

BioModels Database

*Sharing and re-using computational models of
biological processes*

Nicolas Le Novère, Babraham Institute, EMBL-EBI

What happened to Biology at the end of XXth century?

Annu. Rev. Genomics Hum. Genet. 2001. 2:343-72
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A NEW APPROACH TO DECODING LIFE: Systems Biology

Trey Ideker^{1,2}, Timothy Galitski¹, and Leroy Hood^{1,2,3,4,5}
Institute for Systems Biology¹, Seattle, Washington 98105; Departments of

New Generation Computing, 18(2000)199-216
Ohmsha, Ltd. and Springer-Verlag

invited paper

Perspectives on Systems Biology

Hiroaki KITANO
Sony Computer Science Laboratories, Inc.

NEW
GENERATION
COMPUTING

©Ohmsha, Ltd.



What happened to biology at the end of XXth century?

RESEARCH ARTICLE

Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome

Daniel G. Gibson,¹ John I. Glass,¹ Carole Lartigue,¹ Vladimir N. Noskov,¹ Ray-Yuan Chuang,¹ Mikkel A. Algire,¹ Gwynedd A. Benders,² Michael G. Montague,¹ Li Ma,¹ Monzia M. Moodie,¹ Chuck Merryman,¹ Sanjay Vashee,¹ Radha Krishnakumar,¹ Nacyra Assad-Garcia,¹ Cynthia Andrews-Pfannkoch,¹ Evgeniya A. Denisova,¹ Lei Young,¹ Zhi-Qing Qi,¹ Thomas H. Segall-Shapiro,¹ Christopher H. Calvey,¹ Prashanth P. Parmar,¹ Clyde A. Hutchison III,² Hamilton O. Smith,² J. Craig Venter^{1,2*}

2 JULY 2010 VOL 329 SCIENCE www.sciencemag.org

Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors

Cell

Kazutoshi Takahashi¹ and Shinya Yamanaka^{1,2,*}

¹Department of Stem Cell Biology, Institute for Frontier Medical Sciences, Kyoto University, Kyoto 606-8507, Japan

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DOI 10.1016/j.cell.2006.07.024

Cell 126, 663–676, August 25, 2006 ©2006 Elsevier Inc. 663



EXTREME GENETIC ENGINEERING

An Introduction to Synthetic Biology

January 2007

etc group

A synthetic oscillatory network of transcriptional regulators

Michael B. Elowitz & Stanislas Leibler

Departments of Molecular Biology and Physics, Princeton University, Princeton, New Jersey 08544, USA

NATURE | VOL 403 | 20 JANUARY 2000 | www.nature.com

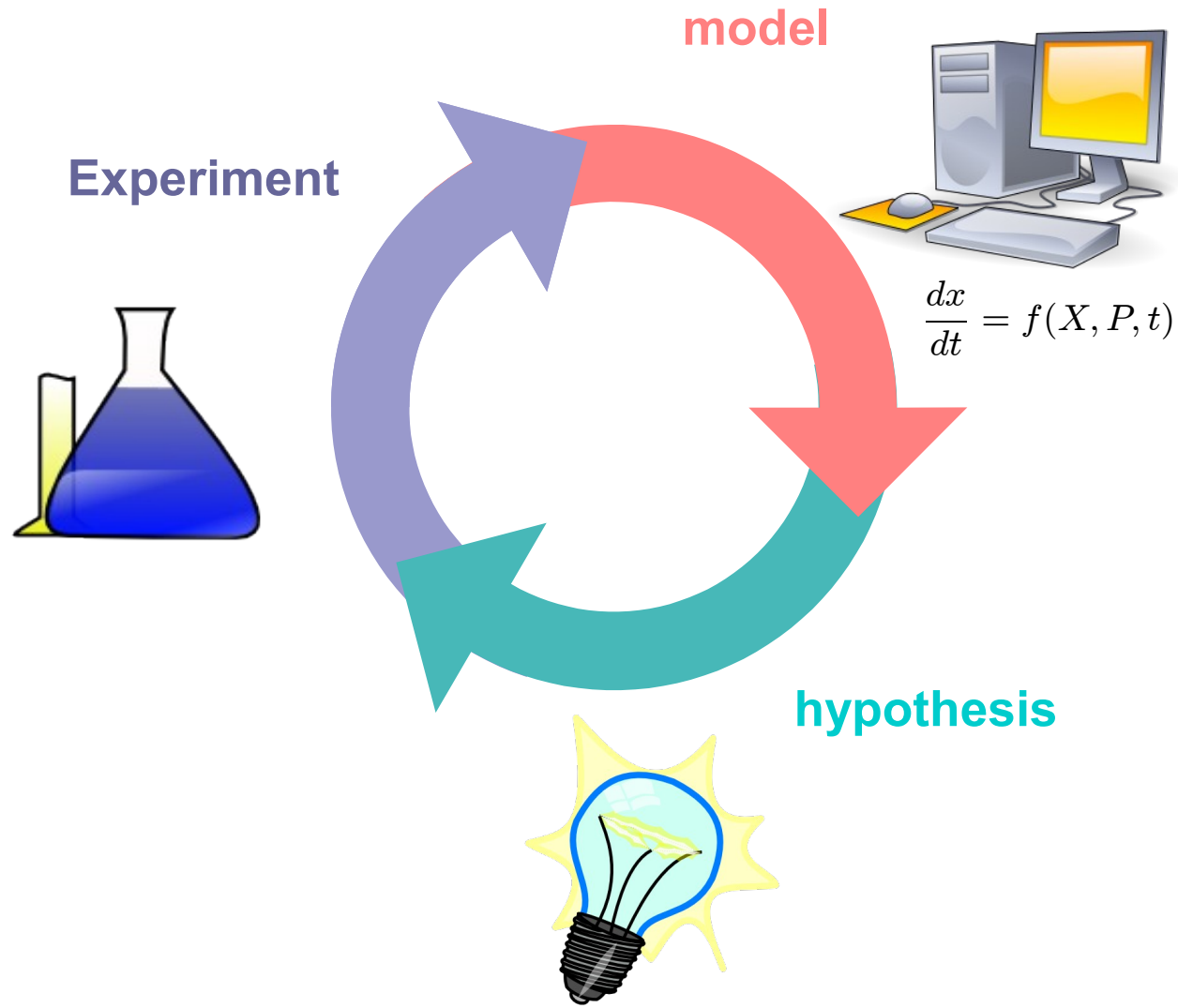


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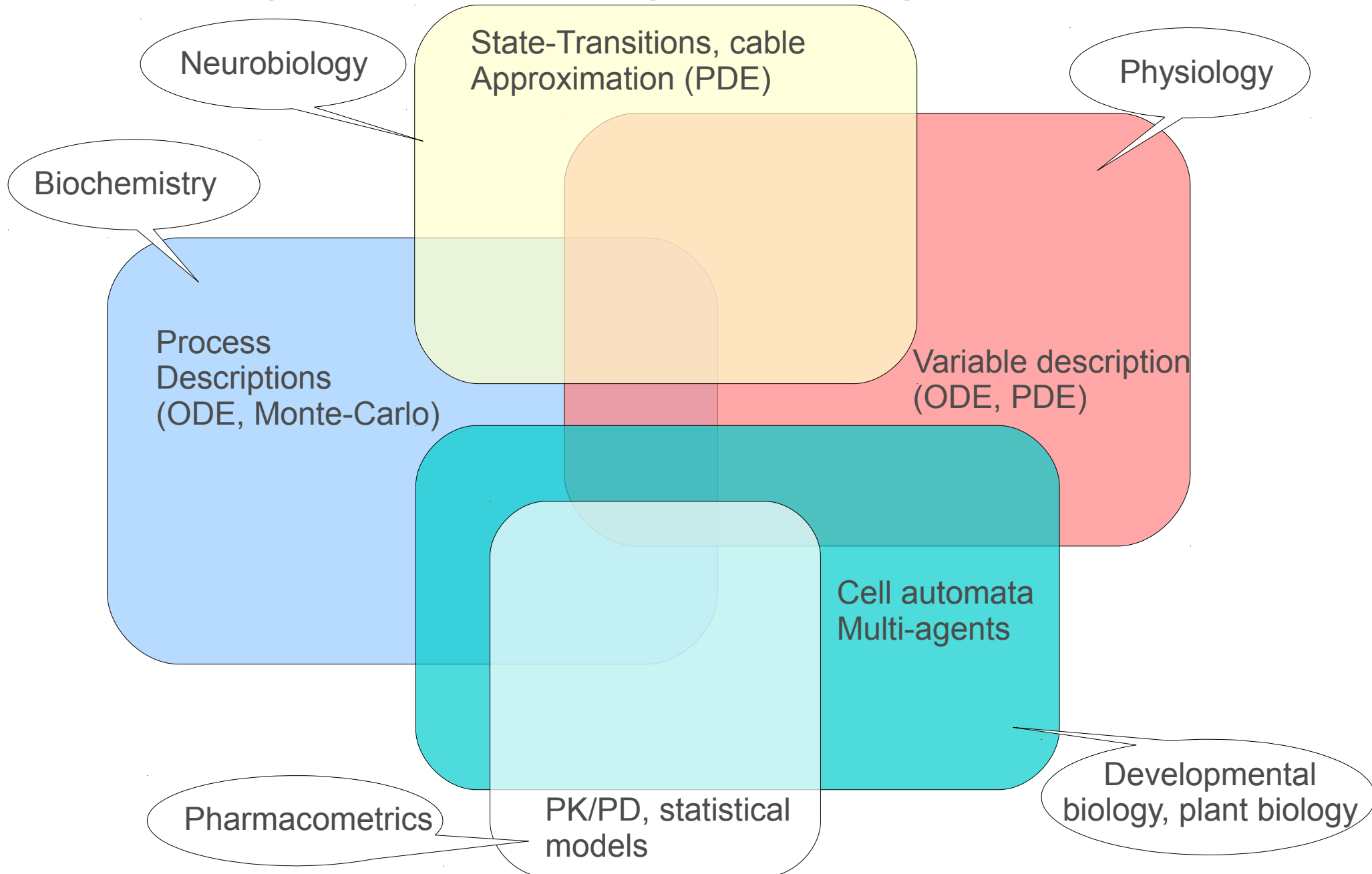
About

The **International Genetically Engineered Machine competition (iGEM)** is a Biology competition. Student teams are given a kit of biological parts at the beginning of the year. Working at their own schools over the summer, they use these parts to create synthetic biological systems.

For all that we need models



Many complementary modelling approaches



Computational modelling left the niches

- **Metabolic networks** Fung et al. A synthetic gene-metabolic oscillator. *Nature* 2005; Herrgård et al. A consensus yeast metabolic network reconstruction obtained from a community approach to systems biology. *Nat Biotechnol* 2008
- **Signalling pathways** Bray et al. Receptor clustering as a cellular mechanism to control sensitivity. *Nature* 1998; Bhalla and Iyengar. Emergent properties of signaling pathways. *Science* 1998; Schoeberl et al. Computational modeling of the dynamics of the MAP kinase cascade activated by surface and internalized EGF receptors. *Nat Biotechnol* 2002; Hoffmann et al. The I κ B-NF- κ B signaling module: temporal control and selective gene activation. *Science* 2002; Smith et al. Systems analysis of Ran transport. *Science* 2002; Bhalla et al. MAP kinase phosphatase as a locus of flexibility in a mitogen-activated protein kinase signaling network. *Science* 2002; Nelson et al. Oscillations in NF- κ B Signaling Control the Dynamics of Gene Expression. *Science* 2004; Werner et al. Stimulus specificity of gene expression programs determined by temporal control of IKK activity. *Science* 2005; Sasagawa et al. Prediction and validation of the distinct dynamics of transient and sustained ERK activation. *Nat Cell Biol* 2005; Basak et al. A fourth I κ B protein within the NF- κ B signaling module. *Cell* 2007; McLean et al. Cross-talk and decision making in MAP kinase pathways. *Nat Genet* 2007; Ashall et al. Pulsatile Stimulation Determines Timing and Specificity of NF- κ B-Dependent Transcription. *Science* 2009; Becker et al. Covering a broad dynamic range: information processing at the erythropoietin receptor. *Science* 2010
- **Gene regulatory networks** McAdams and Shapiro. Circuit simulation of genetic networks. *Science* 1995; Yue et al. Genomic cis-regulatory logic: Experimental and computational analysis of a sea urchin gene. *Science* 1998; Von Dassow et al. The segment polarity network is a robust developmental module. *Nature* 2000; Elowitz and Leibler. A synthetic oscillatory network of transcriptional regulators. *Nature* 2000; Shen-Orr et al. Network motifs in the transcriptional regulation network of Escherichia coli. *Nat Genet* 2002; Yao et al. A bistable Rb-E2F switch underlies the restriction point. *Nat Cell Biol* 2008; Friedland. Synthetic gene networks that count. *Science* 2009
- **Pharmacometrics models** Labrijn et al. Therapeutic IgG4 antibodies engage in Fab-arm exchange with endogenous human IgG4 in vivo. *Nat Biotechnol* 2009
- **Physiological models** Noble. Modeling the heart from genes to cells to the whole organ. *Science* 2002; Izhikevich and Edelman. Large-scale model of mammalian thalamocortical systems. *PNAS* 2008
- **Infectious diseases** Perelson et al. HIV-1 dynamics in vivo: Virion clearance rate, infected cell life-span, and viral generation time. *Science* 1996; Nowak. Population dynamics of immune responses to persistent viruses. *Science* 1996; Neumann et al. Hepatitis C viral dynamics in vivo and the antiviral efficacy of interferon-alpha therapy. *Science* 1998

A Whole-Cell Computational Model Predicts Phenotype from Genotype

Jonathan R. Karr,^{1,4} Jayodita C. Sanghvi,^{2,4} Derek N. Macklin,² Miriam V. Gutschow,² Jared M. Jacobs,² Benjamin Bolival, Jr.,² Nacyra Assad-Garcia,³ John I. Glass,³ and Markus W. Covert^{2,*}

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<http://dx.doi.org/10.1016/j.cell.2012.05.044>

SUMMARY

Understanding how complex phenotypes arise from individual molecules and their interactions is a primary challenge in biology that computational approaches are poised to tackle. We report a whole-cell computational model of the life cycle of the human pathogen *Mycoplasma genitalium* that includes all of its molecular components and their interactions. An integrative approach to modeling that combines diverse mathematics enabled the simultaneous inclusion of fundamentally different cellular processes and experimental measurements. Our whole-cell model accounts for all annotated gene functions and was validated against a broad range of data. The model provides insights into many previously unobserved cellular behaviors, including in vivo rates of protein-DNA association

First, until recently, not enough has been known about the individual molecules and their interactions to completely model any one organism. The advent of genomics and other high-throughput measurement techniques has accelerated the characterization of some organisms to the extent that comprehensive modeling is now possible. For example, the mycoplasmas, a genus of bacteria with relatively small genomes that includes several pathogens, have recently been the subject of an exhaustive experimental effort by a European consortium to determine the transcriptome (Güell et al., 2009), proteome (Kühner et al., 2009), and metabolome (Yus et al., 2009) of these organisms.

The second limiting factor has been that no single computational method is sufficient to explain complex phenotypes in terms of molecular components and their interactions. The first approaches to modeling cellular physiology, based on ordinary differential equations (ODEs) (Atlas et al., 2008; Browning et al., 2004; Castellanos et al., 2004, 2007; Domach et al., 1984; Tomita et al., 1999), were limited by the difficulty in obtaining the necessary model parameters. Subsequently, alternative

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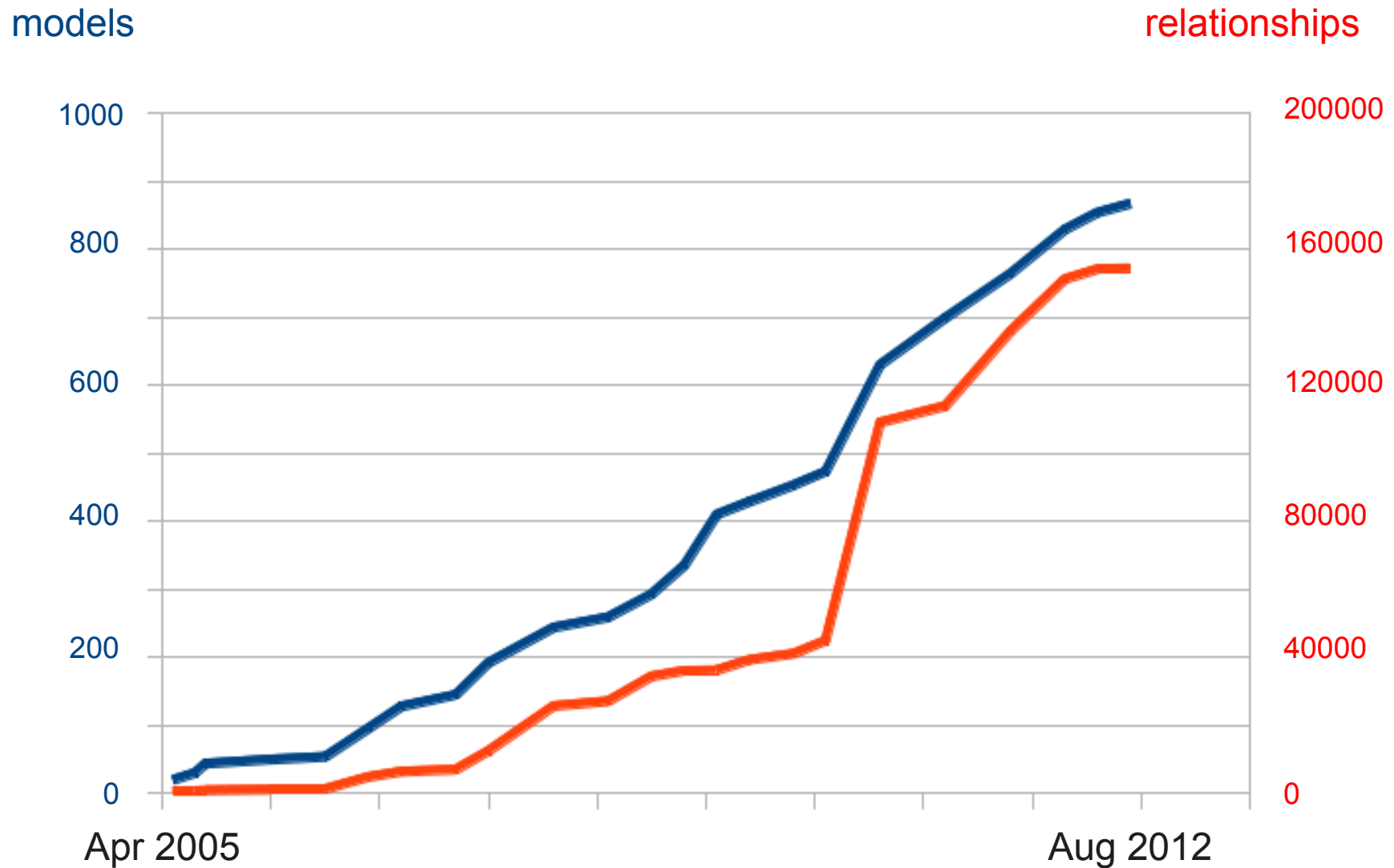
SUMMARY

Understanding how complex phenotypes arise from individual molecules and their interactions is a primary challenge in biology that computational approaches are poised to tackle. We report a whole-cell computational model of the life cycle of the human pathogen *Mycoplasma genitalium* that includes all of its molecular components and their interactions. An integrative approach to modeling that combines diverse mathematics enabled the simultaneous inclusion of fundamentally different cellular processes and experimental measurements. Our whole-cell model accounts for all annotated gene functions and was validated against a broad range of data. The model provides insights into many previously unobserved cellular behaviors, including in vivo rates of protein-DNA association

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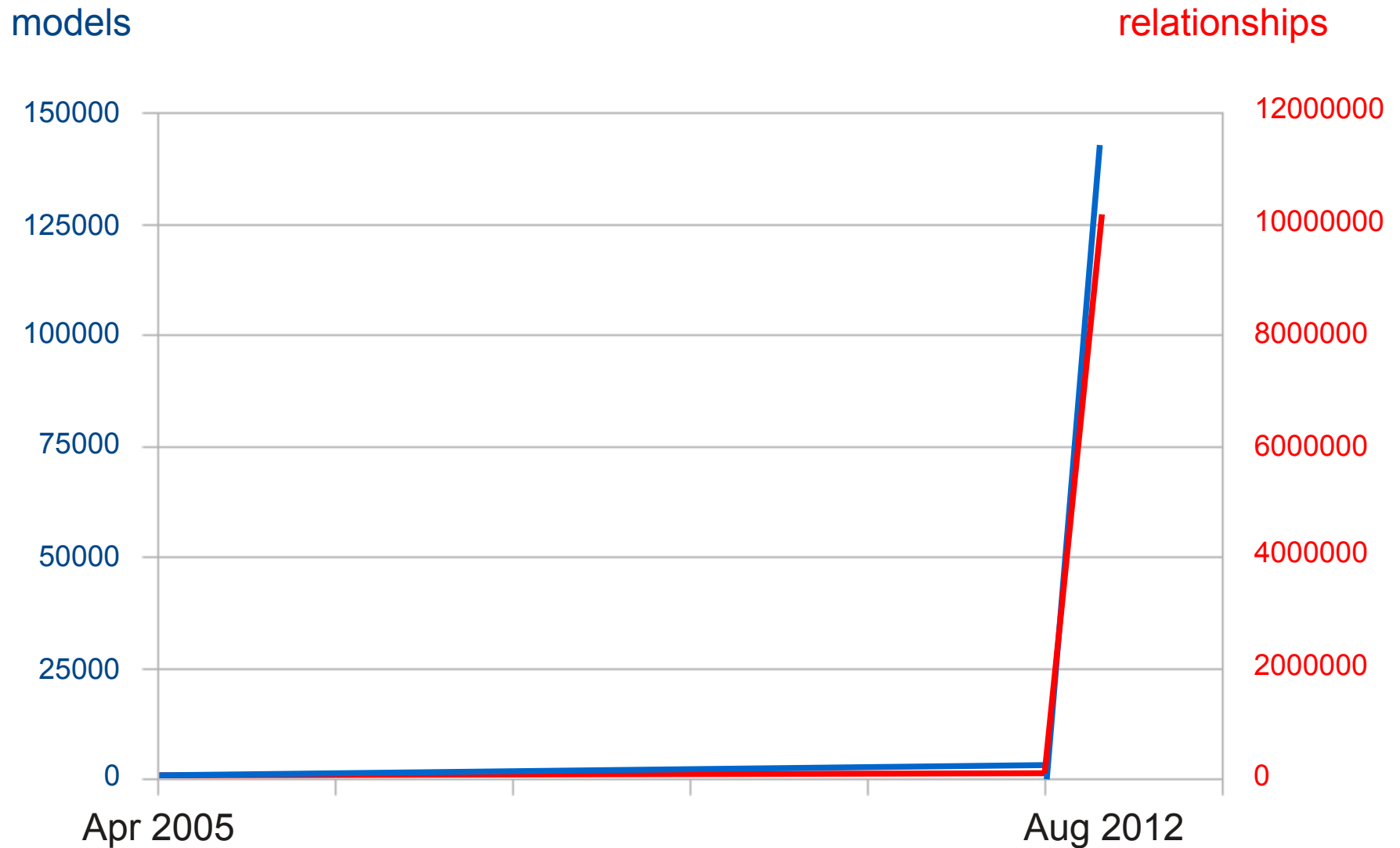
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Computational models on the rise



BioModels Database growth since its creation, published models

Computational models on the rise

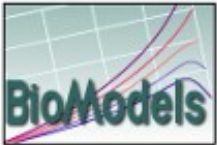


BioModels Database growth since its creation, with Path2Models

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
- Browse curated models using Taxonomy
- Browse non-curated models

Path2Models (new)

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

Links

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

Model of the month

November, 2012

Transforming growth factor β (TGF- β) ligands activate a signaling cascade with multiple cell context dependent outcomes. Disruption or disturbance leads to variant clinical disorders. A mathematical model to determine the relevance of feedback loops in the TGF- β signaling has been presented by Wegner et al. (2011).

[Please read more...](#)

News

7 November 2012
Software developer position available

We are seeking an experienced Software Developer to work on the software infrastructure behind BioModels Database. For more information and application instructions, please refer to the [job description page](#) (closing date: 30 November 2012).

6th September 2012
Introduction to BioModels Database on Train online

The EBI online training platform, [Train online](#), now features an [introduction to BioModels Database](#).

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

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

What is BioModels Database?

- Store and serve quantitative models of **biomedical** interest
- Models described in the **peer-reviewed** scientific literature + models **automatically generated** from pathway resources
- Models are curated: computer software check the **syntax**, while human curators check the **semantics**
- Models are **simulated** to ensure they provide the expected results
- Model components are **annotated**, to improve identification and retrieval
- Models are accepted in **several formats**, and served in several others

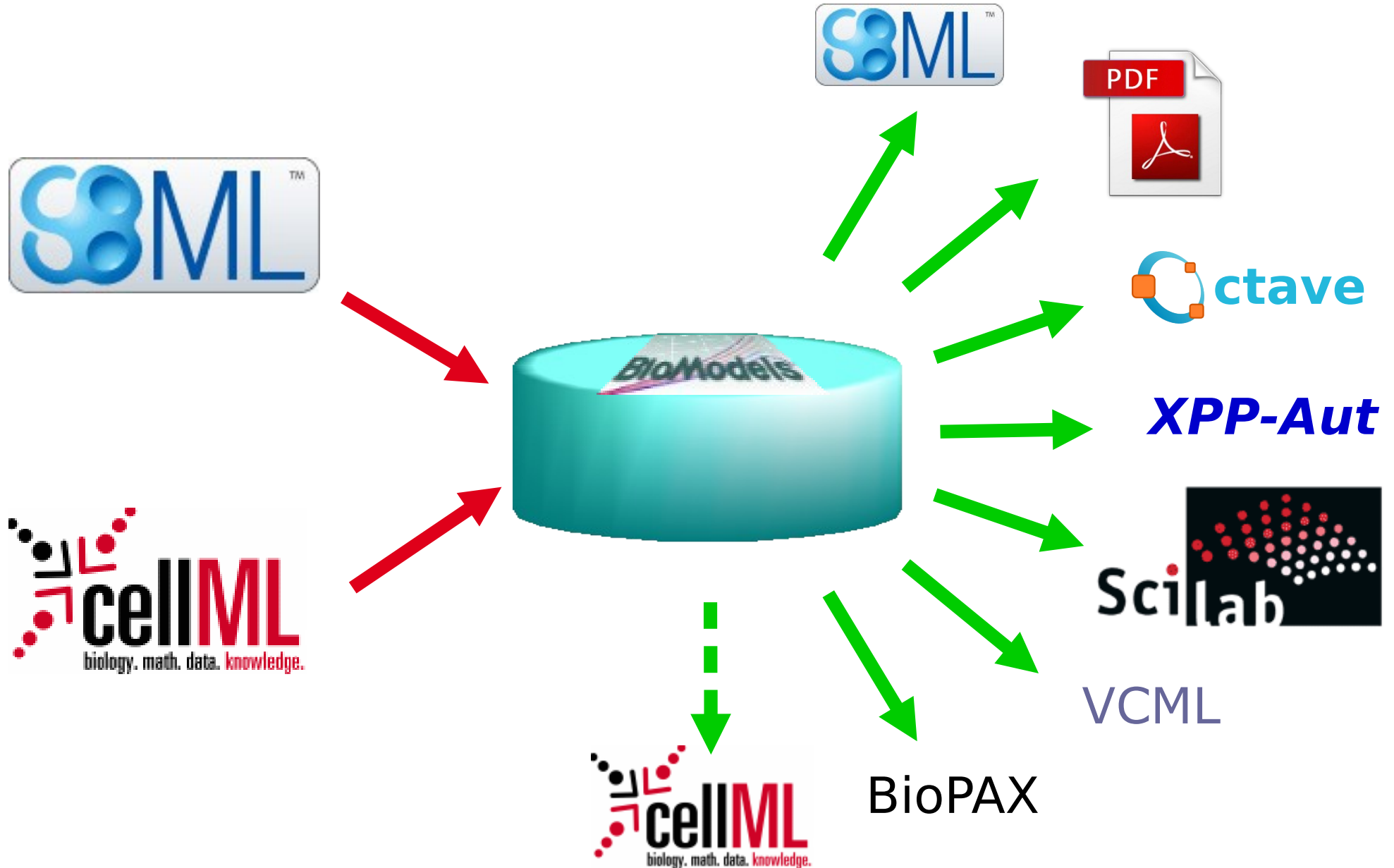
What can-we do with BioModels Database?

- **Search** and **retrieve** quantitative models of biomedical interest
- **Explore** the variables and the structure of the model
- Run timecourse **simulations** of the model
- **Download** the model in many formats
- Do all the above via **Web Services**
- Learn about significant models using the **Model of the Month**

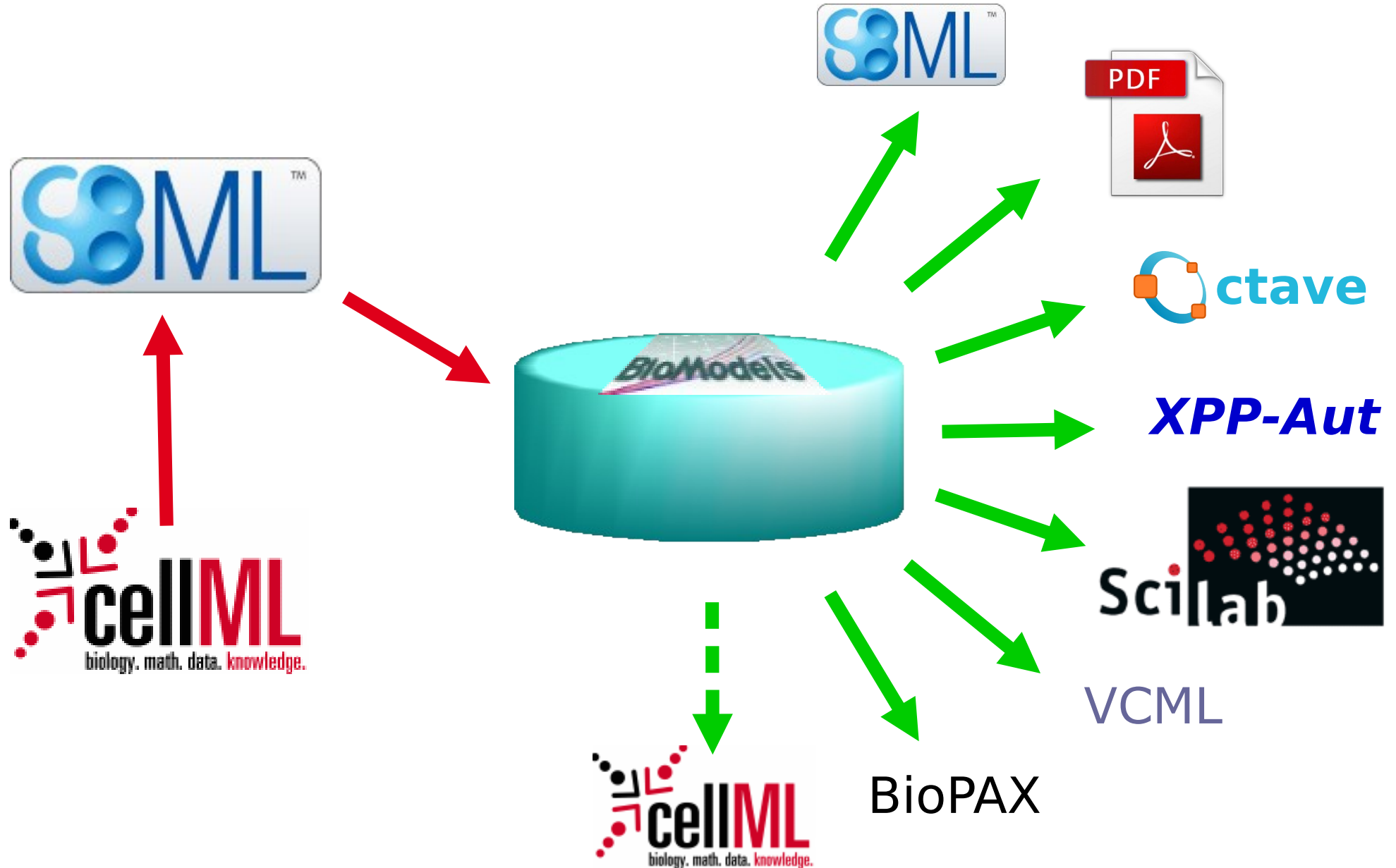
Where do models come from?

- From authors before grant applications or publications
- Over 300 scientific journals advise submission to BioModels Db:
 - Nature Molecular Systems Biology
 - Public Library of Science journals
 - BioMedCentral journals
 - Royal Society of Chemistry
- Various people curated models out of interest.
- Submitted by curators
 - imported from other repositories (DOQCS, CellML)
 - reimplemented from literature

Input and output formats



Input and output formats



SBML core is not limited to biochemistry!

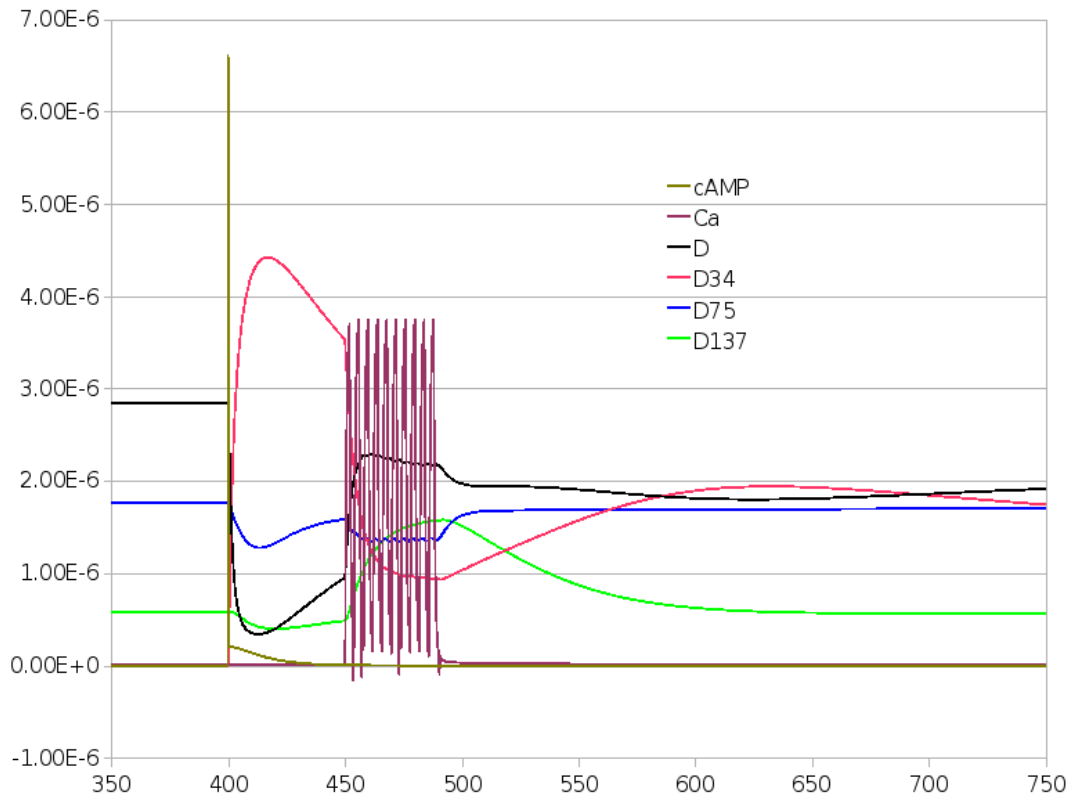
- A **species** is a pool of entities participating to a reaction, **not always** a **chemical** entity
 - It can be a pool of molecules
 - It can be a pool of cells
 - It can be a pool of organs
 - It can be a population of organi
- **Rate Rules** can describe the temporal evolution of any quantitative parameter, e.g. transmembrane voltage, tumour size etc.
- **Events** can describe any discontinuous change, e.g. neurotransmitter release, repolarisation, cell division etc.

→ SBML core is about process descriptions

SBML supporting tools

- Simulators
 - Discrete stochastic (25)
 - Continuous deterministic (42)
 - Spatial (4)
- Modelling and simulation environments (29)
 - Based on Mathematica (3)
 - Based on Matlab (12)
 - Based on Python/SciPy (9)
 - Based on R (3)
- Flux/metabolic analysis (16)
- Integrated framework (3)
- Libraries (3)
- Model Management, Data Integration, and Analysis (12)
- Model development tools (18)
- Model visualisation (7)
- Model Repositories, Test Suites, and Databases (16)
- Converters (7)
- Analysis and utility (12)

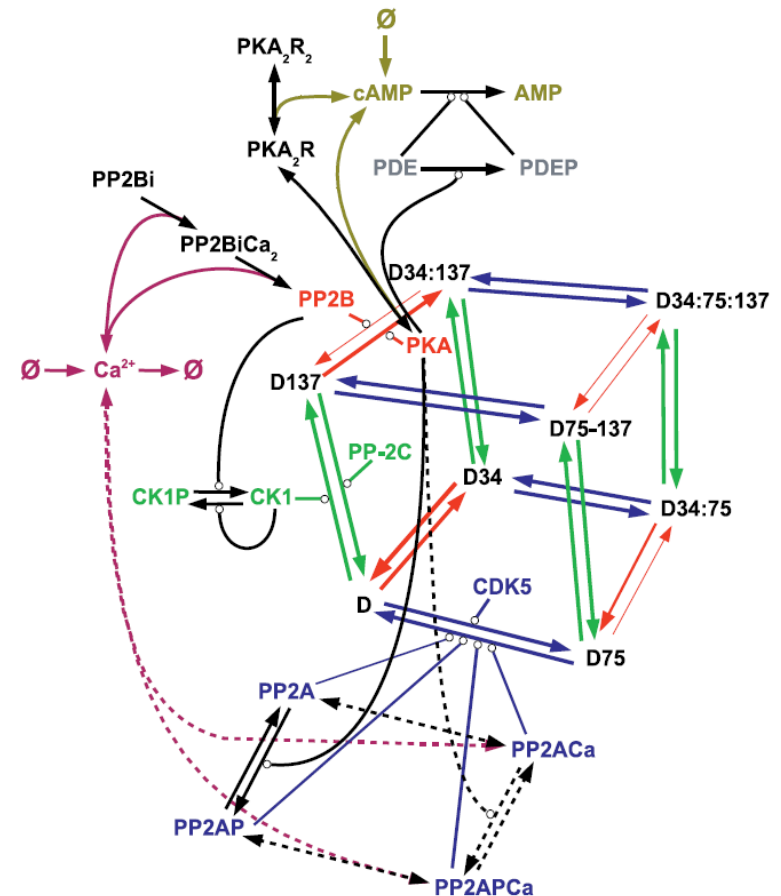
Process based biochemical models



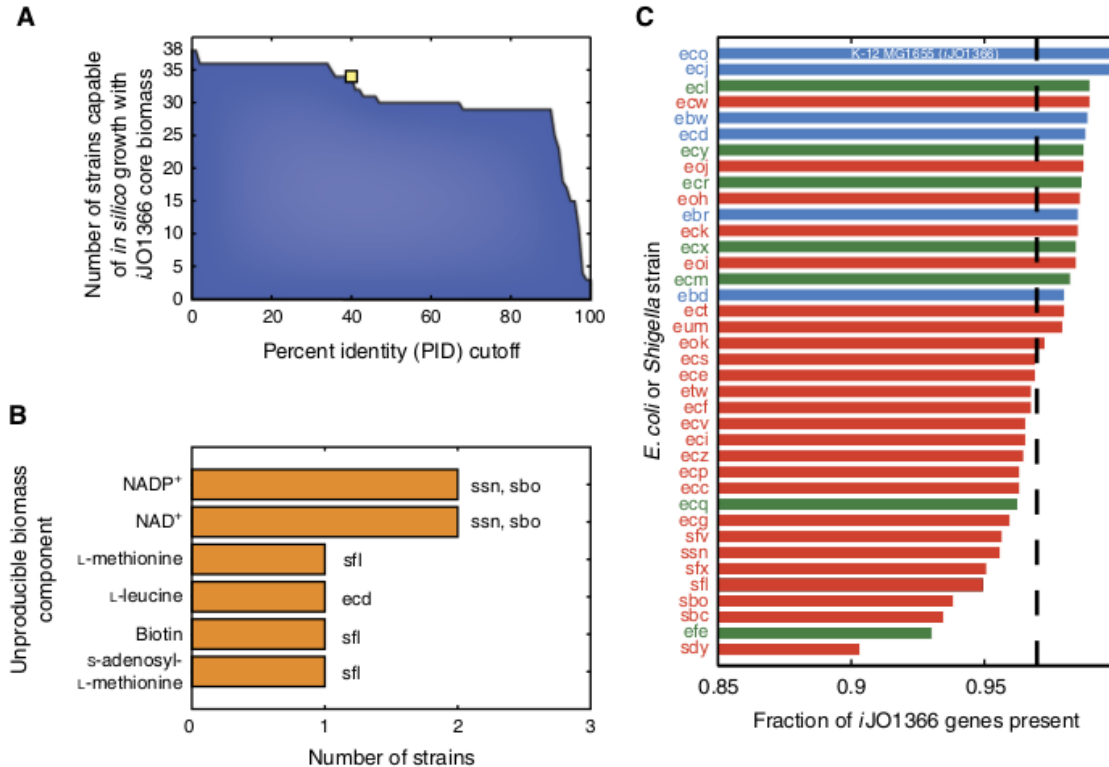
reaction:

$$v_{on1} = k_{on1} \times [D] \times [CDK5] \times Vol$$

Fernandez et al. DARPP-32 is a robust integrator of dopamine and glutamate signals
PLoS Comput Biol (2006) 2: e176.



Flux Balance Analysis models



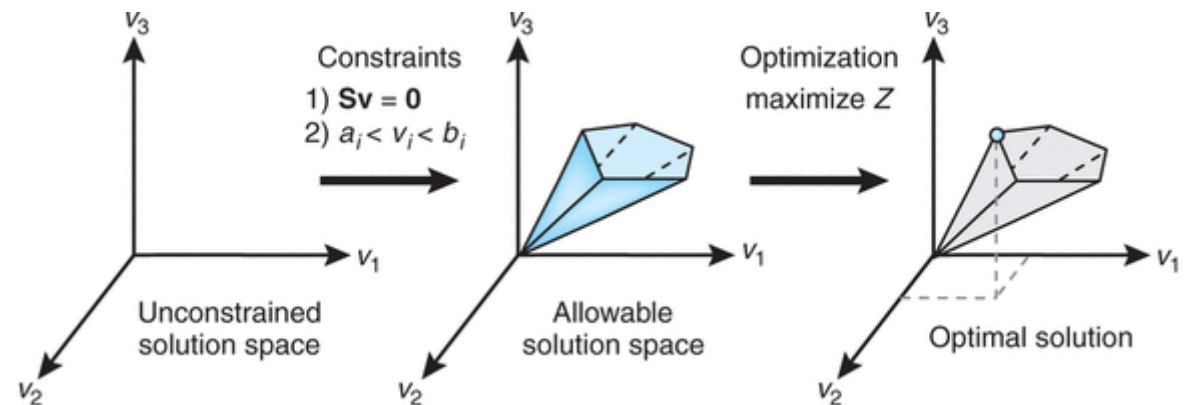
Orth et al. A comprehensive genome-scale reconstruction of *Escherichia coli* metabolism - 2011
Mol Syst Biol (2011);7:535



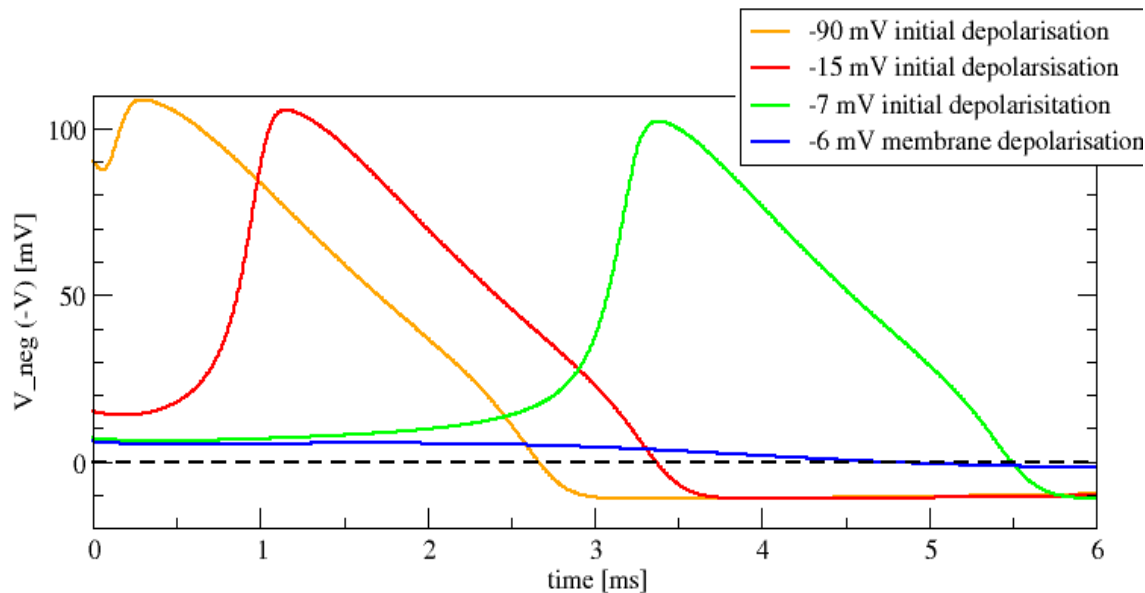
MODEL1108160000

reaction:

$$v_i = flux_i$$



Conductance-based model



Hodgkin AL, Huxley AF.
A quantitative description of
membrane current and its
application to conduction
and excitation in nerve.
J Physiol (1952) 117:500-544.

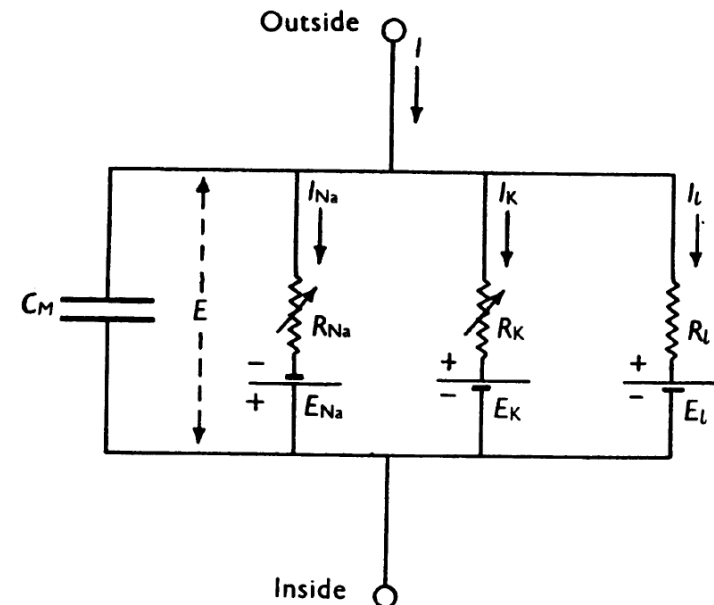


rate rule:

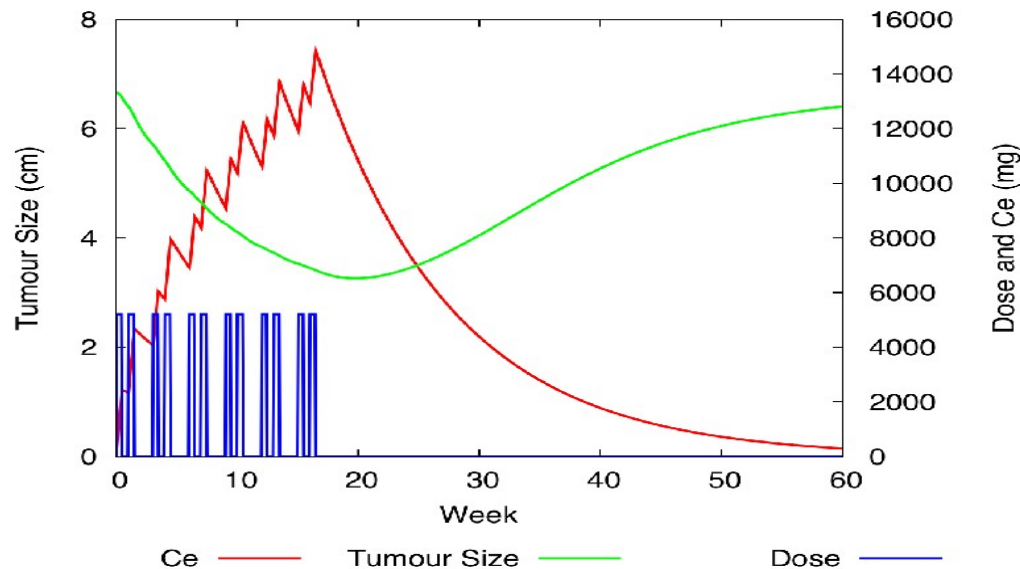
$$\frac{dv}{dt} = \frac{I - (i_{Na} + i_K + i_L)}{C_m}$$

assignment rule:

$$i_{Na} = g_{Na} \times m^3 \times h \times (V - E_{Na})$$



Pharmacometrics models



Tham et al (2008) A pharmacodynamic model for the time course of tumor shrinkage by gemcitabine + carboplatin in non-small cell lung cancer patients. *Clin Cancer Res.* 2008 14(13): 4213-8.



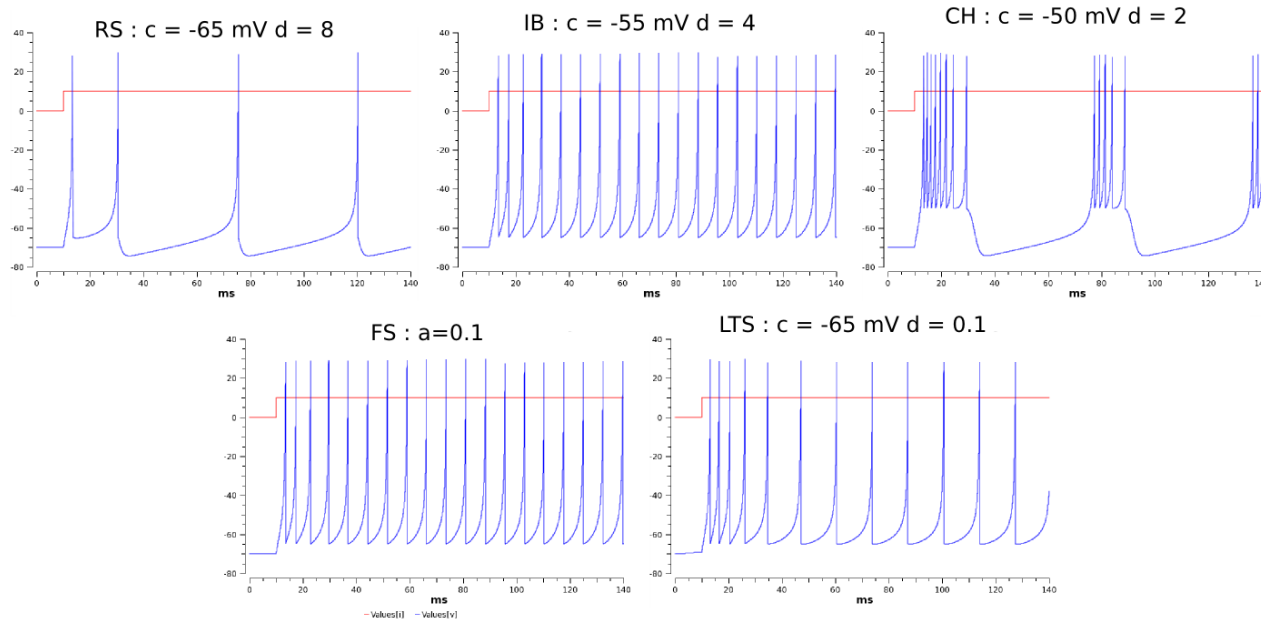
rate rule:

$$\frac{dSize}{dt} = (Rate_{in} \times Effect - K_{over} \times Size) \times Size$$

assignment rule:

$$Effect = 1 - \frac{E_{max} \times Ce}{Amt_{50} + Ce}$$

Single-compartment neurons



Izhikevich EM. Simple model of spiking neurons. *IEEE Trans Neural Netw* (2003) 14(6):1569-1572.



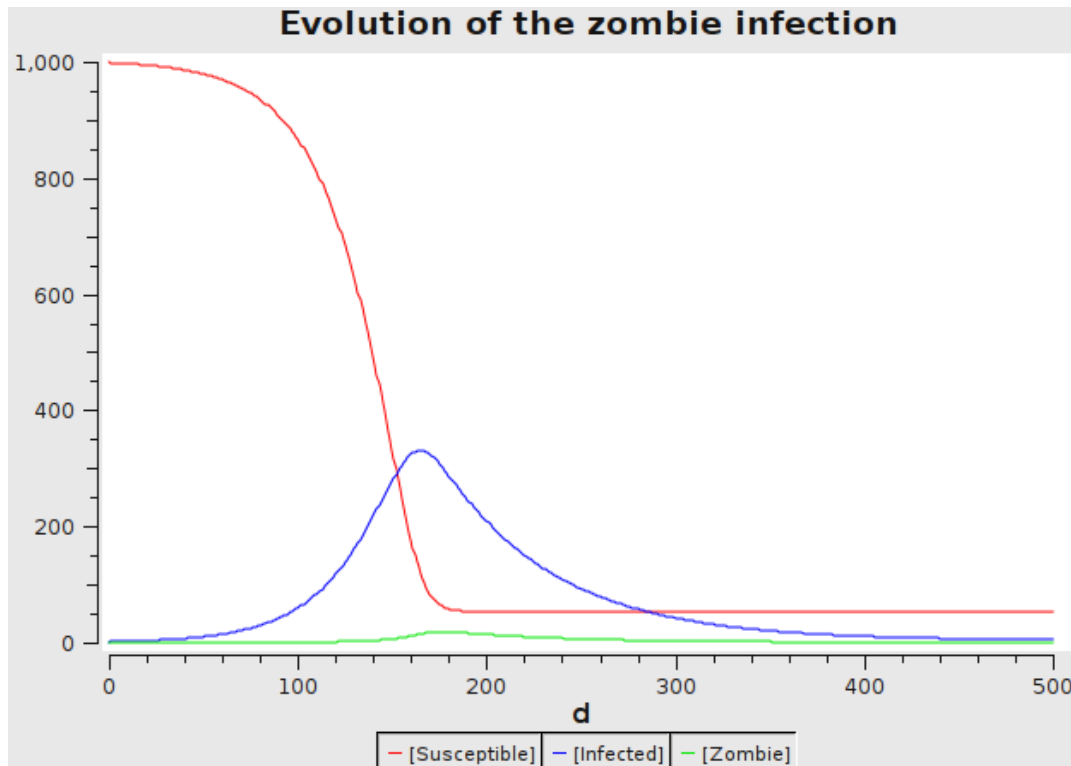
rate rule:

$$\frac{dv}{dt} = 0.04v^2 + 5 \times V + 140 - U + i$$

event:

$$\text{when } v > V_{thresh} \begin{cases} v = c \\ U = U + d \end{cases}$$

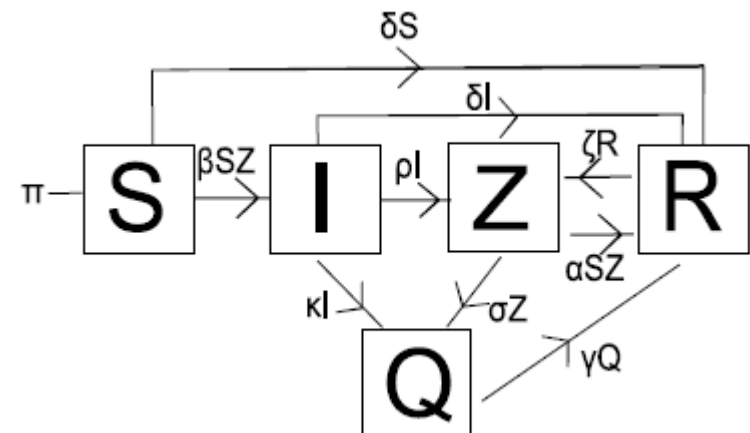
Spread of infection diseases ...



Munz P et al. When zombies attack!: Mathematical modelling of an outbreak of zombie infection. in "Infectious Disease Modelling Research Progress", (2009)133-150



MODEL1008060001



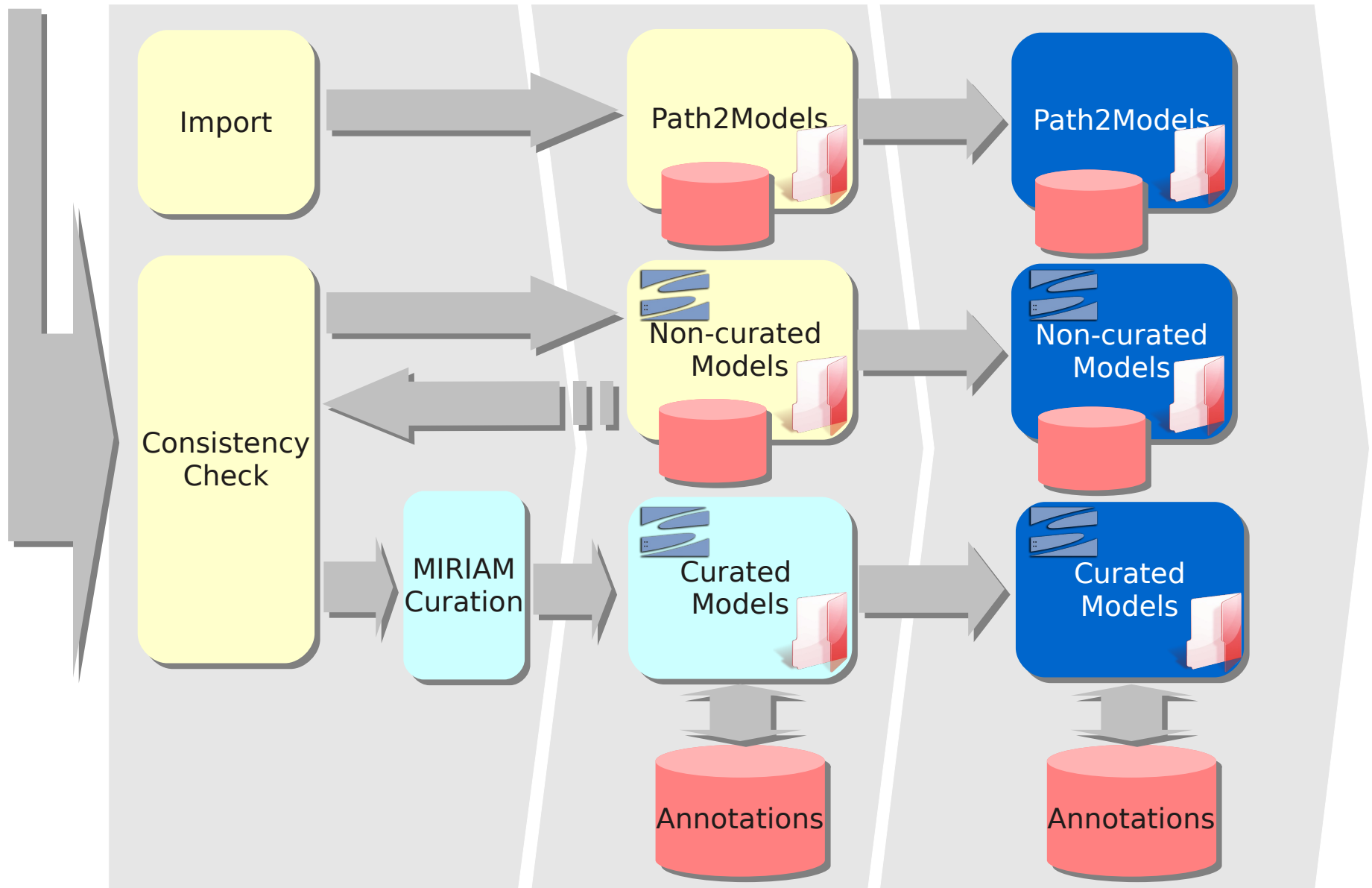
Current production pipeline

Submission

Curation

Annotation

distribution



BioModels Db does not belong to anyone!

CC0 1.0 Universal (CC0 1.0) Public Domain Dedication

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

[Disclaimer](#)

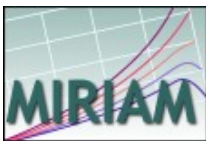
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Minimum Information Required in the Annotation of Models (simplified)

Models must :

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

Curated and Non-curated Models

- Curated models – Comply with the MIRIAM guidelines
- Non-Curated models – valid SBML, not curated or annotated
 - Not MIRIAM compliant:
 - cannot reproduce results published in the paper.
 - differ in model structure
 - non-kinetic models (eg. FBA, stoichiometric maps)
 - MIRIAM compliant:
 - models contain kinetics that we cannot curate at present (e.g. reaction-diffusion models)
 - models are yet to be curated

Why are annotations important?

Annotation of model components are essential to:

- allow efficient search strategies
- unambiguously identify model components
 - improve understanding the structure of the model
 - allow easier comparison of different models
 - ease the integration of models
- add a semantic layer to the model
 - improve understanding of the biology behind the model
 - allow conversion and reuse of the model
 - ease the integration of model and biological knowledge

Enter *identifiers*^o_g (aka new MIRIAM URIs)

`http://` `identifiers.org` `/namespace/` `identifier`

protocol

type of URI

collection

record

`http://identifiers.org/uniprot/P62158`

`http://identifiers.org/ec-code/1.1.1.1`

`http://identifiers.org/obo.go/GO:0000186`



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- Curator Sign in



sourceforge

EBI

>

Groups

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Computational Neurobiology

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Research

>

MIRIAM Registry

MIRIAM Registry

The **MIRIAM Registry** provides a set of online services for the generation of unique and perennial identifiers, in the form of URIs.

The *Registry* was initially created to support [MIRIAM](#), a set of guidelines for the annotation and curation of computational models.

The core of the *Registry* is a catalogue of data collections (corresponding to controlled vocabularies or databases), their URIs and the corresponding physical URLs or resources. Access to this data is made available via exports (XML) and Web Services (SOAP).

The *Registry* is developed and maintained under the [BioModels.net](#) initiative. All provided services and data is free for use by all.



Quick links

Browse by data collection name by tags	Web Services services available usage of the services online demonstration
Search generic search	Exports XML

http://www.ebi.ac.uk/miriam/

Registry

The *MIRIAM Registry* is composed of four components: [a database](#), [some Web Services](#), [a Java library](#) and [this web application](#).

Database

The core of the system is a [MySQL](#) database. It allows us to store the [data collections](#) (which can be controlled vocabularies or databases), their URIs and the corresponding physical URLs, and other [details](#) such as documentation and resource identifier patterns.

Each entry contains a diverse set of details about the data collection: official name and synonyms, root URI, pattern of identifiers, documentation, etc. Moreover, each data collection can be associated with several resources (or physical locations).

Web Services

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

4 physical locations (or resources) are available for accessing *1.1.1.1* (from [Enzyme Nomenclature](#)):

**Enzyme nomenclature database,
ExPASy (Expert Protein Analysis
System)**

Swiss Institute of Bioinformatics

Switzerland

(Uptime: 99%)

[ExploreEnz at Trinity College](#)
[Trinity College, Dublin](#)

[Ireland](#)

(Uptime: 100%)

[KEGG Ligand Database for Enzyme
Nomenclature](#)
[Kyoto University Bioinformatics Center](#)

[Japan](#)

(Uptime: 100%)

[IntEnZ \(Integrated relational Enzyme
database\)](#)
[European Bioinformatics Institute](#)

[United Kingdom](#)

(Uptime: 100%)

Search - Models



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):

Publication 

Annotation (identifier):

Taxonomy 

Annotation (identifier):

KEGG Reaction 

Annotation (identifier):

Enzyme Nomenclature Compose by: ☒ and ☐ or

Search - Models



Query: *Gene Ontology* **cell cycle** [resources]

The search returned **50** models.

↩ [New Search](#)

50 Curated models returned:

BioModels ID ▼	Name	Publication ID	Last Modified
BIOMD0000000003	Goldbeter1991_MinMitOscil	1833774	2012-05-15T15:45:17+00:00
BIOMD0000000004	Goldbeter1991_MinMitOscil_ExpInact	1833774	2012-05-15T15:45:30+00:00
BIOMD0000000005	Tyson1991_CellCycle_6var	1831270	2012-06-18T13:11:11+00:00
BIOMD0000000006	Tyson1991_CellCycle_2var	1831270	2012-05-15T15:45:49+00:00
BIOMD0000000007	Novak1997_CellCycle	9256450	2012-05-15T15:46:12+00:00
BIOMD0000000008	Gardner1998_CellCycle_Goldbeter	9826676	2012-07-11T17:07:14+00:00
BIOMD0000000056	Chen2004_CellCycle	15169868	2012-05-15T21:53:24+00:00
BIOMD0000000069	Fuss2006_MitoticActivation	16873466	2012-05-16T10:20:18+00:00
BIOMD0000000087	Proctor2006_telomere	17015293	2012-07-05T14:40:05+00:00

BIOMD0000000005 - Tyson1991_CellCycle_6var



Download SBML

Other formats (auto-generated)

Actions

[Send feedback](#)**Model**

Overview

Math

Physical entities

Parameters

Curation

Reference Publication**Publication ID:** [1831270](#)

Tyson JJ.
 Modeling the cell division cycle: cdc2 and cyclin interactions.
 Proc Natl Acad Sci U S A 1991 Aug;88(16):7328-32.
 Department of Biology, Virginia Polytechnic Institute and State University, Blacksburg 24061. [\[more\]](#)

Model**Original Model:** [BIOMD0000000005.xml.origin](#)**Submitter:** [Nicolas Le Novère](#)**Submission ID:** MODEL6614644188**Submission Date:** 13 Sep 2005 12:31:08 UTC**Last Modification Date:** 18 Jun 2012 13:11:11 UTC**Creation Date:** 08 Feb 2005 18:28:27 UTC
Encoders: [Bruce Shapiro](#)
[Vijayalakshmi Chelliah](#)

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

Notes

This a model from the article:

BIOMD0000000005 - Tyson1991_CellCycle_6var


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[Other formats \(auto-generated\)](#)
[Actions](#)
[Send feedback](#)

Model

Overview

Math

Physical entities

Parameters

Curation



Spatial dimensions: 3.0 Compartment size: 1.0

EmptySet

Initial amount: 0.0

Compartment: cell

**cdc2k**

Initial amount: 0.0

Compartment: cell

**cdc2k-P**

Initial amount: 0.75

Compartment: cell

**p-cyclin_cdc2**

Initial amount: 0.0

Compartment: cell

Annotations:

set #1 bqbiol:hasPart

[UniProt CDK1 SCHPO](#)
[InterPro IPR006670](#)
**p-cyclin_cdc2-p**

Initial amount: 0.25

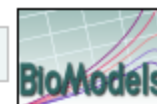
Compartment: cell

**cyclin**

Initial amount: 0.0

Compartment: cell

BIOMD0000000005 - Tyson1991_CellCycle_6var


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[Other formats \(auto-generated\)](#)
[Actions](#)
[Send feedback](#)

Model

Overview

Math

Physical entities

Parameters

Curation

Reactions (9)

☒ **cyclin_cdc2k dissociation** $[p\text{-cyclin_cdc2}] \rightarrow [cdc2k] + [p\text{-cyclin}]$;

☒ **cdc2k phosphorylation** $[cdc2k] \rightarrow [cdc2k\text{-P}]$;

☒ **cdc2k dephosphorylation** $[cdc2k\text{-P}] \rightarrow [cdc2k]$;

☒ **cyclin cdc2k-p association** $[cdc2k\text{-P}] + [cyclin] \rightarrow [p\text{-cyclin_cdc2-p}]$;

☐ **deactivation of cdc2 kinase** $[p\text{-cyclin_cdc2}] \rightarrow [p\text{-cyclin_cdc2-p}]$;

Math: $cell \times k5notP \times M$ [\(Details: !\[\]\(e7807f406269fb58f87257f99da68944_img.jpg\)\)](#)

Annotations:

set #1	bqbiol:isVersionOf	Enzyme Nomenclature 2.7.10.2 Gene Ontology protein phosphorylation Gene Ontology negative regulation of cyclin-dependent protein kinase activity
set #2	bqbiol:hasVersion	Reactome REACT_3178 Reactome REACT_6327

☒ **cyclin biosynthesis** $[EmptySet] \rightarrow [cyclin]$;

☒ **default degradation of cyclin** $[cyclin] \rightarrow [EmptySet]$;

☒ **cdc2 kinase triggered degradation of cyclin** $[p\text{-cyclin_cdc2}] \rightarrow [EmptySet]$;

BIOMD0000000005 - Tyson1991_CellCycle_6var

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

Overview

Math

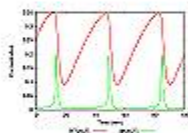
Physical entities

Parameters

Curation

Submodel1

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).

Additional file(s)

■ **Simulation experiment description:**

This SED-ML file allows you to reproduce the curation result (Fig 3a), for example, by loading it into SED-ML Web Tools (http://sysbioapps.dyndns.org/SED-ML_Web_Tools/).

[\[BIOMD0000000005_SED-ML.xml\]](#)

BIOMD0000000005 - Tyson1991_CellCycle_6var

Download SBML

Other formats (auto-generated)

Actions

[Send feedback](#)

Overview

Math

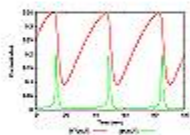
Physical entities

Parameters

Curation

Submodel1

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).

Additional file(s)

■ **Simulation experiment description:**

This SED-ML file allows you to reproduce the curation result (Fig 3a), for example by loading it into SED-ML Web Tools (http://sysbioapps.dyndns.org/SED-ML/BIOMD0000000005_SED-ML.xml)

Reproduction with COPASI

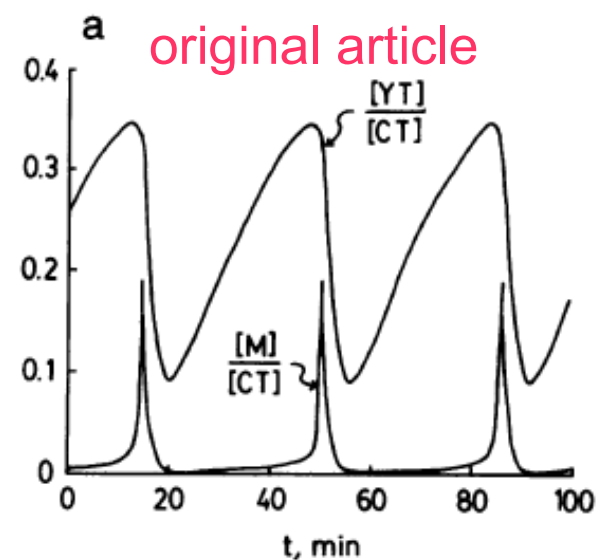
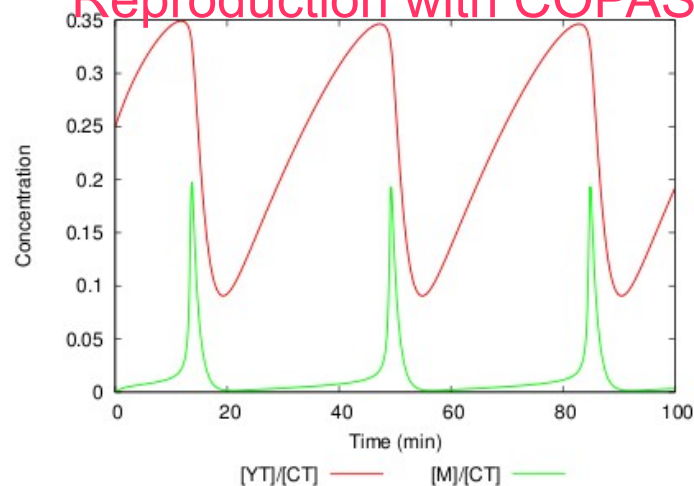
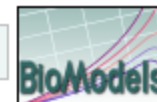


FIG. 3. Dynamical behavior of the cdc2-cyclin relative to total cdc2 ($[CT] = [C2] + [CP] + [nM]$)

BIOMD0000000005 - Tyson1991_CellCycle_6var

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

Model

Overview

Math

Physical entities

Parameters

Curation



Create a submodel with selected elements



Deselect All

ModelPublication ID: [1831270](#)

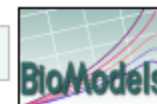
Submission Date: 13 Sep 2005 12:31:08 UTC

Last Modification Date: 18 Jun 2012 13:11:11 UTC

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

Mathematical expressions☐ Reactions☐ [cyclin_cdc2k dissociation](#)☐ [cdc2k phosphorylation](#)☐ [cdc2k dephosphorylation](#)☐ [cyclin cdc2k-p association](#)☐ [deactivation of cdc2 kinase](#)☐ [cyclin biosynthesis](#)☐ [default degradation of cyclin](#)☐ [cdc2 kinase triggered degradation of cyclin](#)☐ [activation of cdc2 kinase](#)**Rules**[Assignment Rule \(variable: total_cyclin\)](#)[Assignment Rule \(variable: total_cdc2\)](#)**Physical entities**☐ Compartments☐ Species

BIOMD0000000005 - Tyson1991_CellCycle_6var



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Other formats (auto-generated)

Actions

[Send feedback](#)

Model

Overview

Math

Physical entities

Parameters

Curation

Create a submodel with selected elements

Deselect All

Model

Publication ID: [1831270](#)

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

Last Modification Date: 18 Jun 2012 13:11:11 UTC

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

Mathematical expressions

☐ Reactions

☐ [cyclin_cdc2k dissociation](#)

☐ [cdc2k phosphorylation](#)

☒ [cdc2k dephosphorylation](#)

☐ [cyclin cdc2k-p association](#)

☐ [deactivation of cdc2 kinase](#)

☐ [cyclin biosynthesis](#)

☐ [default degradation of cyclin](#)

☐ [cdc2 kinase triggered degradation of cyclin](#)

☐ [activation of cdc2 kinase](#)

Rules

[Assignment Rule \(variable: total_cyclin\)](#)

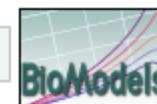
[Assignment Rule \(variable: total_cdc2\)](#)

Physical entities

☐ Compartments

☐ Species

BIOMD0000000005 - Tyson1991_CellCycle_6var



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Other formats (auto-generated)

Actions

[Send feedback](#)

Overview

Math

Physical entities

Parameters

Curation

Submodel1

View the submodel in SBML

Save as

Reactions (1)

cdc2k dephosphorylation [\[cdc2k-P\]](#) → [\[cdc2k\]](#);

Compartments (1)

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

Referred to as: cell

Species (2)

cdc2k Initial amount: 0.0

Compartment: cell

cdc2k-P Initial amount: 0.75

Compartment: cell

Fully valid SBML model containing only the dephosphorylation of cdc2k



BIOMD0000000005 - Tyson1991_CellCycle_6var

- Download SBML
- SBML L2 V1 (auto-generated)
- SBML L2 V2 (auto-generated)
- SBML L2 V3 (auto-generated)
- SBML L2 V4 (curated)

Other form

Automatically generated using libsbml
(<http://sbml.org/Software/libSBML>)

Model Comment/Bug

Parameters

Curation

Reference Publication

Proc Natl Acad Sci U S A 1991 Aug;88(16):7328-32.
Modeling the cell division cycle: cdc2 and cyclin interactions.

Publication ID: [1831270](#)

State University, Blacksburg 24061. [\[more\]](#)

Curated version of the model

Original Model: [BIOMD0000000005](#)

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 UTC

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

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

set #1 bqbiol:isVersionOf

[KEGG Pathway sce04111](#)
[Gene Ontology mitotic cell cycle](#)

bqbiol:occursIn

[Taxonomy Fungi/Metazoa group](#)

Notes

This a model from the article:

Modeling the cell division cycle: cdc2 and cyclin interactions.

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

Abstract:

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

This model originates from BioModels Database: A Database of Annotated Published Models (<http://www.ebi.ac.uk/biomodels/>). It is copyright (c) 2005-2010 The BioModels.net Team.

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

To cite BioModels Database, please use: [Li C, Donizelli M, Rodriguez N, Dharuri H, Endler L, Chelliah V, Li L, He E, Henry A, Stefan MI, Snoep JL, Hucka M, Le Novère N, Laibe C \(2010\) BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models. BMC Syst Biol., 4:92.](#)

BIOMD0000000005 - Tyson1991_CellCycle_6var

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Other formats (auto-generated)

Actions

Submit Model Comment/Bug

Model

Publication ID: [1831270](#)

Original Model

Submitter

Submission

Submission

Last Modified

Creation

Encoders

Other formats (auto-generated)

Octave

PDF

SciLab

VCML (VCell)

XPP

Actions

Reference Publications

Submit Model Comment/Bug

SBML Model Report

Model name: "Tyson1991_CellCycle_6var"

9th February 2009

1 General Overview

This is a document in SBML Level 2 Version 3 format. This model was created by the following two authors: Bruce Shapiro¹ and Vijayalakshmi Chelliah² at February eighth 2005 at 6:28 p.m. and last modified at August 21st 2008 at 11:31 a.m. Table 1 gives an overview of the quantities of all components of this model.

biol:hasVersion

biol:isVersionOf

biol:occursIn

1270,

promoting factor) to

show that the co

We associate the

growth-controlled

f Annotated Pub

riquez N. Dharur,

ted resource for published quantitative kinetic models. BMC Syst Biol., 4:92.

Table 1: The SBML components in this model.

All components are described in more detail in the following sections.

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	9
events	0	constraints	0
reactions	9	function definitions	0
global parameters	0	unit definitions	5
rules	2	initial assignments	0

Model Notes

Cell Cycle Model; Tyson (1991, 6 variables)

Description

¹NASA Jet Propulsion Laboratory, bshapiro@jpl.nasa.gov

²EMBL-EBL, vij@ebi.ac.uk

Produced by SBML2LATEX

1270,

promoting factor) to

show that the co

We associate the

growth-controlled

f Annotated Pub

riquez N. Dharur,

ted resource for published quantitative kinetic models. BMC Syst Biol., 4:92.

BioPAX versions of the model generated from SBML+MIRIAM

```
<?xml version="1.0" encoding="UTF-8"?>
<rdf:RDF xmlns:bp="http://www.biopax.org/release/biopax-level2.owl#"
xmlns:xsd="http://www.w3.org/2001/XMLSchema#"
xmlns:owl="http://www.w3.org/2002/07/owl#"
xmlns:base="http://www.ebi.ac.uk/biomodels/biopax.owl#"
xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#">
  <owl:Ontology rdf:about="">
    <owl:imports rdf:resource="http://www.biopax.org/release/biopax-level2.owl#" />
  </owl:Ontology>

  <bp:physicalEntity rdf:about="EmptySet">
    <bp:NAME rdf:datatype="xsd:string">EmptySet</bp:NAME>
  </bp:physicalEntity>

  <bp:physicalEntityParticipant rdf:about="RIGHT_conversion_Reaction1_C2">
    <bp:PHYSICAL-ENTITY rdf:resource="C2" />
    <bp:CELLULAR-LOCATION rdf:resource="cell" />
    <bp:STOICHIOMETRIC-COEFFICIENT
      rdf:datatype="xsd:double">1.0</bp:STOICHIOMETRIC-COEFFICIENT>
  </bp:physicalEntityParticipant>

  <bp:physicalEntityParticipant rdf:about="LEFT_conversion_Reaction4_CP">
    <bp:PHYSICAL-ENTITY rdf:resource="CP" />
    <bp:CELLULAR-LOCATION rdf:resource="cell" />
    <bp:STOICHIOMETRIC-COEFFICIENT
      rdf:datatype="xsd:double">1.0</bp:STOICHIOMETRIC-COEFFICIENT>
  </bp:physicalEntityParticipant>

  <bp:physicalEntityParticipant rdf:about="LEFT_conversion_Reaction1_M">
    <bp:PHYSICAL-ENTITY rdf:resource="M" />
    <bp:CELLULAR-LOCATION rdf:resource="cell" />
    <bp:STOICHIOMETRIC-COEFFICIENT
      rdf:datatype="xsd:double">1.0</bp:STOICHIOMETRIC-COEFFICIENT>
  </bp:physicalEntityParticipant>
```


http://www.ebi.ac.uk/biomodels/models-main/ode_simu/SIMU1234453623...

BIOMD0000000005 - Tyson1991_CellCycle_6var

Download SBML | Other formats (auto-generated) | Actions

Model | Overview | Math

Publication ID: 1831270

Proc Natl Acad Sci
Modeling the cell di
Tyson JJ.
Department of Biology, Virginia Polytechnic Institute

View Bitmap Reaction Graph

View SVG Reaction Graph

View Dynamic Reaction Graph

View Model of Month

JWS Online Simulation

BioModels Online Simulation

http://jjj.mib.ac.uk/biomodels/Tyson1991/index.html

Biomodels Home

Index

JWS Online

Model

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

Submitter: [Nicolas Le Novère](#)

Submission ID: MODEL6614644188

bqbiol:hasVersion

set#1 bqbiol:isVersionOf

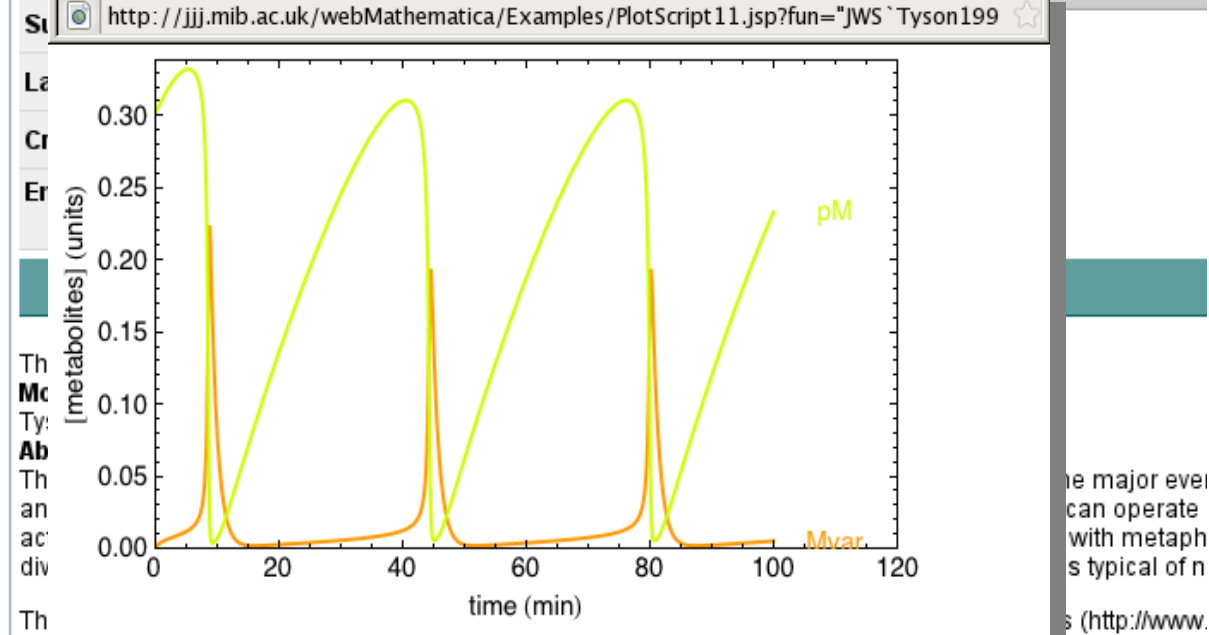
bqbiol:occursIn

[Reactome REACT 152](#)

[KEGG Pathway sce0411](#)

[Gene Ontology mitotic ce](#)

[Taxonomy Fungi/Metazo](#)



Biomodels

Biomodels: BIOMD0000000005

Tyson1991

Powered by JWS Online

JWSApplet - ver 5.0.3 Tyson1991

	Parameter	Value
P1_v1	cell	1
P2_v1	k6	1
P3_v1	k8notP	1.0e6
P4_v1	k9	1000
P5_v1	k3	200
P6_v1	k5notP	0.
P7_v1	k1aa	0.015
P8_v1	k2	0.
P9_v1	k7	0.6
P10_v1	k4	180
P11_v1	k4prime	0.018
E1	EmptySet	0.
I1	C2[0]	0.
I2	CP[0]	1
I3	Mvar[0]	0.
I4	Y[0]	0.
I5	YP[0]	0.
I6	pM[0]	0.3

POWERED BY

webMATHEMATICA2

Reset

Evaluate Model

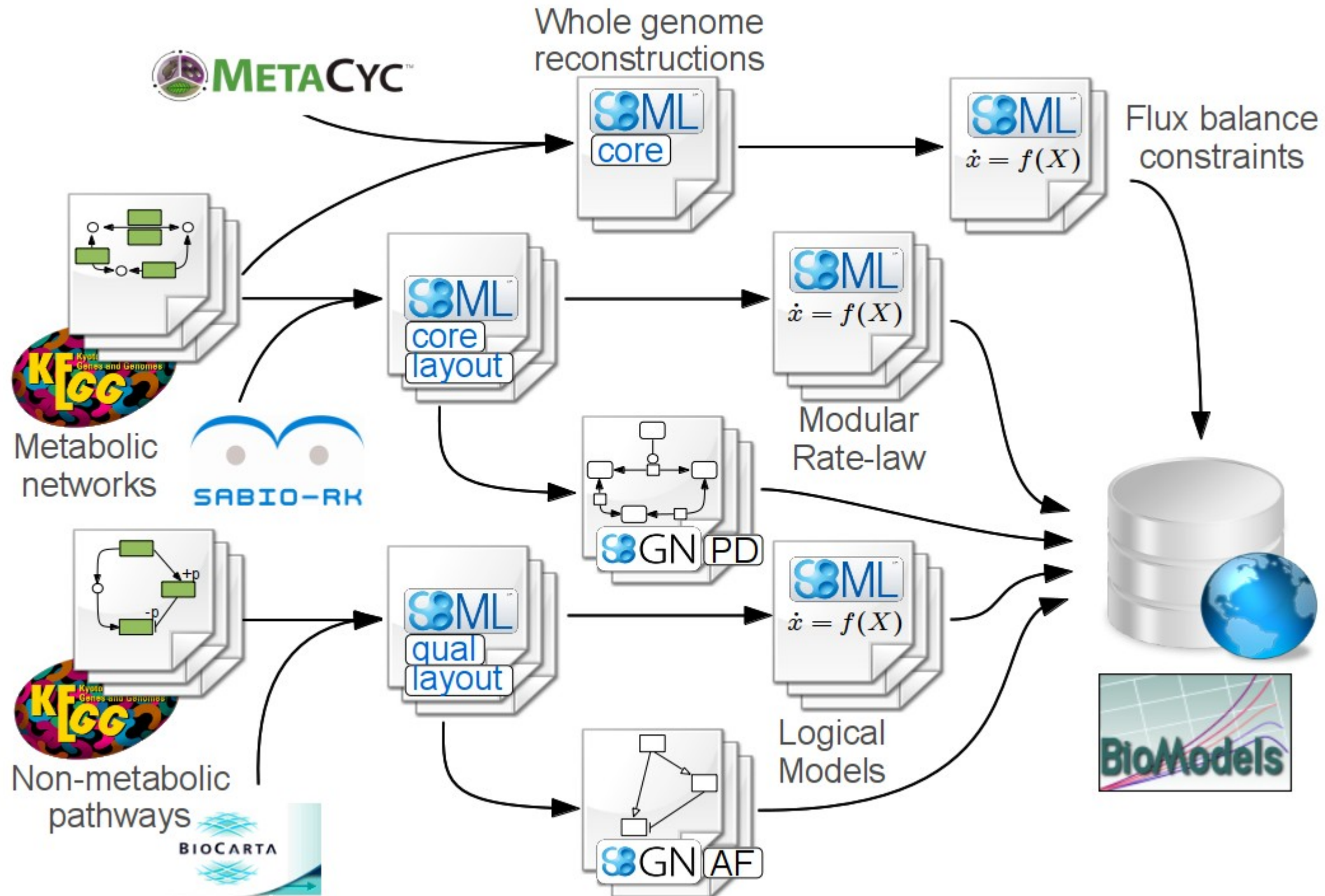
Sim State

StartTime EndTime

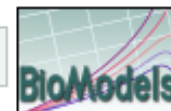
0 100

☐ Rates ☒ Metabolites

Type	Output	Plot
M1	C2	☐
M2	CP	☐
M3	Mvar	☒
M4	Y	☐
M5	YP	☐
M6	pM	☒
F1	vRea...	☐
F2	vRea...	☐
F3	vRea...	☐
F4	vRea...	☐
F5	vRea...	☐
F6	vRea...	☐
F7	vRea...	☐
F8	vRea...	☐



Path2Models



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

Browse models

Models from this project are classified in 3 distinct categories:

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

One can also browse those models by organism:

- [list of all organisms](#)

Search models

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

Help about the search

- The keywords *AND* or *OR* (in upper cases) are available to refine the search. By default, if more than one word is present in a query, *OR* will be used to combine them.
- Double quotes (") can be used to force the search engine to match a whole expression containing several words.
- The colon character (:) must be escaped in the queries; one can use a backslash for this purpose (\:).

Download all models

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



Path2Models:

Here are all the whole genome metabolism models available:

- [Acaryochloris marina \(strain MBIC 11017\)](#)
- [Accumulibacter phosphatis \(strain UW-1\)](#)
- [Acetobacter pasteurianus \(strain NBRC 3283 / LMG 1513 / CCTM 1153\)](#)
- [Acetobacter pasteurianus IFO 3283-01-42C](#)
- [Acetobacter pasteurianus IFO 3283-03](#)
- [Acetobacter pasteurianus IFO 3283-07](#)
- [Acetobacter pasteurianus IFO 3283-12](#)
- [Acetobacter pasteurianus IFO 3283-22](#)
- [Acetobacter pasteurianus IFO 3283-26](#)
- [Acetobacter pasteurianus IFO 3283-32](#)
- [Acetobacterium woodii \(strain ATCC 29683 / DSM 1030 / JCM 2381 / KCTC 1655\)](#)
- [Acetohalobium arabaticum \(strain ATCC 49924 / DSM 5501 / Z-7288\)](#)
- [Acholeplasma laidlawii \(strain PG-8A\)](#)
- [Achromobacter xylosoxidans \(strain A8\)](#)
- [Acidaminococcus fermentans \(strain ATCC 25085 / DSM 20731 / VR4\)](#)
- [Acidaminococcus intestini \(strain RyC-MR95\)](#)
- [Acidianus hospitalis \(strain W1\)](#)
- [Acidilobus saccharovorans \(strain DSM 16705 / VKM B-2471 / 345-15\)](#)
- [Acidimicrobium ferrooxidans \(strain DSM 10331 / JCM 15462 / NBRC 103882 / ICP\)](#)
- [Acidiphilium cryptum \(strain JF-5\)](#)
- [Acidiphilium multivorum \(strain DSM 11245 / JCM 8867 / AIU301\)](#)
- [Acidithiobacillus caldus \(strain SM-1\)](#)
- [Acidithiobacillus ferrivorans SS3](#)
- [Acidithiobacillus ferrooxidans \(strain ATCC 23270 / DSM 14882 / NCIB 8455\)](#)



Whole Genome Metabolism - Homo sapiens

Download SBML

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Model information

Identifier: [BMID000000140905](#)

Format: SBML L2 V4

Project: [path2models](#)

Categories: [genome-scale](#)

Submission: 19 May 2012 15:48:00 UTC

Last modified: 08 Aug 2012 21:02:14 UTC

Published: 19 May 2012 23:49:21 UTC

Annotations

[occursIn](#)

[Homo sapiens](#)

Taxonomy

Notes

Whole Genome Metabolism of "Homo sapiens"

This is a whole genome metabolism model of Homo sapiens.

This model has been automatically generated by the [SuBliMinaL Toolbox](#) using information coming from KEGG and MetaCyc.

This model has been produced by the [path2models](#) project and is currently hosted on [BioModels Database](#) and identified by: [BMID000000140905](#).

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.

BioModels Web Services

Available features

With BioModels Web Services, users can access the up-to-date resources in BioModels Database without installing a local copy of the database. There are a range of available features for searching and retrieving models. Furthermore, some features can help users to extract interesting parts from a large model and construct them into a submodel. For any comments or new feature enquiries, please feel free to [contact us](#).

- [Available features](#)
- [javadoc](#)
- [WSDL](#)

The WSDL (Web Services Description Language) defines and describes the available features in an XML format file. This enables third-party software to automate parsing all available features of BioModels Web Services. Comparing with WSDL, Javadoc is API documentation which provides more information to the developers.

Download

We provide two versions of the library for querying BioModels Database Web Services. These are available for download from the [SourceForge project download page](#) (latest release: 1.12):

- [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 only needed by 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.

Basics - Getting Started

First, download the library we provide.

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

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

public class HelloBioModels
{
```

Index of ftp://ftp.ebi.ac.uk/pub/databases/biomodels/weekly_archives/2012/

[↑ Up to higher level directory](#)

Name	Size	Last Modified
 BioModels-Database-weekly-2012-01-02-sbmls.tar.gz	11734 KB	22/03/12 00:00:00
 BioModels-Database-weekly-2012-01-09-sbmls.tar.gz	11735 KB	22/03/12 00:00:00
 BioModels-Database-weekly-2012-01-16-sbmls.tar.gz	11734 KB	22/03/12 00:00:00

Index of <ftp://ftp.ebi.ac.uk/pub/databases/biomodels/releases/>

[↑ Up to higher level directory](#)

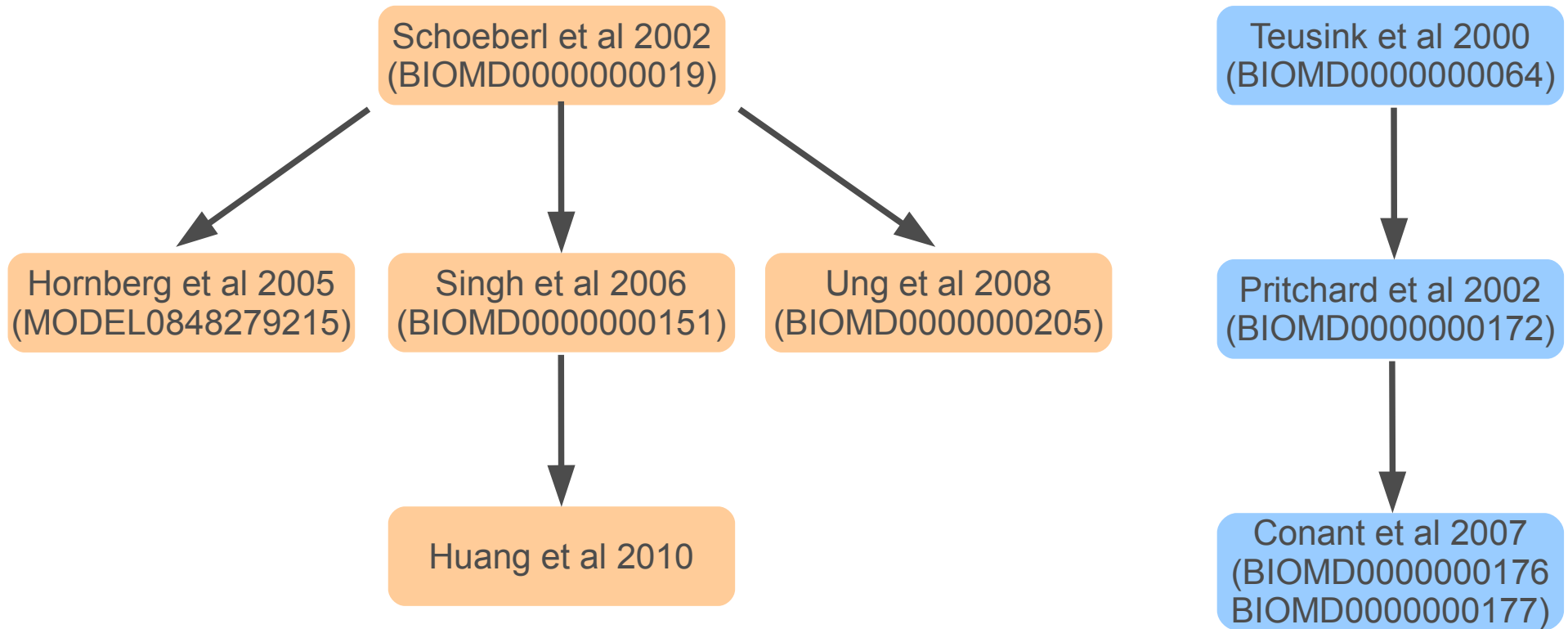
Name	Size	Last Modified
 2005-04-11		08/02/12 00:00:00
 2005-06-01		08/02/12 00:00:00
 2005-07-28		08/02/12 00:00:00
 2006-01-31		08/02/12 00:00:00

Index of <ftp://ftp.ebi.ac.uk/pub/databases/biomodels/releases/latest/>

[↑ Up to higher level directory](#)

Name	Size	Last Modified
 BioModels_Database-r23_p2m-metabolic.tar.bz2	1966032 KB	10/08/12 15:19:00
 BioModels_Database-r23_p2m-non_metabolic.tar.bz2	78726 KB	10/08/12 15:19:00
 BioModels_Database-r23_p2m-whole_genome_metabolism.tar.bz2	509109 KB	10/08/12 15:20:00
 BioModels_Database-r23_pub-all_files.tar.bz2	601968 KB	10/08/12 21:03:00
 BioModels_Database-r23_pub-sbml_files.tar.bz2	10992 KB	11/08/12 13:10:00

Direct model re-use: e.g. EGFR signalling and glycolysis



Standard formats generate new research

- Herrgård et al (2008) A consensus yeast metabolic network reconstruction obtained from a community approach to systems biology. *Nature Biotechnol*, 26: 1155-1160



MODEL0072364382: 2152 species, 1857 reactions

- stoichiometric map, no concentrations, no kinetics
- Smallbone et al (2010) Towards a genome-scale kinetic model of cellular metabolism. *BMC Syst Biol*, 4:6



MODEL1001200000: 1748 species, 1059 reactions

- Concentrations and flux from BioModels Database
- Constraint-based model and simplified linlog kinetics
- Dobson et al (2010) Further developments towards a genome-scale metabolic model of yeast. *BMC Syst Biol*, 4:145



MODEL1012110000: 2657 species, 1865 reactions

- Li et al (2010) Systematic integration of experimental data and models in systems biology. *BMC Bioinfo*, 11: 582



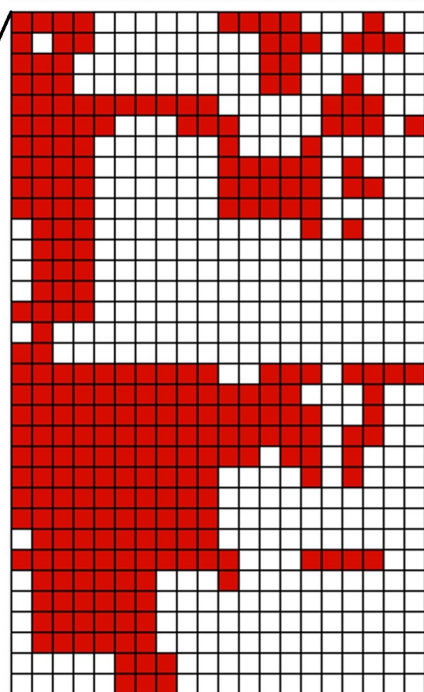
MODEL1012110001

- Workflows using experimental kinetic information database (SABIO-RK) plus metabolomics and proteomics database
- Full quantitative chemical kinetics descriptions

Clustering models (and data) based on metadata

Schulz M. et al (2010)
Retrieval, alignment, and clustering of computational models based on semantic Annotations. *Mol Syst Bio*, 7: 512

BIOMD00000000010_0
BIOMD00000000009_0
BIOMD00000000011_0
BIOMD00000000014_0
BIOMD00000000026_0
BIOMD00000000028_0
BIOMD00000000030_0
BIOMD00000000029_0
BIOMD00000000027_0
BIOMD00000000031_0
BIOMD00000000032_0
BIOMD000000000116_0
BIOMD00000000084_0
BIOMD000000000149_0
BIOMD00000000033_0
BIOMD00000000048_0
BIOMD00000000049_0
BIOMD000000000205_0
BIOMD00000000019_0
BIOMD000000000175_0



ATP:protein_phosphotransferase_(non-specific)
RAF_proto-oncogene_serine/threonine-protein_kinase
inactivation_of_MAPKKK_activity
inactivation_of_MAPKKK_activity
protein_amino_acid_dephosphorylation
protein_amino_acid_phosphorylation
MAP_kinase_kinase_kinase_kinase_activity
MAP_kinase_kinase_kinase_activity
activation_of_MAPKKK_activity
activation_of_MAPKKK_activity
Ras_small_GTPase_Ras_type
mitogen-activated_protein_kinase_kinase_kinase_binding
urn:miriam:reactome:REACT_143
urn:miriam:reactome:REACT_996
urn:miriam:reactome:REACT_614
Serine/threonine-protein_kinase_mos
urn:miriam:reactome:REACT_525
Mitogen-activated_protein_kinase_1
ATP:protein_phosphotransferase_(MAPKKK-activated)
MAP_kinase_kinase_activity
activation_of_MAPK_activity
inactivation_of_MAPK_activity
Dual_specificity_mitogen-activated_protein_kinase_kinase_1
urn:miriam:reactome:REACT_136
urn:miriam:reactome:REACT_2247
urn:miriam:uniprot:Q90W58
phosphoprotein_phosphatase_activity
mitogen-activated_protein_kinase_binding
mitogen-activated_protein_kinase_kinase_binding
urn:miriam:reactome:REACT_1780
urn:miriam:reactome:REACT_495
peptidyl-threonine_phosphorylation
peptidyl-tyrosine_phosphorylation

Ranking and retrieval of models

Model	BioModel	Score	p-val num	
Huang1996_MAPK_ultrasens	BIOMD0000000009	1.000	< 1/1000	
Levchenko2000_MAPK_noScaffold	BIOMD0000000011	0.925	< 1/1000	
Levchenko2000_MAPK_Scaffold	BIOMD0000000014	0.865	< 1/1000	
Kholodenko2000_MAPK_feedback	BIOMD0000000010	0.816	< 1/1000	
Markevich2004_MAPK_orderedElementary	BIOMD0000000026	0.737	< 1/1000	
Markevich2004_MAPK_phosphoRandomElementary	BIOMD0000000028	0.690	< 1/1000	
Markevich2004_MAPK_AllRandomElementary	BIOMD0000000030	0.690	< 1/1000	
Markevich2004_MAPK_orderedMM	BIOMD0000000027	0.673	< 1/1000	
Markevich2004_MAPK_orderedMM2kinases	BIOMD0000000031	0.673	< 1/1000	
Markevich2004_MAPK_phosphoRandomMM	BIOMD0000000029	0.617	< 1/1000	
Hornberg2005_ERKcascade	BIOMD0000000084	0.468	< 1/1000	
McClean2007_CrossTalk	BIOMD0000000116	0.397	< 1/1000	
Kofahl2004_pheromone	BIOMD0000000032	0.348	< 1/1000	
Kim2007_Wnt_ERK_Crosstalk	BIOMD0000000149	0.323	< 1/1000	
Brown2004_NGF_EGF_signaling	BIOMD0000000033	0.260	< 1/1000	
Goldbeter1995_CircClock	BIOMD0000000016	0.244	< 1/1000	
Sasagawa2005_MAPK	BIOMD0000000049	0.240	< 1/1000	
Ung2008_EGFR_Endocytosis	BIOMD0000000205	0.234	< 1/1000	
Leloup1999_CircClock	BIOMD0000000021	0.229	< 1/1000	
Goldbeter1991_MinMitOscil_ExpInact	BIOMD0000000004	0.222	< 1/1000	
Goldbeter1991_MinMitOscil	BIOMD0000000003	0.214	< 1/1000	
Leloup1998_CircClock_LD	BIOMD0000000171	0.201	< 1/1000	
Tyson1991_CellCycle_6var	BIOMD0000000005	0.199	< 1/1000	
Veening2008_DegU_Regulation	BIOMD0000000240	0.180	< 1/1000	
Neves2008_Cell_Shape	BIOMD0000000182	0.168	4.0e-03	
Fisher2006_Ca_Oscillation_dpdnt_NFAT_dynamics	BIOMD0000000122	0.164	5.0e-03	
Leloup2003_CircClock_DD	BIOMD0000000073	0.163	5.0e-03	

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MAPK

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Leloup2003_CircClock_DD	BIOMD0000000073	0.163	5.0e-03	

MAPK

Other kinase cascades

FOSS house made of FOSS bricks

- **BioModels Db** [GPLv2] → <http://sourceforge.net/projects/biomodels/>
- **LibSBML** [LGPLv2] → <http://sourceforge.net/projects/sbml/>
- **JSBML** [LGPLv2] → <http://sourceforge.net/projects/jsbml/>
- **Systems Biology Format Converter** [GPLv2] → <http://sourceforge.net/projects/sbfc/>
- **Tomcat** [Apache v2] → <http://tomcat.apache.org/>
- **MySQL** [Oracle FOSS] → <http://dev.mysql.com/>
- **Subversion** [Apache v2] → <http://subversion.apache.org/>
- **Lucene** [Apache v2] → <http://lucene.apache.org/>
- **Axis** [Apache v2] → <http://axis.apache.org/>
- **SOSlib** [GPLv2] → <http://www.tbi.univie.ac.at/~raim/odeSolver/>
- **Gnuplot** [own opensource license] → <http://www.gnuplot.info/>
- + 33 FOSS libraries

Future directions for BioModels Database

- Improvement of the software infrastructure
 - More portable (mirrors, re-use in other projects)
 - Better authentication, logging and security
 - More flexible: groups of models, or users, more converters, views, services ...
 - Community development model
- Extension of the coverage
 - Different types of models: Neuroscience, PK/PD, physiology ...
 - Parametrisation procedures, simulation descriptions ...
 - Large scale project (e.g. Path2Models)



**Just a Model Management Platform
(JUMMP)**

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Just a Model Management Platform

Clone this repository (size: 22.6 MB): [HTTPS](#) / [SSH](#)

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$ git clone https://jumps@bitbucket.org/jumps/jumps.git
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JUMMP

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

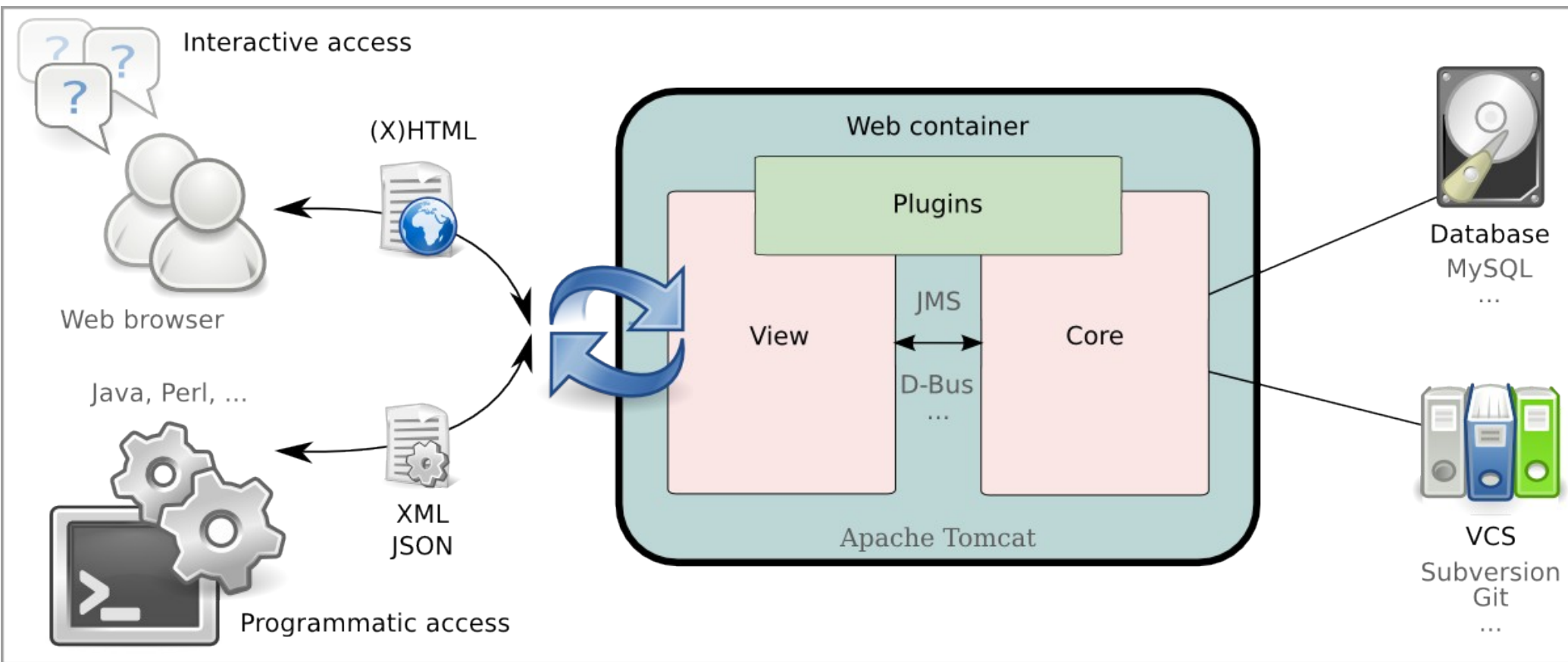
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<https://bitbucket.org/jumps/jumps/>

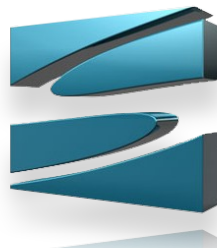
- 2012-08-16: JUMMP is presented at [COMBINE 2012](#). A publicly-available instance of it is also released at [EBI](#).
- 2012-03-19: First presentation of JUMMP to a developer audience at the [Systems Biology Data Management Foundry Workshop](#) in Vienna at 19./20. of March.
- 2011-05-05: presentation of the software infrastructure behind [BioModels Database](#) and the JUMMP project at the *Data Management for Systems Biology and the Life Sciences* workshop, Heidelberg, Germany
- 2011-02-04: official announcement at EBI and DKFZ
- 2010-12-22: starting work on a first testing prototype
- 2010-12-07: project created on Bitbucket
- 2010-10-08: initial announcement during [COMBINE 2010](#)

JUMMP architecture



FOSS again

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



Many many thanks

EMBL-EBI

- **Developers**

Mélanie Courtot, Alexander Broicher, Finja Büchel, [Marco Donizelli](#), Marine Dumousseau, Gael Jalowicki, [Mihai Glont](#), Ron Henkel, Arnaud Henri, [Sarah Keating](#), Christian Knuepfer, [Camille Laibe](#), [Chen Li](#), Lu Li, Florian Mittag, Kedar Nath Natarajan, Jean-Baptiste Pettit, [Nicolas Rodriguez](#), Karim Tazibt, Martijn van Iersel, Dagmar Waltemath, [Sarala Wimalaratne](#), Yangyang Zhao, Anna Zhukova

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- [Henning Hermjakob](#), Janet Thornton

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- **Scientific Advisory Board**

Upi Bhalla, [Carole Goble](#), [Thomas Lemberger](#), [Pedro Mendes](#), Ion Moraru, [Wolfgang Müller](#), [Philippe Sanseau](#), Herbert Sauro, Jacky Snoep

- All the computational systems Biology community, in particular: Rainer Machne, Bruce Shapiro, Kieran Smallbone

[Current member coordinator](#)

Generous funders



EMBL-EBI



Innovative Medicines Initiative

