\ M, [Ca_{out}] = [IP3] = [PLC_{act}] = 0\ M$$

$$\frac{d[Ca_{out}]}{dt} = \frac{k_1[IP3R] * ([Ca_{in}] - [Ca_{out}])}{Km_1 + |[Ca_{in}] - [Ca_{out}]|} * \frac{[IP3]^m}{K_A + [IP3]^m}$$

$$\frac{d[IP3]}{dt} = \frac{k_2[PLC_{act}] * [PIP2]}{Km_2 + [PIP2]} - \frac{k_3[IP3_{ase}] * [IP3]}{Km_3 + [IP3]}$$

$$\frac{d[PLC_{act}]}{dt} = \frac{[G_q]^n}{\alpha + [G_q]^n} * [PLC_{tot}]$$

creators	Joe User (juser@eden.com), Anne Other (aother@eden.com)
creation date	01 January 0000
last modification	31 May 2005

Constituent	Data Type	Identifier	Qualifier	Meaning
model	http://www.pubmed.gov/	0000000		
	http://www.ncbi.nlm.nih.gov/Taxonomy/	9606		*Homo sapiens*
	http://www.geneontology.org/	GO:0007204	IsVersionOf	*positive regulation of cytosolic [ca^{2+}]*
	http://www.geneontology.org/	GO:0051279	IsVersionOf	*regulation of release of sequestered ca^{2+} into cytop*
	http://www.genome.jp/kegg/pathway/	hsa04020	IsPartOf	*Calcium signaling pathway - H sapiens*
	http://www.genome.jp/kegg/pathway/	hsa04070	IsPartOf	*Phosphatidylinositol signaling system - H sapiens*
compartment ER	http://www.geneontology.org/	GO:0005790		*smooth endoplasmic reticulum*
reactant Ca_{in}	http://www.ebi.ac.uk/chebi/	CHEBI:29108		*calcium(2+)*
cytoplasm	http://www.geneontology.org/	GO:0005737		*cytoplasm*
reactant Ca_{out}	http://www.ebi.ac.uk/chebi/	CHEBI:29108		*calcium(2+)*
reactant IP3	http://www.ebi.ac.uk/chebi/	CHEBI:16595		*1D-myo-inositol 1,4,5-tris(dihydrogen phosphate)*
reactant PIP2	http://www.ebi.ac.uk/chebi/	CHEBI:18348		*1-phosphatidyl-1D-myo-inositol 4,5-bisphosphate*
reactant IP3R	http://www.uniprot.org/	Q14643	HasVersion	*Inositol 1,4,5-trisphosphate receptor type 1*
	http://www.uniprot.org/	Q14571	HasVersion	*Inositol 1,4,5-trisphosphate receptor type 2*
	http://www.uniprot.org/	Q14573	HasVersion	*Inositol 1,4,5-trisphosphate receptor type 3*
reactant PLC_{act}	http://www.uniprot.org/	Q9NQ66	IsVersionOf	*PIP2 phosphodiesterase β1*
reactant PLC_{tot}	http://www.uniprot.org/	Q9NQ66		*PIP2 phosphodiesterase β1*
reactant $IP3_{ase}$	http://www.uniprot.org/	Q14642		*Type I inositol-1,4,5-trisphosphate 5-phosphatase*
reactant G_q	http://www.uniprot.org/	Q6NT27		*Guanine nucleotide binding protein Gq*
reaction $Ca_{release}$	http://www.geneontology.org/	GO:0005220		*IP3-sensitive calcium-release channel activity*
	http://www.geneontology.org/	GO:0008095	IsVersionOf	*IP3 receptor activity*
reaction $IP3_{production}$	http://www.geneontology.org/	GO:0004435	IsVersionOf	*phosphoinositide phospholipase C activity*
	http://www.ebi.ac.uk/intenz/	3.1.4.11	IsVersionOf	*phosphoinositide phospholipase C*
reaction $IP3_{degradation}$	http://www.ebi.ac.uk/intenz/	3.1.3.56	IsVersionOf	*inositol-polyphosphate 5-phosphatase*
reaction $PLC_{activation}$	http://www.geneontology.org/	GO:0007200		*G-protein signaling coupled to IP3 2nd messenger*

BioModels Database: A Free, Centralized Database of Curated, Published, Quantitative Kinetic Models of Biochemical and Cellular Systems

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 M.

Nucleic Acids Research, (2006), 34: in the press

BioModels Database

- Store and serve quantitative models of biomedical interest
- BioModels Database goes further than MIRIAM: 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.
- Models are accepted in several format, and served in several others.
- Aims to be the Swiss-Prot of quantitative modelling.

Where are the models coming from

I) Repositories

- SBML repository
- JWS Online
- E-Cell Developer Network

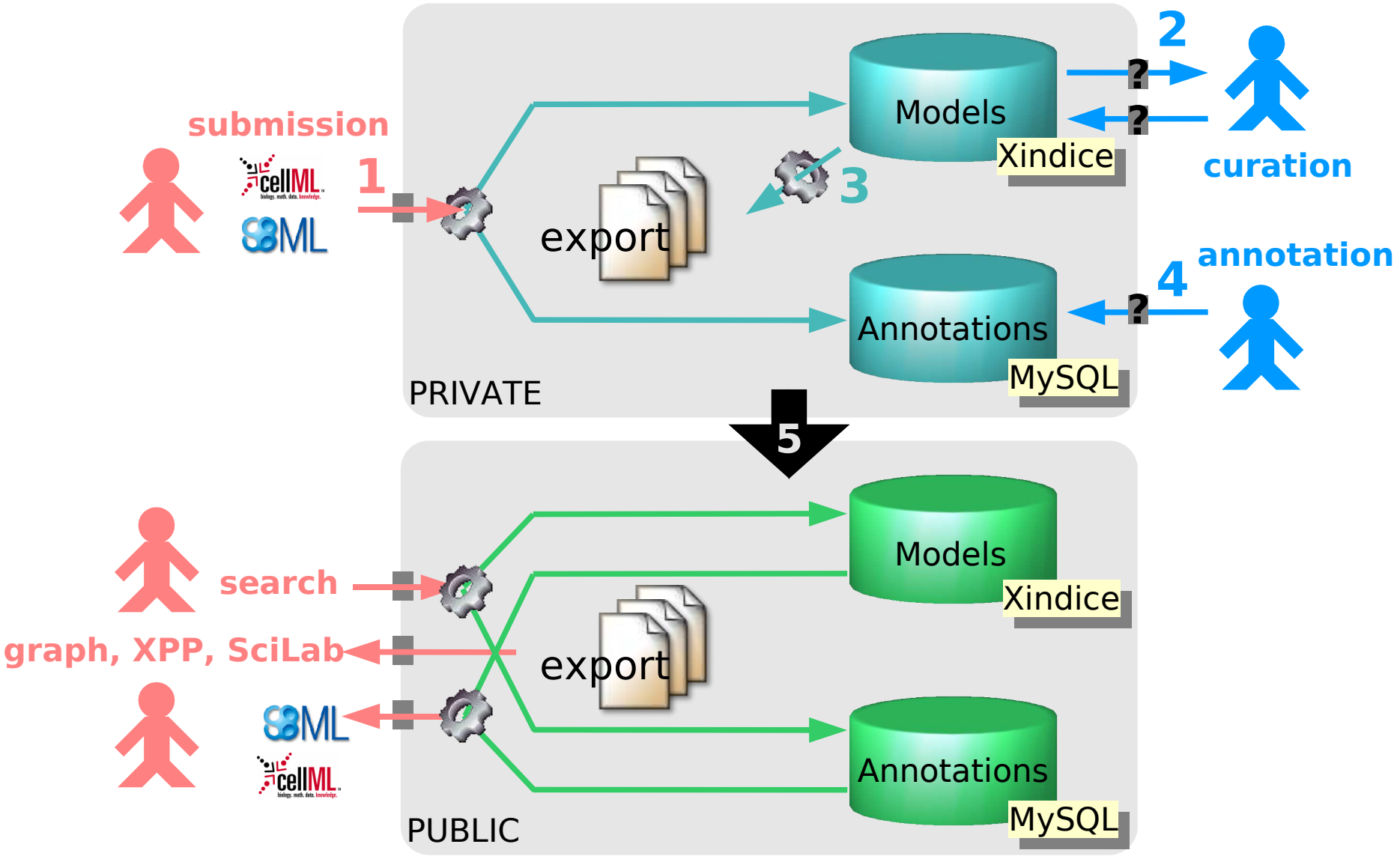
II) Individuals

- Members of the SBML community (developers+modelers)
- Authors

III) Journals (NPG/EMBO MSB; cf JWS)

IV) BioModels Database curators

Structure of BioModels Database



Detailed pipeline

1) Non-authenticated submission: SBML or CellML
   - Annotation in the model (<notes>, <annotation>)
   - Annotation entered through submission form
2) [Transformation into SBML Level 2 Version 1]
3) XML schema validation
4) Consistency check
5) Generation of export formats (SBML, CellML, SciLab, XPP, dot)
6) Authenticated semantic curation (correspondence with paper)
7) 3 to 5 again
8) Authenticated annotation
   - SBML annotation in the RDF format proposed by Le Novère and Finney is recognised and reused!

Model annotation

model	Submitter, Creators, publication, Gene Ontology, ICD10, KEGG pathway, OMIM, Reactome, Taxonomy
compartment	Gene Ontology
species	BIND complex, ChEBI, Ensembl, Gene Ontology, InterPro, KEGG compound, OMIM, Taxonomy, UniProt
rule	BIND interaction, EC code, Gene Ontology, IntAct, KEGG pathway, KEGG Reaction, Reactome
reaction	BIND interaction, EC code, Gene Ontology, IntAct, KEGG pathway, KEGG Reaction, Reactome
event	BIND interaction, EC code, Gene Ontology, IntAct, KEGG pathway, KEGG Reaction, Reactome

Reference Publication

PubMed ID: 2732237

J Biol Chem. 1989 Jun 25;264(18):10552-66.
Folate cycle kinetics in human breast cancer cells.
Morrison PF, Allegra CJ.

Model

Submitter: Nicolas Le Novère

Submission Date: 2005-03-09T00:38:18

Last Modification Date: 2005-06-29T11:23:01

Creators: Tomas Radivoyevitch
Nicolas Le Novere

Gene Ontology	GO:0046655
KEGG Pathway	map00670 map00790
Taxonomy	9606
ICD10	C50

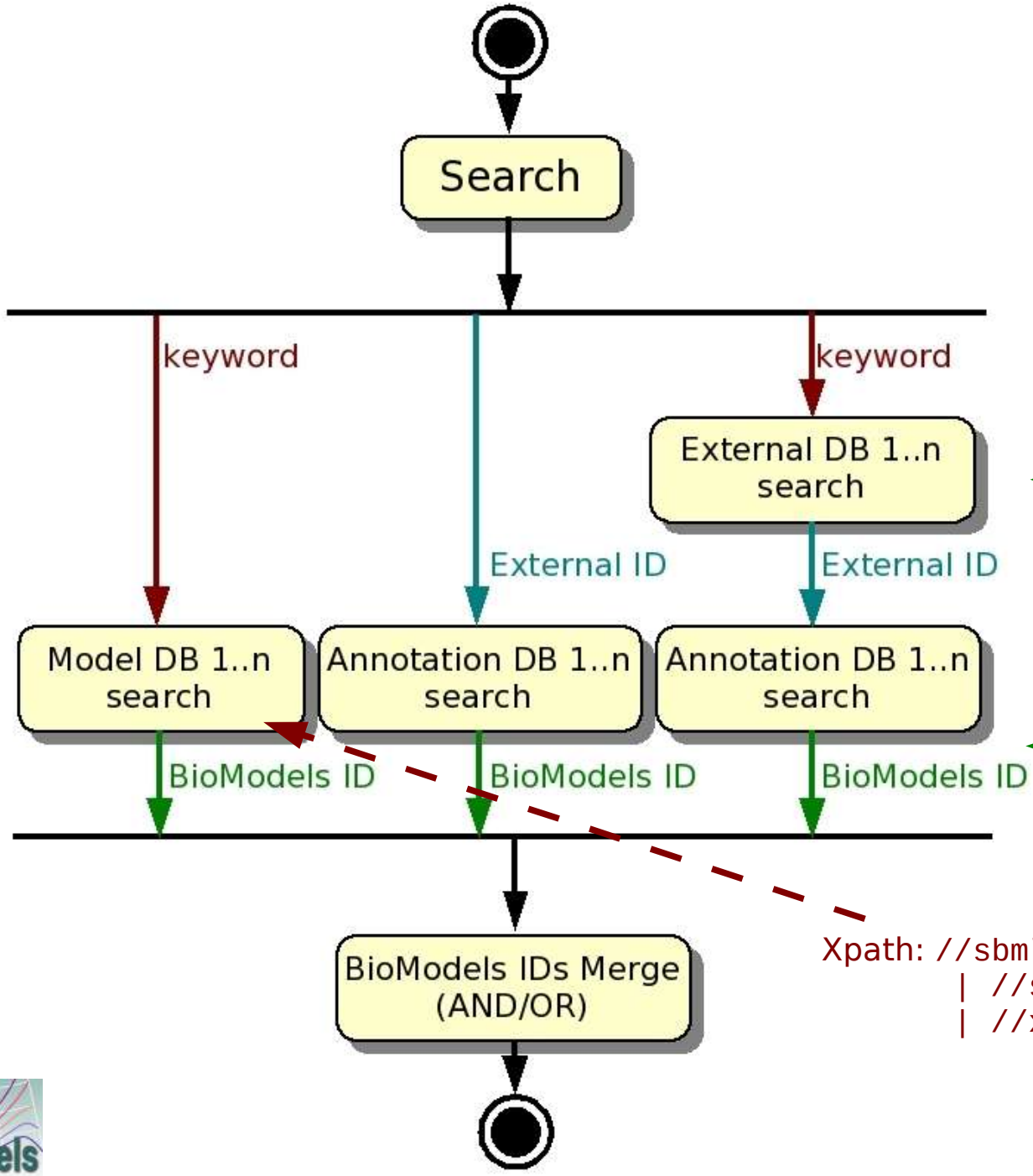
Compartments (2)

cell	**Gene Ontology**	GO:0005623
ext	**Gene Ontology**	GO:0005615

Species (33)

dihydrofolate free Compartment: cell Initial Concentration: 0.0012	**ChEBI**	CHEBI:15633
	KEGG Compound	C00415
dihydrofolate bound Compartment: cell Initial Concentration: 0.0024	**ChEBI**	CHEBI:15633
	KEGG Compound	C00415
dihydrofolate reductase free Compartment: cell Initial Concentration: 0.64	**UniProt**	P00374
dihydrofolate reductase total Compartment: cell Initial Concentration: 0.64	**UniProt**	P00374
tetrahydrofolate Compartment: cell Initial Concentration: 0.46	**ChEBI**	CHEBI:20506
	KEGG Compound	C00101
5,10-methylene-tetrahydrofolate Compartment: cell Initial Concentration: 0.26	**ChEBI**	CHEBI:15636
	KEGG Compound	C00143

Search strategy



GO, UniProt Oracle database
ChEBI, PubMed WebServices

BioModels MySQL database

Xpath:
```
//sbml:*[contains(@id,'TEXT')]
| //sbml:*[contains(@name,'TEXT')]
| //xhtml:*[contains(text(),'TEXT')]
```

Curate Models

News
FAQ
Terms of Use
Related Software
Contact

BIOMODELS.NET

- *BioModels ID* → Search BioModels Database for *exact* BioModels identifiers (for example *BIOMD0000000007* 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 for SBML elements by either name or *notes* content (for example *Edelstein* or *nicotinic*).
- *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:0007049* or *cell cycle* for Gene Ontology, *P04551* or *cell division* for UniProt).
- *Resource ID* → 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 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.

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 ID:

Person:

SBML Elements:

Resource: Publication

Resource: Gene Ontology — cell cycle

Resource:

Publication
ChEBI
Gene Ontology
UniProt

Resource ID:

Resource ID: BIND

Resource ID: BIND

Compose by: and or

Search Reset

BIOMODELS.NET

BioModels Database
- Browse
- Search

Submit Your Model

Curators Sign In

FAQ

Terms of Use

Contact

Search Models

The search returned **6** models.

New Search

BioModels ID	Name	PubMed Id	Last Modified	
BIOMD0000000003	Goldbeter1991_MinMitOscil	1833774	2005-06-27T16:53:31	SBML
BIOMD0000000004	Goldbeter1991_MinMitOscil_ExplInact	1833774	2005-06-27T16:53:42	SBML
BIOMD0000000005	Tyson1991_CellCycle_6var	1831270	2005-06-27T16:54:42	SBML
BIOMD0000000006	Tyson1991_CellCycle_2var	1831270	2005-06-27T16:54:55	SBML
BIOMD0000000007	Novak1997_CellCycle	9256450	2005-06-27T16:56:33	SBML
BIOMD0000000008	Gardner1998_CellCycle_Goldbeter	9826676	2005-06-27T16:56:45	SBML

New Search

Browse
Search

Submit Your Model

Curate Models

News
FAQ
Terms of Use
Related Software
Contact

BIOMODELS.NET

BIOMD0000000007 Novak1997_CellCycle

SBML L2 V1 | CellML | XPP

View Model Graph

Submit Model Comment/Bug

Reference Publication

Publication ID: 9256450

Proc Natl Acad Sci U S A 1997 Aug;94(17):9147-52.
Modeling the control of DNA replication in fission yeast.
Novak B, Tyson JJ.
Department of Agricultural Chemical Technology, Technical University of Budapest, 1521 Budapest, St. Gellert ter 4, Hungary.

Model

Submitter: Nicolas Le Novère

Submission Date: 2005-09-13T13:33:30

Last Modification Date: 2005-09-13T13:33:30

Creation Date: 2005-02-09T13:27:02

Creators: Bruce Shapiro

Gene Ontology mitotic cell cycle
KEGG Pathway sce04110
Reactome 69278
Taxonomy 4896

Compartments (1)

Species (22)

Rules (15)

Reactions (25)

Events (2)

1: Proc Natl Acad Sci U S A. 1997 Aug 19;94(17):9147-52.

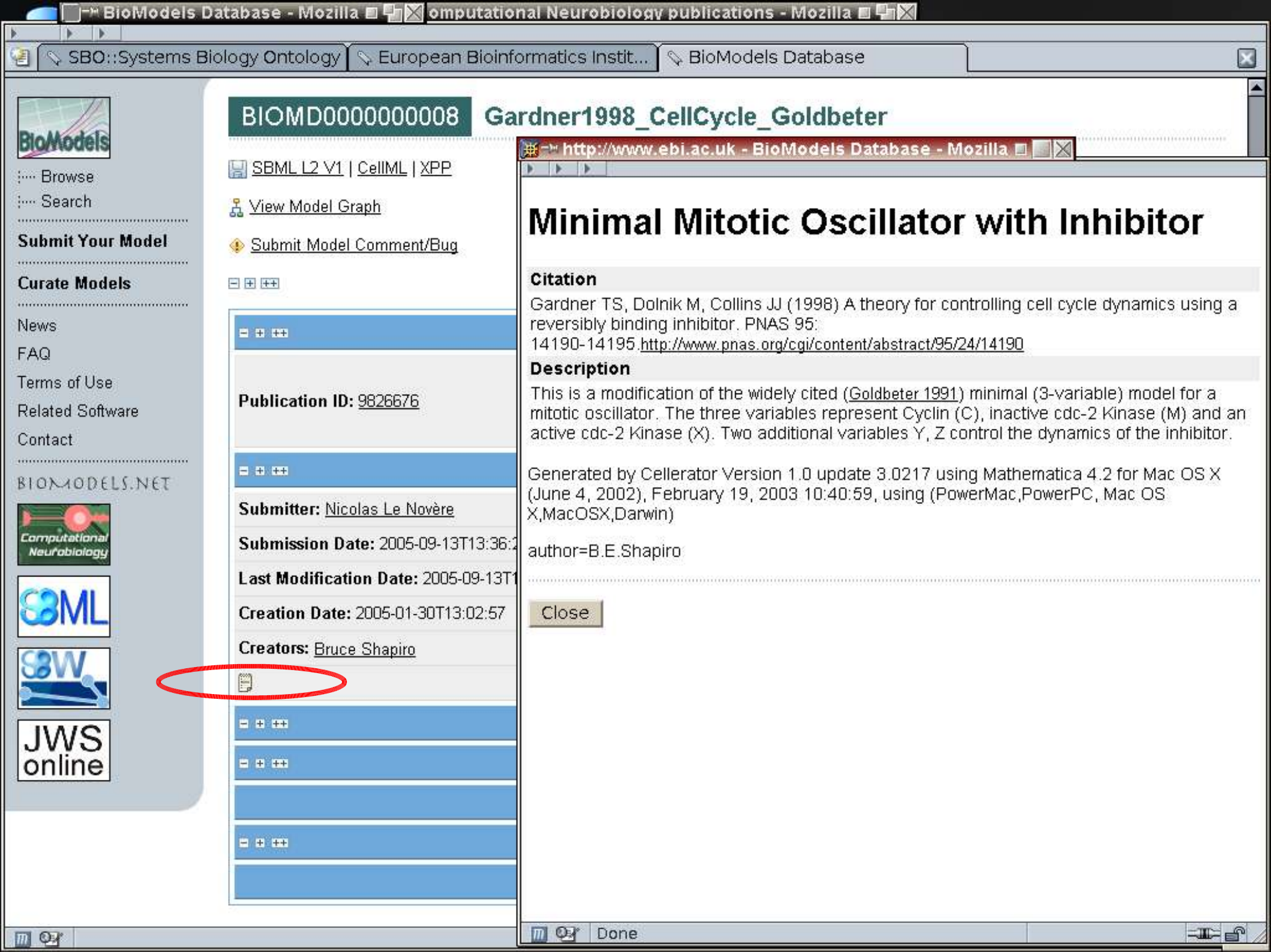
Modeling the control of DNA replication in fission yeast.

Novak B, Tyson JJ.

Department of Agricultural Chemical Technology, Technical University of Budapest, 1521 Budapest, St. Gellert ter 4, Hungary.

A central event in the eukaryotic cell cycle is the decision to commence DNA replication (S phase). Strict controls normally operate to prevent repeated rounds of DNA replication without intervening mitoses ("endoreplication") or initiation of mitosis before DNA is fully replicated ("mitotic catastrophe"). Some of the genetic interactions involved in these controls have recently been identified in yeast. From this evidence we propose a molecular mechanism of "Start" control in Schizosaccharomyces pombe. Using established principles of biochemical kinetics, we compare the properties of this model in detail with the observed behavior of various mutant strains of fission yeast: wee1(-) (size control at Start), cdc13Delta and rum1(OP) (endoreplication), and wee1(-) rum1Delta (rapid division cycles of diminishing cell size). We discuss essential features of the mechanism that are responsible for characteristic properties of Start control in fission yeast, to expose our proposal to crucial experimental tests.

PMID: 9256450 [PubMed - indexed for MEDLINE]


BioModels Database - Mozilla
omputational Neurobiology publications - Mozilla
SBO::Systems Biology Ontology
European Bioinformatics Instit...
BioModels Database
BioModels
Browse
Search
Submit Your Model
Curate Models
News
FAQ
Terms of Use
Related Software
Contact
BIOMODELS.NET
Computational Neurobiology
SBML
SBW
JWS online
BIOMD0000000008
Gardner1998_CellCycle_Goldbeter
SBML L2 V1 | CellML | XPP
View Model Graph
Submit Model Comment/Bug
Publication ID: 9826676
Submitter: Nicolas Le Novère
Submission Date: 2005-09-13T13:36:
Last Modification Date: 2005-09-13T1
Creation Date: 2005-01-30T13:02:57
Creators: Bruce Shapiro
http://www.ebi.ac.uk - BioModels Database - Mozilla
Minimal Mitotic Oscillator with Inhibitor
Citation
Gardner TS, Dolnik M, Collins JJ (1998) A theory for controlling cell cycle dynamics using a reversibly binding inhibitor. PNAS 95: 14190-14195.http://www.pnas.org/cgi/content/abstract/95/24/14190
Description
This is a modification of the widely cited (Goldbeter 1991) minimal (3-variable) model for a mitotic oscillator. The three variables represent Cyclin (C), inactive cdc-2 Kinase (M) and an active cdc-2 Kinase (X). Two additional variables Y, Z control the dynamics of the inhibitor.
Generated by Cellerator Version 1.0 update 3.0217 using Mathematica 4.2 for Mac OS X (June 4, 2002), February 19, 2003 10:40:59, using (PowerMac,PowerPC, Mac OS X,MacOSX,Darwin)
author=B.E.Shapiro
Close
Done

BioModels Database - Mozilla

Computational Neurobiology publications - Mozilla

SBO::Systems Biology Ontology | European Bioinformatics Instit... | BioModels Database

EMBL-EBI
European Bioinformatics Institute

EBI Home | About EBI | Groups | Services

BioModels

Browse
Search

Submit Your Model

Curate Models

News
FAQ
Terms of Use
Related Software
Contact

BIOMODELS.NET

Computational Neurobiology

SBML

SBW

JWS online

BIOMD0000000035 Vil

SBML L2 V1 | CellML | XPP

View Model Graph

Submit Model Comment/Bug

Publication ID: 11972055

Submitter: Nicolas Le Novère

Submission Date: 2005-09-13T14:54:3

Last Modification Date: 2005-09-13T1

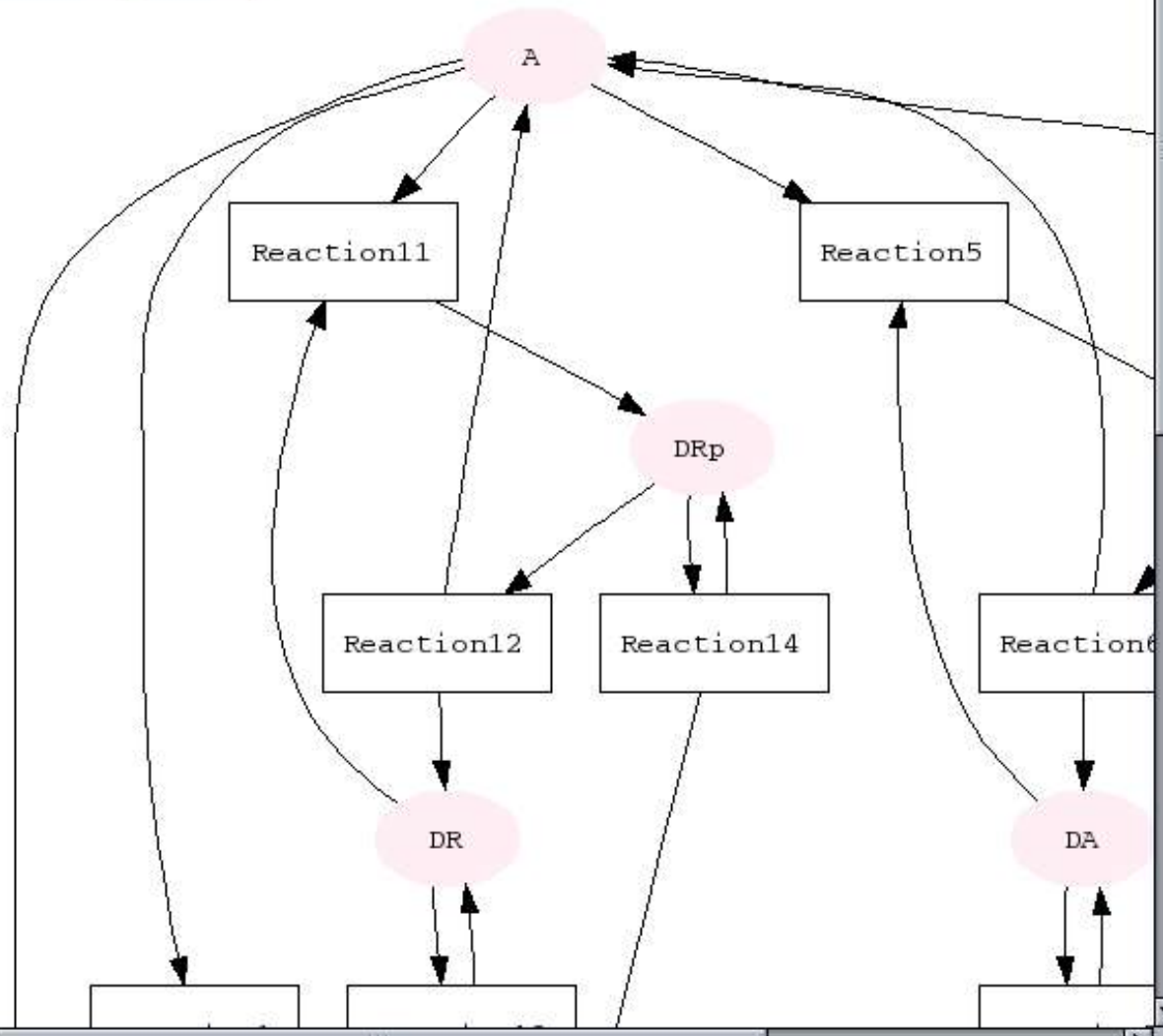
Creation Date: 2005-06-30T11:20:37

Creators: Bruce Shapiro

http://www.ebi.ac.uk - BioModels Database - Mozilla

BIOMD0000000035 Vilar2002_Oscillator

Refresh | Close



Browse
Search
Submit Your Model
Curate Models
News
FAQ
Terms of Use
Related Software
Contact
BIOMODELS.NET

BIOMD0000000007 Novak1997_CellCycle

SBML L2 V1 | CellML | XPP

View Model Graph

Submit Model Comment/Bug

Reference Publication

Publication ID: 9256450

Proc Natl Acad Sci U S A 1997 Aug;94(17):9147-52.
Modeling the control of DNA replication in fission yeast.
Novak B, Tyson JJ.
Department of Agricultural Chemical Technology, Technical University of Budapest, 1521 Budapest, St. Gellert ter 4, Hungary.

Model

Submitter: Nicolas Le Novère

Submission Date: 2005-09-13T13:33:30

Last Modification Date: 2005-09-13T13:33:30

Creation Date: 2005-02-09T13:27:02

Creators: Bruce Shapiro

Gene Ontology mitotic cell cycle
KEGG Pathway sce04110
Reactome 69278
Taxonomy 4896

Compartments (1)

Species (22)

Rules (15)

Reactions (25)

Cdc13_Cdc2 creation
Reactants:
Products: Cdc13_Cdc2

Reactome 68910
Reactome 69282

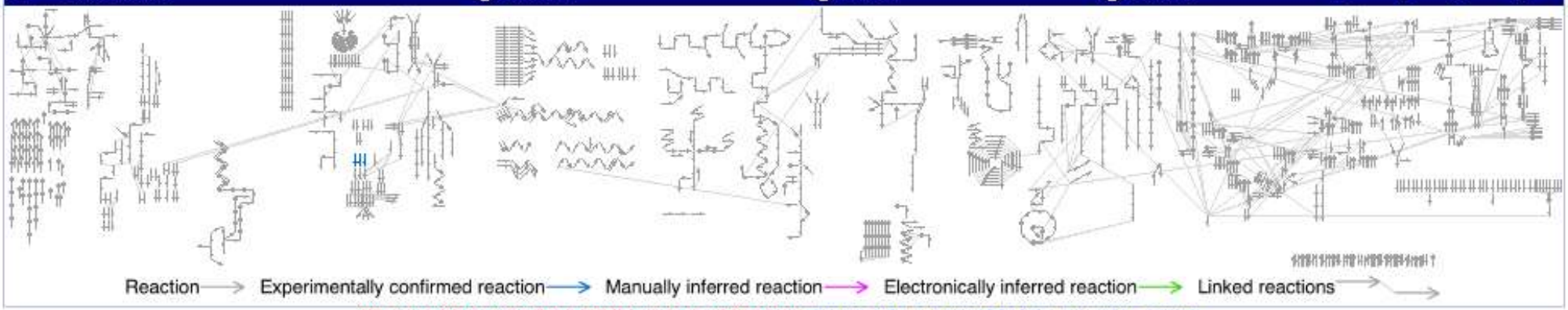
Reactome: Formation of Cyclin A/B1:Cdc2 complexes - Mozilla

BioModels Database - Mozilla

Home | About | TOC | User Guide | Data Model | Schema | Extended search | PathFinder | SkyPainter | Download | Linking | Citing

Find everything with ALL of the words in Homo sapiens Go!

Click on the map: shifts focus zooms in zooms out



We appreciate your feedback and thoughts about Reactome. **Please take a moment to take our online survey.**

[Reactome Home]

+ Cell Cycle, Mitotic

+ G2/M Transition

+ Cyclin A/B1 associated events during G2/M transition

- **Formation of Cyclin A/B1:Cdc2 complexes [Homo sapiens]**

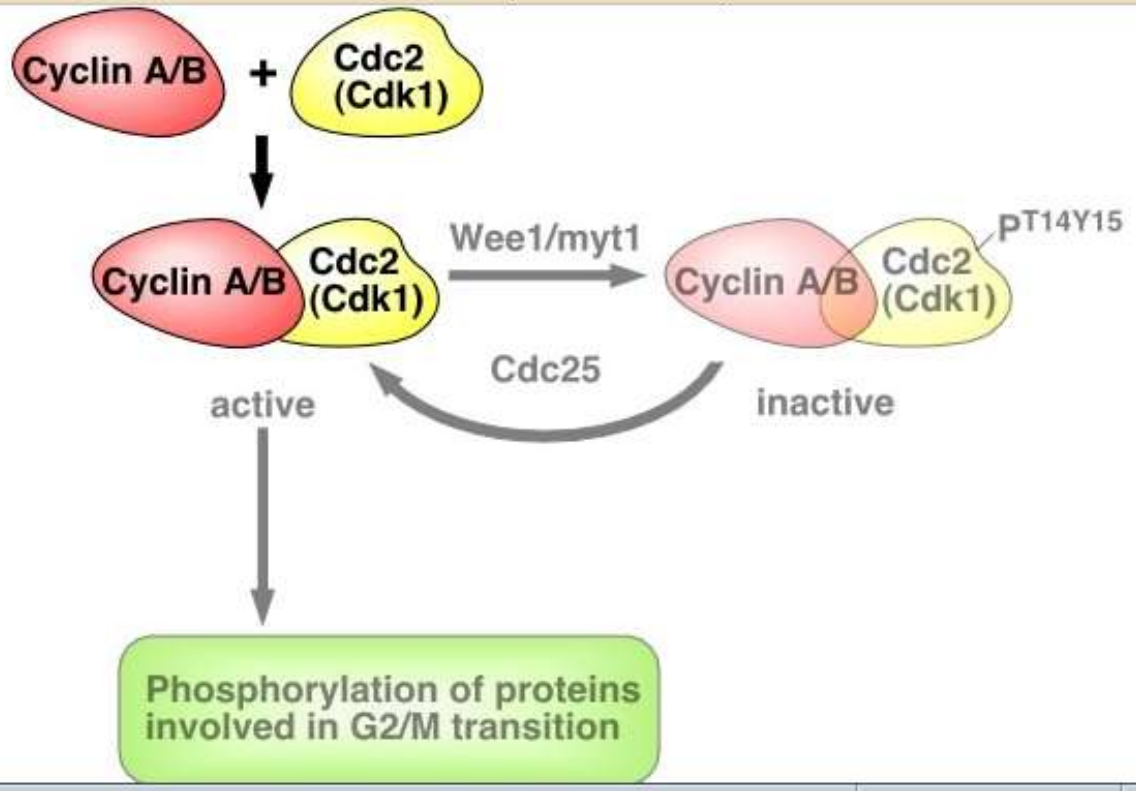
Formation of Cyclin A1:Cdc2 complexes

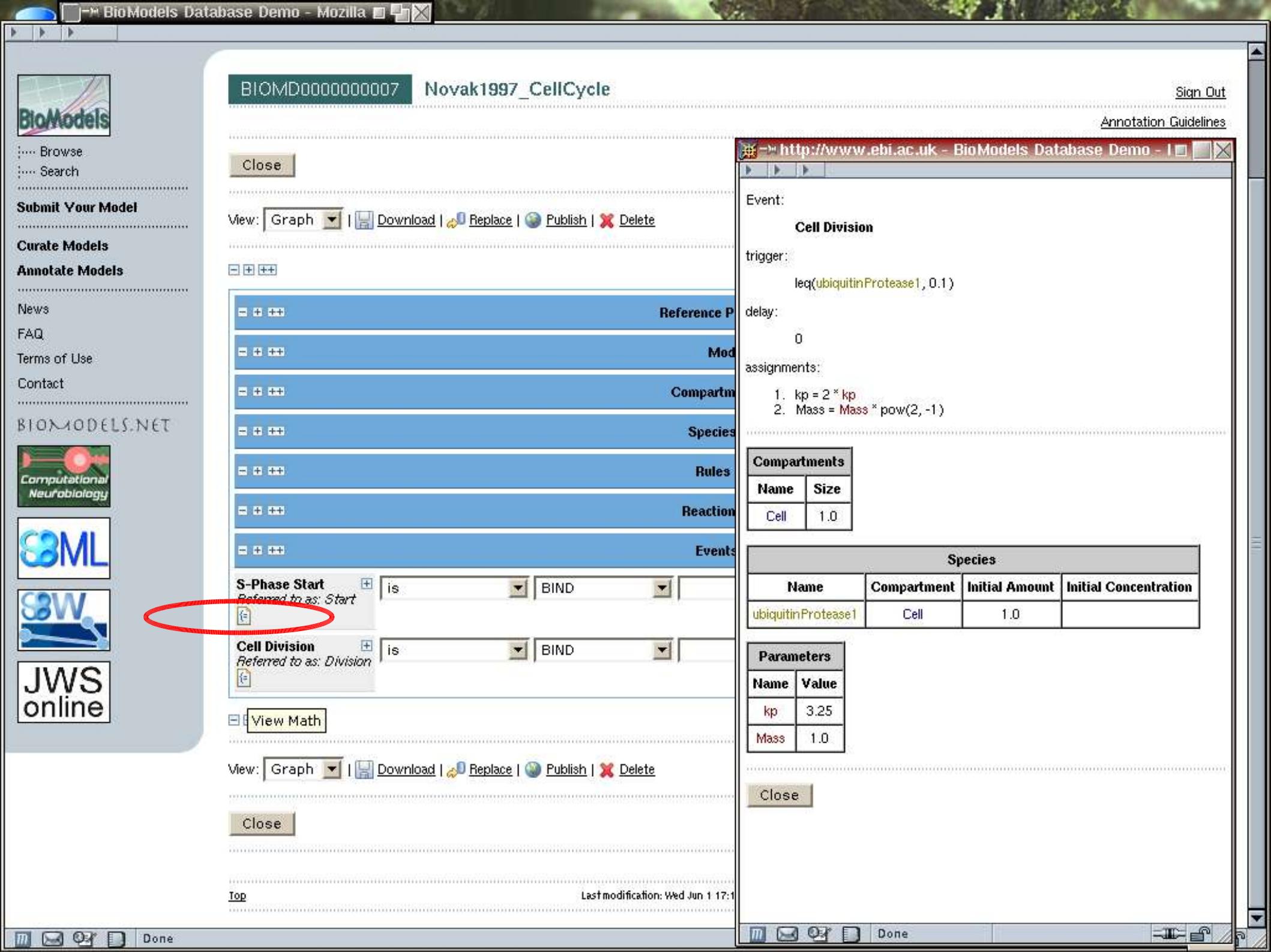
Formation of Cyclin A2:Cdc2 complexes

Formation of Cyclin B1:Cdc2 complexes

Show hierarchy types

Formation of Cyclin A/B1:Cdc2 complexes




BioModels Database Demo - Mozilla
BioModels
Browse
Search
Submit Your Model
Curate Models
Annotate Models
News
FAQ
Terms of Use
Contact
BIOMODELS.NET
Computational Neurobiology
SBML
SBW
JWS online
BIOMD0000000007
Novak1997_CellCycle
Sign Out
Annotation Guidelines
Close
View: Graph | Download | Replace | Publish | Delete
Reference P
Mod
Compartm
Species
Rules
Reaction
Events
S-Phase Start
Referred to as: Start
is
BIND
Cell Division
Referred to as: Division
is
BIND
View Math
View: Graph | Download | Replace | Publish | Delete
Close
Top
Last modification: Wed Jun 1 17:1
Done
http://www.ebi.ac.uk - BioModels Database Demo - I
Event:
Cell Division
trigger:
leq(ubiquitinProtease1, 0.1)
delay:
0
assignments:
1. kp = 2 * kp
2. Mass = Mass * pow(2, -1)
Compartments
Name
Size
Cell
1.0
Species
Name
Compartment
Initial Amount
Initial Concentration
ubiquitinProtease1
Cell
1.0
Parameters
Name
Value
kp
3.25
Mass
1.0
Close
Done

BioModels
Browse
Search

Submit Your Model

Curate Models

Annotate Models

News
FAQ
Terms of Use
Contact

BIOMODELS.NET

Computational Neurobiology

SBML

SBW

JWS online

BIOMD0000000007 **Novak1997_CellCycle**

Sign Out

Annotation Guidelines

Close

View: Graph | Download | Replace | Publish | Delete

Reference Publication

Publication ID: 9256450 Edit

Proc Natl Acad Sci U S A 1997 Aug;94(17):9147-52.
Modeling the control of DNA replication in fission yeast.
Novak B, Tyson JJ.
Department of Agricultural Chemical Technology, Technical University of Budapest, 1521 Budapest, St. Gellert ter 4, Hungary.

Model

Submitter: Nicolas Le Novère

Submission Date: 2005-08-29T23:18:57

Last Modification Date: 2005-08-29T23:18:57

Creation Date: 2005-08-29T23:18:57

Creators: Bruce Shapiro Remove

Add

is set #1

Gene Ontology mitotic cell cycle Remove

KEGG Pathway sce04110 Remove

Reactome 69278 Remove

Taxonomy 4896 Remove

Gene Ontology | GO: | Add

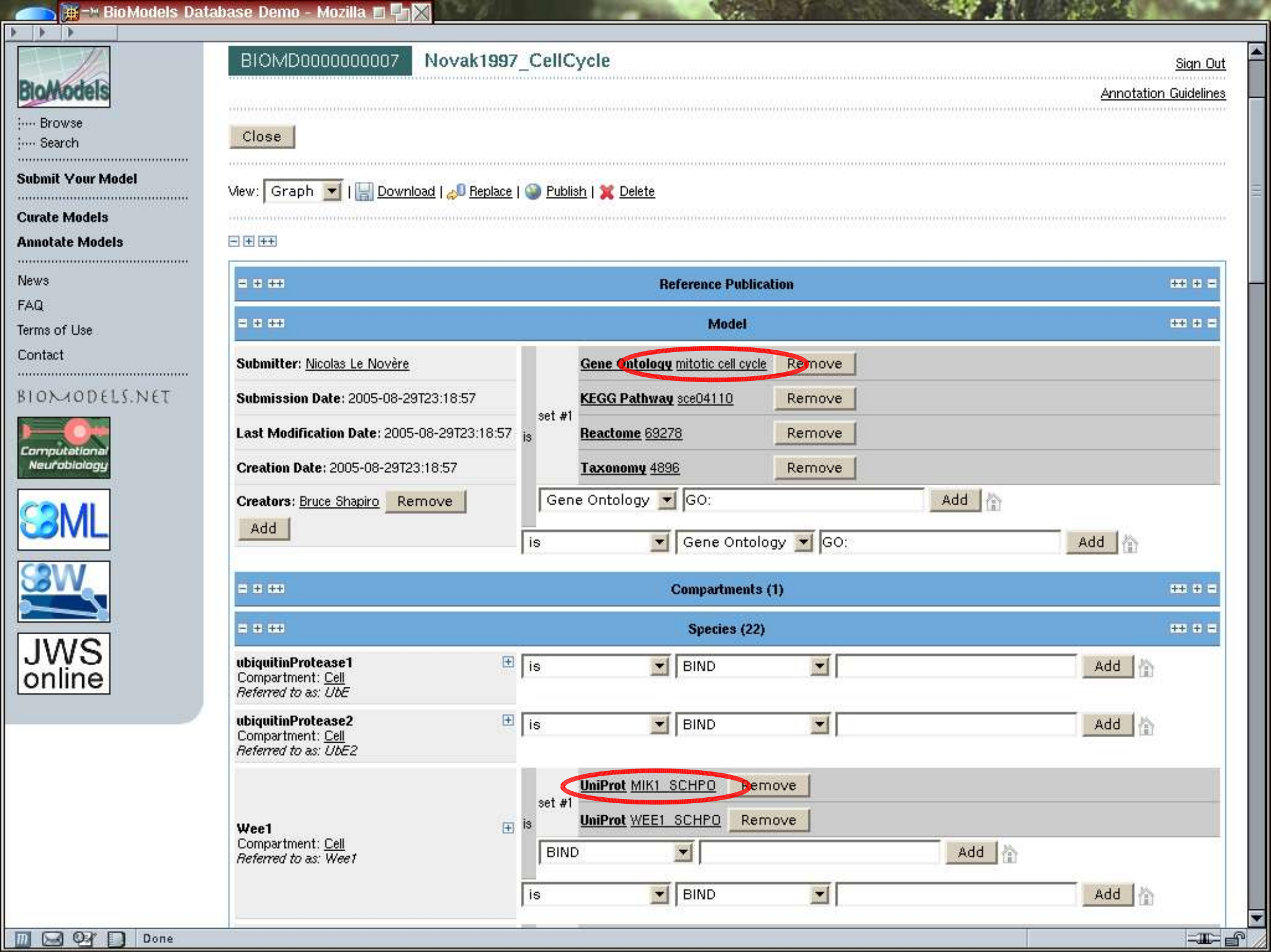
is | Gene Ontology | GO: | Add

is
has part
is part of
is version of
has version
is referenced by

Compartments (1)

Species (22)

Rules (15)


BioModels Database Demo - Mozilla
BioModels
Browse
Search
Submit Your Model
Curate Models
Annotate Models
News
FAQ
Terms of Use
Contact
BIOMODELS.NET
Computational Neurobiology
SBML
SBW
JWS online
BIOMD0000000007
Novak1997_CellCycle
Sign Out
Annotation Guidelines
Close
View: Graph | Download | Replace | Publish | Delete
Reference Publication
Model
Submitter: Nicolas Le Novère
Submission Date: 2005-08-29T23:18:57
Last Modification Date: 2005-08-29T23:18:57
Creation Date: 2005-08-29T23:18:57
Creators: Bruce Shapiro Remove
Add
set #1
is
Gene Ontology mitotic cell cycle Remove
KEGG Pathway sce04110 Remove
Reactome 69278 Remove
Taxonomy 4896 Remove
Gene Ontology GO: Add
is Gene Ontology GO: Add
Compartments (1)
Species (22)
ubiquitinProtease1
Compartment: Cell
Referred to as: UbE
is BIND Add
ubiquitinProtease2
Compartment: Cell
Referred to as: UbE2
is BIND Add
Wee1
Compartment: Cell
Referred to as: Wee1
set #1
is
UniProt MIK1_SCHPO Remove
UniProt WEE1_SCHPO Remove
BIND Add
is BIND Add
Done

Browse
Search

Submit Your Model

Curate Models

News
FAQ
Terms of Use
Related Software
Contact

BIOMODELS.NET

BIOMD0000000007 Novak1997_CellCycle

SBML L2 V1 | CellML | XPP

View Model Graph

Submit Model Comment/Bug

Reference Publication

Publication ID: 9256450

Proc Natl Acad Sci U S A 1997 Aug;94(17):9147-52.
Modeling the control of DNA replication in fission yeast.
Novak B, Tyson JJ.
Department of Agricultural Chemical Technology, Technical University of Budapest, 1521 Budapest, St. Gellert ter 4, Hungary.

Model

Submitter: Nicolas Le Novère

Submission Date: 2005-09-13T13:33:30

Last Modification Date: 2005-09-13T13:33:30

Creation Date: 2005-02-09T13:27:02

Creators: Bruce Shapiro

Gene Ontology mitotic cell cycle
KEGG Pathway sce04110
Reactome 69278
Taxonomy 4896

Compartments (1)

Species (22)

Rules (15)

Reactions (25)

Cdc13_Cdc2 creation
Reactants:
Products: Cdc13_Cdc2

Reactome 68910
Reactome 69282

COPASI (4.0 Build 12 test version)

rxvt <2>

File Tools Help

Copasi
- Model
- Tasks
  - Steady-State
  - Stoichiometry
  - Time Course
    - Result
  - Metabolic Control Analysis
- Output
  - Plots
    - ConcentrationPlot
  - Reports
- Functions

Task Name: Trajectory Task — Task Executable

Start Time: 0 — End Time: 400

Interval size: 4 — Intervals: 100

store time series in memory

Method: Deterministic (LSODA)

Parameter value

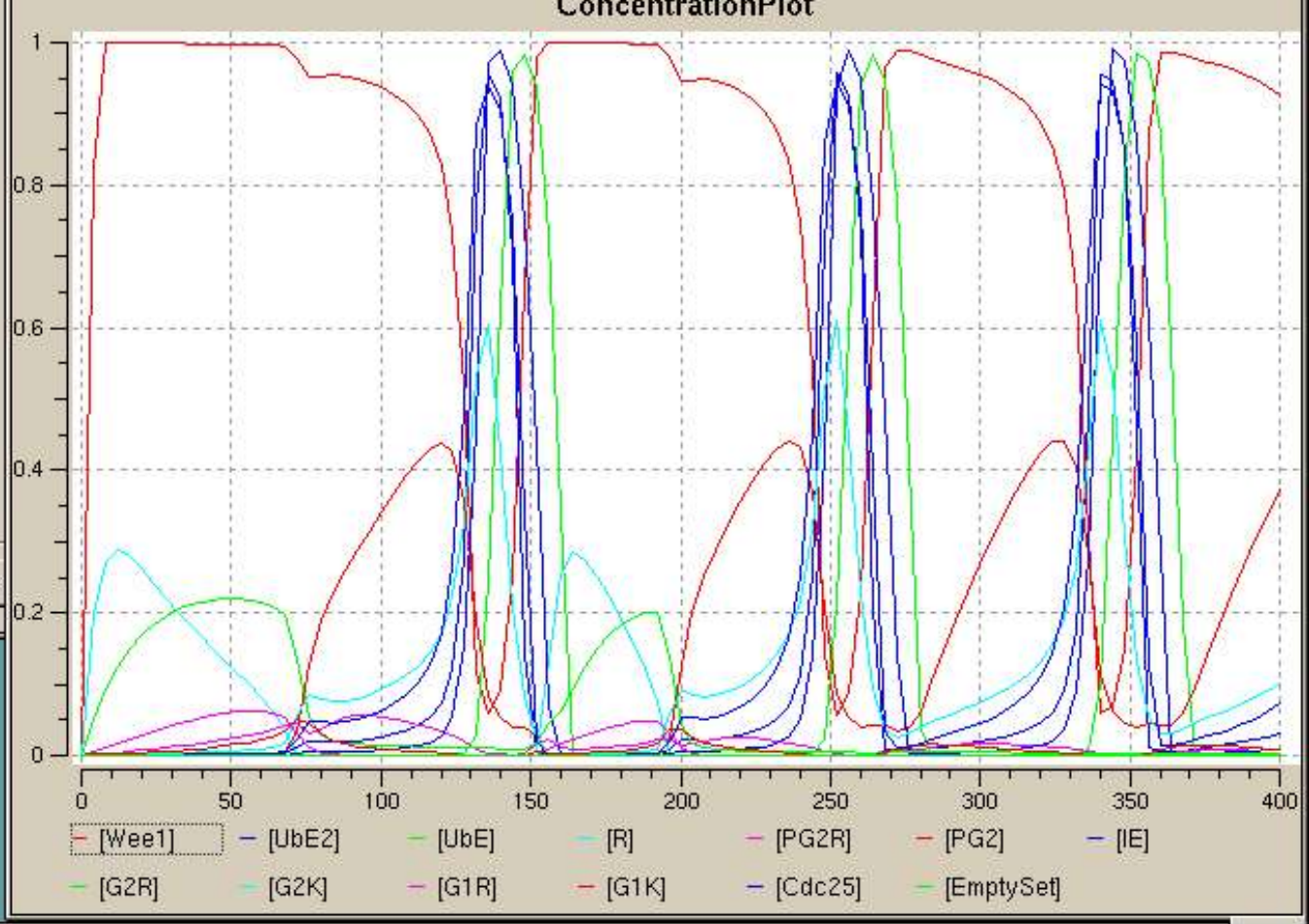
	Value
LSODA.RelativeTolerance	1e-06

Run

```
PlotItem_0
** compiling a CModel is requested.
PlotItem_0
** compiling a CModel is requested.
PlotItem_0
** compiling a CModel is requested.
PlotItem_0
** compiling a CModel is requested.
PlotItem_0
```

Copasi Plot: ConcentrationPlot

Zoom Print

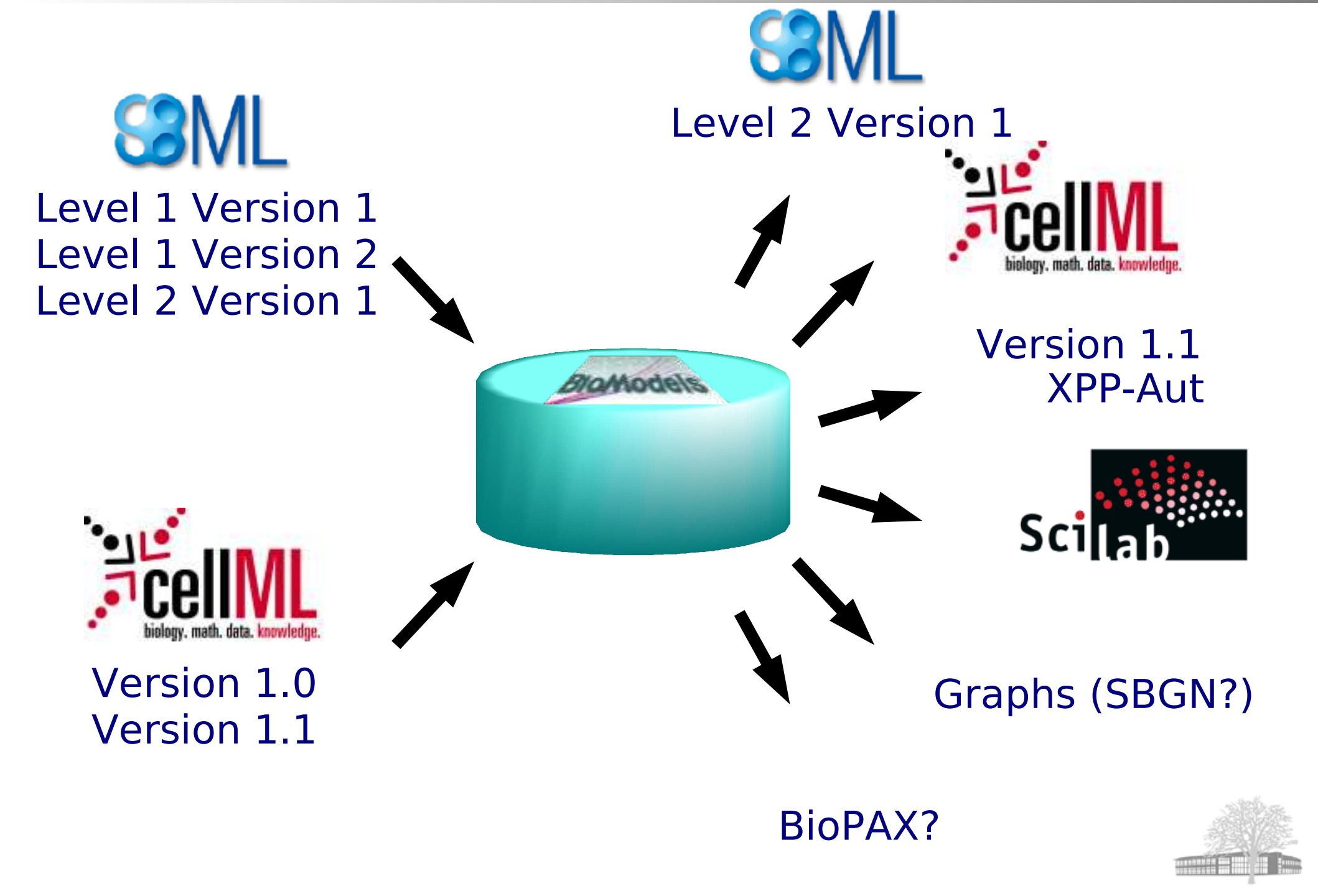


Steady increase

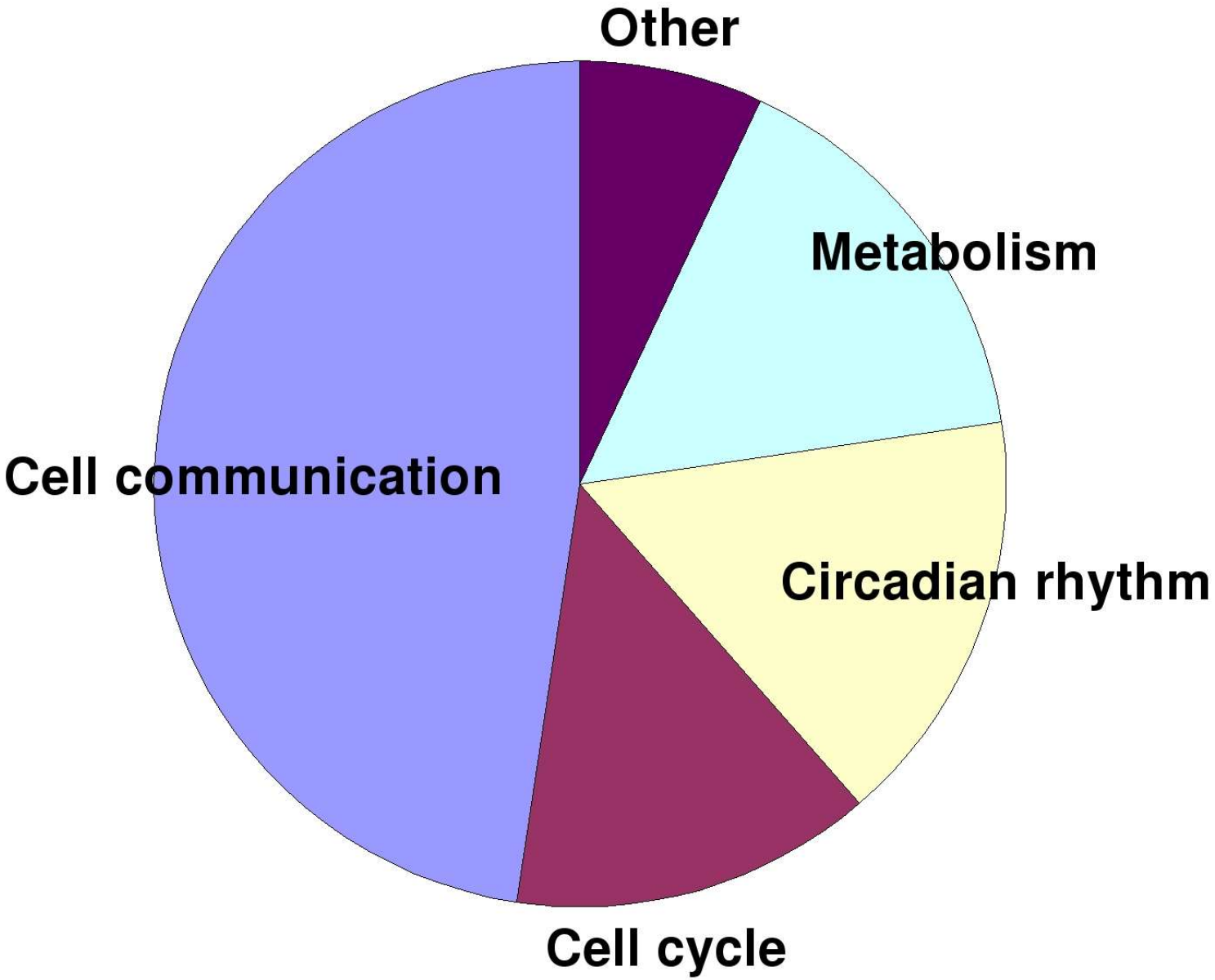
Release	# models	# reactions	#annotations
11 April 2005	20	631	1084
01 June 2005	30	736	1609
28 July 2005	44	943	2373
?? Decemberish	~75		

- Still important legacy from JWS Online, DOQCS, CellML Repo
- Supported by Nature Publishing Group and BioMedCentral. MSB advices deposition, and forward supplementary material
- Curation teams encode new models from literature

Compatibility



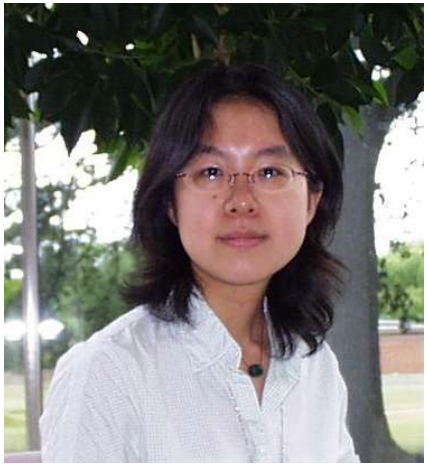
Topical repartition



The EBI team

Marco Donizelli, Chen Li: Tomcat/Xindice/Web interface

Melanie Courtot: MySQL



Lu Li: Graph, CellML, XPP, SciLab exports and curation

Curation

An international collaboration

- EBI
  - Nicolas Le Novère
  - Marco Donizelli
  - Mélanie Courtot
  - Chen Li
  - Lu Li
  - Nicolas Rodriguez
  - Alexander Broicher
- SBML team
  - Michael Hucka
  - Andrew Finney
  - Bruce Shapiro
  - Benjamin Borstein
  - Maria Schilstra
  - Sarah Keating
- Keck Graduate Institute
  - Herbert Sauro
  - Harish Dharuri
- Systems Biology Institute
  - Hiroaki Kitano
  - Akira Funahashi
- Stellenbosh University
  - Jacky Snoep
- External contributors
  - Samuel Bandara
  - Upinder Bhalla
  - Christoph Flamm
  - Ryan Gutenkunst
  - Adam Halasz
  - Ken Lau
  - Rainer Machné
  - Marc Poolman
  - Tomas Radivoyevitch
  - Oleg Sokolsy
  - Joanne Matthews
  - Les Grivell
  - Boris Kholodenko
  - Tjeerd olde Scheper
  - Birgit Schoeberl
  - Paul Smolen
  - Yukiko Matsuoka
- Programs used for curation
  - COPASI
  - SBMLodeSolver
  - Jarnac/JDesigner

European Bioinformatics Institute

British outstation of the European Molecular Biology Laboratory

- Data resources
  - Sequences, structures
  - Transcriptomics, Proteomics pathways, models
  - Controlled vocabularies and dictionaries

    + ~200 other resources

- Research groups
  - Comparative genomics (Ouzounis)
    Structural Genomics (Thornton)
    Molecular Evolution (Goldman)
  - Text-Mining (Rebholz-Schumman)
    Computational Systems Biology (Le Novère)
    Statistical array analysis (Huber)
    Genomic analysis of regulatory systems (Luscombe)

Marie Curie Training site Fellowships: 3-6 months. Fully funded.