



Sharing enriched computational models, a cornerstone for Integrative Biology

Nicolas Le Novère, EMBL-EBI

European Molecular Biology Laboratory

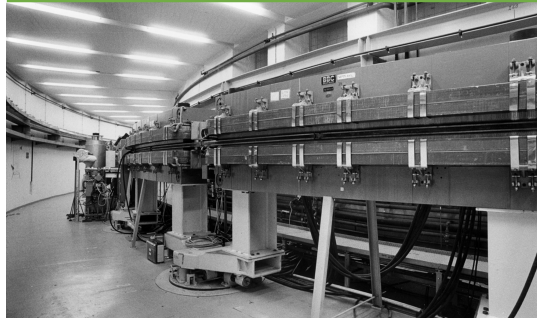
- EMBL is a basic research institute funded by public research monies from 20 member states and numerous external funding sources
- 1530 staffs, over 60 nationalities

Heidelberg



Basic research in molecular
biology
Administration
EMBO

Hamburg



Structural biology

Hinxton



Bioinformatics

Grenoble



Structural biology

Monterotondo

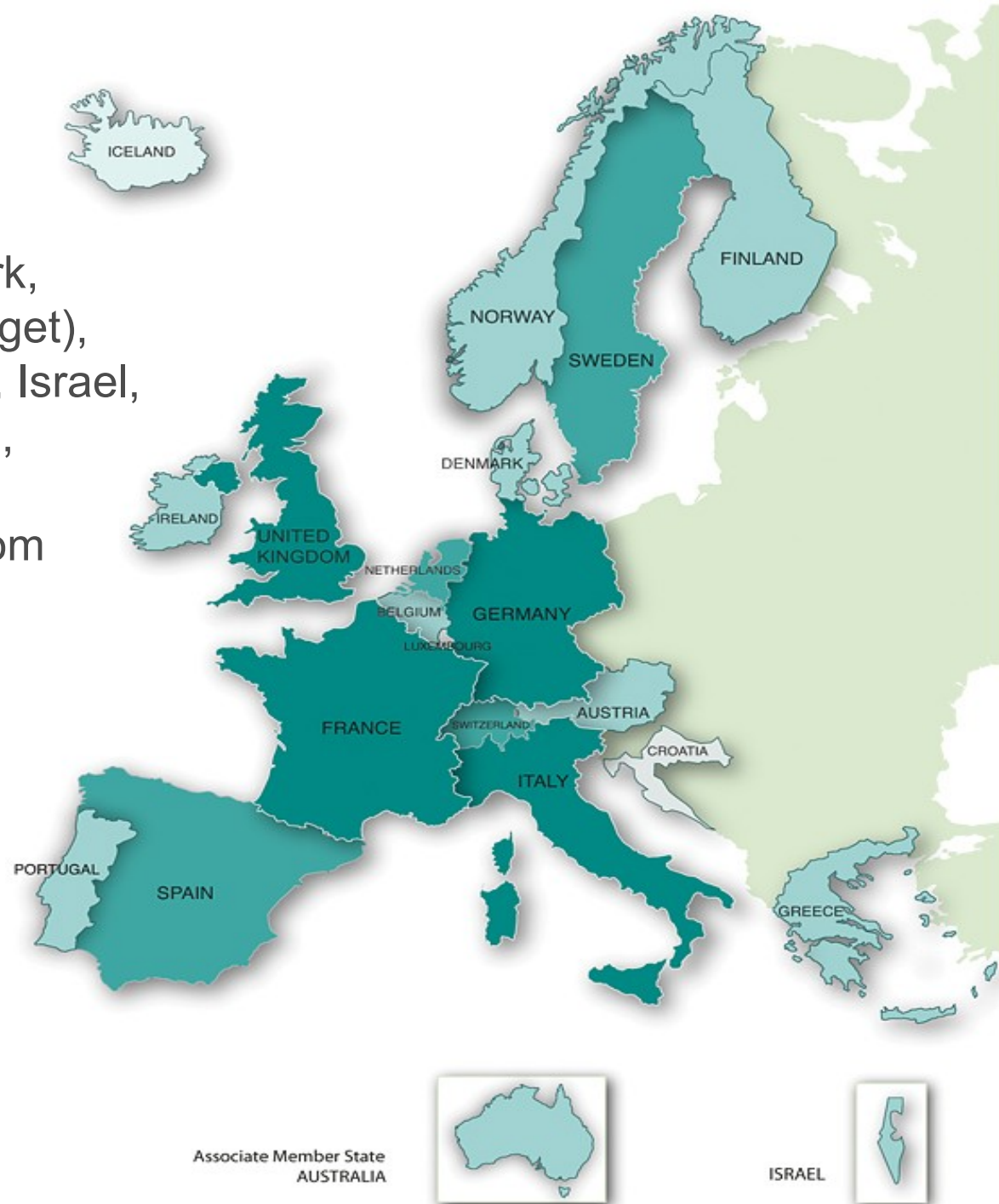


Mouse biology

EMBL member states

Austria, Belgium, Croatia, Denmark, Finland, France (16 % of 2009 budget), Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and the United Kingdom

Associate member state: Australia



EMBL-European Bioinformatics Institute



Provision of services, research
and training in Bioinformatics

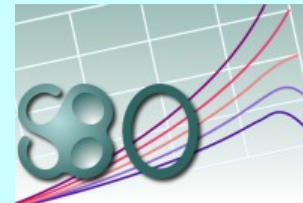
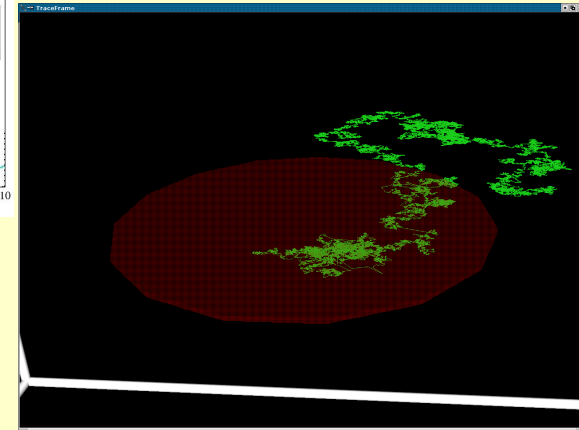
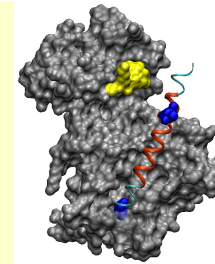
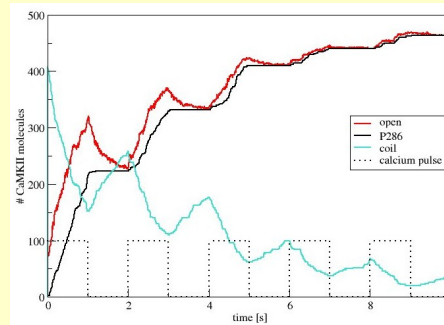
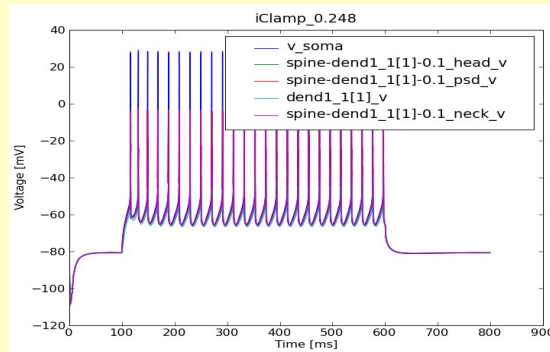
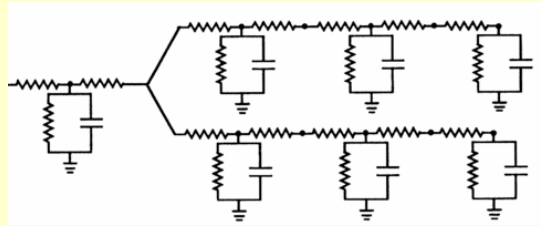
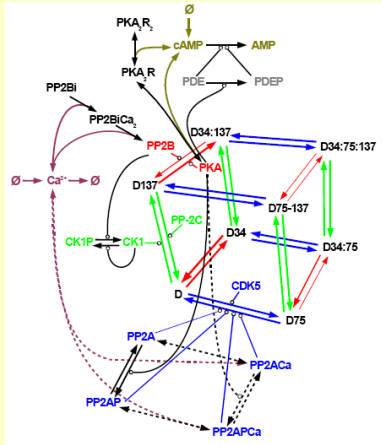
From the molecule to the cell,
and the genome to the individual

Based on the Wellcome-Trust
Genome Campus near Cambridge,
UK

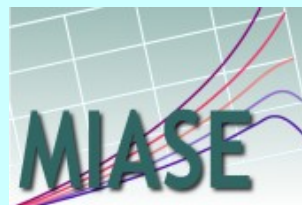


Themes and projects of the “compneur” group

Computational Neurobiology

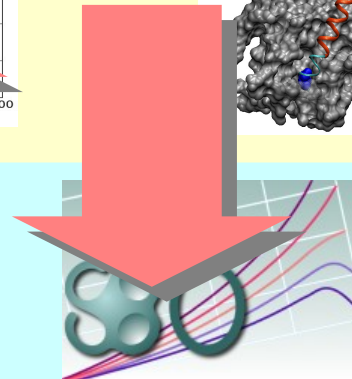
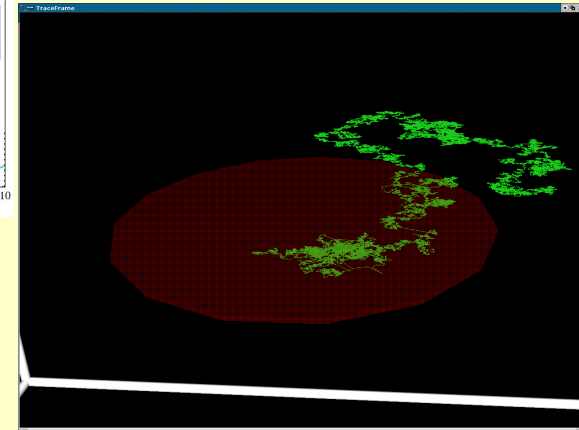
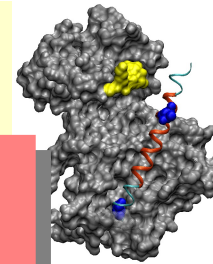
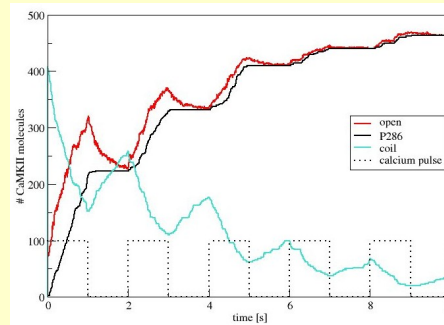
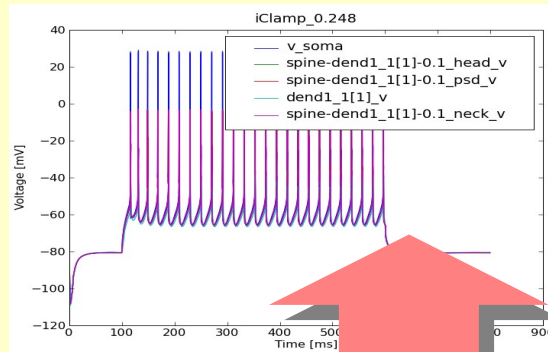
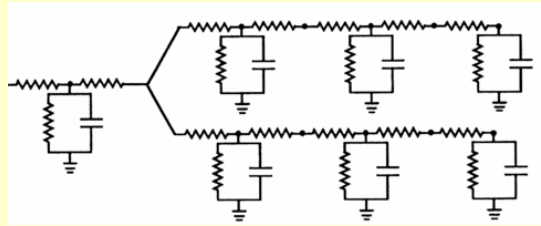
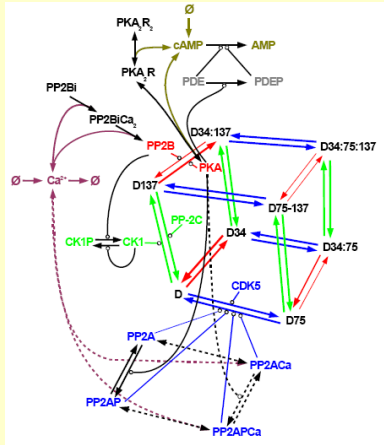


Computational Systems Biology

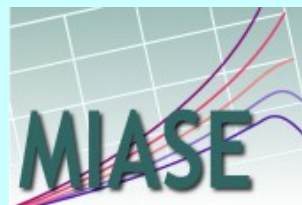


Themes and projects of the “compneur” group

Computational Neurobiology



Computational Systems Biology



What happened to biology at the end of XXth century?



Federal Ministry
of Education
and Research

Annu. Rev. Genomics Hum. Genet. 2001. 2:343-72
Copyright © 2001 by Annual Reviews. All rights reserved

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

REVIEW

Systems Biology: A Brief Overview

Hiroaki Kitano

1 MARCH 2002 VOL 295 SCIENCE www.sciencemag.org

Basic science

Systems of Life

Systems Biology



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

²CREST, Japan Science and Technology Agency, Kawaguchi 332-0012, Japan

*Contact: yamanaka@frontier.kyoto-u.ac.jp

DOI 10.1016/j.cell.2006.07.024

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

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



EXTREME GENETIC ENGINEERING

An Introduction to Synthetic Biology

Technology

January 2007

etc group



page discussion view source history teams

About

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

Nobel Symposium on Systems Biology (June 2009)

networks

Leroy Hood
Marc Vidal
Mike Snyder
Marc Kirschner
Charlie Boone
Ruedi Aebersold
Terence Hwa
Erin O'Shea
Jussi Taipale

models

Eric Davidson
Stanislas Leibler
Michel Savageau
Hans Westerhoff
Roger Brent
Francois Nedelec
Uwe Sauer
Jim Ferrell
Jorg Stelling
Edda Klipp
Boris Kholodenko
Bela Novak
Hiroaki Kitano
Stefan Hohmann
Harley McAdams
William Bialek
Mans Ehrenberg

Nobel Symposium on Systems Biology (June 2009)

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Stefan Hohmann
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Mans Ehrenberg

synthetic biology cell reprogramming

Avid Regev
Jeff Hasty
Michael Elowitz
Yoshihide Hayashizaki
Richard Young

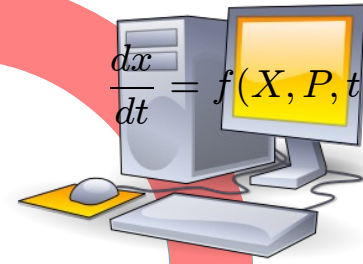
Consequences of this revolution on our activity

Needs for interplay between models and reality tests

Experiment

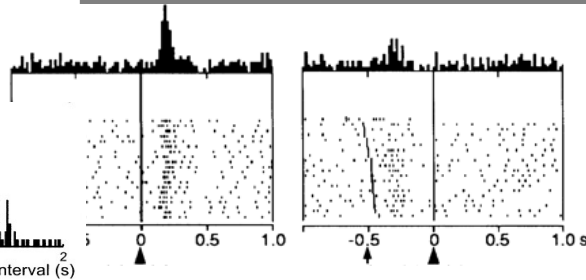
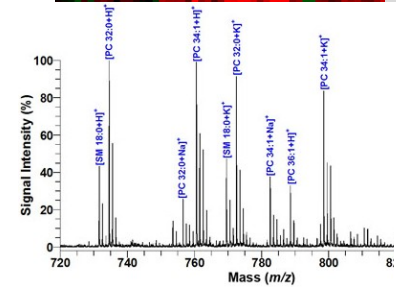
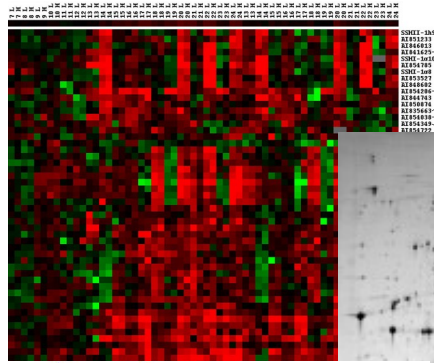
model

$$\frac{dx}{dt} = f(X, P, t)$$

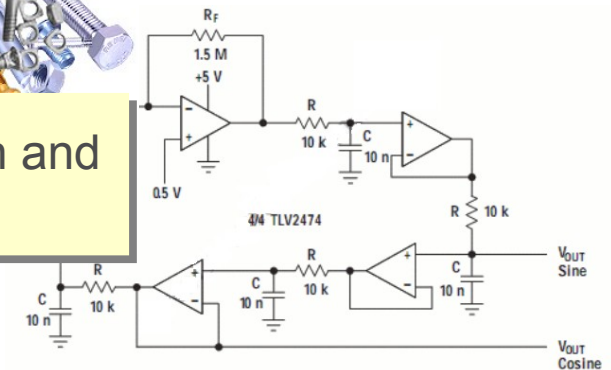


hypothesis

Needs for systems thinking and integration of heterogeneous knowledge



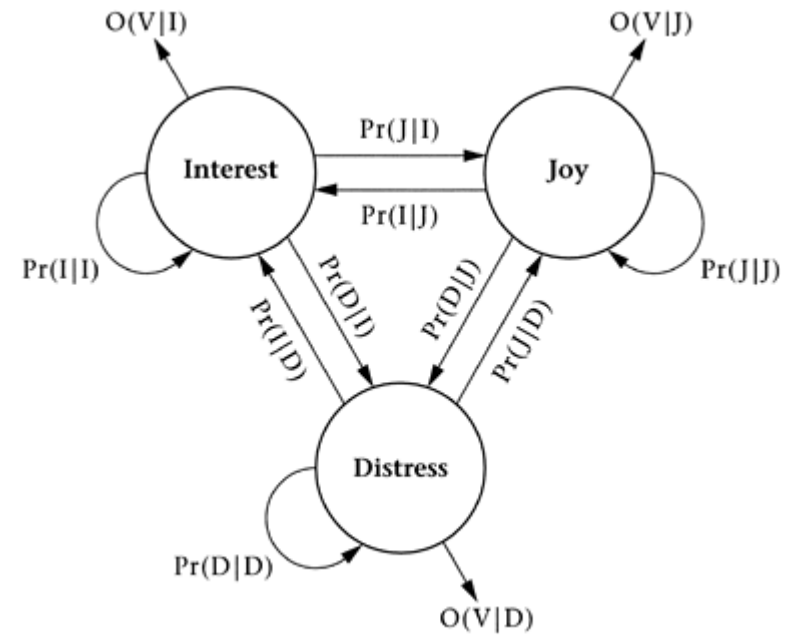
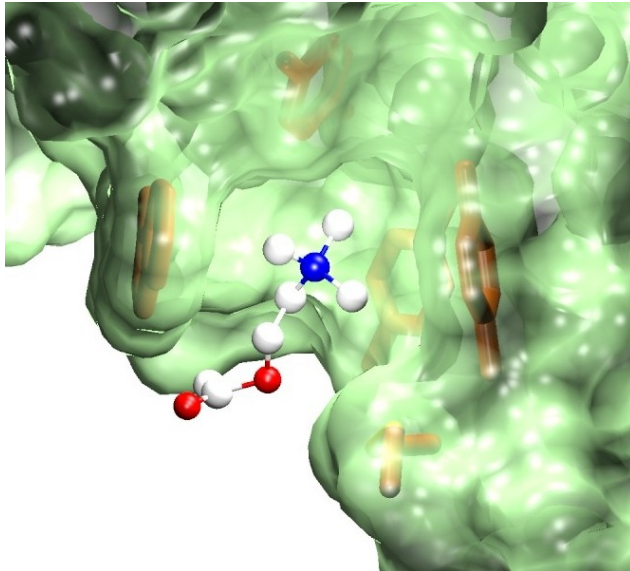
Needs for cooperation and standardisation



The models I am not talking about



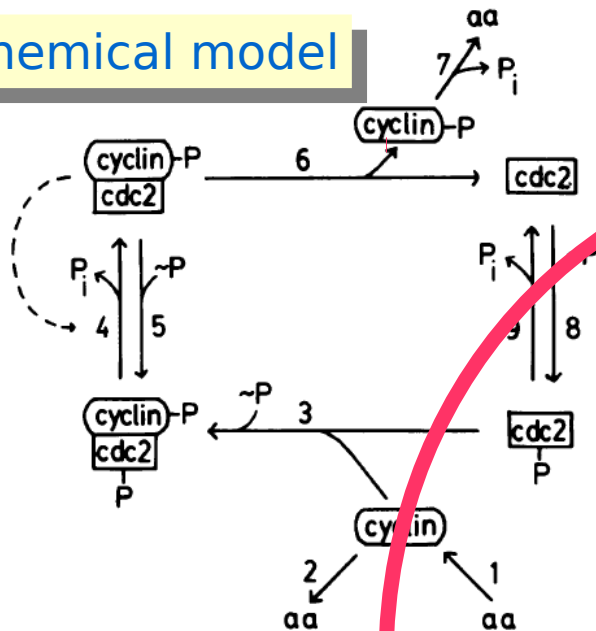
The models I am not talking about



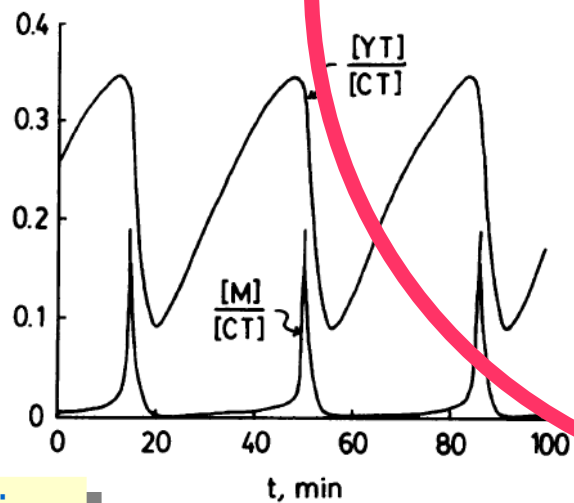
The models I am talking about

biochemical model

mathematical model



$$\begin{aligned} \frac{d[C2]}{dt} &= k_6[M] - k_8[\sim P][C2] + k_9[CP] \\ \frac{d[CP]}{dt} &= -k_3[CP][Y] + k_8[\sim P][C2] - k_9[CP] \\ \frac{d[pM]}{dt} &= k_3[CP][Y] - [pM]F([M]) + k_5[\sim P][M] \\ \frac{d[M]}{dt} &= [pM]F([M]) - k_5[\sim P][M] - k_6[M] \\ \frac{d[Y]}{dt} &= k_1[aa] - k_2[Y] - k_3[CP][Y] \\ \frac{d[YP]}{dt} &= k_6[M] - k_7[YP] \end{aligned}$$



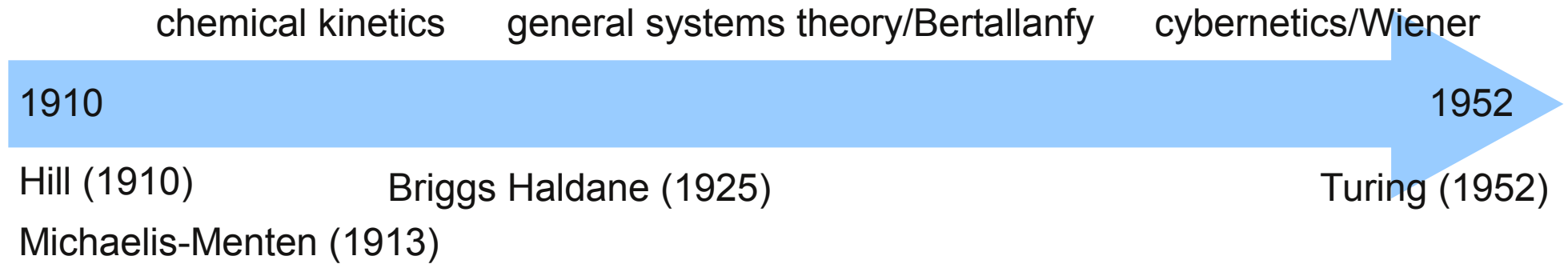
Parameter	Value	Notes
$k_1[aa]/[CT]$	0.015 min^{-1}	*
k_2	0	†
$k_3[CT]$	200 min^{-1}	*
k_4	$10\text{--}1000 \text{ min}^{-1}$ (adjustable)	
k_4'	0.018 min^{-1}	
$k_5[\sim P]$	0	‡
k_6	$0.1\text{--}10 \text{ min}^{-1}$ (adjustable)	
k_7	0.6 min^{-1}	†
$k_8[\sim P]$	$\gg k_9$	§
k_9	$\gg k_6$	§

simulation

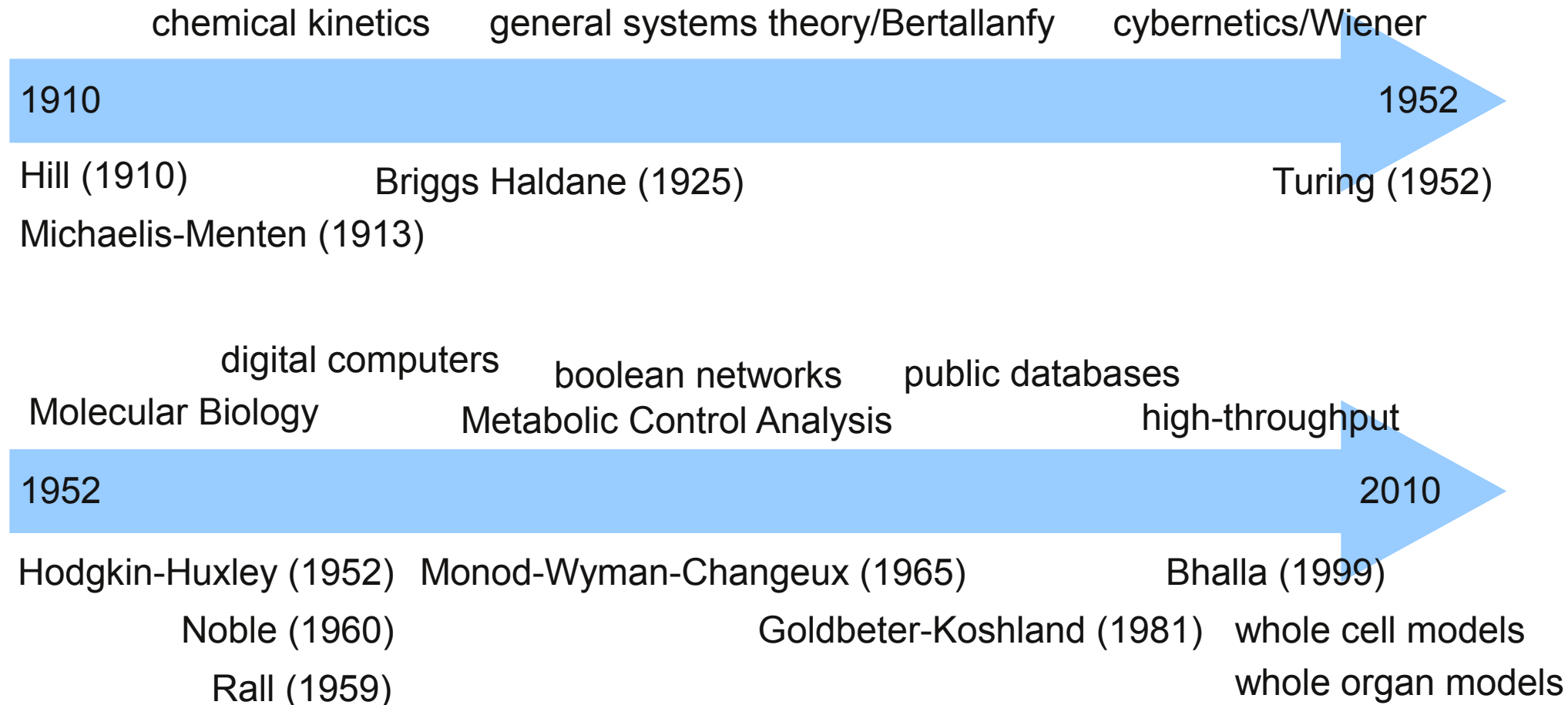
Tyson et al (1991) PNAS 88(1):7328-32

computational model

Phenomenological (descriptive) models



Mechanistic (explanatory) models



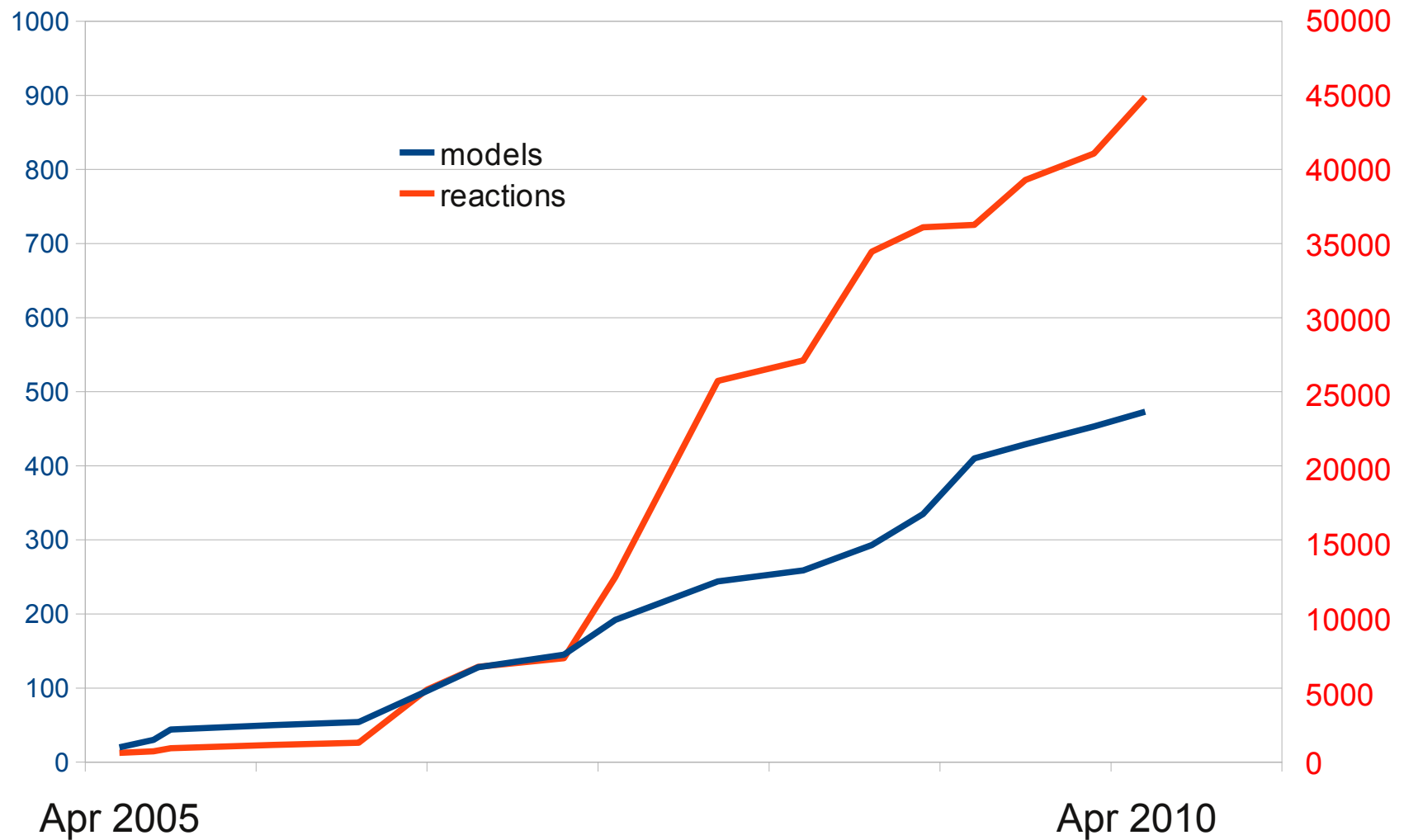
Systems Biology: Where it comes from, what it is, and what it does:

http://www.ebi.ac.uk/~lenov/LECTURES/LeNovere_SystemsBiology-EBI_WT.pdf

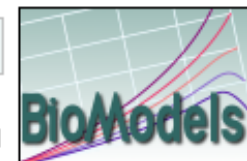
Computational modelling for biology and medicine left the niches in the last decades

- **Metabolic networks** (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; Nelson et al. Oscillations in NF- κ B Signaling Control the Dynamics of Gene Expression. *Science* 2004; Ashall et al. Pulsatile Stimulation Determines Timing and Specificity of NF- κ B-Dependent Transcription. *Science* 2009)
- **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)
- **Pharmacokinetic/dynamic 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; Neumann et al. Hepatitis C viral dynamics in vivo and the antiviral efficacy of interferon-alpha therapy. *Science* 1998)

Computational models on the rise



Growth of BioModels Database between its creation and release 17

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

Go to the model

[Advanced search](#)**Browse models**

- [Curated models \(249\)](#)
- [Browse models using GO](#)
- [Non-curated models \(224\)](#)

Simulate in JWS Online**Submit a model**

Mirror at California Institute of Technology <http://biomodels.caltech.edu>

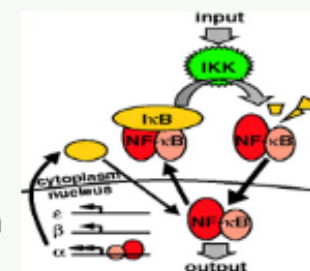
BioModels AT SourceForge <http://sourceforge.net/projects/biomodels/>

Web Services <http://www.ebi.ac.uk/biomodels-main/webservices>

Download archived models <http://www.ebi.ac.uk/biomodels/models-main/tars/>

Model of the month**July, 2010**

The activity of the transcription factor NF- κ B, is largely controlled by three I κ B isoforms (I κ B α , I κ B β , I κ B ϵ) which upon binding to NF- κ B, prevents its association with DNA causing its localization to the cytoplasm. A computational model that describes the temporal control of NF- κ B activation by I κ B proteins is described here.

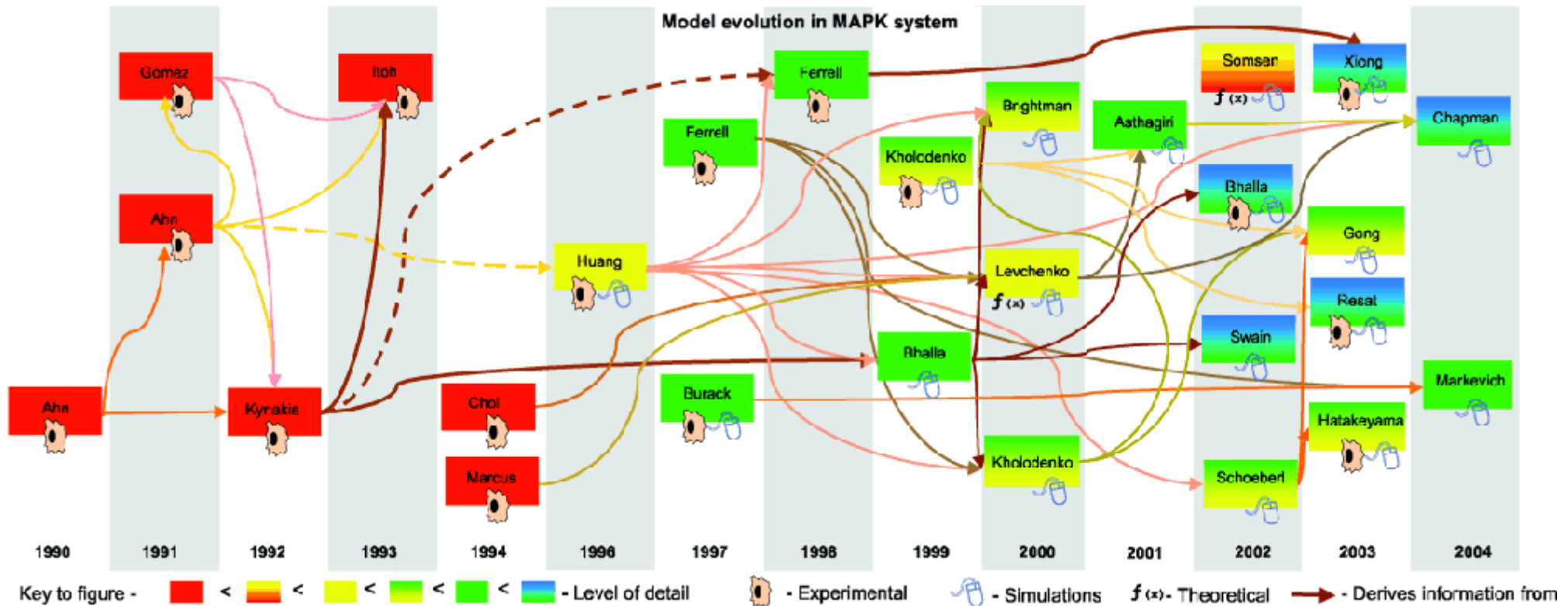
[Read more...](#)**News**

29 June 2010 New BioModels Database publication
[New BioModels Database paper published in BMC Systems Biology: BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models.](#)

2nd June 2010 SBML to VCML converter updated
The Virtual Cell recently released a new version of

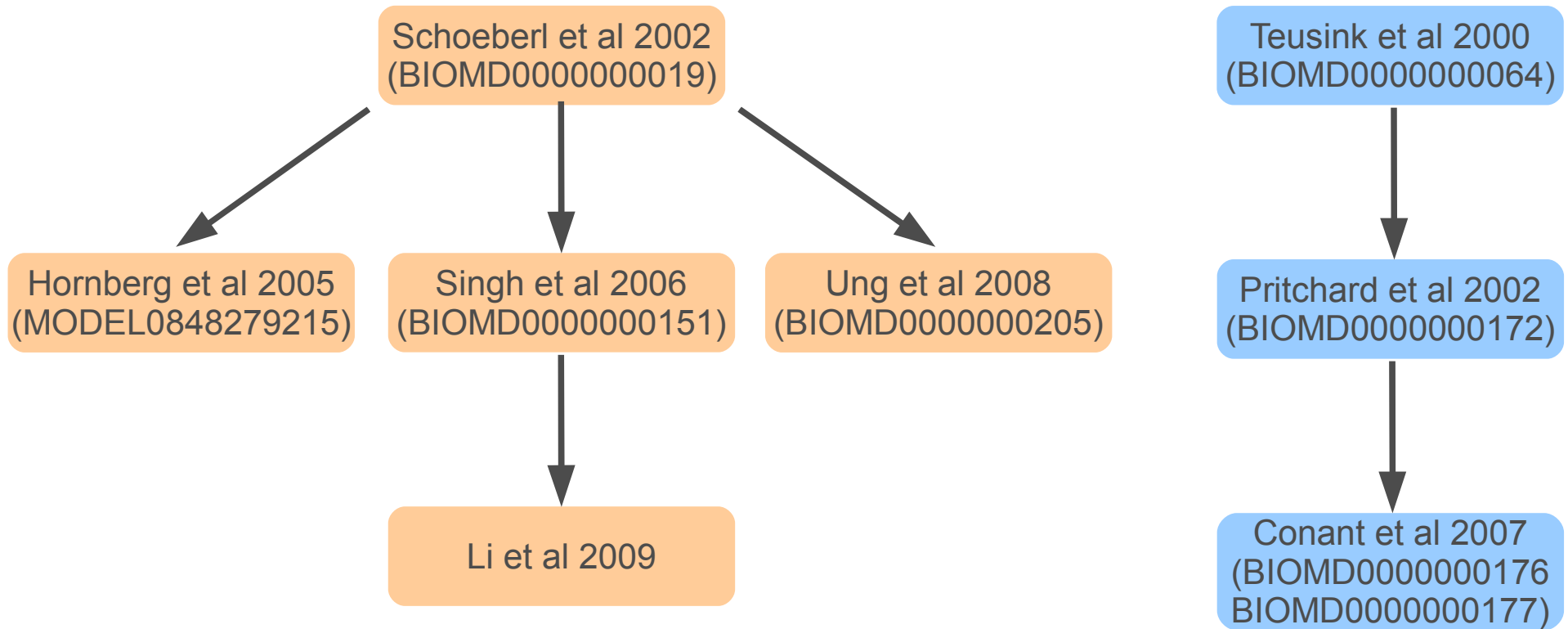
N. Le Novère, B. Bornstein, A. Broicher, M. Courtot, M. Donizelli, H. Dharuri, L. Li, H. Sauro, M. Schilstra, B. Shapiro, J.L. Snoep, M. Hucka. BioModels Database: A Free, Centralized Database of Curated, Published, Quantitative Kinetic Models of Biochemical and Cellular Systems. (2006) *Nucleic Acids Research*, 34: D689-D691.

Indirect model re-use: MAPK cascade



S.J. Vayttaden, S.M. Ajay, and U.S. Bhalla (2004). A spectrum of models of signaling pathways. *Chembiochem*, 5(10):1365-1374.

Direct model re-use: EGFR signalling and glycolysis



Models at the core of integrative systems bio/physio/neurobiology

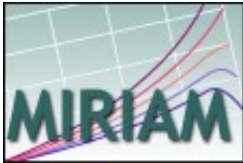
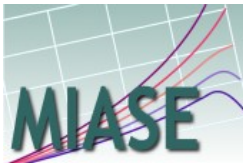
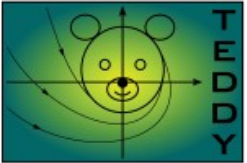
- As any kind of output from scientific research, models must be available to the scientific community: Results based on a model that is not distributed cannot be verified and falsified. This is not valid and useful science
- Computational models must be exchanged:
computer storable and readable
- Computational models must be related to relevant experimental datasets:
expressive relationships and robust links
- Computational models must be amenable to many different analyses:
standard API
- Computational models must allow modification, split, merge:
Encoded according a suitable design

Models at the core of integrative systems bio/physio/neurobiology

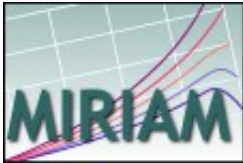
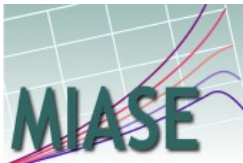
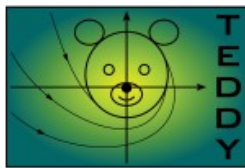
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Encoded according a suitable design

→ **Standardisation is unavoidable!**

A “complete” (?) mosaic of standards for Computational Systems Biology models

	Models	Simulation	Results
Minimal requirements			
Data-models	 		SBRML
Ontologies			

Model description

	Models	Simulation	Results
Minimal requirements			
Data-model	 		SBRML
Ontologies			

Welcome to the portal for the **Systems Biology Markup Language (SBML)**, a computer-readable format for representing models of biological processes. SBML is suitable for models of metabolism, cell signaling, and other processes, and has been evolving since 2000 thanks to an international community of researchers.



For the curious

What *is* SBML? Read our [introduction](#), then perhaps browse the [mailing lists](#) to get a sense for what's going on with SBML today.



For modelers

Looking for software that supports SBML? Our [software guide](#) lists over **180** systems today. Are you instead looking for models? Visit the [BioModels Database](#), where you can find hundreds!



For software developers

Interested in supporting SBML in your software? Read our [basic introduction](#) and then the [SBML specifications](#) to understand how to use SBML. After that, you may want to look at [libSBML](#).

No matter how you use SBML, we invite you to sign up for news updates either through our [RSS feed](#), our [Twitter feed](#), or one of the [mailing lists](#), and get involved with [community efforts](#) to help keep improving SBML. You can also

SBML News

SBMLToolbox 3.1.2!

(27 Apr.'10) Another minor bug-fix release of our free MATLAB toolbox for SBML is now available.

SBMLToolbox 3.1.1!

(12 Apr.'10) A minor bug-fix release of our free MATLAB toolbox for SBML is now available.

[Older news ...](#)

Community News

Cain 1.4 released!

(31 May.'10) **Cain** is a stochastic simulator with highly efficient implementations of many methods.

SBW 2.8.0 released!

(10 May.'10) SBW is a component-based application framework. The update improves support for simulation of SBML models and Windows 7 support.

CBO workshop @ ICSB

(2 May.'10) There will be a



Hucka M., Bolouri H., Finney A., Sauro H.M., Doyle J.C., Kitano H., Arkin A.P., Bornstein B.J., Bray D., Cornish-Bowden A., Cuellar A.A., Dronov S., Ginkel M., Gor V., Goryanin I.I., Hedley W.J., Hodgman T.C., Hunter P.J., Juty N.S., Kasberger J.L., Kremling A., Kummer U., Le Novère N., Loew L.M., Lucio D., Mendes P., Mjolsness E.D., Nakayama Y., Nelson M.R., Nielsen P.F., Sakurada T., Schaff J.C., Shapiro B.E., Shimizu T.S., Spence H.D., Stelling J., Takahashi K., Tomita M., Wagner J., Wang J. et al (2003). The Systems Biology Markup Language (SBML): A Medium for Representation and Exchange of Biochemical Network Models. *Bioinformatics*, 19: 524-531.

What is SBML?

The Systems Biology Markup Language is a way to **exchange and reuse** (and hopefully **interface**) descriptions of quantitative models in “Systems Biology”, in fact mostly well-stirred chemical kinetics so far.



It is not a procedural language.

It is not a programming language.

It is not a format for specific software configuration files (only 3 of the 7 SBML founding software still in operation).

Development philosophy: Start small, get good support, extend.

SBML itself re-uses other standards: MathML, XHTML, RDF, existing ontologies.

It is supported by a community large, diverse, active and **evolving**.

The Extensible Markup Language (XML)

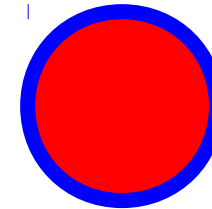
- **HTML**

A **strong word** and an
hyperlink

A strong word and an [hyperlink](#)

- **SVG**

```
<circle r="100" fill="red"
stroke="blue" stroke-width="10" />
```



- **MathML**

```
<apply>
  <int/>
  <bvar><ci> x </ci></bvar>
  <lowlimit><cn> 0 </cn></lowlimit>
  <uplimit><ci> a </ci></uplimit>
  <apply><ci> f </ci><ci> x </ci></apply>
</apply>
```

$$\int_0^a f(x) \, dx$$

- **Excel**

```
<row r="1">
  <c r="A1"><v>1</v></c>
  <c r="B1">
    <f>C11*E11</f>
    <v>102</v>
  </c>
</row>
```

	A	B	C	D
1	1	102		
2				

Global structure of a SBML file

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="3" version="1"
      xmlns="http://www.sbml.org/sbml/level3/version1/core">
  <model>
    <listOfFunctionDefinitions> <!-- --> </listOfFunctionDefinitions>
    <listOfUnitDefinitions> <!-- --> </listOfUnitDefinitions>
    <listOfCompartments> <!-- --> </listOfCompartments>
    <listOfSpecies> <!-- --> </listOfSpecies>
    <listOfParameters> <!-- --> </listOfParameters>
    <listOfInitialAssignments> <!-- --> </listOfInitialAssignments>
    <listOfRules> <!-- --> </listOfRules>
    <listOfConstraints> <!-- --> </listOfConstraints>
    <listOfReactions> <!-- --> </listOfReactions>
    <listOfEvents> <!-- --> </listOfEvents>
  </model>
</sbml>
```


Global structure of a SBML file

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="3" version="1".
  xmlns="http://www.sbml.org/sbml/level3/version1/core">
  <model>
    <listOfFunctionDefinitions> <!-- --> </listOfFunctionDefinitions>
    <listOfUnitDefinitions> <!-- --> </listOfUnitDefinitions>
    <listOfCompartments> <!-- --> </listOfCompartments>
    <listOfSpecies> <!-- --> </listOfSpecies>
    <listOfParameters> <!-- --> </listOfParameters>
    <listOfInitialAssignments> <!-- --> </listOfInitialAssignments>
    <listOfRules> <!-- --> </listOfRules>
    <listOfConstraints> <!-- --> </listOfConstraints>
    <listOfReactions> <!-- --> </listOfReactions>
    <listOfEvents> <!-- --> </listOfEvents>
  </model>
</sbml>
```

variables

relationships



A very simple SBML file

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="2" version="4" xmlns="http://www.sbml.org/sbml/level2/version4">
  <model>
    <listOfCompartments>
      <compartment id="cell" />
    </listOfCompartments>
    <listOfSpecies>
      <species id="A" compartment="cell" initialConcentration="1"/>
      <species id="B" compartment="cell" initialConcentration="0"/>
    </listOfSpecies>
    <listOfParameters>
      <parameter id="kon" value="1"/>
    </listOfParameters>
    <listOfReactions>
      <reaction>
        <listOfReactants>
          <speciesReference species="A" />
        </listOfReactants>
        <listOfProducts>
          <speciesReference species="B" />
        </listOfProducts>
        <kineticLaw>
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <apply>
              <times />
              <ci>kon</ci>
              <ci>A</ci>
              <ci>cell</ci>
            </apply>
          </math>
        </kineticLaw>
      </reaction>
    </listOfReactions>
  </model>
</sbml>
```

A very simple SBML file

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="2" version="4" xmlns="http://www.sbml.org/sbml/level2/version4">
  <model>
    <listOfCompartments>
      <compartment id="cell" />
    </listOfCompartments>
    <listOfSpecies>
      <species id="A" compartment="cell" initialConcentration="1"/>
      <species id="B" compartment="cell" initialConcentration="0"/>
    </listOfSpecies>
    <listOfParameters>
      <parameter id="kon" value="1"/>
    </listOfParameters>
    <listOfReactions>
      <reaction>
        <listOfReactants>
          <speciesReference species="A" />
        </listOfReactants>
        <listOfProducts>
          <speciesReference species="B" />
        </listOfProducts>
        <kineticLaw>
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <apply>
              <times />
              <ci>kon</ci>
              <ci>A</ci>
              <ci>cell</ci>
            </apply>
          </math>
        </kineticLaw>
      </reaction>
    </listOfReactions>
  </model>
</sbml>
```

A very simple SBML file

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="2" version="4" xmlns="http://www.sbml.org/sbml/level2/version4">
  <model>
    <listOfCompartments>
      <compartment id="cell" />
    </listOfCompartments>
    <listOfSpecies>
      <species id="A" compartment="cell" initialConcentration="1"/>
      <species id="B" compartment="cell" initialConcentration="0"/>
    </listOfSpecies>
    <listOfParameters>
      <parameter id="kon" value="1"/>
    </listOfParameters>
    <listOfReactions>
      <reaction>
        <listOfReactants>
          <speciesReference species="A" />
        </listOfReactants>
        <listOfProducts>
          <speciesReference species="B" />
        </listOfProducts>
        <kineticLaw>
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <apply>
              <times />
              <ci>kon</ci>
              <ci>A</ci>
              <ci>cell</ci>
            </apply>
          </math>
        </kineticLaw>
      </reaction>
    </listOfReactions>
  </model>
</sbml>
```

A very simple SBML file

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="2" version="4" xmlns="http://www.sbml.org/sbml/level2/version4">
  <model>
    <listOfCompartments>
      <compartment id="cell" />
    </listOfCompartments>
    <listOfSpecies>
      <species id="A" compartment="cell" initialConcentration="1"/>
      <species id="B" compartment="cell" initialConcentration="0"/>
    </listOfSpecies>
    <listOfParameters>
      <parameter id="kon" value="1"/>
    </listOfParameters>
    <listOfReactions>
      <reaction>
        <listOfReactants>
          <speciesReference species="A" />
        </listOfReactants>
        <listOfProducts>
          <speciesReference species="B" />
        </listOfProducts>
        <kineticLaw>
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <apply>
              <times />
              <ci>kon</ci>
              <ci>A</ci>
              <ci>cell</ci>
            </apply>
          </math>
        </kineticLaw>
      </reaction>
    </listOfReactions>
  </model>
</sbml>
```

A very simple SBML file

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="2" version="4" xmlns="http://www.sbml.org/sbml/level2/version4">
  <model>
    <listOfCompartments>
      <compartment id="cell" />
    </listOfCompartments>
    <listOfSpecies>
      <species id="A" compartment="cell" initialConcentration="1"/>
      <species id="B" compartment="cell" initialConcentration="0"/>
    </listOfSpecies>
    <listOfParameters>
      <parameter id="kon" value="1"/>
    </listOfParameters>
    <listOfReactions>
      <reaction>
        <listOfReactants>
          <speciesReference species="A" />
        </listOfReactants>
        <listOfProducts>
          <speciesReference species="B" />
        </listOfProducts>
        <kineticLaw>
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <apply>
              <times />
              <ci>kon</ci>
              <ci>A</ci>
              <ci>cell</ci>
            </apply>
          </math>
        </kineticLaw>
      </reaction>
    </listOfReactions>
  </model>
</sbml>
```


A very simple SBML file

```
<?xml version="1.0" encoding="UTF-8"?>
<sbml level="2" version="4" xmlns="http://www.sbml.org/sbml/level2/version4">
  <model>
    <listOfCompartments>
      <compartment id="cell" />
    </listOfCompartments>
    <listOfSpecies>
      <species id="A" compartment="cell" initialConcentration="1"/>
      <species id="B" compartment="cell" initialConcentration="0"/>
    </listOfSpecies>
    <listOfParameters>
      <parameter id="kon" value="1"/>
    </listOfParameters>
    <listOfReactions>
      <reaction>
        <listOfReactants>
          <speciesReference species="A" />
        </listOfReactants>
        <listOfProducts>
          <speciesReference species="B" />
        </listOfProducts>
        <kineticLaw>
          <math xmlns="http://www.w3.org/1998/Math/MathML">
            <apply>
              <times />
              <ci>kon</ci>
              <ci>A</ci>
              <ci>cell</ci>
            </apply>
          </math>
        </kineticLaw>
      </reaction>
    </listOfReactions>
  </model>
</sbml>
```

A more realistic example ...

```

<species.
  id="A".
  name="a-tubulin"
  compartment="cell"
  initialAmount="1000"
  substanceUnits="item"
  hasOnlySubstanceUnits="true"
  boundaryCondition="true"
  constant="false"
  charge="0"
  metaid="PX"
  sboTerm="SBO:0000245" >
<notes>
  <body xmlns="http://www.w3.org/1999/xhtml">
    <p>One of the components of a microtubule</p>
  </body>
</notes>
<annotation>
  <rdf:RDF.
    xmlns:bqbiol="http://biomodels.net/biology-qualifiers/"
    xmlns:bqmodel="http://biomodels.net/model-qualifiers/"
    xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#">
    <rdf:Description rdf:about="#PX">
      <bqbiol:is>
        <rdf:Bag>
          <rdf:li rdf:resource="urn:miriam:uniprot:P68370"/>
          <rdf:li rdf:resource="urn:miriam:obo.go:GO:0045298"/>
        </rdf:Bag>
      </bqbiol:is>
    </rdf:Description>
  </rdf:RDF>
</annotation>
</species>

```



SBML is not limited to biochemistry!

Rate Rules can describe the temporal evolution of any quantitative parameter, e.g. transmembrane voltage;

Events can describe any discontinuous change, e.g. neurotransmitter release or repolarisation;

A **species** is an entity participating to a reaction, **not always a chemical** entity:

- It can be a molecule

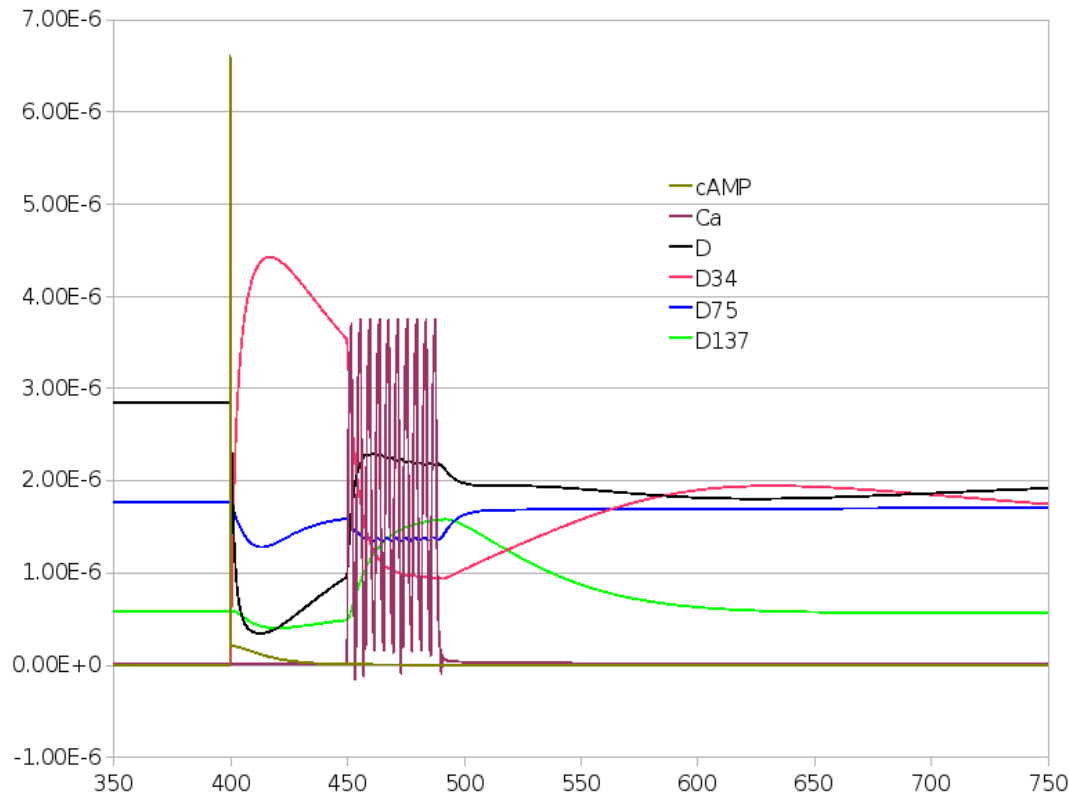
- It can be a cell

- It can be an organ

- It can be an organism

→ SBML is about process descriptions

Model of signalling pathways

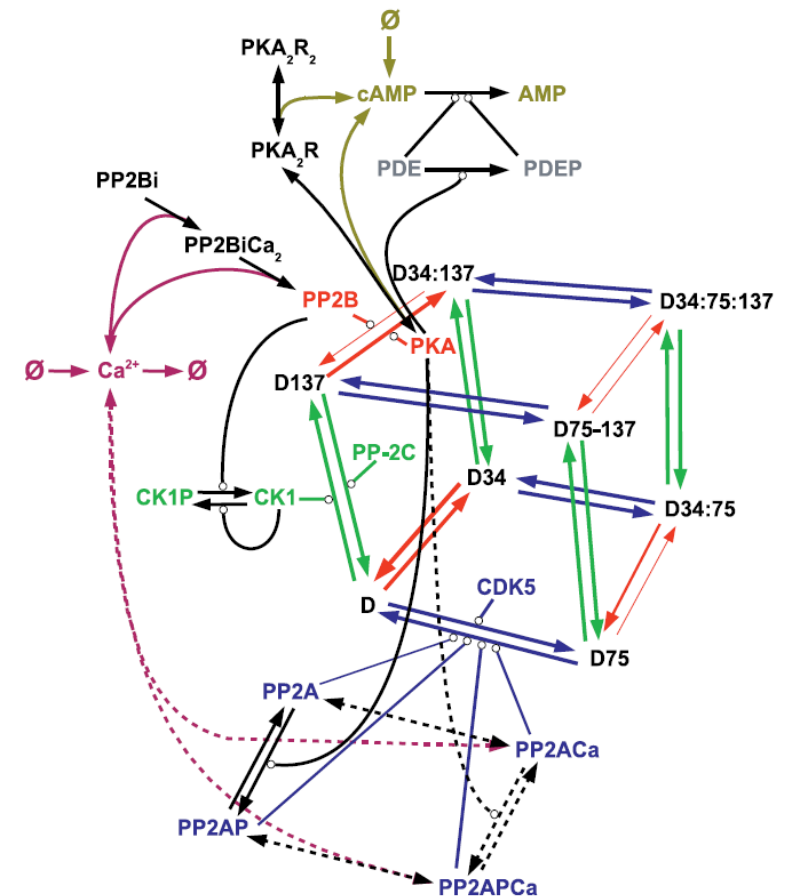


reaction:

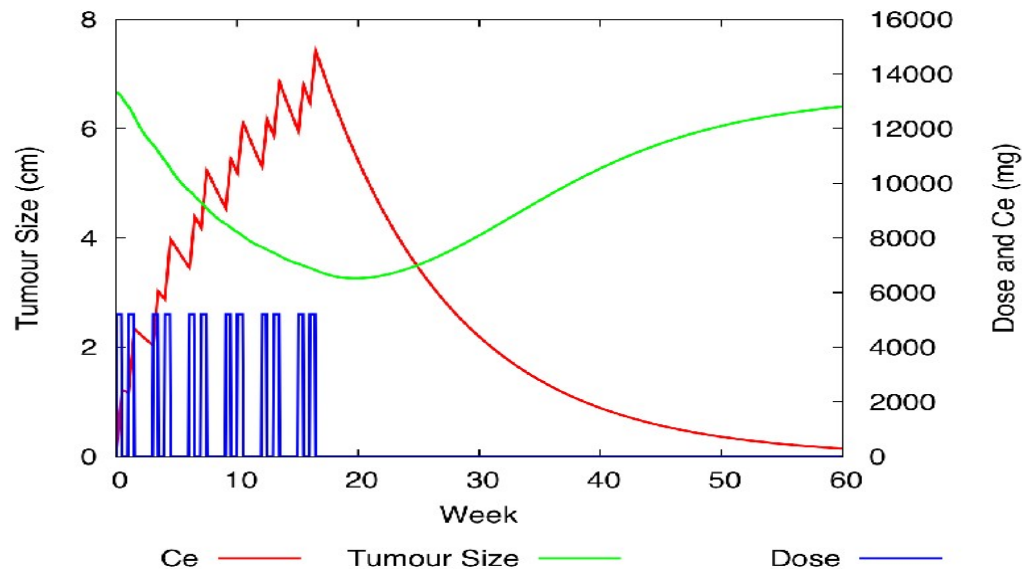
$$v_{on1} = k_{on1} \times [D] \times [CDK5] \times Vol$$

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

BIOMD0000000153



Pharmacokinetic/dynamic model



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.

BIOMD0000000234

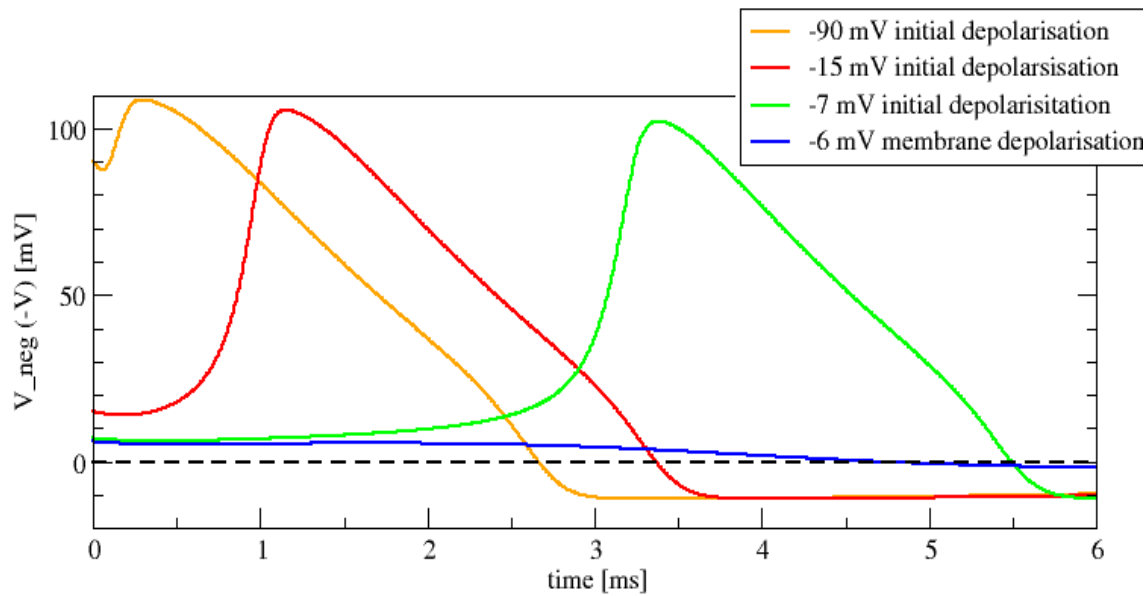
rate rule:

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

assignment rule:

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

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.

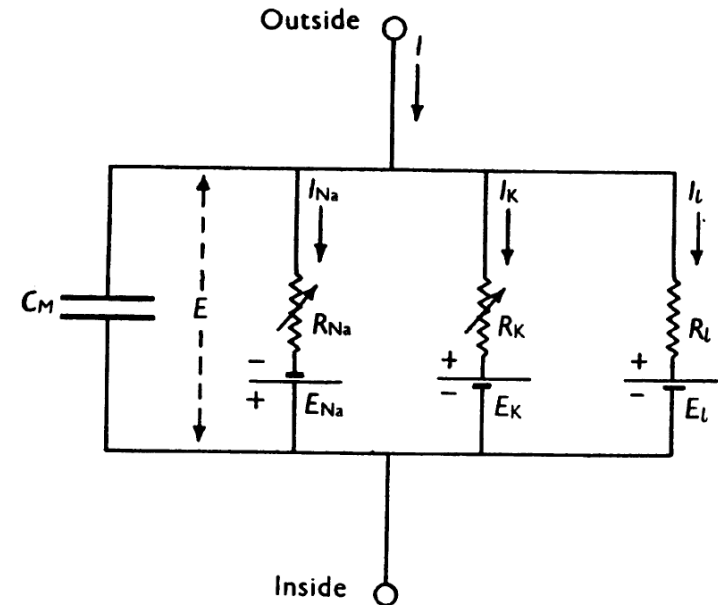
BIOMD0000000020

rate rule:

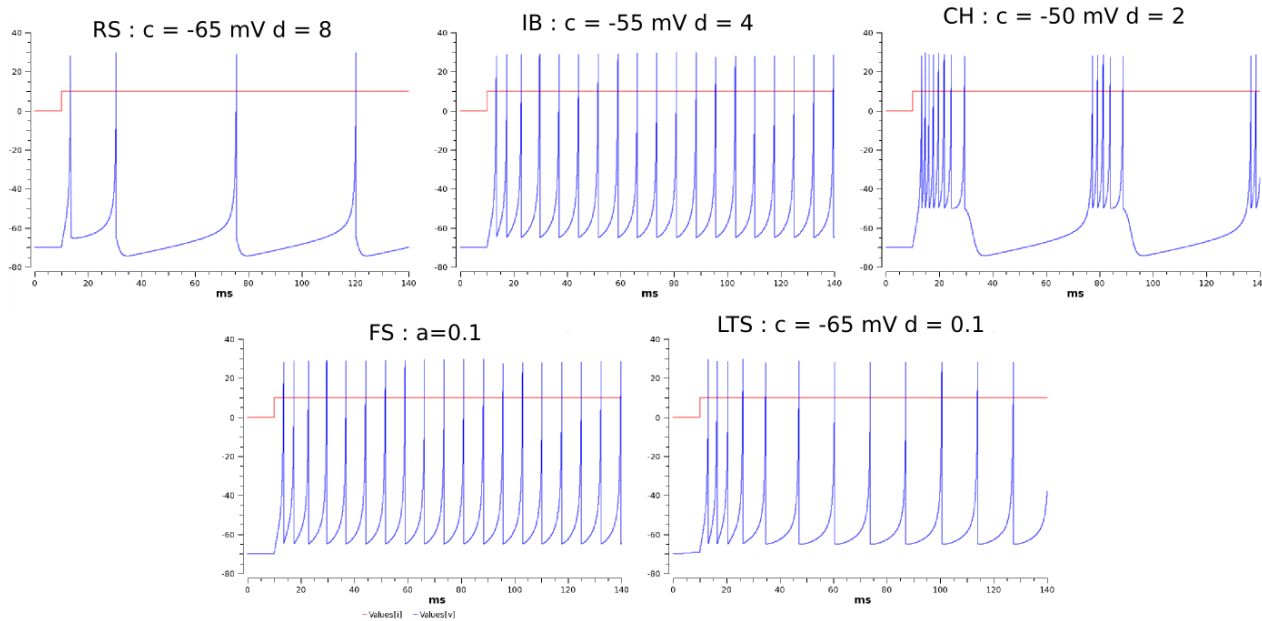
$$\frac{dv}{dt} = \frac{I - (i_{Na} + i_K + i_L)}{C_m}$$

assignment rule:

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



Single-compartment neurons



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

BIOMD0000000127

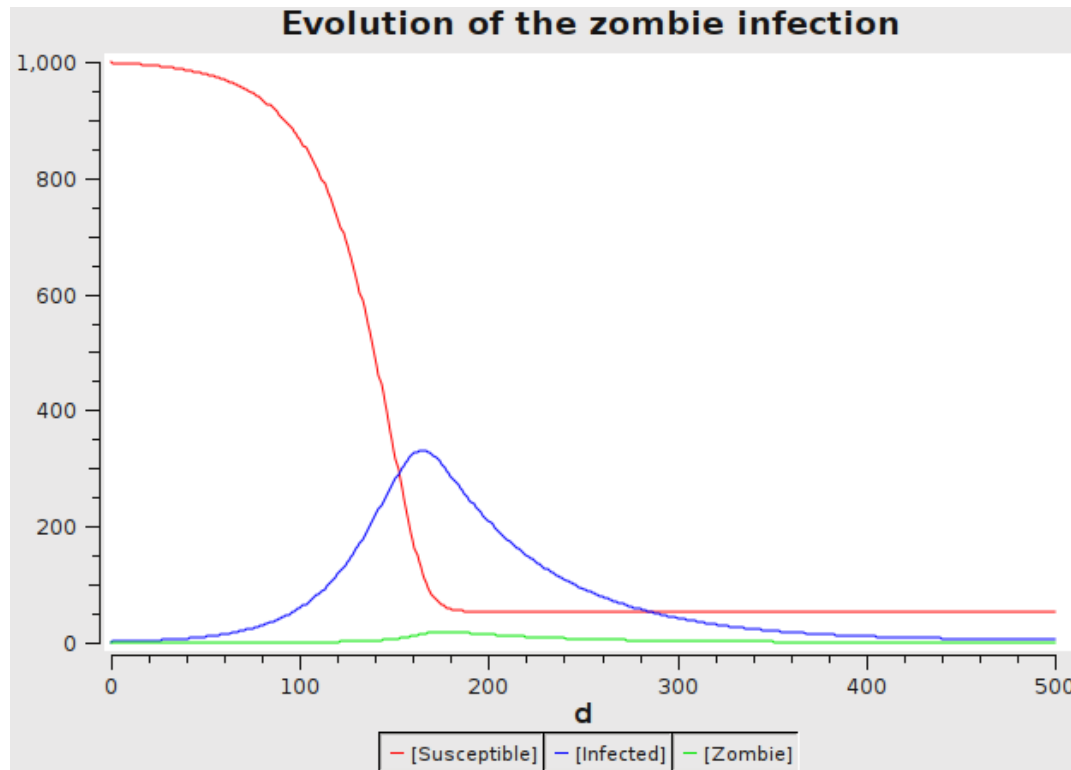
rate rule:

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

event:

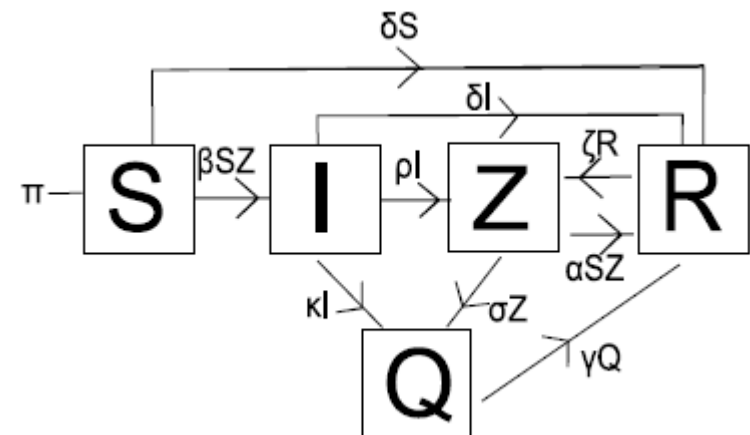
$$\text{when } v > V_{thresh} \begin{cases} v = c \\ U = U + d \end{cases}$$

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



Number of software packages listed in the matrix today: **188**

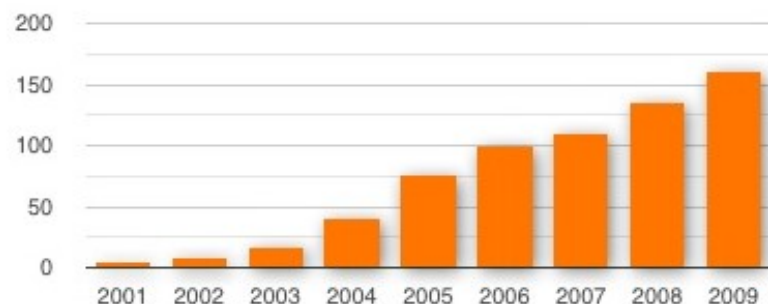
Please **use the survey form** [🔗](#) to notify us about additions and suggestions.

Go to the SBML Software Matrix

[Go to the SBML Software Summary](#)

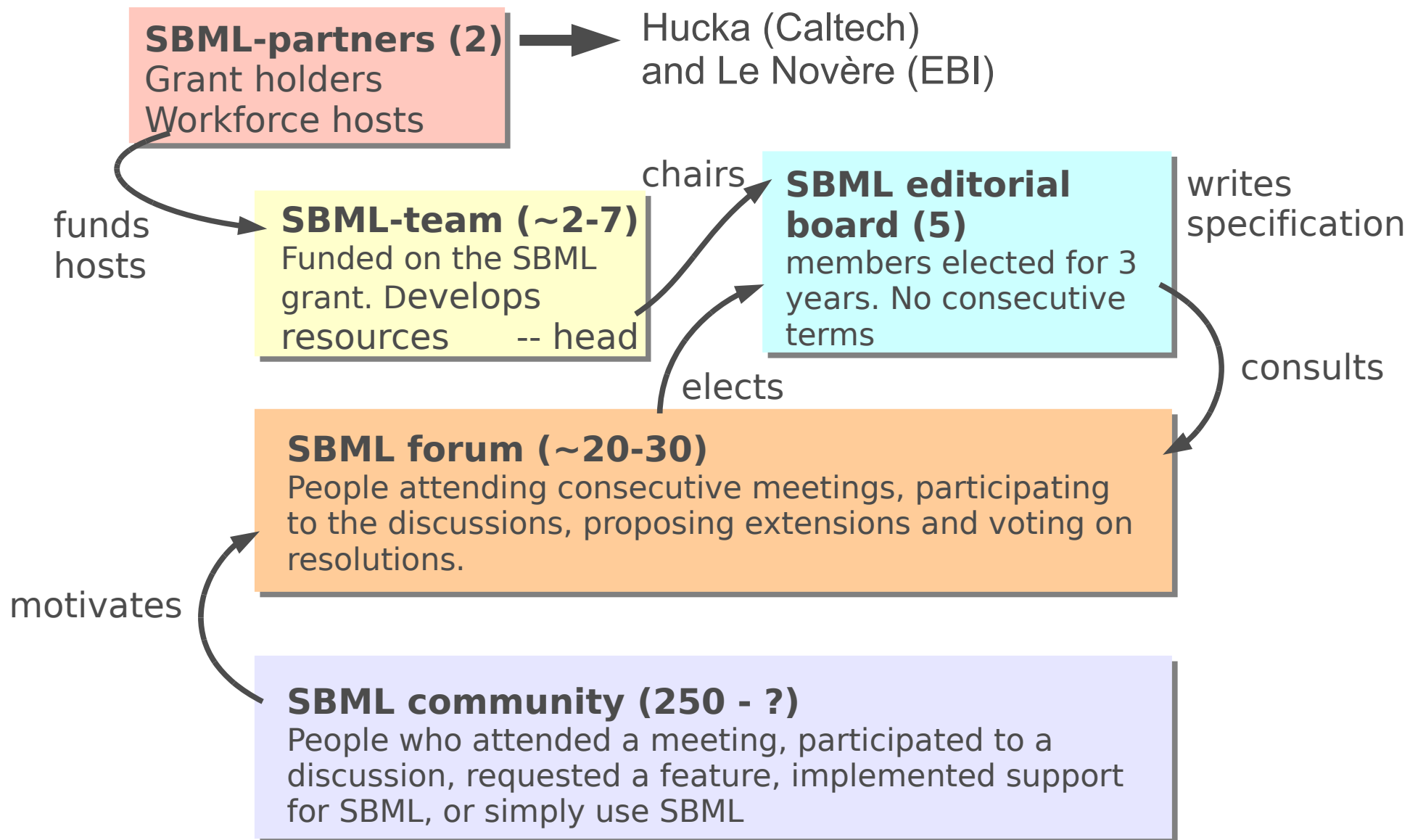
Historical trend

The following graph shows the total number of known SBML-compatible software packages each year, as counted by the SBML Team. The counts shown are for approximately the middle of each year.

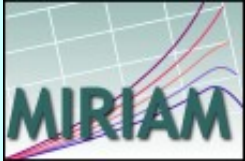
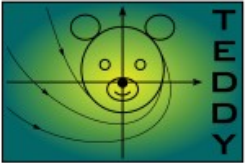


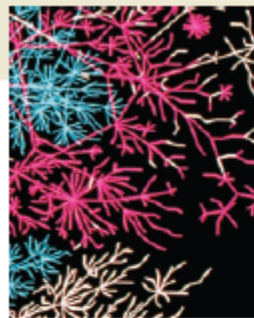
(Note: the flat period in 2007 is an artifact of inadequate record keeping rather than a lull in SBML software development.)

Current structure of the SBML community



Model semantics

	Models	Simulation	Results
Minimal requirements			
Data-models	 		SBRML
Ontologies			

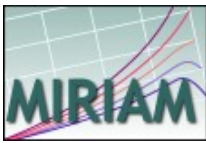


Minimum information requested in the annotation of biochemical models (MIRIAM)

Nicolas Le Novère^{1,15}, Andrew Finney^{2,15}, Michael Hucka³, Upinder S Bhalla⁴, Fabien Campagne⁵, Julio Collado-Vides⁶, Edmund J Crampin⁷, Matt Halstead⁷, Edda Klipp⁸, Pedro Mendes⁹, Poul Nielsen⁷, Herbert Sauro¹⁰, Bruce Shapiro¹¹, Jacky L Snoep¹², Hugh D Spence¹³ & Barry L Wanner¹⁴

Most of the published quantitative models in biology are lost for the community because they are either not made available or they are insufficiently characterized to allow them to be reused. The lack of a standard description format, lack of stringent reviewing and authors' carelessness are the main causes for incomplete model descriptions. With today's increased interest in detailed biochemical models, it is necessary to define a minimum quality standard for the encoding of those models. We propose a set of rules for curating quantitative models of biological systems. These rules define procedures for encoding and annotating models represented in machine-readable form. We believe their

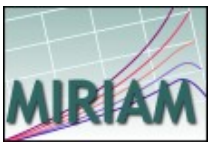
During the genomic era we have witnessed a vast increase in availability of large amounts of quantitative data. This is motivating a shift in the focus of molecular and cellular research from qualitative descriptions of biochemical interactions towards the quantification of such interactions and their dynamics. One of the tenets of systems biology is the use of quantitative models (see Box 1 for definitions) as a mechanism for capturing precise hypotheses and making predictions^{1,2}. Many specialized models exist that attempt to explain aspects of the cellular machinery. However, as has happened with other types of biological information, such as sequences, macromolecular structures or



MIRIAM compliance

Models must :

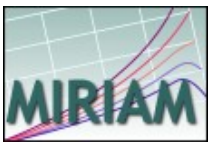
- be encoded in a public machine-readable format
- be clearly linked to a single reference description
- reflect the structure of the biological processes described in the reference paper (list of reactions etc.)
- be instantiable in a simulation (possess initial conditions etc.)
- be able to reproduce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



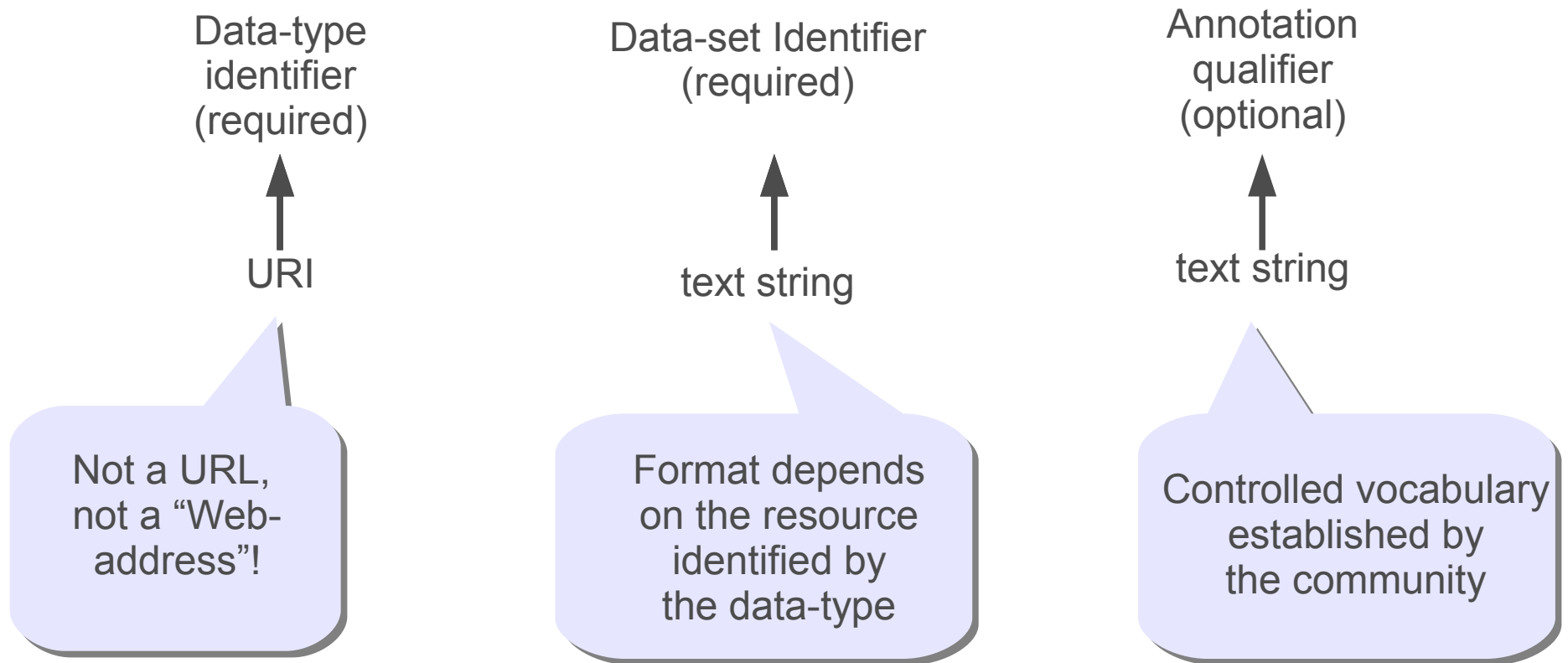
Why are annotations important?

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



MIRIAM cross-references



UniProt and P62158 (human calmodulin)

urn:miriam:uniprot:P62158

EC code and 1.1.1.1 (alcohol dehydrogenase)

urn:miriam:ec-code:1.1.1.1

Gene Ontology and GO:0000186 (activation of MAPKK activity)

urn:miriam:obo.go:GO%3A0000186



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- Documents
 - MIRIAM Standard
 - FAQ
 - Documentation
 - News
 - BioModels.net
 - Qualifiers

- MIRIAM on SourceForge

- Support
- Contact

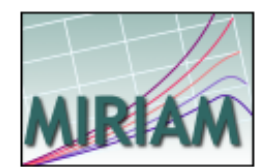


EBI > Groups > Computational Neurobiology > Research > MIRIAM Resources

MIRIAM Resources

MIRIAM Resources are a set of online services created to support [MIRIAM Standard](#).

The core of *MIRIAM Resources* is a catalogue of data types (these can be 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).



Quick links

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

Resources

MIRIAM Resources are 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 types (which can be controlled vocabularies or databases), their URIs and the corresponding physical URLs or resources.

Moreover,

Laibe C., Le Novère N. MIRIAM Resources: tools to generate and resolve robust cross-references in Systems Biology. BMC Systems Biology (2007), 1: 58.

...ve model annotations, but also to generate the correct URIs based on resource name and accession numbers. You have access to the [list of services available](#), an

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 - BioModels.net
 - Qualifiers

- MIRIAM on SourceForge

- Support
- Contact



SOURCEFORGE.NET

Data type: *Enzyme Nomenclature*

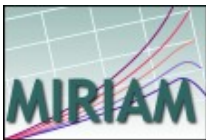
General Tags Annotation

General Information about the data type

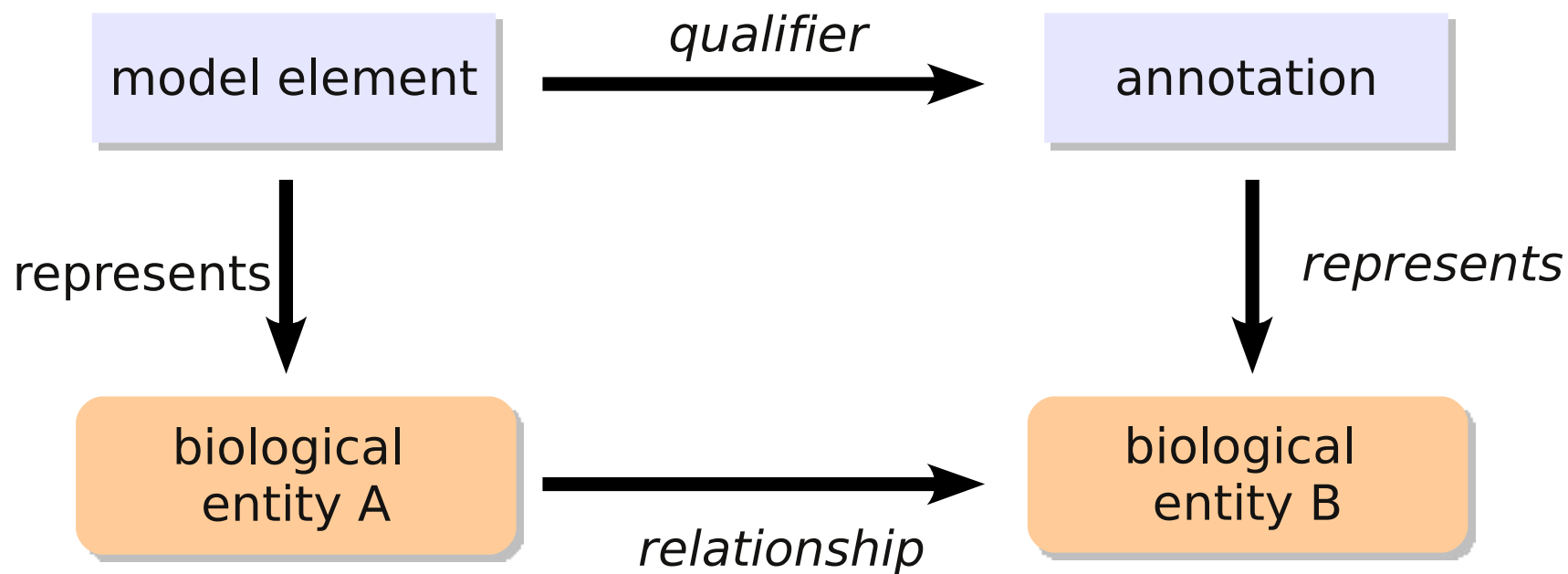
Name		
Identifier	MIR:00000004	
Name	Enzyme Nomenclature	
Synonyms	EC code	
	Enzyme Classification	
	EC	
URLs		
Official URN	urn:miriam:ec-code	
Deprecated	http://www.ec-code.org/	
	urn:lsid:ec-code.org	
	http://www.ebi.ac.uk/IntEnz/	
Information		
Definition	The Enzyme Classification contains the recommendations of the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology on the nomenclature and classification of enzyme-catalysed reactions.	
Identifier Pattern	^\\d+\\.\\-\\.\\-\\.\\d+\\.\\d+\\.\\-\\.\\d+\\.\\d+\\.\\d+\\.\\d+\\.\\d+\\.\\d+\\.\\d+\\.\\d+\$	
Physical Locations		
Resource #1	Data Entry	http://www.ebi.ac.uk/intenz/query?cmd=SearchEC&ec=\$id [Example: 1.1.1.1 
	Data Resource	http://www.ebi.ac.uk/intenz/
	Information	IntEnZ (Integrated relational Enzyme database)
	Institution	European Bioinformatics Institute, United Kingdom
Resource #2	Data Entry	http://www.genome.jp/dbget-bin/www_bget?ec:\$id [Example: 1.1.1.1 
	Data Resource	http://www.genome.jp/dbget-bin/www_bfind?enzyme
	Information	KEGG Ligand Database for Enzyme Nomenclature
	Institution	Kyoto University Bioinformatics Center, Japan
Resource #3	Data Entry	http://us.expasy.org/cgi-bin/nicezyme.pl?\$id [Example: 1.1.1.1 
	Data Resource	http://us.expasy.org/enzyme/
	Information	Enzyme nomenclature database, ExPASy (Expert Protein Analysis System)
	Institution	Swiss Institute of Bioinformatics, Switzerland
Documentation		
URL(s)	http://www.chem.qmul.ac.uk/iubmb/enzyme/	
	 http://srs.ebi.ac.uk/srsbin/cgi-bin/wgetz?-view+MedlineFull+[medline-PMID:10812475]	
Miscellaneous		
Date of creation	2006-08-14 19:38:06 GMT	
Date of last modification	2009-05-08 14:59:31 GMT	

 [Go back to the list of data types](#)

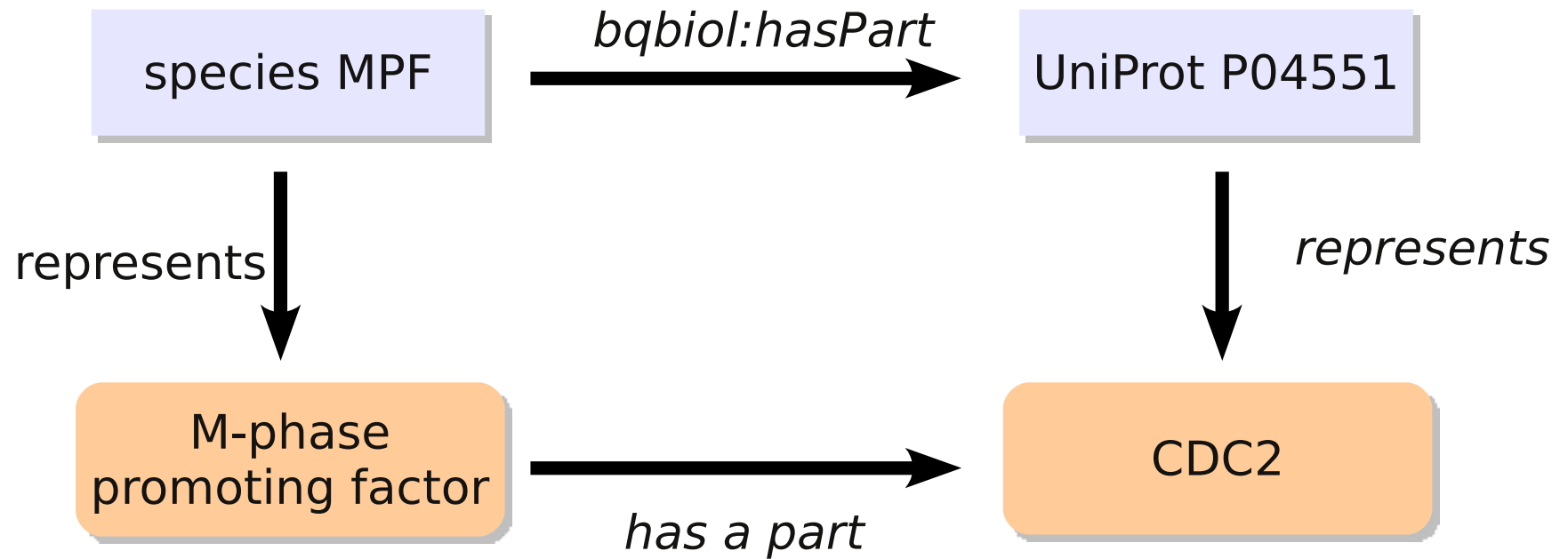
 [Edit this data type](#)

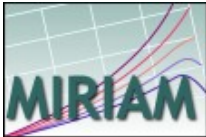


Qualification of annotation



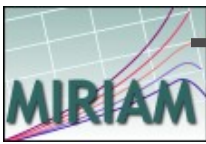
Qualification of annotation





SBML and MIRIAM cross-references

```
<species id="Ca_calmodulin" metaid="cacam">
  <annotation>
    <rdf:RDF
      xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#"
      xmlns:bqbiol="http://biomodels.net/biology-qualifiers/"
      <rdf:Description rdf:about="#cacam">
        <bqbiol:hasPart>
          <rdf:Bag>
            <rdf:li rdf:resource="urn:miriam:uniprot:P62158"/>
            <rdf:li rdf:resource="urn:miriam:obo.chebi:CHEBI%3A29108"/>
          </rdf:Bag>
        </bqbiol:hasPart>
      </rdf:Description>
    </rdf:RDF>
  </annotation>
</species>
```



Tools developing support for MIRIAM identifiers

- Data resources
 - BioModels Database (kinetic models)
 - PSI consortium (protein interactions)
 - Reactome (pathways)
 - Pathway commons (pathways)
 - SABIO-RK (reaction kinetics)
 - Yeast consensus model database
 - Human consensus model database
 - E-MeP (structural genomics)
- MIRIAM Resources statistics
 - ~5000 web page requests per month
 - ~550000 web service requests per month
- Application software
 - ARCADIA (graph editor)
 - BIOUML (modeling and simulation)
 - COPASI (Simulation)
 - libAnnotationSBML
 - libSBML
 - SAINT (semantic annotation)
 - SBML2BioPAX
 - SBML2LaTeX
 - SBMLEditor (model editor)
 - SemanticSBML (annotation and merging)
 - Snazer (Network analysis, Simulations)
 - Systems Biology Workbench (model design and simulation)
 - The Virtual Cell (Simulation)

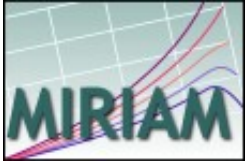
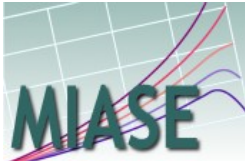
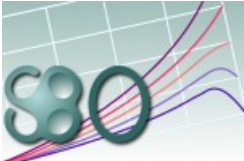
BioModels Similar to BIOMD0000000009.xml

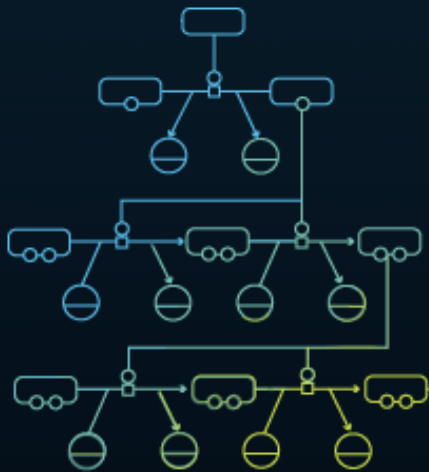
Model	BioModel	Score	Bar Chart
Huang1996_MAPK_ultrasens	BIOMD0000000009	1.0	
Levchenko2000_MAPK_noScaffold	BIOMD0000000011	0.925093068877	
Levchenko2000_MAPK_Scaffold	BIOMD0000000014	0.86507748228	
Kholodenko2000_MAPK_feedback	BIOMD0000000010	0.816212542046	
Markevich2004_MAPK_orderedElementary	BIOMD0000000026	0.737035170293	
Markevich2004_MAPK_phosphoRandomElementary	BIOMD0000000028	0.68757623681	
Markevich2004_MAPK_AlrRandomElementary	BIOMD0000000030	0.68757623681	
Markevich2004_MAPK_orderedMM	BIOMD0000000027	0.67292654353	
Markevich2004_MAPK_orderedMM2kinases	BIOMD0000000031	0.67292654353	
Markevich2004_MAPK_phosphoRandomMM	BIOMD0000000029	0.614419563376	
Hornberg2005_ERKcascade	BIOMD0000000084	0.467502293047	
McClean2007_CrossTalk	BIOMD0000000116	0.396968852299	
Kofahl2004_pheromone	BIOMD0000000032	0.347654497489	
Kim2007_Wnt_ERK_Crosstalk	BIOMD0000000149	0.323862350322	
Brown2004_NGF_EGF_signaling	BIOMD0000000033	0.259659012885	
Goldbeter1995_CircClock	BIOMD0000000016	0.243985892215	
Sasagawa2005_MAPK	BIOMD0000000049	0.239991163172	
Ung2008_EGFR_Endocytosis	BIOMD0000000205	0.233723629425	
Leloup1999_CircClock	BIOMD0000000021	0.22918483858	
Goldbeter1991_MinMitOscil_ExpInact	BIOMD0000000004	0.222401483635	
Goldbeter1991_MinMitOscil	BIOMD0000000003	0.213676433868	
Leloup1998_CircClock_LD	BIOMD00000000171	0.201464719898	
Tyson1991_CellCycle_6var	BIOMD0000000005	0.199125864464	
Veening2008_DegU_Regulation	BIOMD0000000240	0.179667408207	
Neves2008_Cell_Shape	BIOMD0000000182	0.168237862604	
Fisher2006_Ca_Oscillation_dpdnt_NFAT_dynamics	BIOMD0000000122	0.163742528861	
Leloup2003_CircClock_DD	BIOMD0000000073	0.163249339887	
Leloup2003_CircClock_LD	BIOMD0000000078	0.163249339887	
Novak2001_FissionYeast_CellCycle	BIOMD0000000111	0.158121867453	
Kholodenko1999_EGFRsignaling	BIOMD0000000048	0.157261597224	
Swat2004_Mammalian_G1_S_Transition	BIOMD0000000228	0.153857976349	
Chen2004_CellCycle	BIOMD0000000056	0.153626682372	

R. Henkel, L. Endler, A. Peters, N. Le Novère, D. Waltemath (2010) Ranked Retrieval of Computational Biology Models. *BMC Bioinformatics*, 11:423

M Schulz, F Krause, N Le Novère, E Klipp, and W Liebermeister: Comparison and clustering of biochemical network models based on semantic annotations. *submitted*

Visual representation of models

	Models	Simulation	Results
Minimal requirements			
Data-model	 	 ML	SBRML
Ontologies			



A Visual Notation for Network Diagrams in Biology

SBGN.org is the global portal for documentation, news, and other information about the Systems Biology Graphical Notation (SBGN) project, an effort to standardize the graphical notation used in maps of biochemical and cellular processes studied in systems biology.

Standardizing the visual representation is crucial for more efficient and accurate transmission of biological knowledge between different communities in research, education, publishing, and more. When biologists are as familiar with the notation as electronics engineers are familiar with the notation of circuit schematics, they can save the time and effort required to familiarize themselves with different notations, and instead spend more time thinking about the biology being depicted.

SBGN is made up of [three orthogonal languages](#), representing different visions of biological systems. Each language defines a comprehensive set of symbols with precise semantics, together with detailed syntactic rules how maps are to be interpreted.

On this site, you can browse some [example maps](#) to get a feeling for SBGN, read the SBGN [specification documents](#), [software supporting SBGN](#), get answers to [frequent questions about SBGN](#), access join [online discussions](#), see current working documents in the [SBGN wiki](#), and much more.

SBGN is the work of many people. It would not have been possible without the generous [support of multiple organizations](#) over the years, for which we are very thankful.

To quote SBGN as a whole, please use:

Le Novère N, Hucka M, Mi H, Moodie S, Schreiber F, Sorokin A, Demir E, Wegner K, Aladjem MI, Wimalaratne SM, Bergman FT, Gauges R, Ghazal P, Kawaji H, Li L,

SBGN News

(23 Apr.'10) The first [annual competition](#) is opened, with categories such as Best Software, Best Map and Best Outreach.

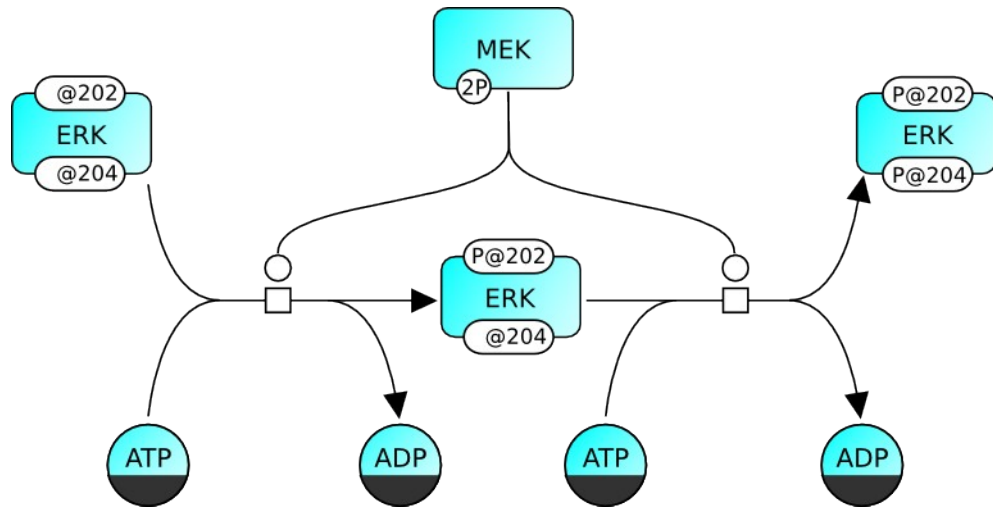
N. Le Novère, M. Hucka, H. Mi, S. Moodie, F. Shreiber, A. Sorokin, et al (2009). The Systems Biology Graphical Notation. *Nature Biotechnology*, 27: 735-741.

What is SBGN?

- An unambiguous way of graphically describing and interpreting biochemical and cellular events
- Limited amount of symbols
Re-use existing symbols
 - ☞ Smooth learning curve
- Can represent logical or mechanistic models, biochemical pathways, at different levels of granularity
- Detailed technical specification, precise data-models and growing software support
- Developed over four years by a diverse community, including biologists, modellers, computer scientists etc.

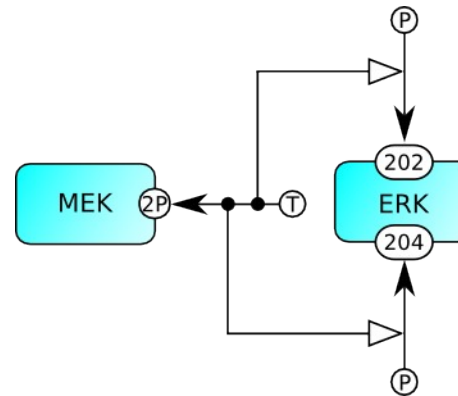
Graph trinity: three languages in one notation

Process Descriptions



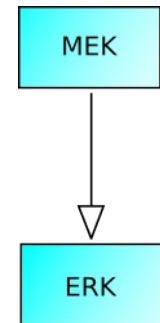
- Unambiguous
- Mechanistic
- Sequential
- Combinatorial explosion

Entity Relationships



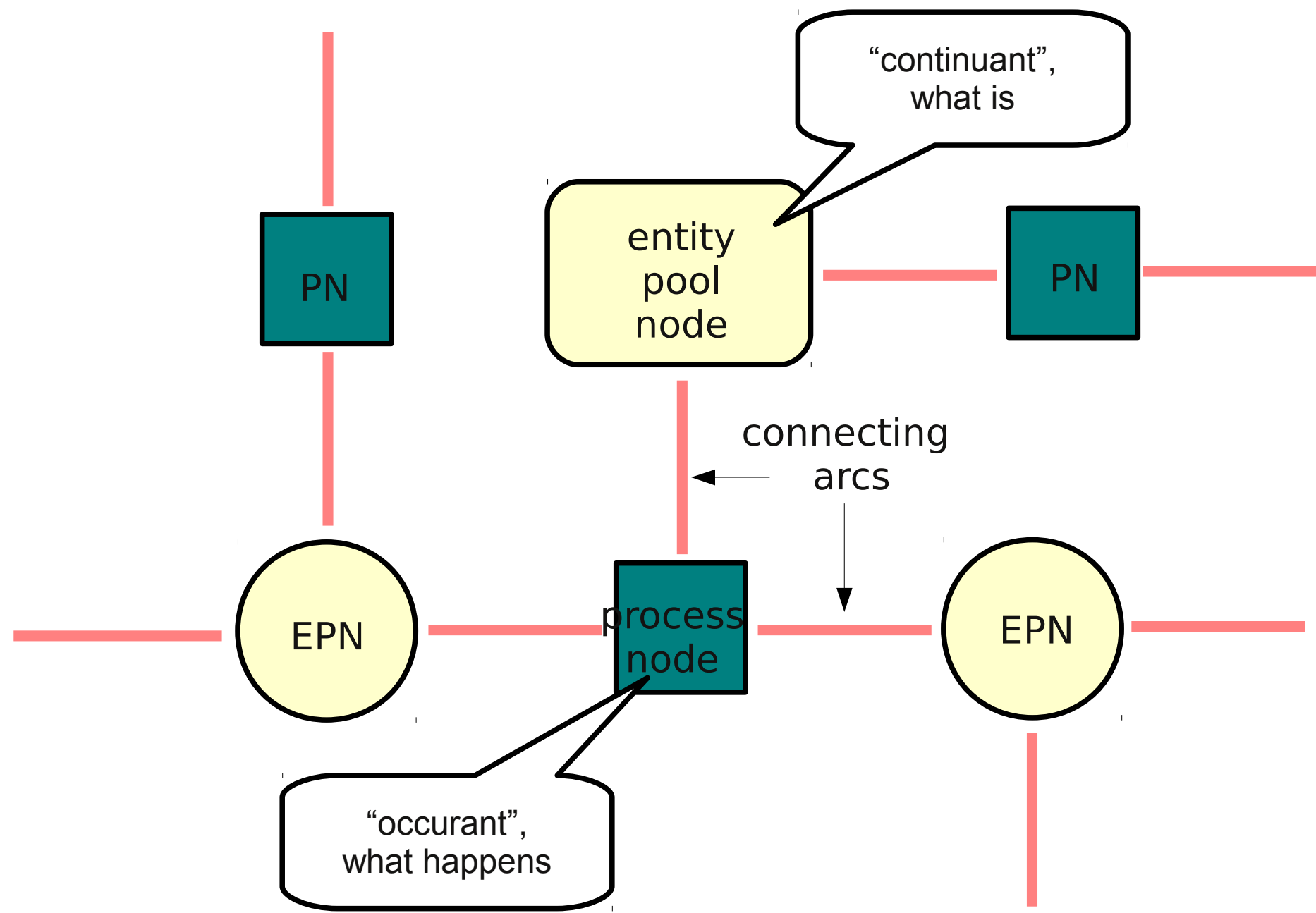
- Unambiguous
- Mechanistic
- Non-sequential
- Independence of relationships

Activity Flows

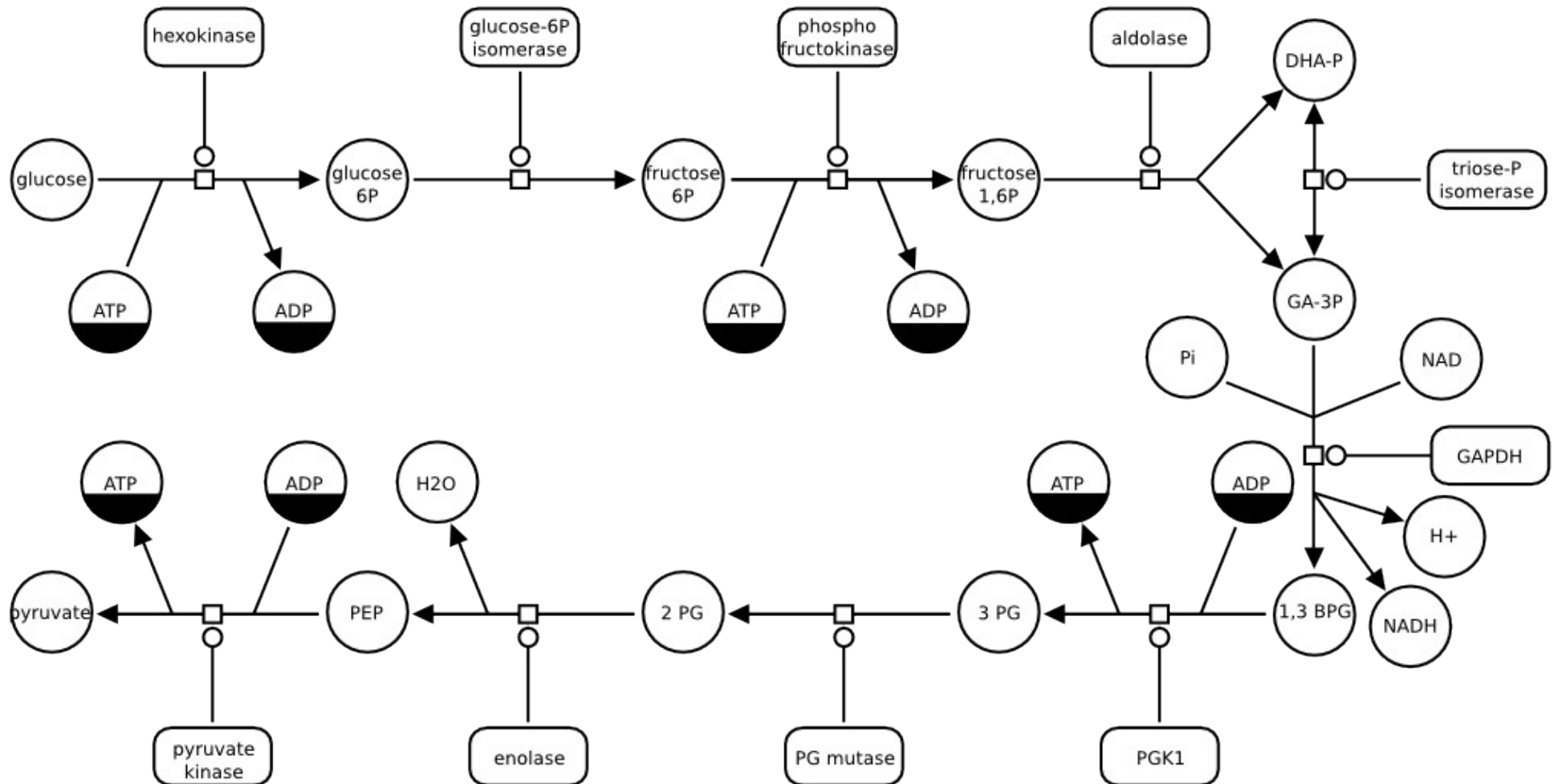


- Ambiguous
- Conceptual
- Sequential

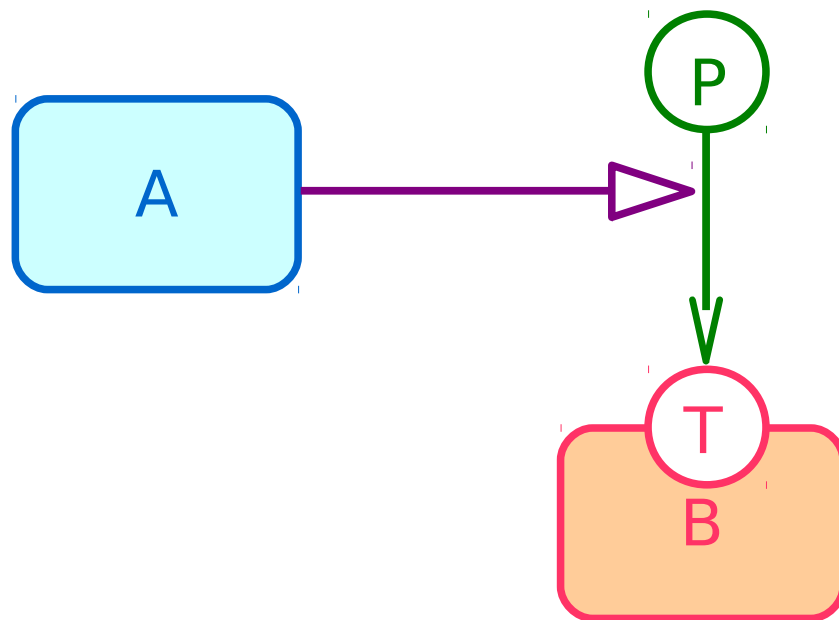
Process Descriptions are bipartite graphs



Metabolic network in Process Description Language



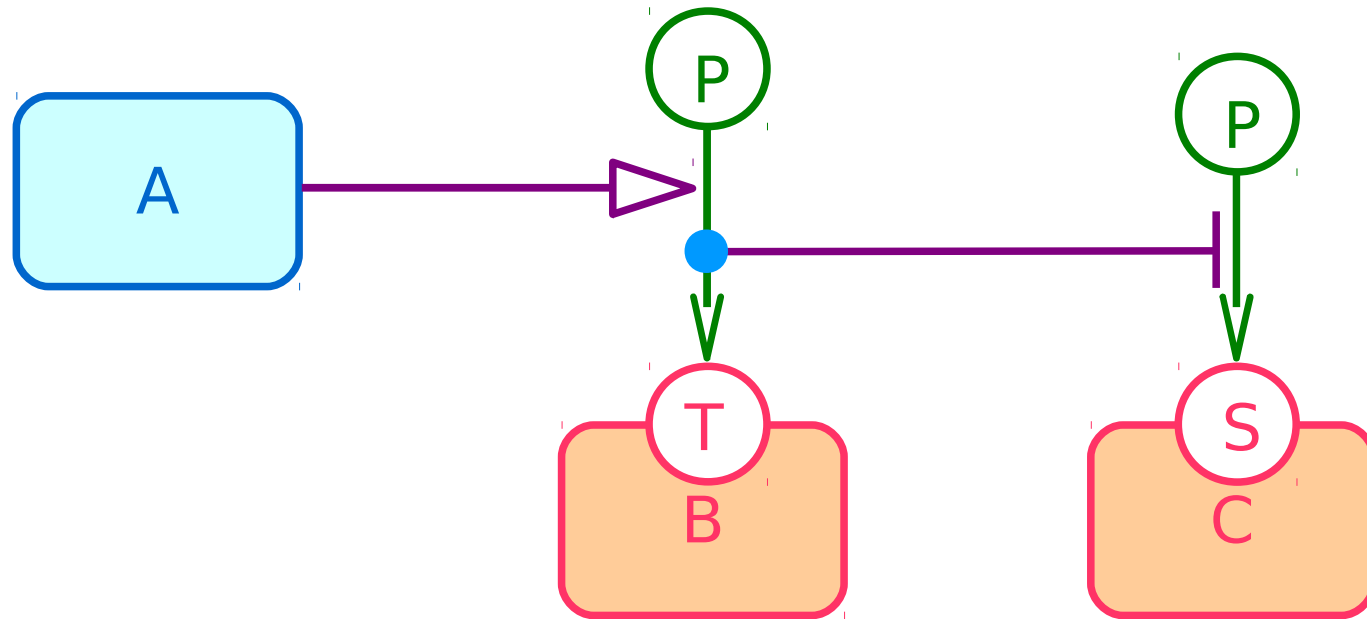
Entity Relationships can be viewed as rules



If **A exists**, the **assignment of the value P** to the **state variable T of B** is **increased**

(**A stimulates** the **phosphorylation** of **B on the threonine**)

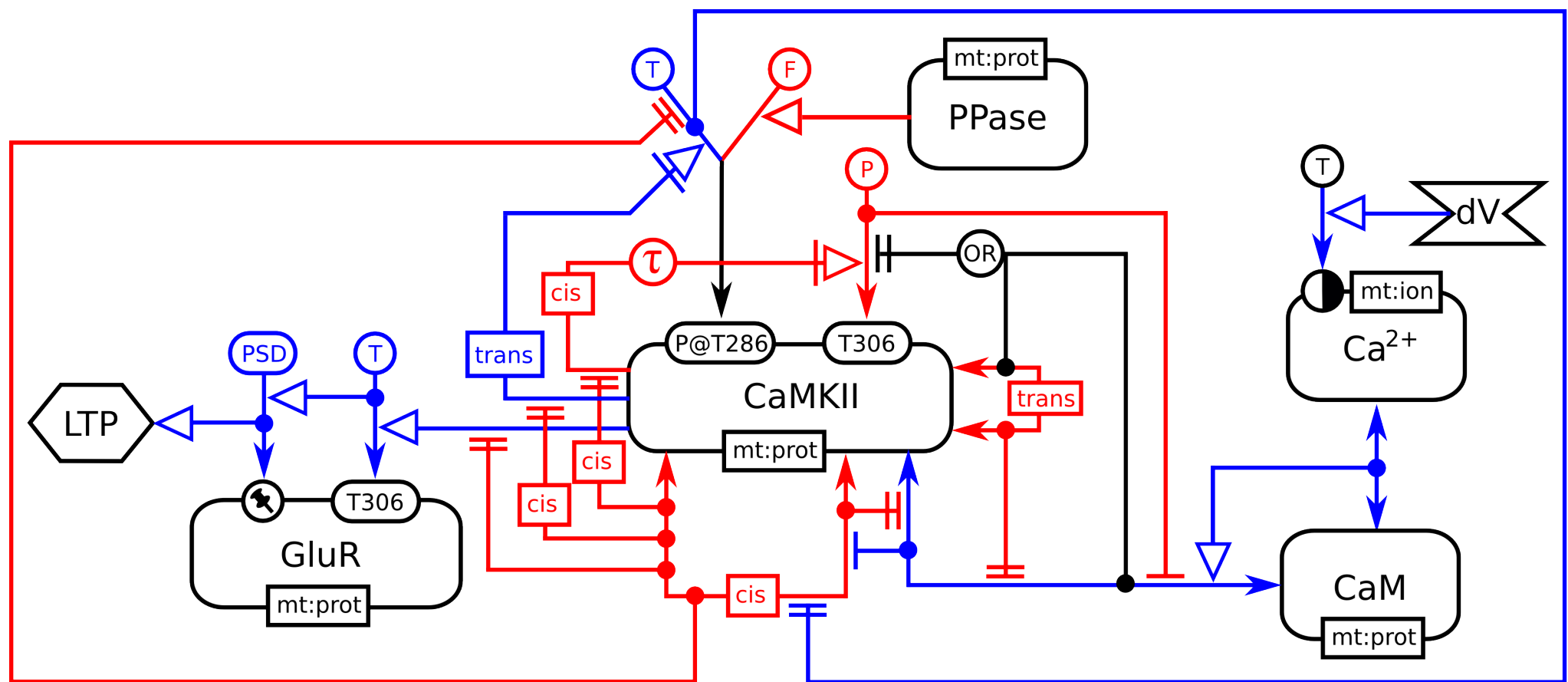
Entity Relationships can be viewed as rules



If **A exists**, the **assignment of the value P** to the **state variable T of B** is **increased**

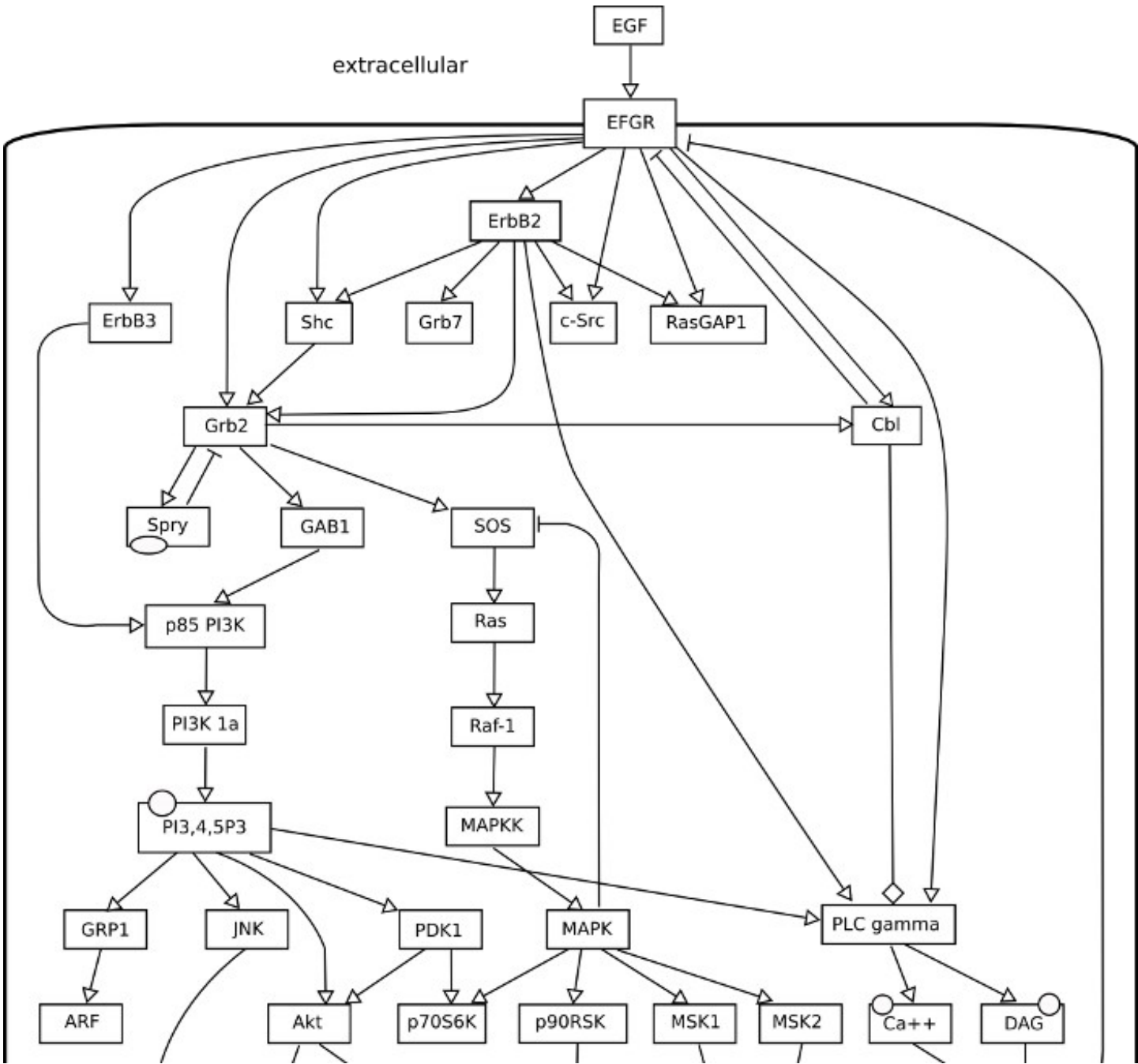
If **P is assigned to the state variable T of B**, the **assignment of the value P** to the **state variable S of B** is **decreased**

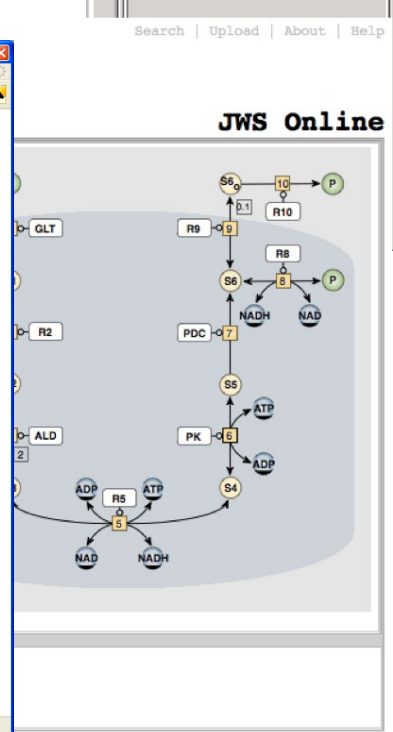
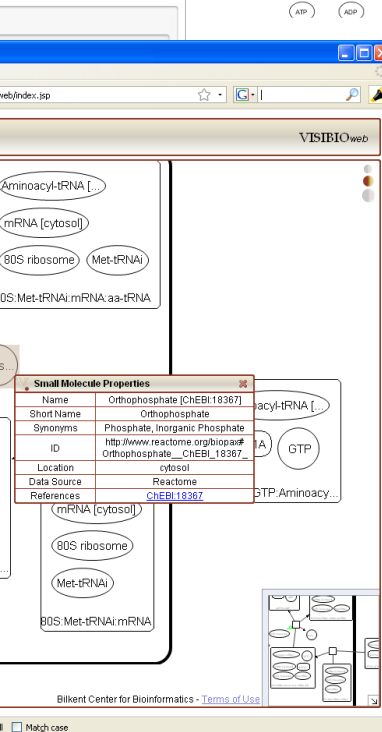
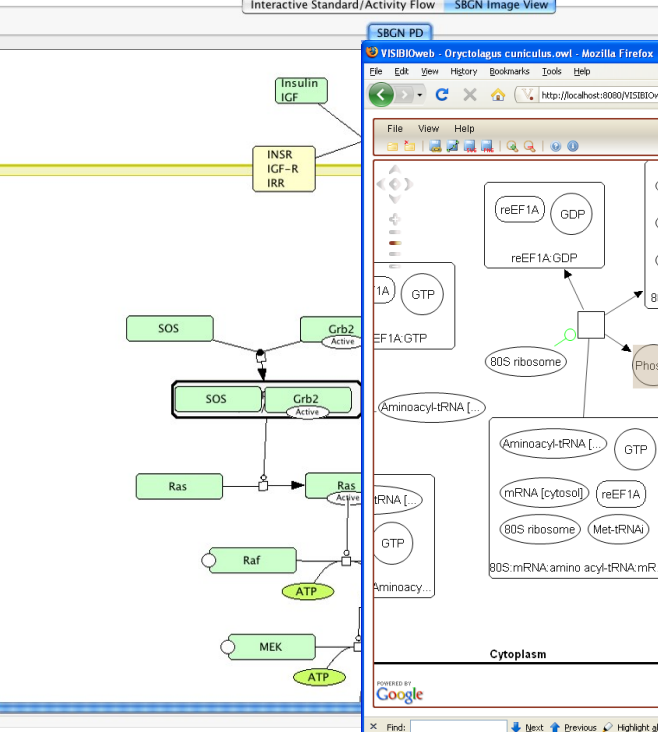
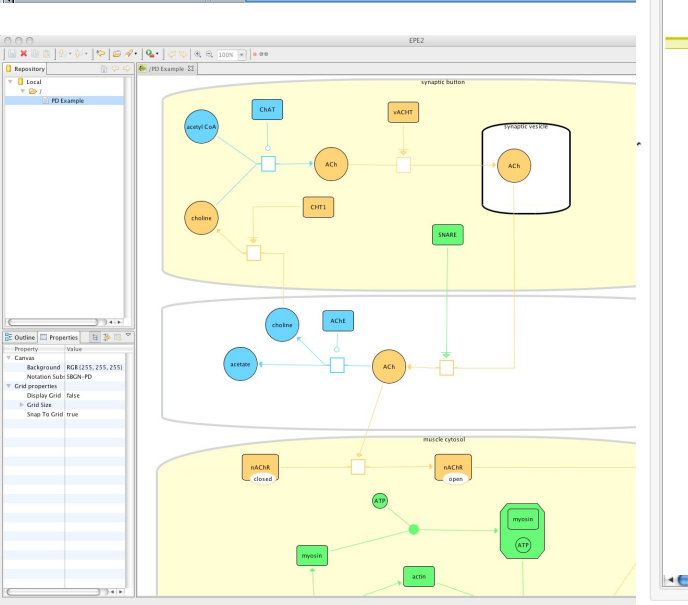
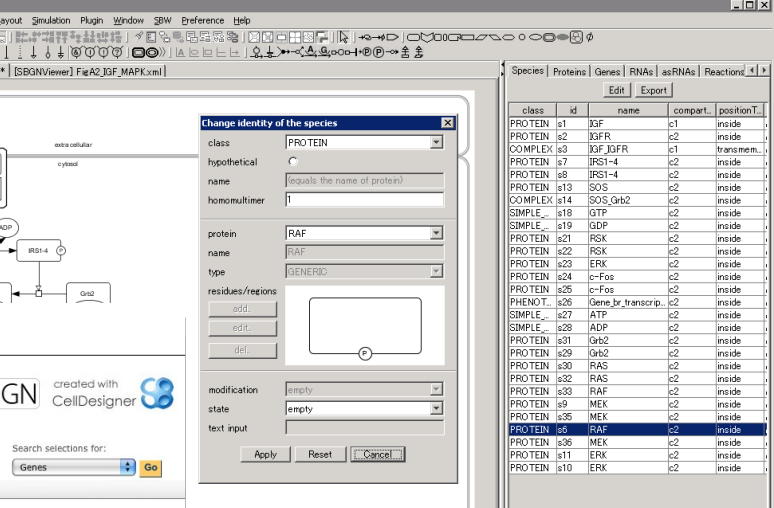
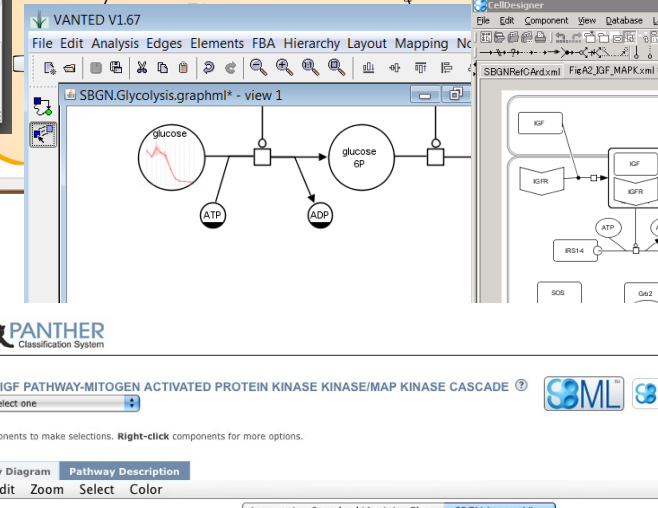
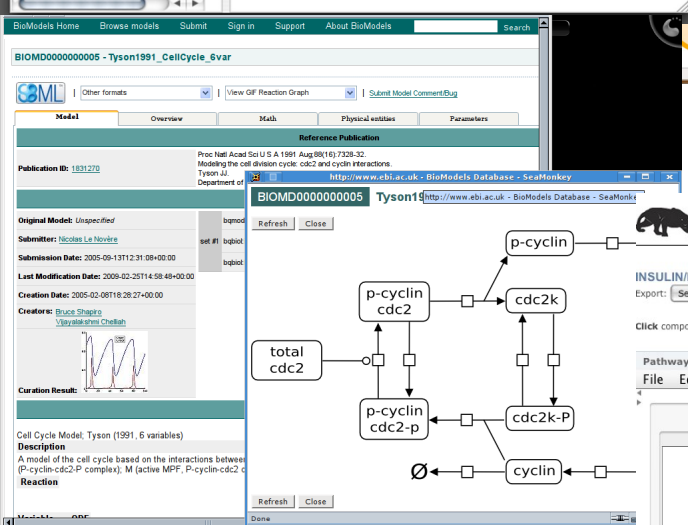
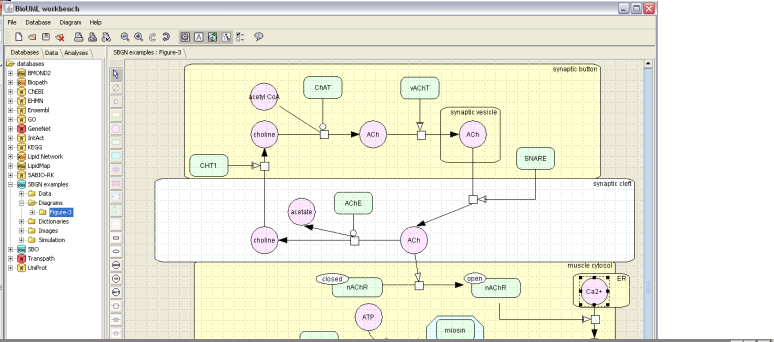
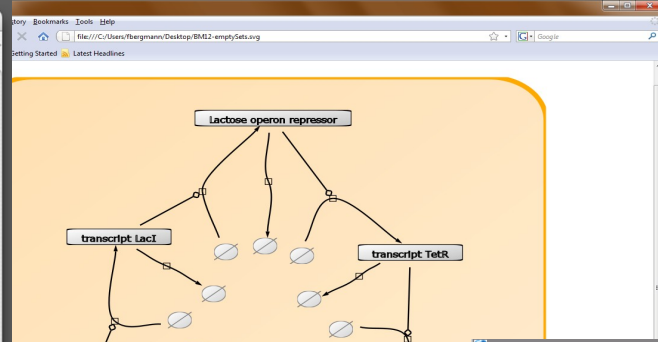
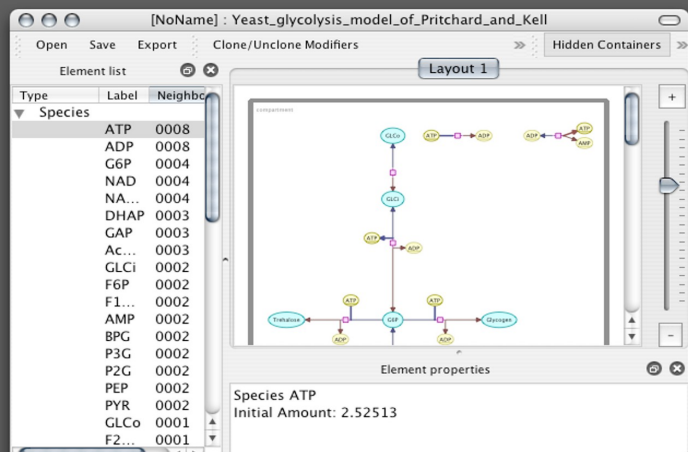
GNER map of calcium-regulated synaptic plasticity



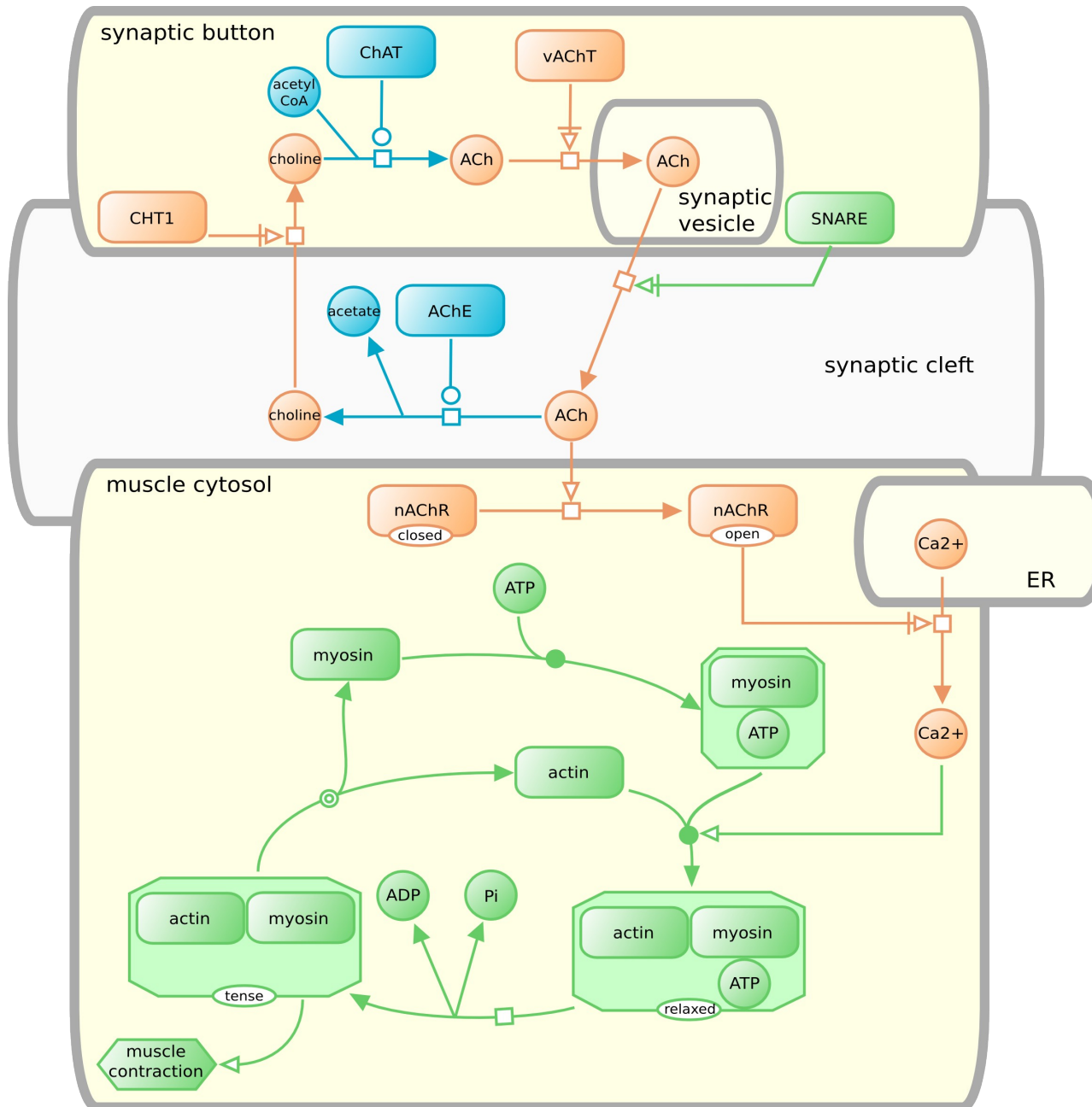
increases synaptic weight
decreases synaptic weight

Example of Activity Flow map

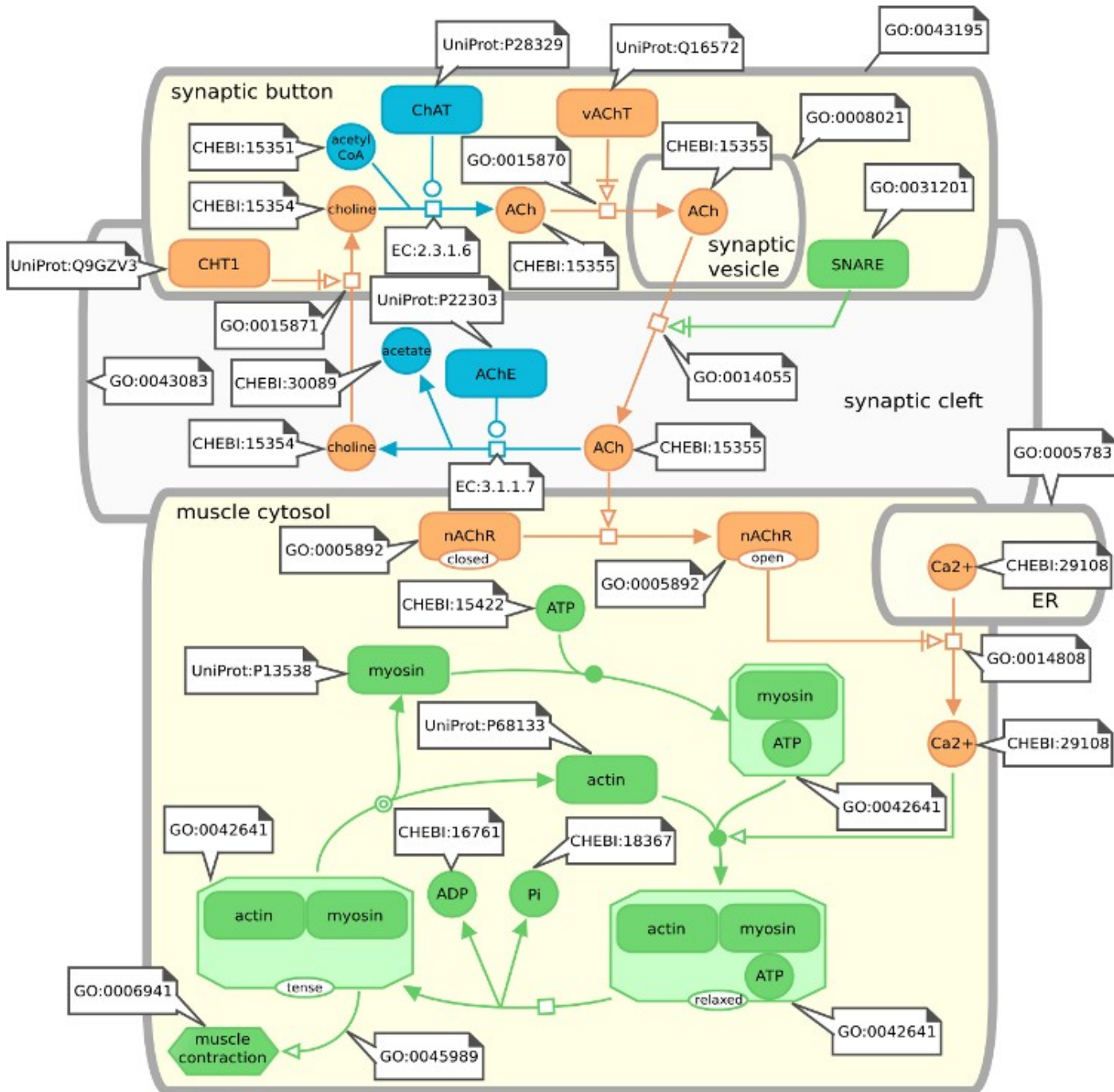




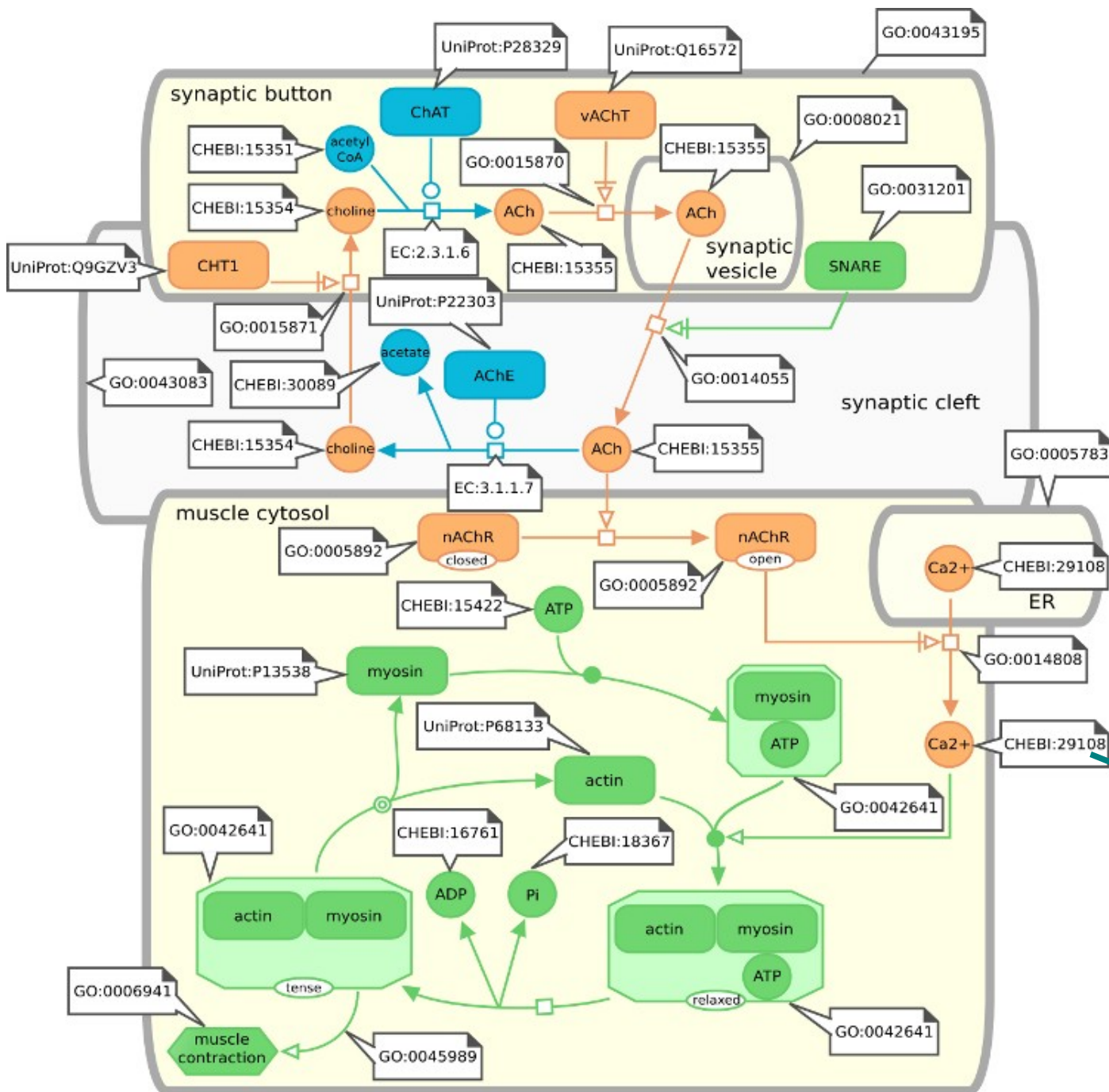
Linking SBGN maps to external information



Linking SBGN maps to external information



Linking SBGN maps to external information



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Main Automatic Xrefs

Ca²⁺

ChEBI Name calcium(2+)
ChEBI ID CHEBI:29108
Last Modified 10 March 2008

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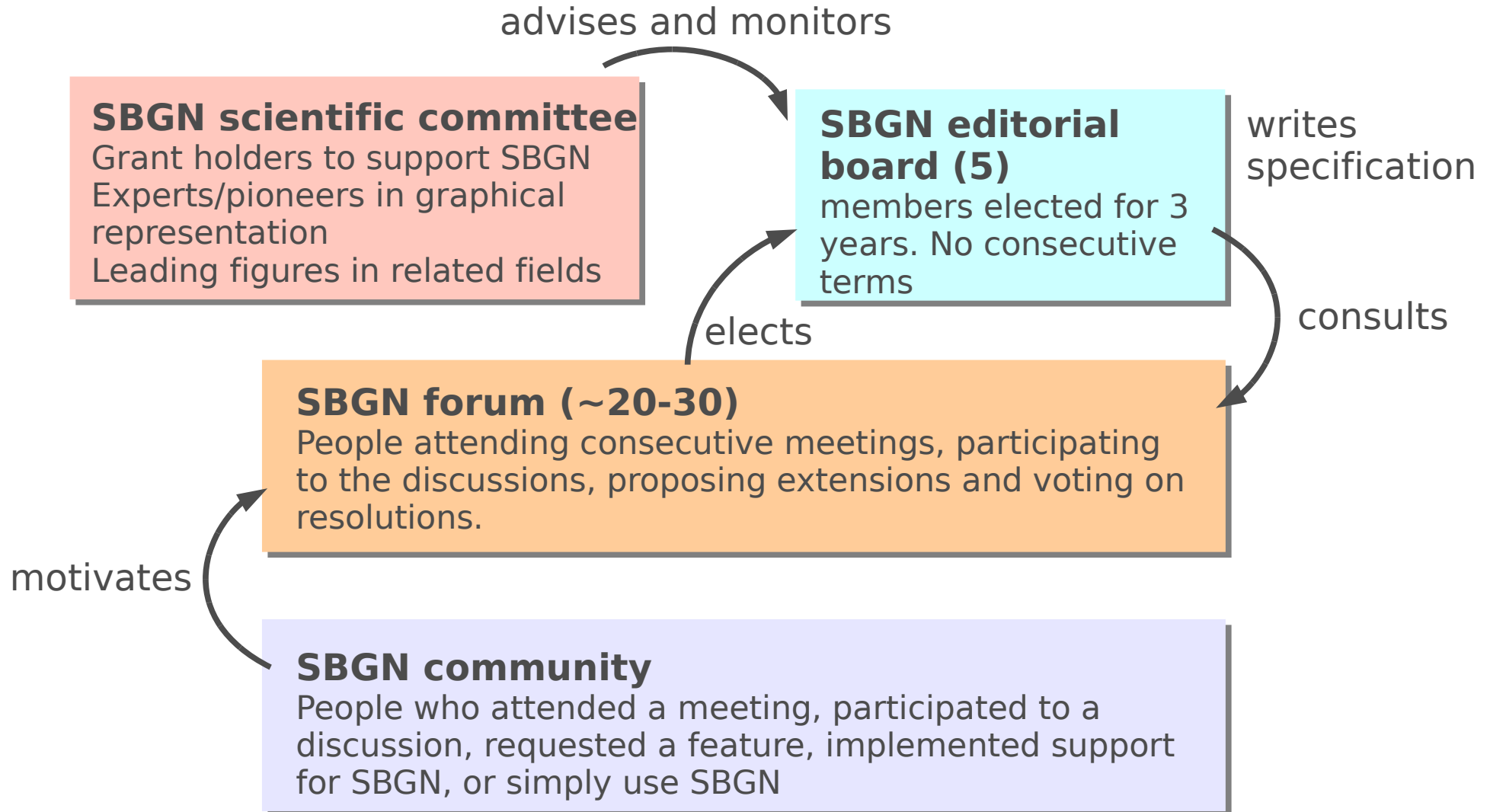
Molfile
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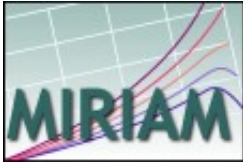
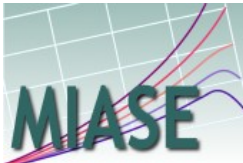
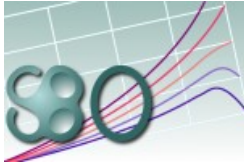
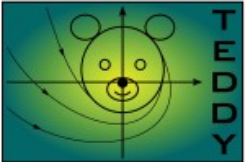
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Current structure of the SBGN community



Is the mosaic of standards complete?

	Models	Simulation	Results
Minimal requirements			
Data-models			SBRML
Ontologies			

Disentangling the model life-cycle

PMML



SBRML

model generation

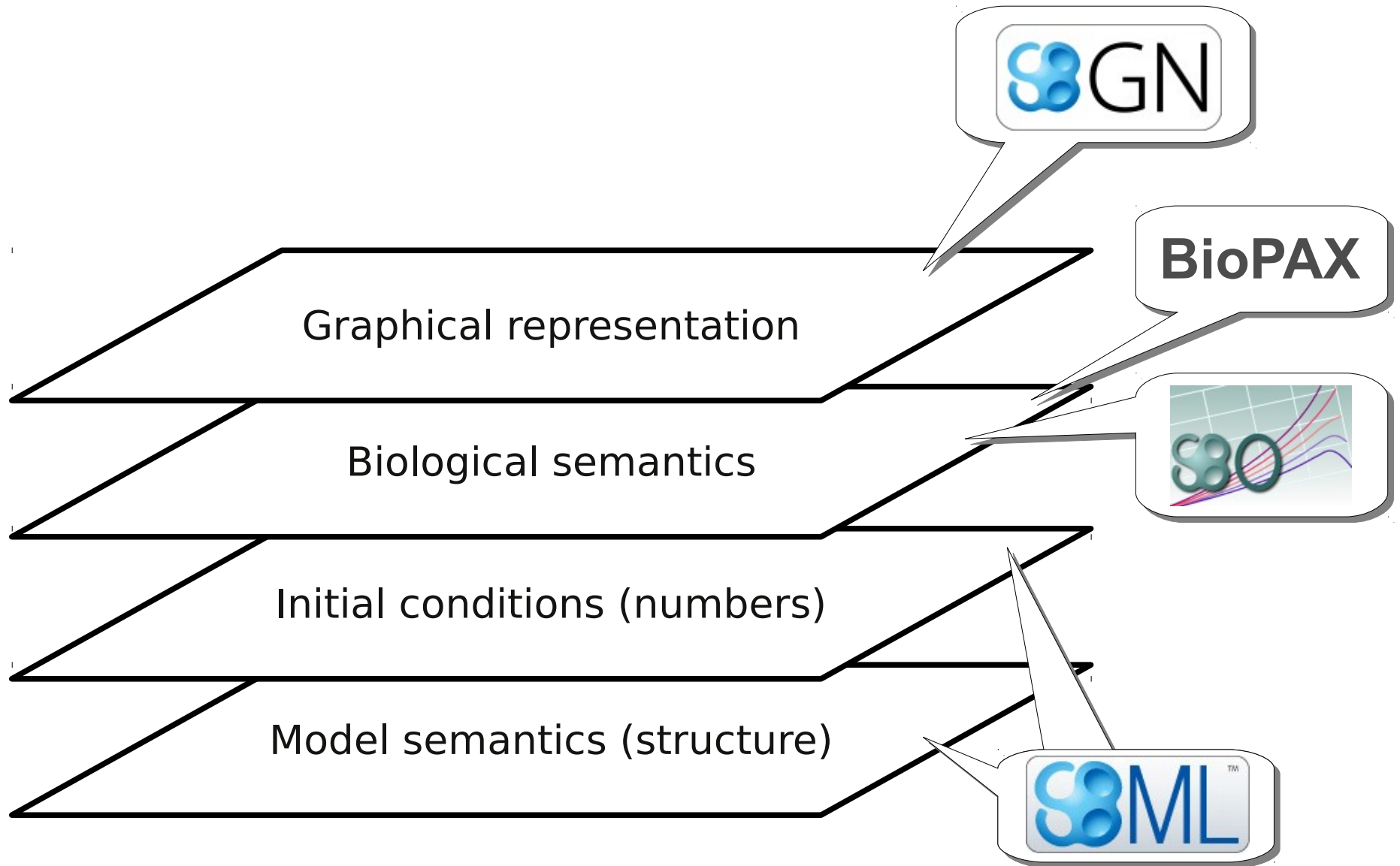
model description

parametrisation

simulation and analysis

numerical results

Disentangling the level of discourse



Biological semantics

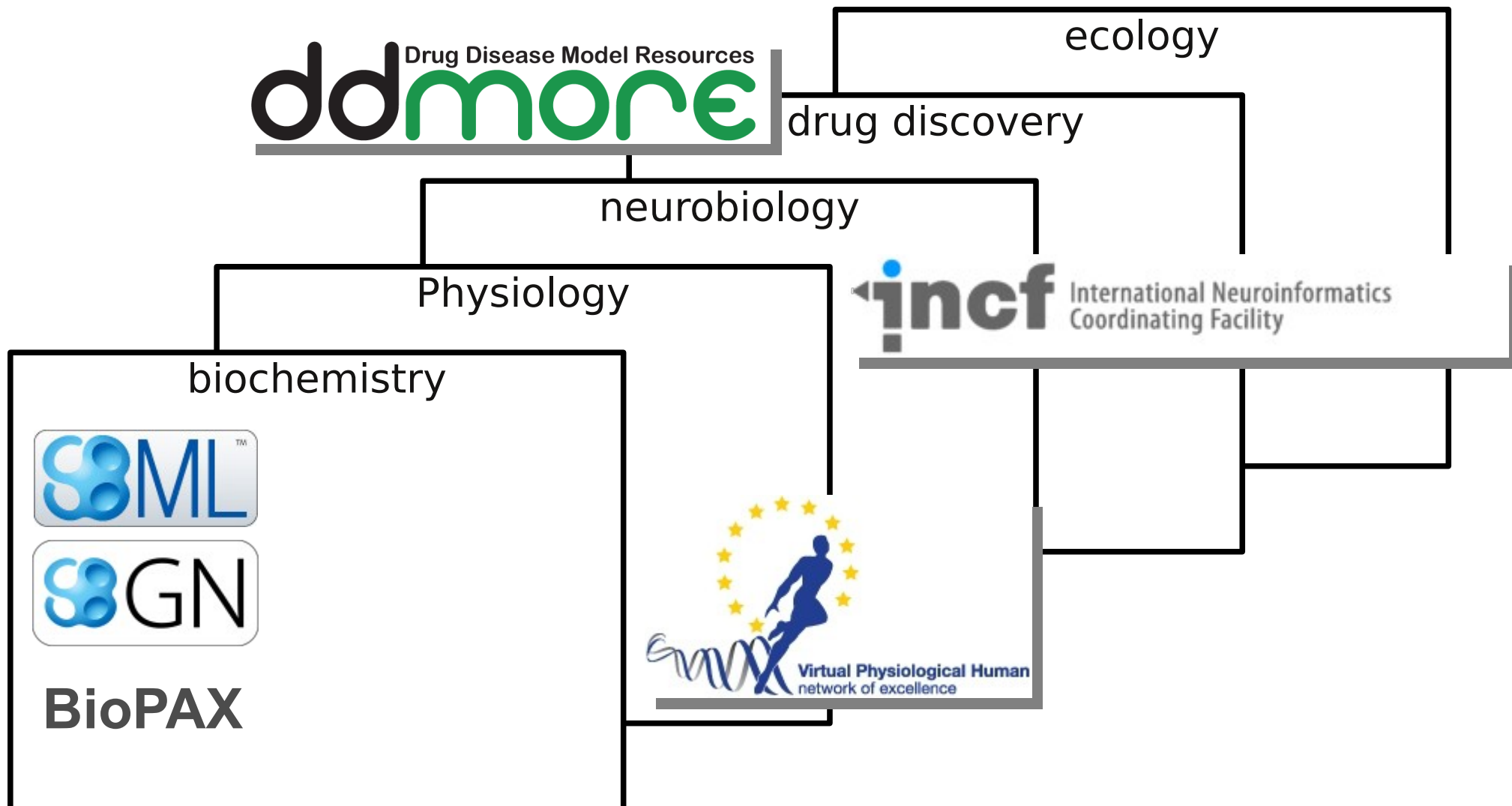
Systems Biology Ontology (SBO) Set of linked controlled vocabularies, defining and relating concepts used in computational modelling in biology. Used in SBML, SBGN, NeuroML

Le Novère N., Courtot M., Laibe C. Adding semantics in kinetics models of biochemical pathways. *Proc 2nd Intl Symp on experimental standard conditions of enzyme characterizations* (2007), 137-153.

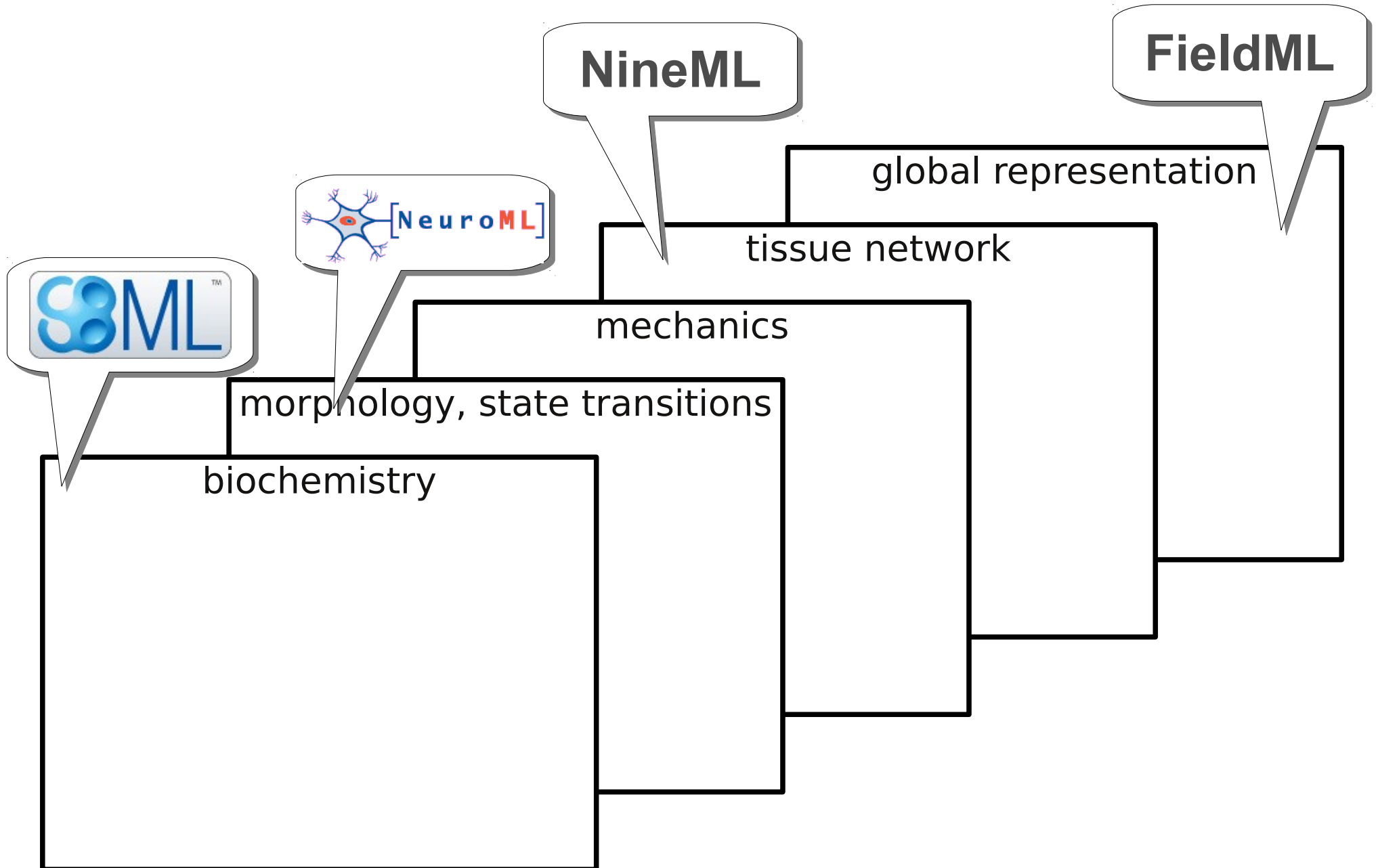
Biological Pathway Exchange (BioPAX) Standard language to represent biological pathways at the molecular and cellular level and to facilitate the exchange of pathway data. Used by most major pathways databases

Demir E, Cary MP, Paley S, Fukuda K, Lemer C, Vastrik I, Wu G, D'Eustachio P, Schaefer C, Luciano J, Schacherer F, Martinez-Flores I, Hu Z, Jimenez-Jacinto V, Joshi-Tope G, Kandasamy K, Lopez-Fuentes AC, Mi H, Pichler E, Rodchenkov I, Splendiani A, Tkachev S, Zucker J, Gopinathrao G, Rajasimha H, Ramakrishnan R, Shah I, Syed M, Anwar N, Babur O, Blinov M, Brauner E, Corwin D, Donaldson S, Gibbons F, Goldberg R, Hornbeck P, Luna A, Murray-Rust P, Neumann E, Reubenacker O, Samwald M, van Iersel M, Wimalaratne S, Allen K, Braun B, Carrillo M, Cheung KH, Dahlquist K, Finney A, Gillespie M, Glass E, Gong L, Haw R, Honig M, Hubaut O, Kane D, Krupa S, Kutmon M, Leonard J, Marks D, Merberg D, Petri V, Pico A, Ravenscroft D, Ren L, Shah N, Sunshine M, Tang R, Whaley R, Letovksy S, Buetow KH, Rzhetsky A, Schachter V, Sobral BS, Dogrusoz U, McWeeney S, Aladjem M, Birney E, Collado-Vides J, Goto S, Hucka M, Le Novère N, Maltsev N, Pandey A, Thomas P, Wingender E, Karp PD, Sander C, Bader GD. BioPAX – A Community Standard for Pathway Data Sharing. *Nat Biotechnol* (2010), 28: 935–942

Parallel and redundant efforts



Non-overlapping languages to cover all models



Standards interoperability along the 3 dimensions

- SBML to BioPAX: conversion using metadata (MIRIAM annotations and SBO terms), e.g.
 - mapping between Species and PhysicalEntity
 - mapping between Reactions and PhysicalInteraction
- Conversion of SBML or BioPAX descriptions to SBGN map
- Usage of SBML descriptions (or CellML or VCML) in SED-ML: Identification of variables using XPath
- Descriptions using SBML and NeuroML: Interface based on XPath

Requirements for a overarching standardisation structure

- What?
 - Set of interoperable description languages
 - Cover all aspects of modelling and simulation, all types of descriptions / views of the real
 - Role of community-maintained ontologies.
- How?
 - Independence towards Institutions, funders and individuals
 - Role of European Research Infrastructures? (ELIXIR, ISBE)
- Who?
 - Communities developing their standards: Systems Biology, Physiology (VPH), Neuroscience (INCF), Drug discovery (DDMoRe)
 - Other players in knowledge-representation (W3C, ...)
 - Academic and corporate users: Modeling platforms (MatWorks ...), Pharma (Pistoia alliance) ...

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**COmputational Modeling in Biology NEtwork
(COMBINE)** forthcoming: <http://co.mbine.org>

COMBINE 2010

- 6 to 9 October 2010, Edinburgh, before the ICSB
- 75 registrations so far (forecast was 50 max ...)
- 14 sessions, plus breakouts, 42 presentations, 30 posters

Physiome standards

SED-ML

SBGN languages

libSBGN and SBGN support

Encoding graph layouts

Interactions and reactions

Semantics and metadata resources

Encoding and using semantics

Format conversion

Software support

BioPAX levels

What is not covered yet

SBML Level 3

libSBML and SBML support

followed by:

SBML 10th anniversary



ABOUT W3C

The World Wide Web Consortium (W3C) is an international community where [Member organizations](#), a full-time staff, and the public work together to develop [Web standards](#). Led by Web inventor [Tim Berners-Lee](#) and CEO [Jeffrey Jaffe](#), W3C's mission is to lead the Web to its full potential. [Contact W3C](#) for more information.



W3C Mission

► Principles, vision, ...



Facts About W3C

► People, organization, revenues, process, patent policy, history, ...



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► Press releases, requests for photos and interviews, ...



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W3C Mission

► Principles, vision, ...

QUICK LINKS

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for the modeling in life-sciences**



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► Employment opportunities, fellows, ...

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Acknowledgements

Visionary: **Hiroaki Kitano**

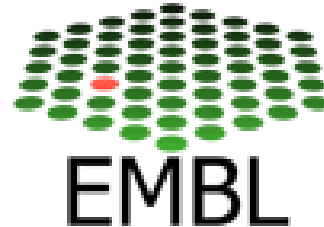
SBML editors: Frank Bergmann, *Andrew Finney*, *Stefan Hoops*, ***Michael Hucka***, *Nicolas Le Novère*, *Sarah Keating*, *Sven Sahle*, *Herbert Sauro*, Jim Schaff, Lucian Smith, Darren Wilkinson

SGN editors: Emek Demir, *Michael Hucka*, *Nicolas Le Novère*, Huaiyu Mi, Stuart Moodie, Falk Schreiber, *Anatoly Sorokin*

MIRIAM: Nick Juty, Camille Laibe

The whole community of Computational Systems Biology

The EBI group Computational Systems Neurobiology



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Group Leader
Joint appointment
with the
[Mouse Biology Unit](#)



[Tracey Andrew](#)
Administrative
assistant



[Benedetta Frida Baldi](#)
PhD student



[Stuart Edelstein](#)
Visiting professor



[Kathryn Hardwick](#)
Administrative
assistant



[Christine Hoyer](#)
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[Lu Li](#)
PhD student



[Michele Mattioni](#)
PhD student



[Melanie Stefan](#)
Post-doc



Yang Zhan
Post-doc
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[Cornelius Gross](#)

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[BioModels.net](#)
coordinator



[Vijayalakshmi Chelliah](#)
Database curator



[Lukas Endler](#)
Database curator



[Nick Juty](#)
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Ontology Curator



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Koray Dogan Kaya
Marie Curie PhD



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Software Engineer



Marine Dumousseau
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