Data Integration and Semantic Enrichment of Systems Biology Models and Simulations

Nicolas Le Novère, EMBL-EBI

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The models I am not going to talk about

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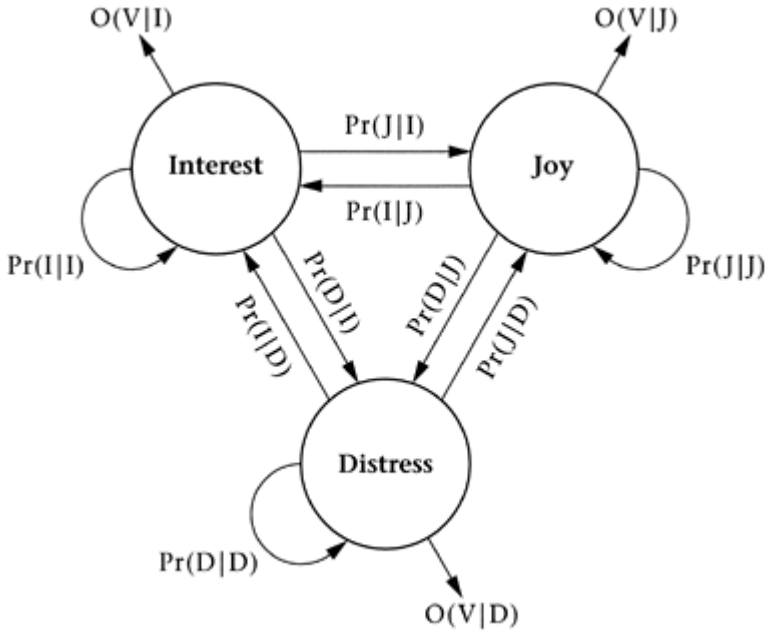

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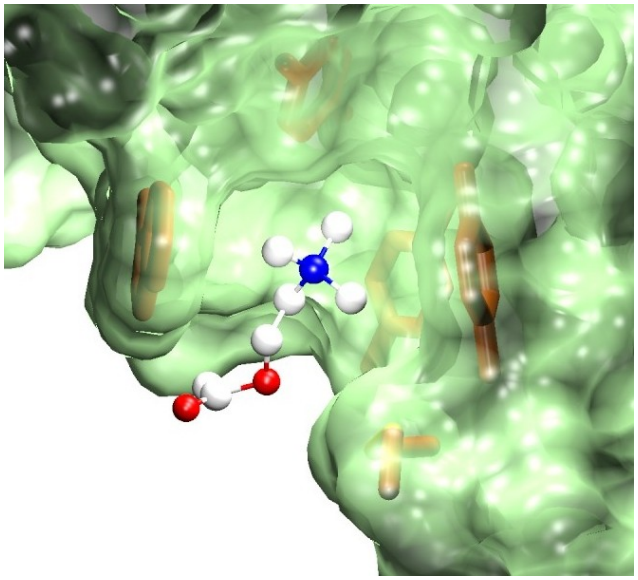

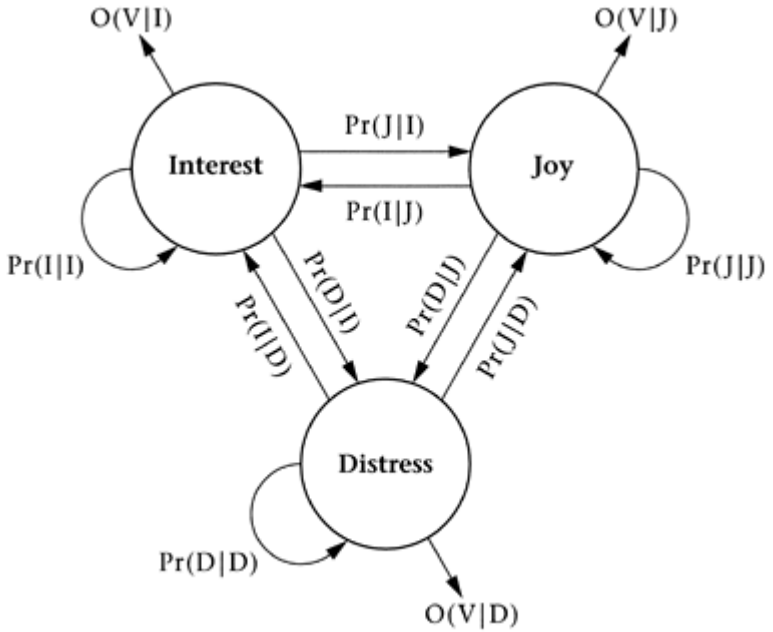

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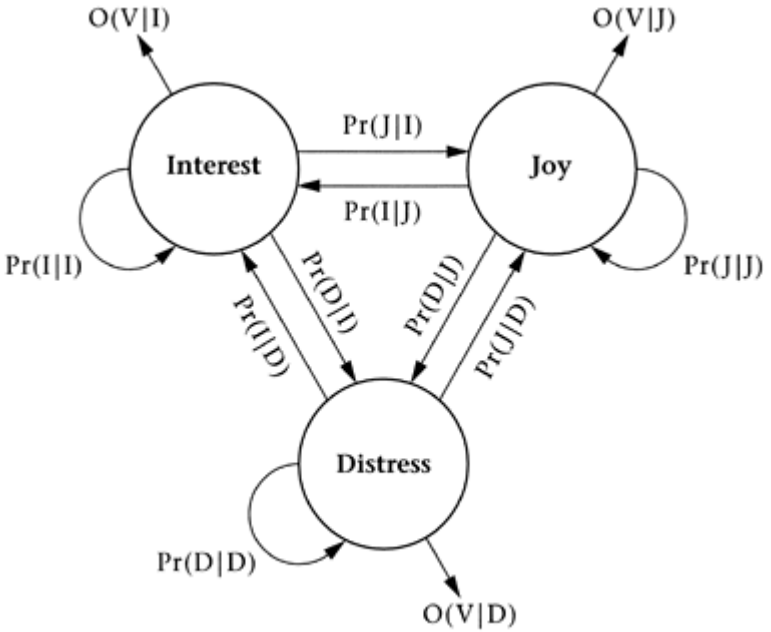
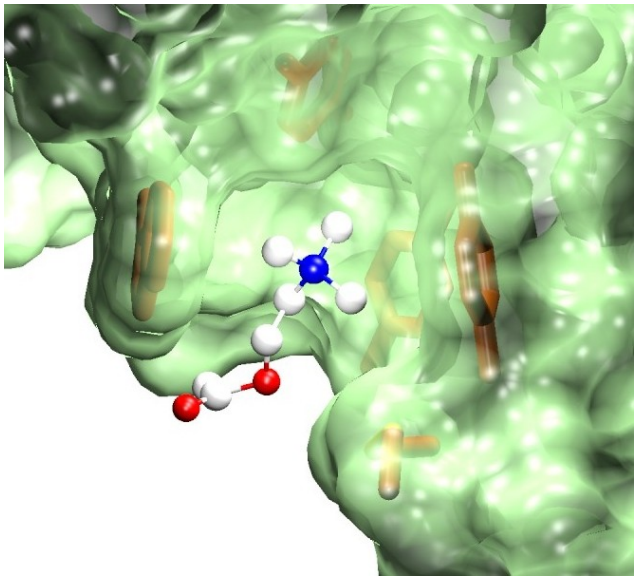
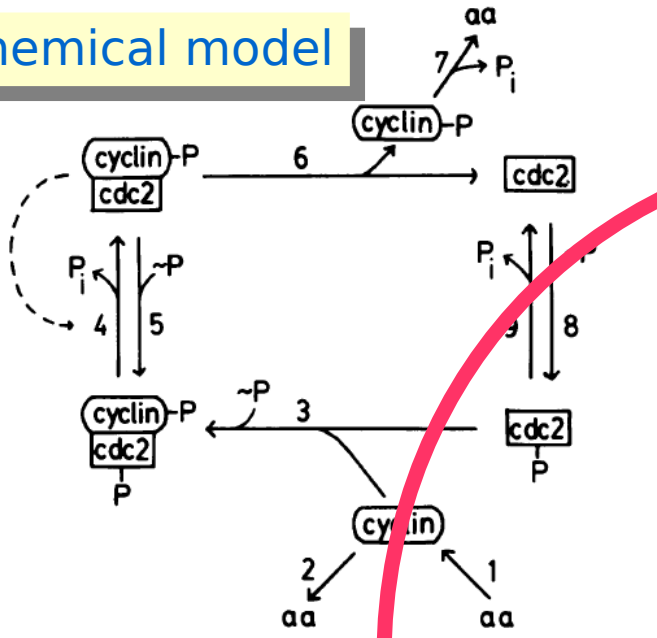
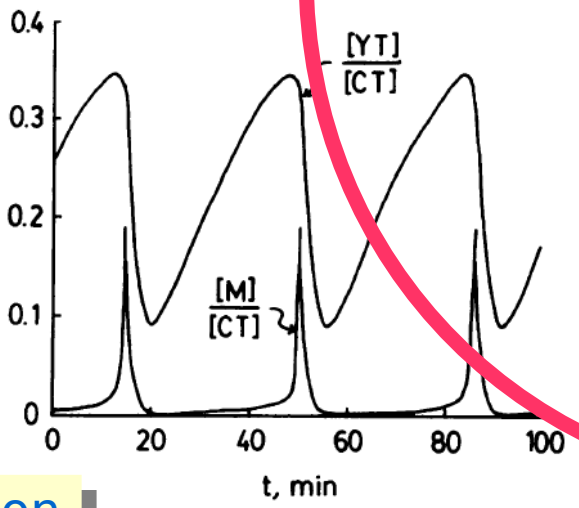




The models I am going to talk about

biochemical model





simulation

mathematical model

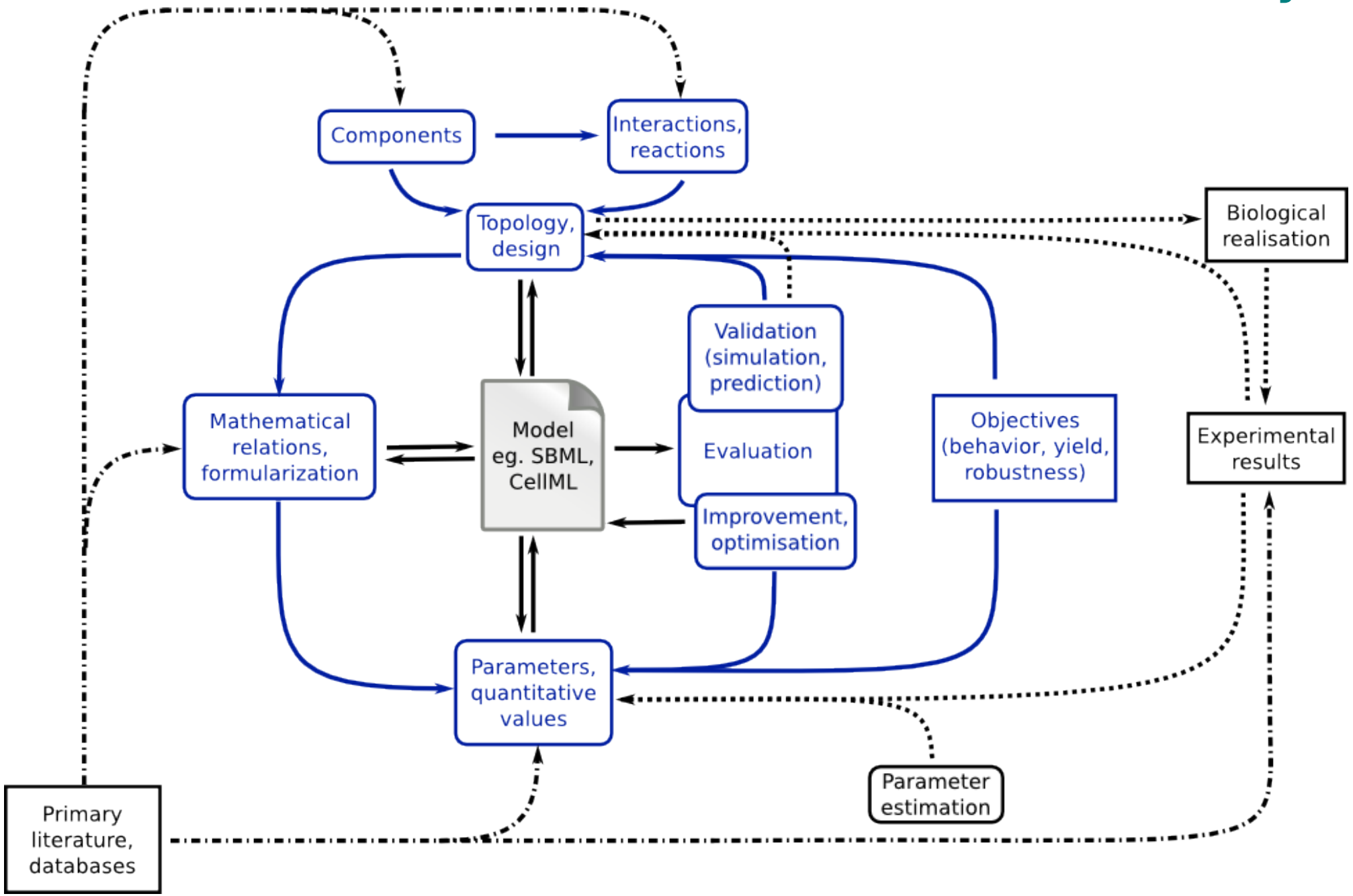
$$
\begin{aligned}
d[C2]/dt &= k_6[M] - k_8[\sim P][C2] + k_9[CP] \\
d[CP]/dt &= -k_3[CP][Y] + k_8[\sim P][C2] - k_9[CP] \\
d[pM]/dt &= k_3[CP][Y] - [pM]F([M]) + k_5[\sim P][M] \\
d[M]/dt &= [pM]F([M]) - k_5[\sim P][M] - k_6[M] \\
d[Y]/dt &= k_1[aa] - k_2[Y] - k_3[CP][Y] \\
d[YP]/dt &= k_6[M] - k_7[YP]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

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

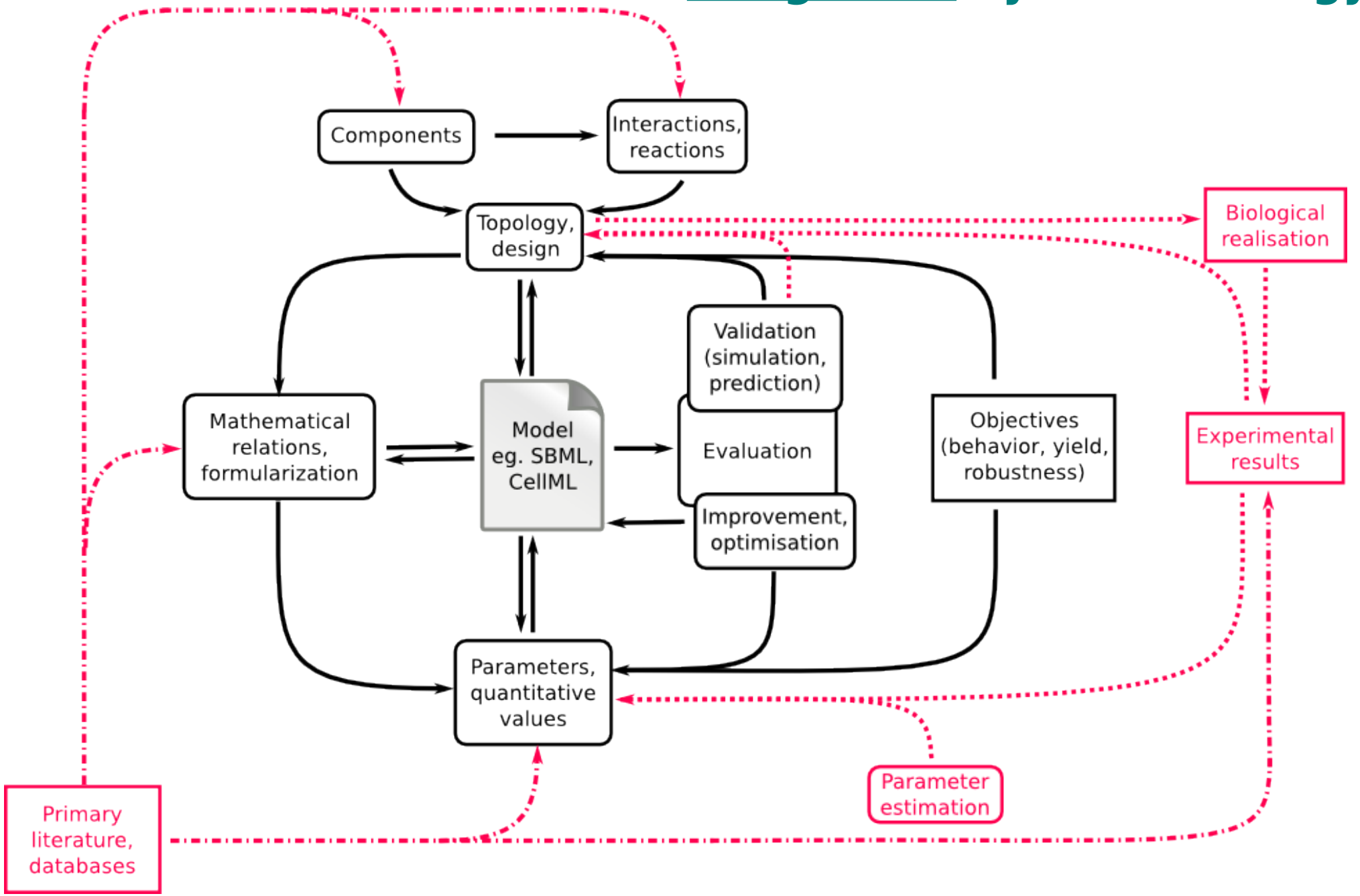
computational model

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

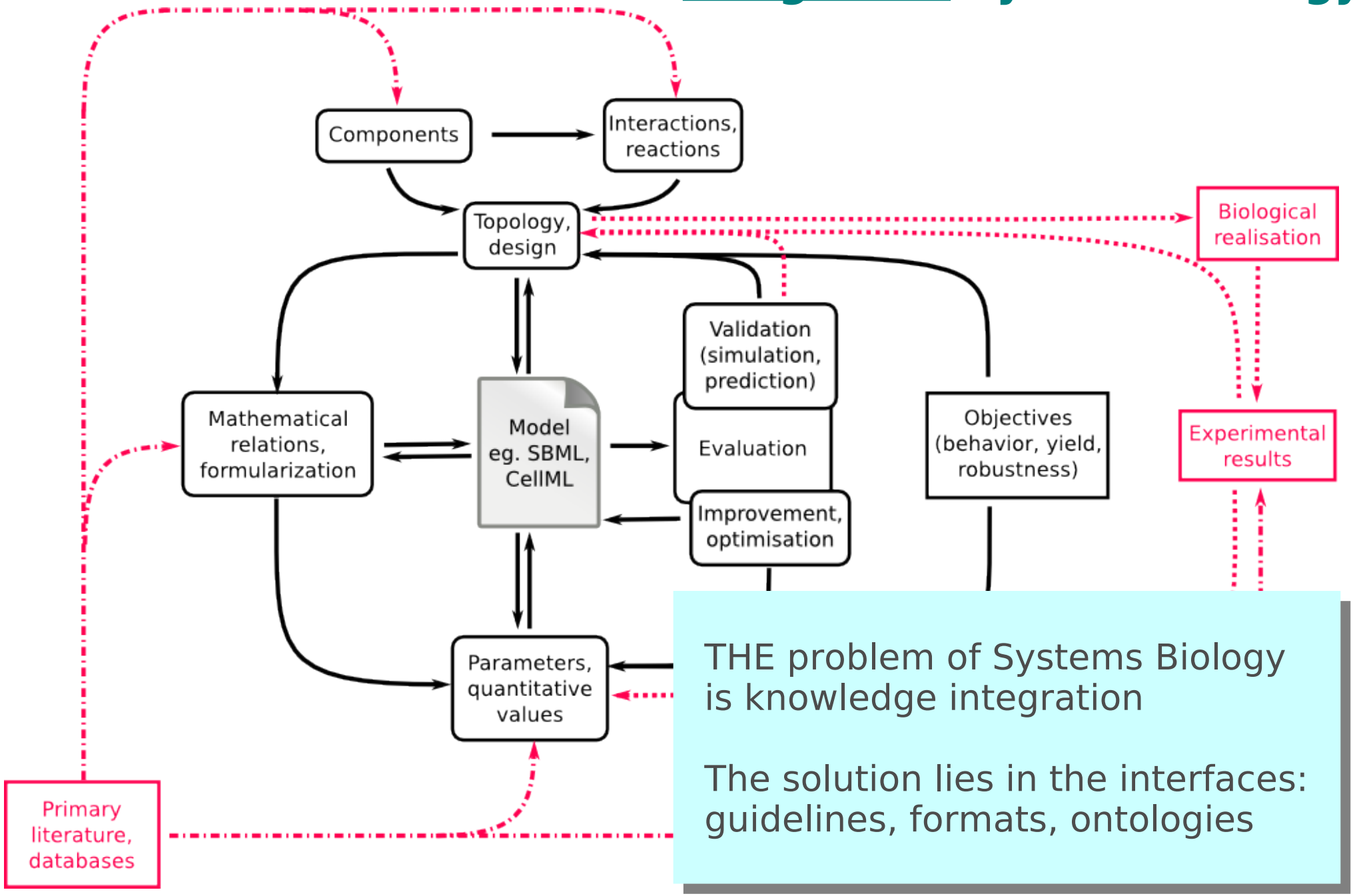
Model life-cycle



Integrative Systems Biology



Integrative Systems Biology



THE problem of Systems Biology is knowledge integration

The solution lies in the interfaces: guidelines, formats, ontologies

Table 1. Kinetic equations governing the cyclin–cdc2 cycle in Fig. 1

$$
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d[\mathrm{C2}]/dt &= k_6[\mathrm{M}] - k_8[\sim P][\mathrm{C2}] + k_9[\mathrm{CP}] \\
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d[\mathrm{Y}]/dt &= k_1[\mathrm{aa}] - k_2[\mathrm{Y}] - k_3[\mathrm{CP}][\mathrm{Y}] \\
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???

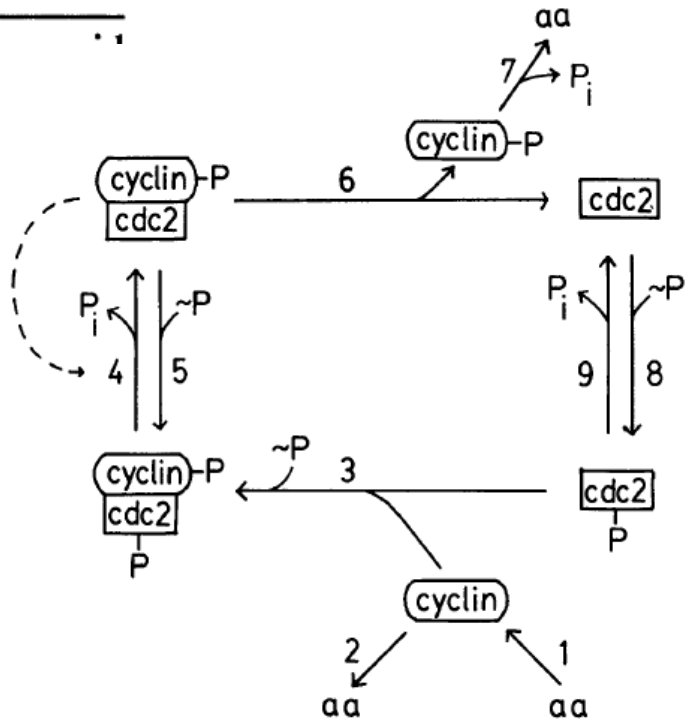

FIG. 1. The relationship between cyclin and cdc2 in the cell cycle. In step 1, cyclin is synthesized *de novo*. Newly synthesized

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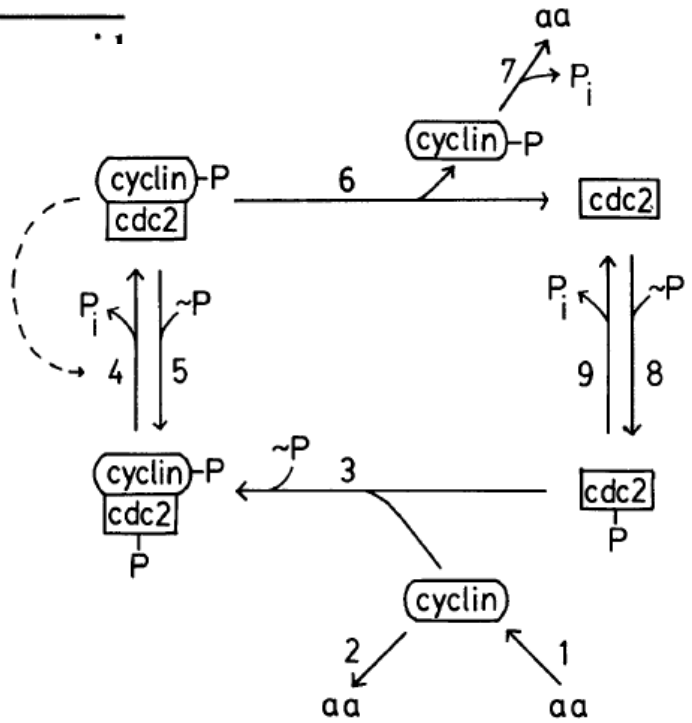
Not a bimolecular interaction



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Understanding models in biology

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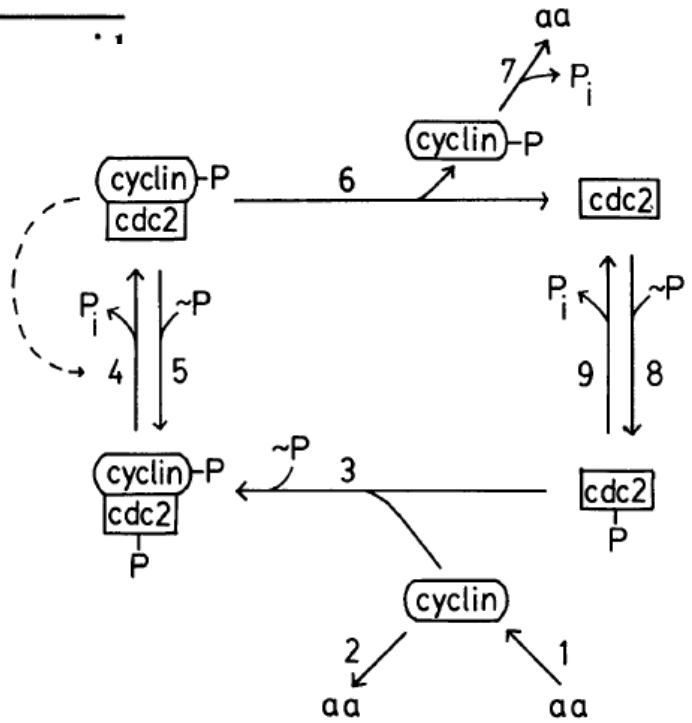
Not a bimolecular interaction

Not a single reaction



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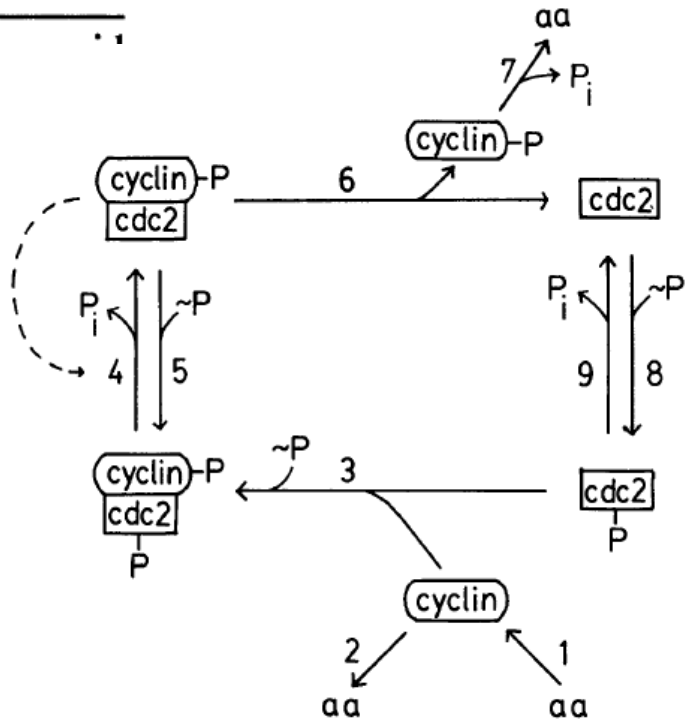
Not a bimolecular interaction

Not a single reaction

complexes



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Understanding models in biology

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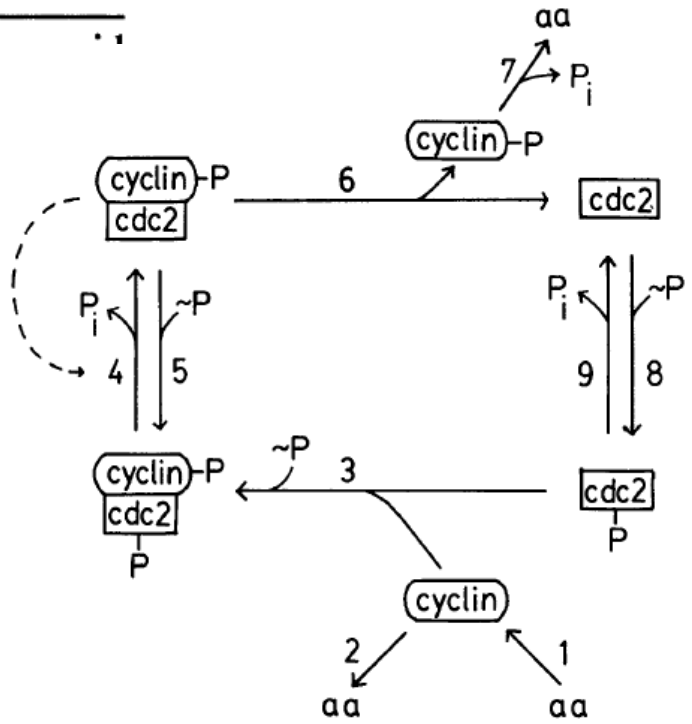
Not a bimolecular interaction

Not a single reaction

complexes

phosphorylated and non-phosphorylated forms of the “same” entity



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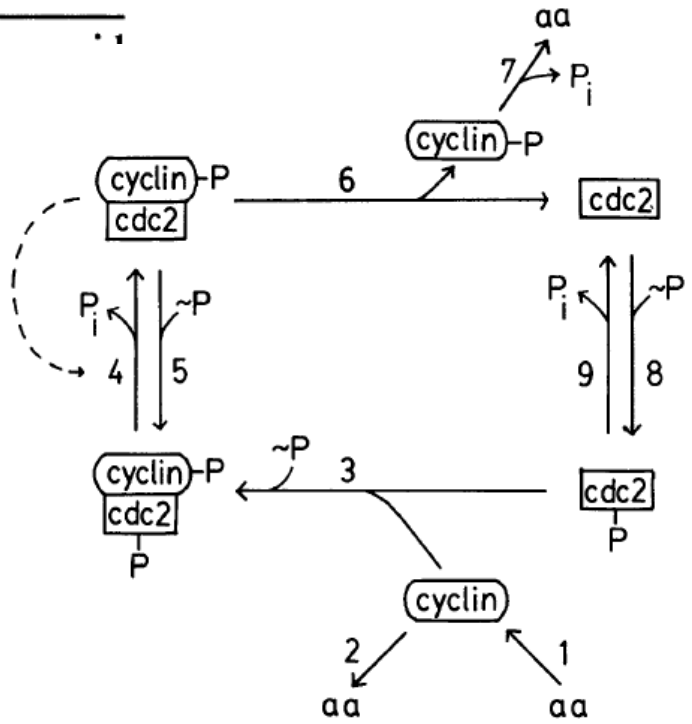
Not a bimolecular interaction

Not a single reaction

complexes

Why not C2P?

phosphorylated and non-phosphorylated forms of the “same” entity



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Entity-based Vs. process-based modeling

- Traditional mathematical modeling in biochemistry is oriented toward the evolution of reacting entities (ODEs).
- Process-based modeling is focusing on reactions, events and relationships. The evolution of entities emerges from all the processes they are involved in.
- Process-based models can be simulated with different approaches. This includes hybrid methods, where different processes are simulated using different algorithms (e.g. discrete and continuous).
- Process-based models lend themselves to modularity and encapsulation. Therefore they are easier to maintain, modify and re-use.

“Most often systems biologists use ODE-based models, that are not realistic, cannot scale and cannot be simulated by discrete methods”

Typical quote from someone wanting to sale a new discrete method (e.g. Process-algebra, rule-based models etc.)

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Typical quote from someone wanting to sale a new discrete method (e.g. Process-algebra, rule-based models etc.)

The design of most models in Systems Biology is actually process-based! ODEs are reconstructed at runtime

SBML.org — The Systems Biology Markup Language

The **Systems Biology Markup Language** (**SBML**) is a computer-readable format for representing models of biological processes. It's applicable to simulations of metabolism, cell-signaling, and many other topics. SBML has been evolving since mid-2000 thanks to an international community of software developers and users. This website is the global portal for the SBML effort; here you can find information about all aspects of SBML.

For the curious

What *is* SBML? Read our **basic introduction** and then perhaps browse the **mailing lists** to get a sense for what's currently going on in the world of SBML.

For modelers

Are you looking for ready-to-run software that supports SBML? The **SBML Software Guide** lists over **170** systems today. Are you instead looking for ready-to-use models? Visit the **BioModels Database**, where you can find hundreds!

For software developers

Are you interested in developing SBML support for 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**, an API library supporting many programming languages.

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 call attention to your project's support of SBML by displaying the **SBML logo**.

SBML News

More errata for L2v4r1
(11 July '09) A few more issues have been noted recently on the SBML Level 2 Version 4 **errata list**.

SBML Level 3 plans updated
(8 Jul. '09) The SBML Editors have updated the **plans for SBML Level 3 Core** and are seeking feedback.

SBML FAQ updated
(1 Jul. '09) FAQ item #3.6 now features an expanded explanation of SBML Level 2 annotations.

Older news ...

Community News

BioModels Database rel. 14
(16 Jun.'09) **BioModels Database**, a free database of published models, now contains 216 curated and 196 uncurated models.

MCSim supports SBML
(25 Apr.'09) **GNU MCSim** lets you design statistical or simulation models & perform Bayesian inference.

Pathway Tools workshop
(24 Apr.'09) Tutorial & workshop on SRI's Pathway Tools and BioCyc database in August '09.

Older news ...

None of this would be possible without the support of multiple agencies and organizations. Visit our **acknowledgements** page to learn about the visionary funding agencies that have backed SBML over the years.

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        </kineticLaw>
      </reaction>
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```

>170 tools supporting SBML

SBML Software Matrix

This matrix provides an at-a-glance summary of software known to us to provide some degree of support for reading, writing, or otherwise working with SBML. The columns' meanings are explained below. For a list of longer descriptions grouped into themes, please see our **SBML Software Summary** page.

	Capabilities					Frameworks							API	Dep.	Platforms	SBML		Availabil.		
	Creation	Simulation	Analysis	Database	Utility	ODE	DAE	PDE	Stochastic	Events	Logical	Other				Import	Export	Open source	Academic use	Commercial use
acslXtreme	•														W	•			$	$
ALC	•					•	•		•			•			L, W, M, B		•	•	F	F
Asmparts	•				•	•									L,W	•	•	•	F	F
Antimony	•				•								C, C++		L, W, M	•	•	•	F	F
AutoSBW			•			•							SBW	SBW	L, W, M	•	•	•	F	F
AVIS												•		various	L	•		•	F	F
BALSA	•													Sigtran						
BASIS	•	•		•					•	•			WS		B	•	•	•	F	F
BetaWB	•	•	•						•	•					L,W,M		•		F	F
BiNoM	•		•		•							•			L, W, M	•	•	•	F	F
BiNoM Cytoscape Plugin	•		•		•							•		Cytoscape	L, W, M	•	•	•	F	F
BIOCHAM		•			•	•									L,W,M		•	•	F	F
BioCharon	•	•	•		•	•								CHARON						
Biological Networks	•		•		•										L,W,M	•	•		F	$
BioCyc				•													•		F	$
BioGrid																				

The columns of this table should be read in the following way:

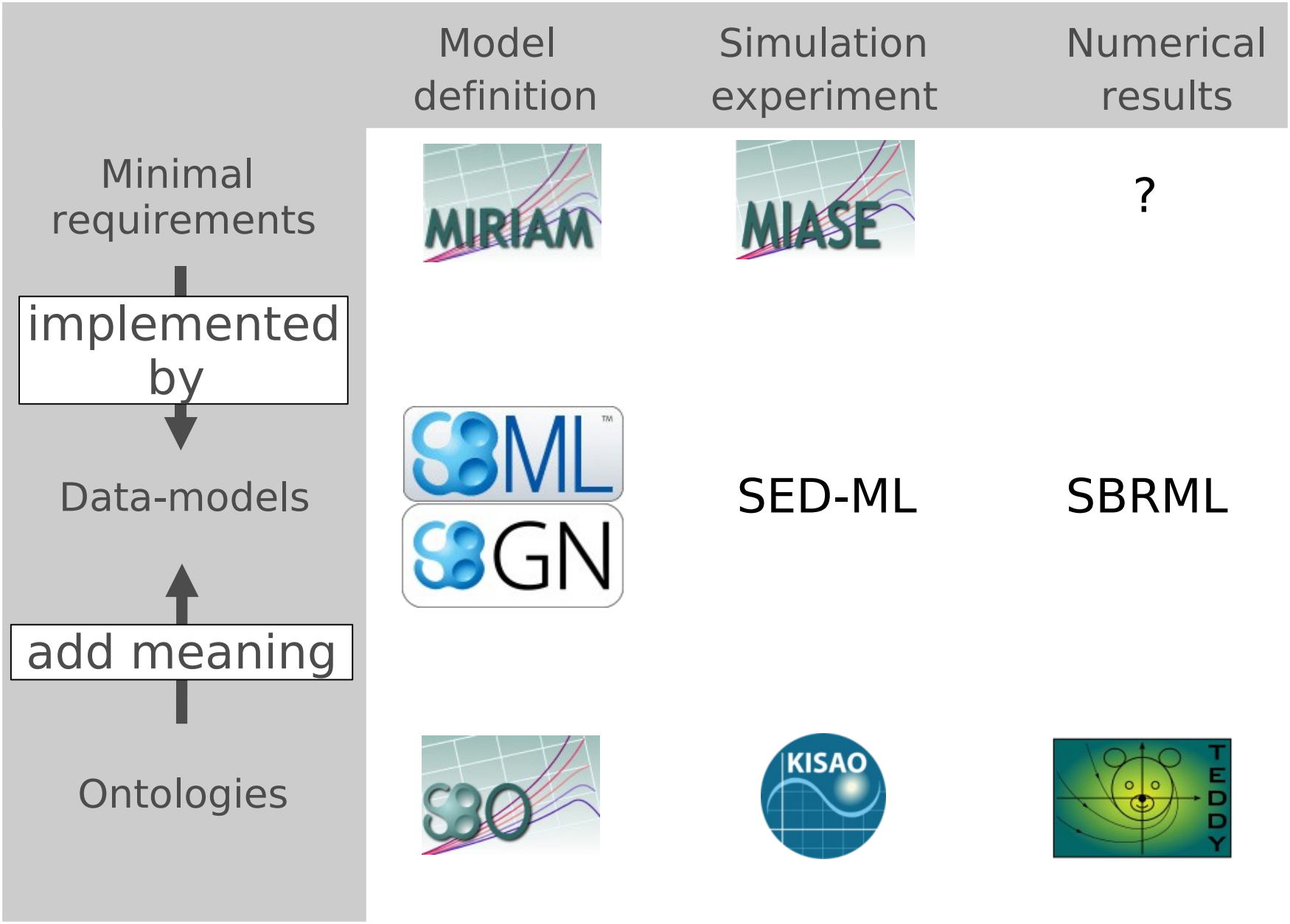
- *Capabilities* summarizes the facilities that a package provides by itself (i.e., without invoking another package) for working with SBML: "Creation" = creating/editing models, "Simulation" = performing time-series simulation of models, "Analysis" = analyzing models (e.g., sensitivity analysis, flux-balance analysis, etc.), "Database" = providing a database of models, and "Utility" = providing other utility functions (e.g., translating SBML to/from other formats).
- *Frameworks* summarizes the modeling frameworks supported by a package, regardless of whether the package

Is SBML enough? What's missing?

- An SBML model lists participants, but does not identify them.
- An SBML model contains mathematical expressions, but does not tell-us what they “mean”, and how they are derived.
- An SBML model constructed for a certain modelling approach cannot be used straight-away within another modelling framework.

⇒ **SBML models cannot be easily searched**
SBML models cannot be easily converted
SBML models cannot be easily merged

Complete mosaic of standards



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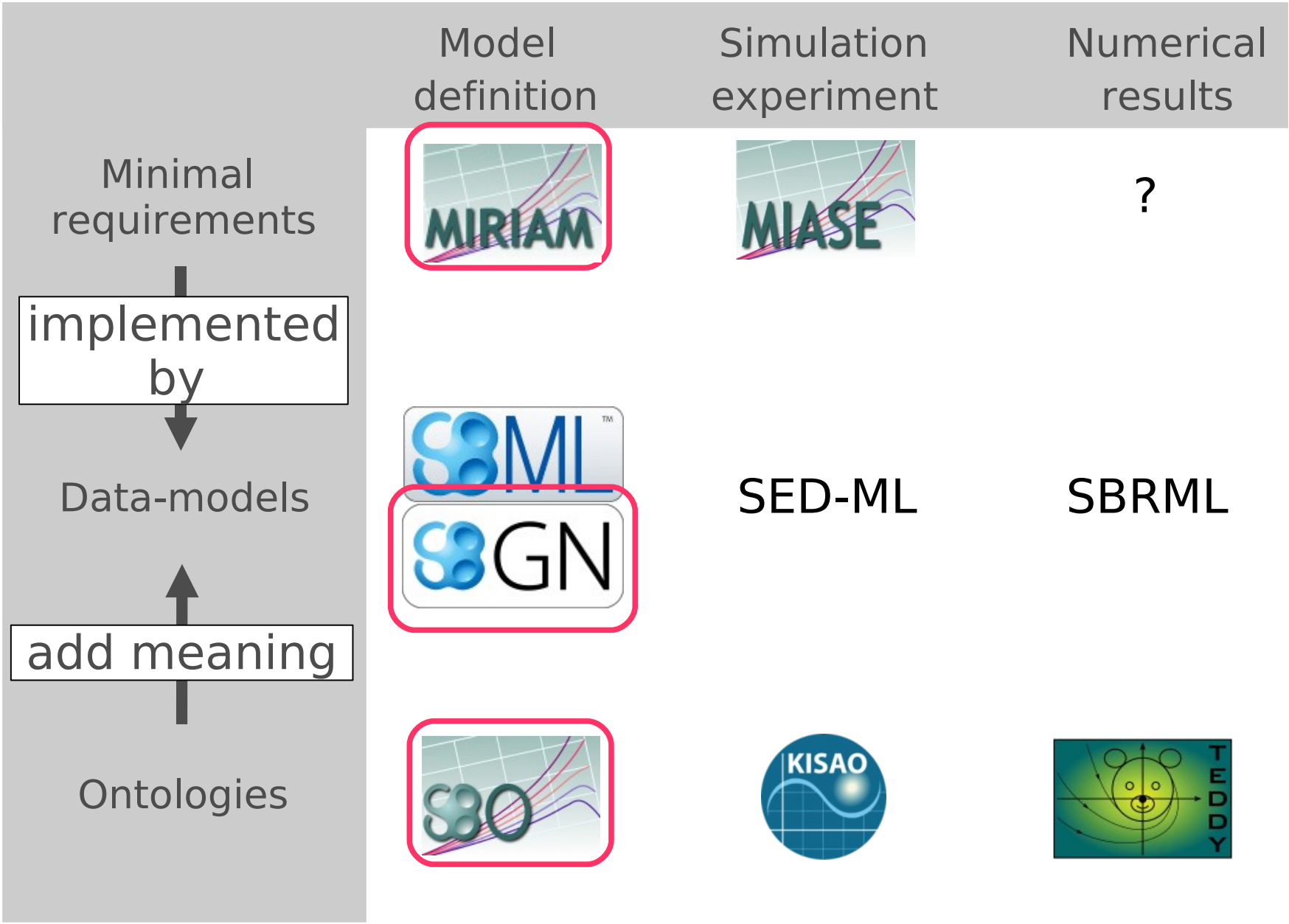
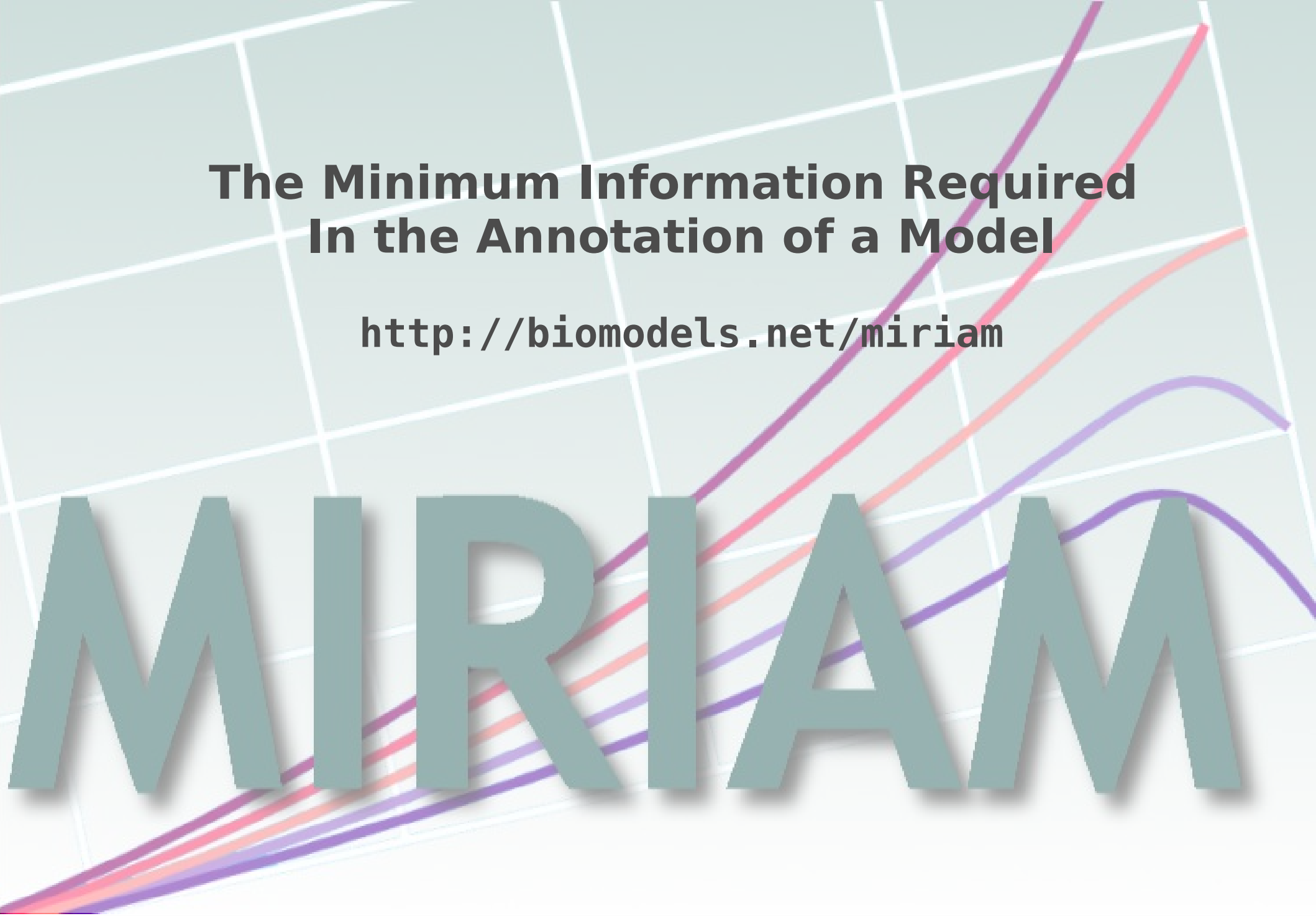


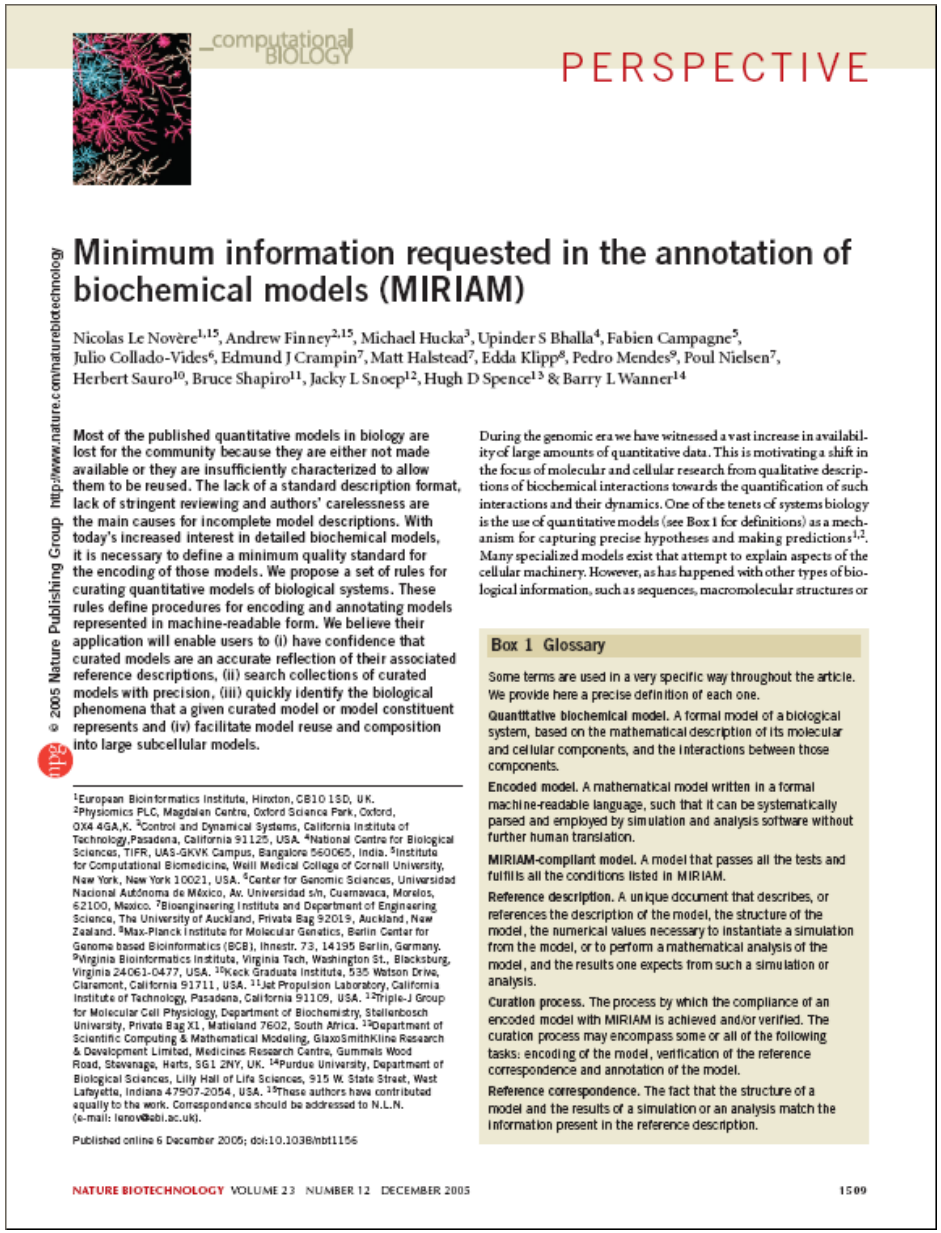
The Minimum Information Required In the Annotation of a Model

http://biomodels.net/miriam



MIRIAM guidelines

- Reporting guidelines for curation of quantitative models
  - Specifically about encoding & annotation
  - Limited for the moment to models that can be numerically evaluated
- Not specific to SBML; applicable to any structured model format



_computational BIOLOGY

PERSPECTIVE

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

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

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

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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

Box 1 Glossary

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

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

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

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

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

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

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

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:

- unambiguously identify model components
  - improve understanding the structure of the model
  - allow easier comparison of different models
  - ease the integration of models
- allow efficient search strategies
- 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

Why annotations should not be raw text

- EMBL bank version 45 (04-DEC-1995):
  /db_xref="PID:g984120"
- EMBL bank version 47 (07-JUN-1996):
  /db_xref="PID:g984120"
  /db_xref="SWISS-PROT:P49581"
- EMBL bank version 60 (03-SEP-1999):
  /db_xref="SWISS-PROT:P49581"
  /protein_id="CAA58766.1"
- EMBL bank version 73 (30-NOV-2002):
  /db_xref="SWISS-PROT:P49581"
  /protein_id="CAA58766.1"
  /db_xref="GOA:P49581"
- EMBL bank version 79 (08-JUN-2004):
  /db_xref="UniProt/Swiss-Prot:P49581"
  /protein_id="CAA58766.1"
  /db_xref="GOA:P49581"
- EMBL bank version 84 (12-SEP-2005):
  /db_xref="UniProtKB/Swiss-Prot:P49581"
  /protein_id="CAA58766.1"
  /db_xref="GOA:P49581"

Why annotations should not be uncontrolled XML

Extracted from a BioPAX version of "Signaling by EGFR":

```
<bp:unificationXref rdf:ID="UniProt_P01133">
    <bp:DB rdf:datatype="http://www.w3.org/2001/XMLSchema#string">UniProt</bp:DB>
    <bp:ID rdf:datatype="http://www.w3.org/2001/XMLSchema#string">P01133</bp:ID>
</bp:unificationXref>
```

What is “UniProt”?

- CGD is the official acronym for:
  - Candida Genome Database
  - Cattle Genome Database
  - Comparative Genomics Database
  - Chronic Granulomatous Disease

Why annotations should not be uncontrolled URLs

http://srs6.ebi.ac.uk/srs6bin/cgi-bin/wgetz?[swissprot-AccNumber:P01133]+-e

http://www.ebi.uniprot.org/uniprot-srv/uniProtView.do?proteinId=P01133

http://www.ebi.uniprot.org/entry/P01133

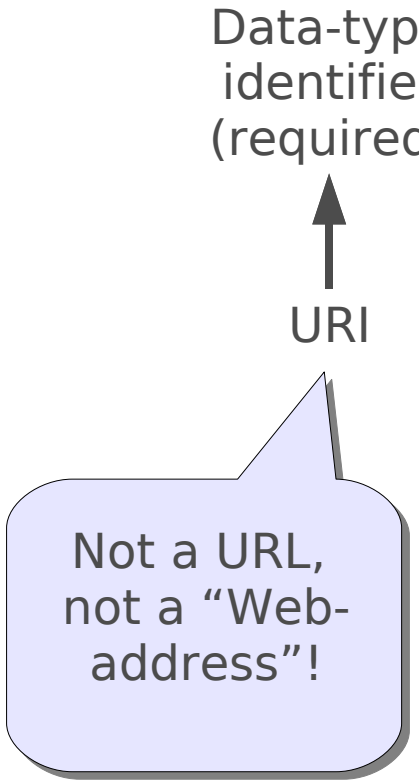
http://www.uniprot.org/uniprot/P01133?proteinId=P01133

http://www.uniprot.org/uniprot/P01133

Characteristics of a useful identifier

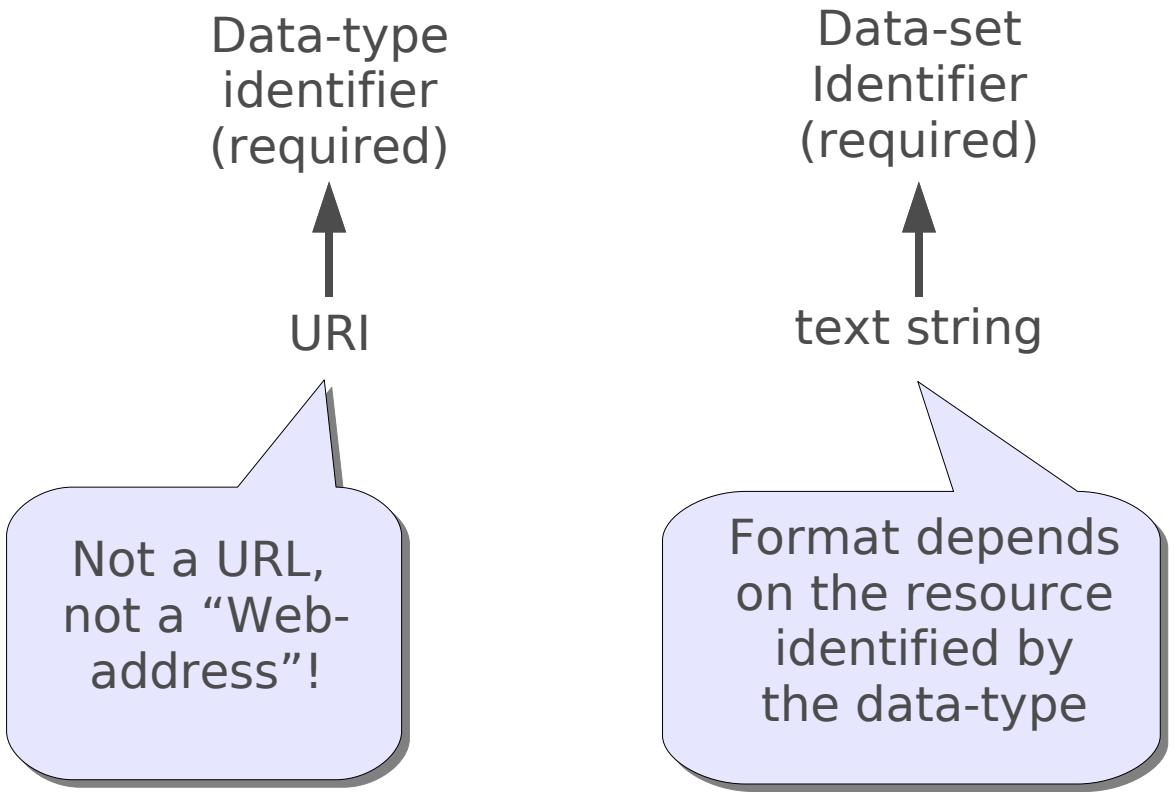
- **Unique**
  an identifier must never be assigned to two different objects;
- **Perennial**
  the identifier is constant and its lifetime is permanent;
- **Standards compliant**
  must conform on existing standards, such as URI;
- **Resolvable**
  identifiers must be able to be transformed into locations of online resources storing the object or information about the object;
- **Free of use**
  everybody should be able to use and create identifiers, freely and at no cost.

MIRIAM annotation

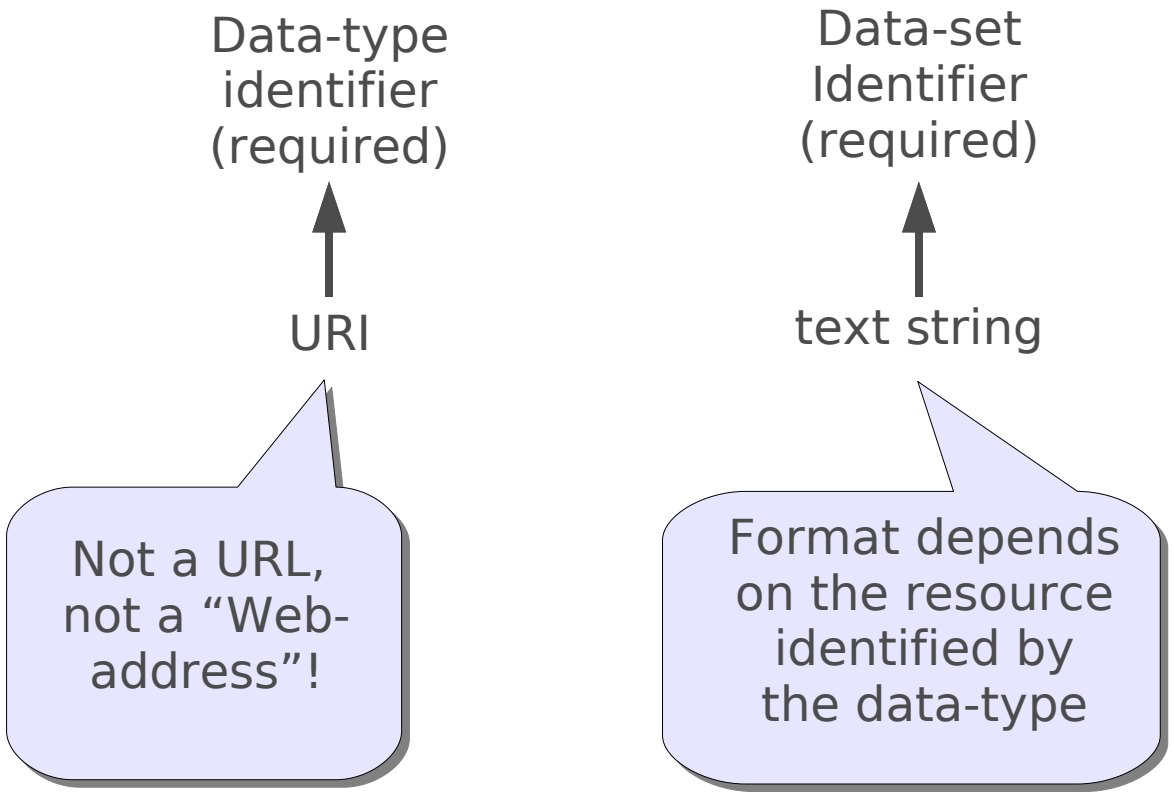


Corresponds to a namespace

MIRIAM annotation



MIRIAM annotation

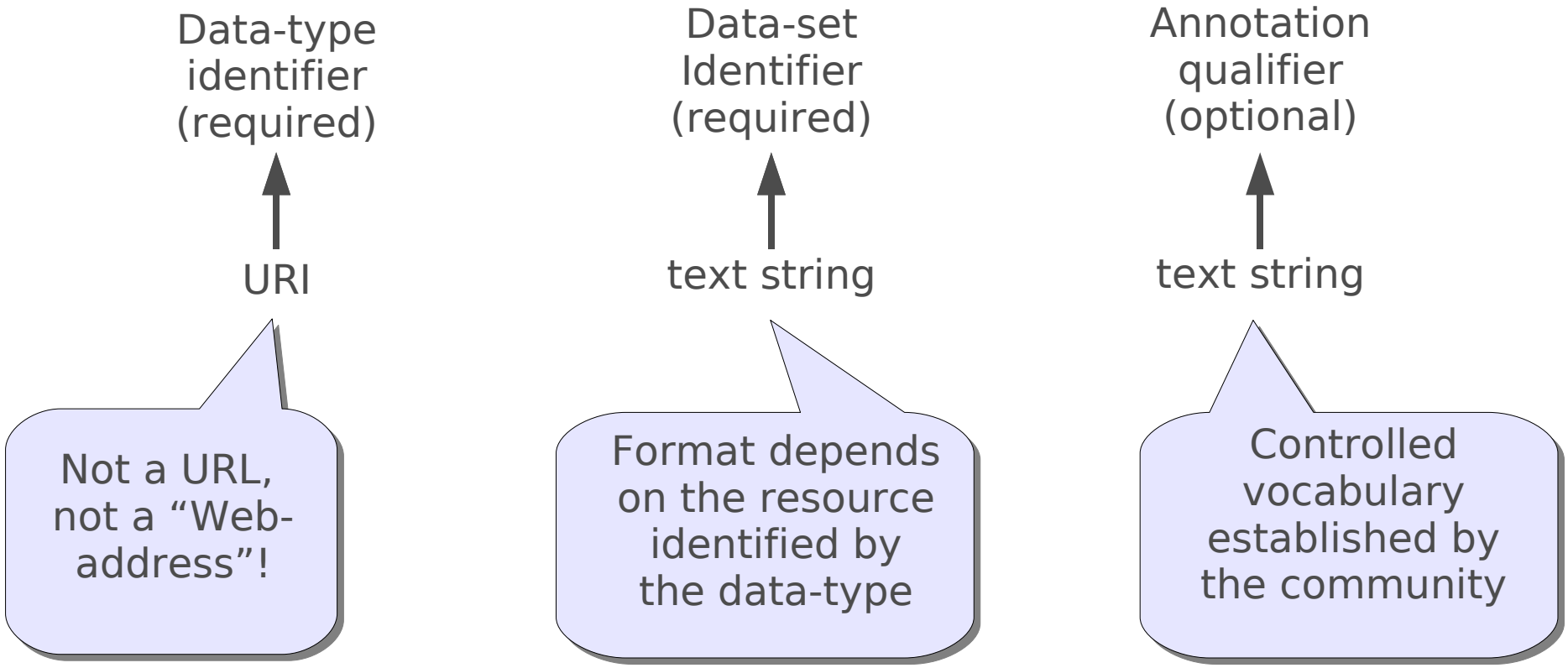


UniProt and P62158 (human calmodulin)
→ urn:miriam:uniprot:P62158

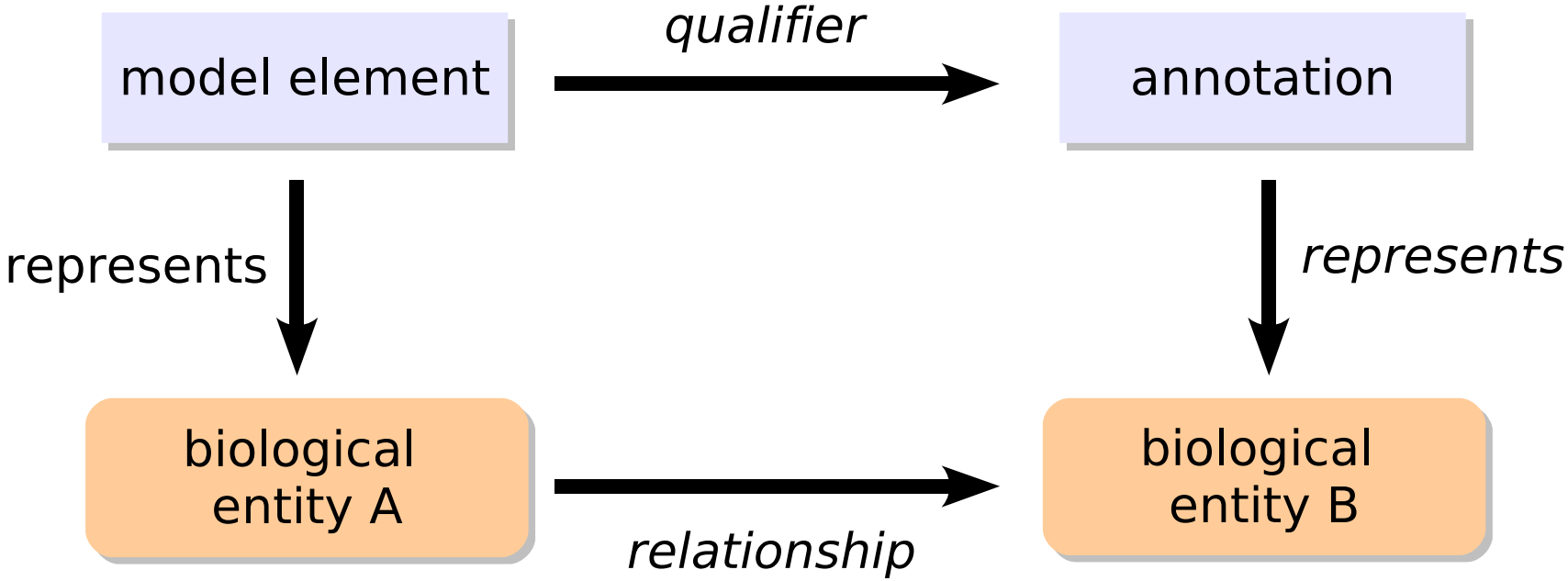
EC code and 1.1.1.1 (alcohol dehydrogenase)
→ urn:miriam:ec-code:1.1.1.1

Gene Ontology and GO:0000186 (activation of MAPKK activity)
→ urn:miriam:obo.go:GO%3A0000186

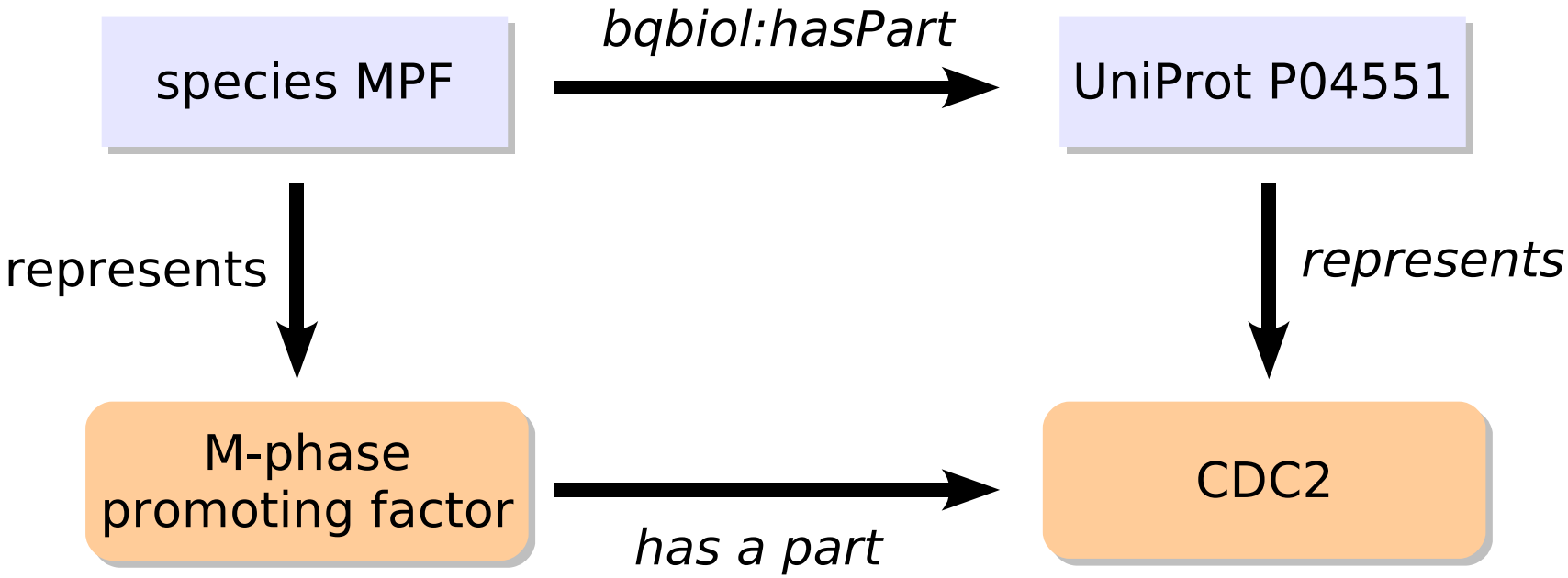
MIRIAM annotation



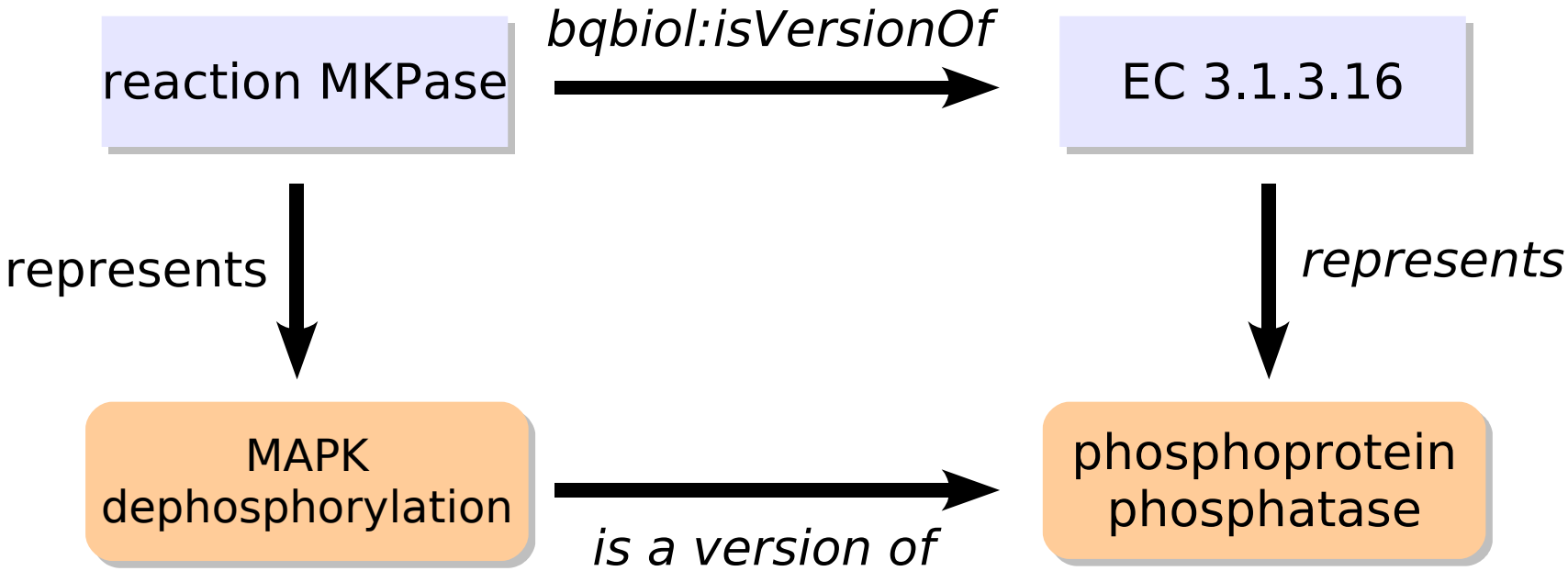
Qualification of annotation



Qualification of annotation



Qualification of annotation



Current BioModels.net Qualifiers

- **bqmodel:is** The modelling object represented by the model component is the subject of the referenced resource.
- **bqmodel:isDescribedBy** The modelling object represented by the component of the encoded model is described by the referenced resource.
- **bqbiol:is** The biological entity represented by the model component is the subject of the referenced resource.
- **bqbiol:hasPart** The biological entity represented by the model component includes the subject of the referenced resource, either physically or logically.
- **bqbiol:isPartOf** The biological entity represented by the model component is a physical or logical part of the subject of the referenced resource
- **bqbiol:isVersionOf** The biological entity represented by the model component is a version or an instance of the subject of the referenced resource.
- **bqbiol:hasVersion** The subject of the referenced resource is a version or an instance of the biological entity represented by the model component.
- **bqbiol:isHomologTo** The biological entity represented by the model component is homolog, to the subject of the referenced resource, i.e. they share a common ancestor.
- **bqbiol:isDescribedBy** The biological entity represented by the model component is described by the referenced resource.

Current BioModels.net Qualifiers

- **bqbiol:encodes** The biological entity represented by the model component encodes, directly or by transitivity the subject of the referenced resource.
- **bqbiol:isEncodedBy** The biological entity represented by the model component is encoded, directly, or by transitivity, by the subject of the referenced resource.
- **bqbiol:occursIn** The biological entity represented by the model component takes place in the subject of the referenced resource.

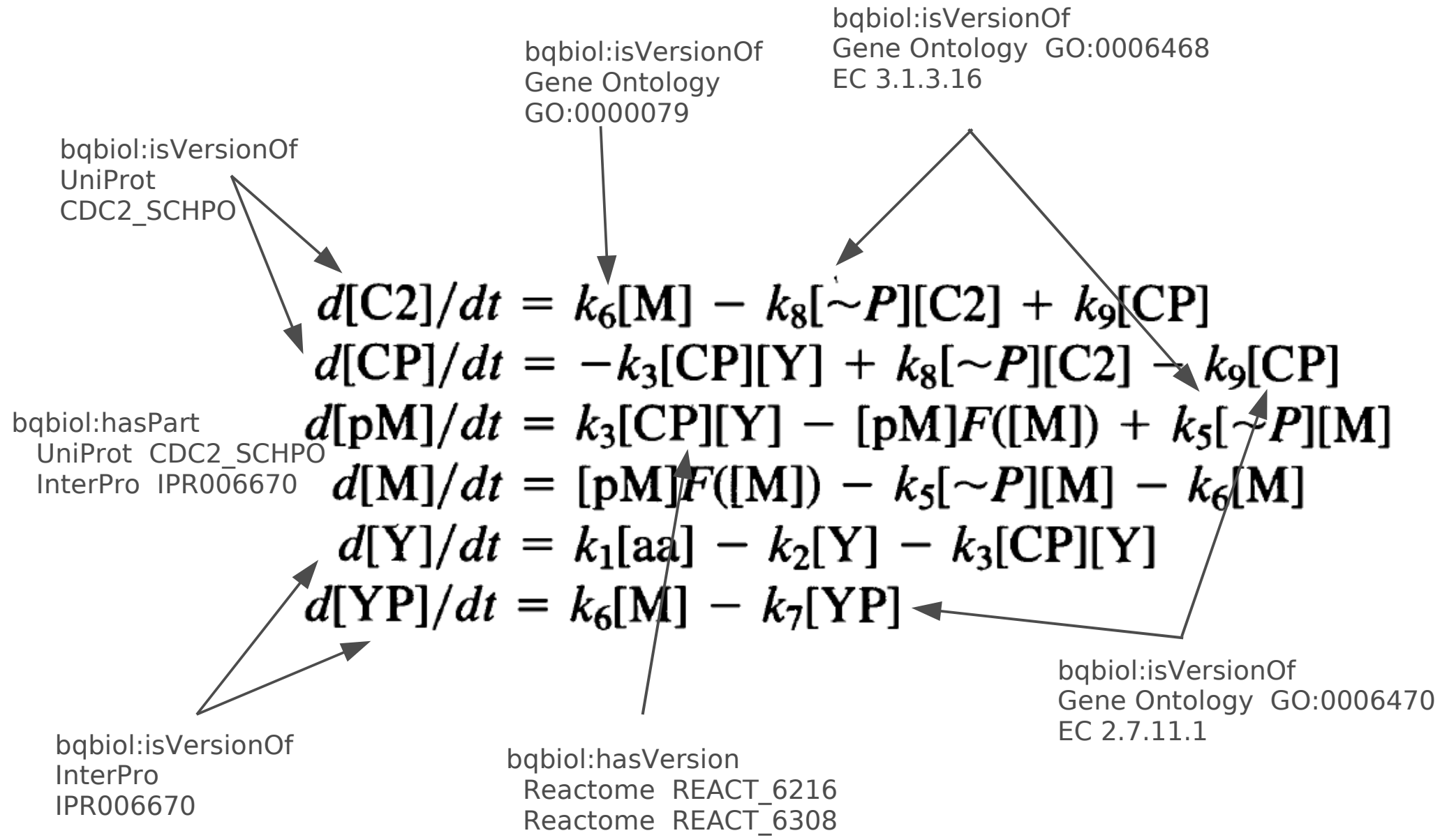
PROPOSED

- **bqbiol:isPropertyOf** The biological entity represented by the model component is a property of the subject of the referenced resource.
- **bqbiol:hasProperty** The subject of the referenced resource is a property of the biological entity represented by the model component .

SBML and MIRIAM

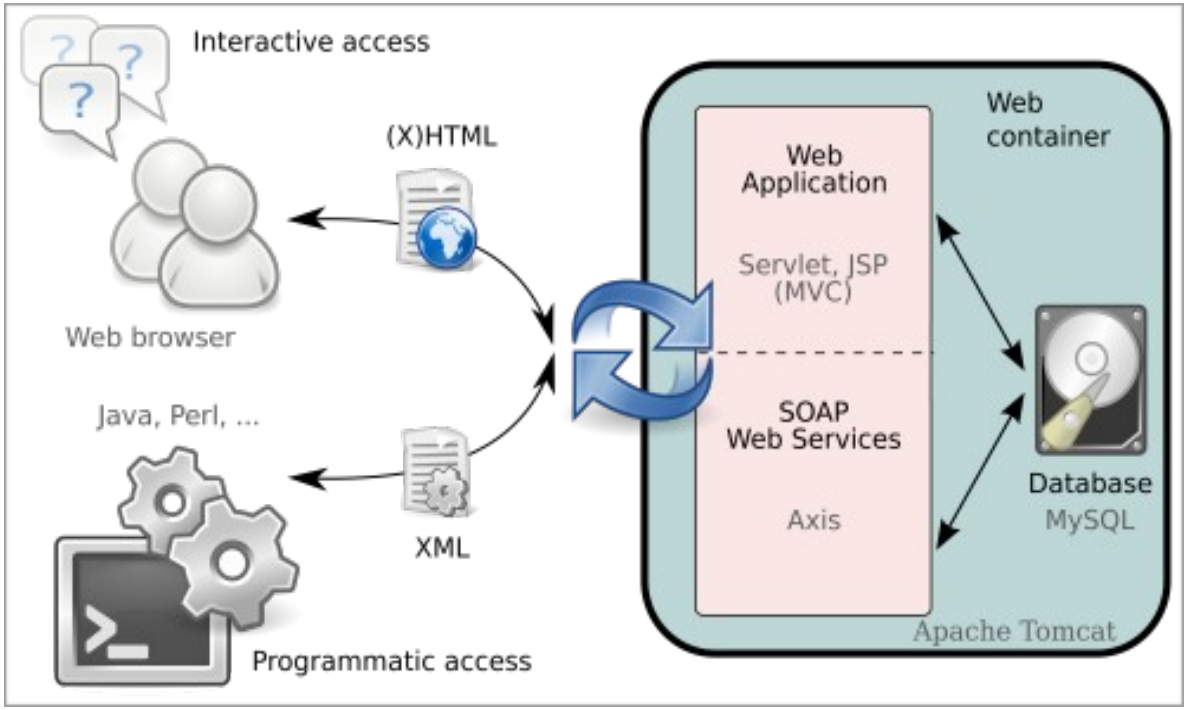
```
<species id="Ca_calmodulin" metaid="cacam">
  <annotation>
    <rdf:RDF
        xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#"
        xmlns:bqbiol="http://biomodels.net/biology-qualifiers/">
      <rdf:Description rdf:about="#cacam">
        <bqbiol:hasPart>
          <rdf:Bag>
            <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>
```

The model revealed



MIRIAM Resources

- **MIRIAM Database**
  Core element of the resource, storing all the information about the data-types and associated information;
- **MIRIAM Web Services**
  SOAP-based application programming interface (API) for querying MIRIAM Database
- **MIRIAM Library**
  Library to use MIRIAM Web Services
- **MIRIAM Web Application**
  Interactive web interface for browsing and querying MIRIAM Database, and submit or edit data-types.



- Browse
- Search
- Tags
- Query services
- Submit new
- Export
- Sign In

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

- MIRIAM on SourceForge

- Support
- Contact

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.

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

Web Services

Programmatic access to the data is available via Web Services (based on Apache Axis and SOAP messages). This API permits not only to resolve 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

MIRIAM Resources

Browse the data types

Brief overview of the different data types stored in *MIRIAM Database*.

Next page

Display: 10 | 20 | 30 | All

Name	URI	Definition
3DMET	urn:miriam:3dmet	3DMET is a database collecting three-dimensional structures of natural metabolites.
Aclame	urn:miriam:aclame	ACLAME is a database dedicated to the collection and classification of mobile genetic elements (MGEs) from various sources, comprising all known phage genomes, plasmids and transposons.
ArrayExpress	urn:miriam:arrayexpress	ArrayExpress is a public repository for microarray data, which is aimed at storing MIAME-compliant data in accordance with Microarray Gene Expression Data (MGED) recommendations.
arXiv	urn:miriam:arxiv	arXiv is an e-print service in the fields of physics, mathematics, non-linear science, computer science, and quantitative biology.
BioGRID	urn:miriam:biogrid	BioGRID is a database of physical and genetic interactions in Saccharomyces cerevisiae, Caenorhabditis elegans, Drosophila melanogaster, Homo sapiens, and Schizosaccharomyces pombe.
BioModels Database	urn:miriam:biomodels.db	BioModels Database is a data resource that allows biologists to store, search and retrieve published mathematical models of biological interests.
BRENDA	urn:miriam:brenda	BRENDA is a collection of enzyme functional data available to the scientific community. Data on enzyme function are extracted directly from the primary literature The database covers information on classification and nomenclature, reaction and specificity, functional parameters, occurrence, enzyme structure and stability, mutants and enzyme engineering, preparation and isolation, the application of enzymes, and ligand-related data.
ChEBI	urn:miriam:obo.chebi	Chemical Entities of Biological Interest (ChEBI) is a freely available dictionary of molecular entities focused on 'small' chemical compounds.
CluSTr	urn:miriam:clustr	The CluSTr database offers an automatic classification of UniProt Knowledgebase and IPI proteins into groups of related proteins. The clustering is based on analysis of all pairwise comparisons (Smith-Waterman) between protein sequences.
Database of Interacting Proteins	urn:miriam:dip	The database of interacting protein (DIP) database stores experimentally determined interactions between proteins. It combines information from a variety of sources to create a single, consistent set of protein-protein interactions
DOI	urn:miriam:doi	The Digital Object Identifier System is for identifying content objects in the digital environment.
Ensembl	urn:miriam:ensembl	Ensembl is a joint project between EMBL - EBI and the Sanger Institute to develop a software system which produces and maintains automatic annotation on selected eukaryotic genomes.
Entrez Gene	urn:miriam:entrez.gene	Entrez Gene is the NCBI's database for gene-specific information, focusing on completely sequenced genomes, those with an active research community to contribute gene-specific information, or those that are scheduled for intense sequence analysis.
Enzyme Nomenclature	urn:miriam:ec-code	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.
Evidence Code	urn:miriam:obo.eco	Evidence codes can be used to specify the type of supporting evidence for a piece of knowledge. This allows inference of a 'level of support' between an entity and an annotation made to an entity.
FlyBase	urn:miriam:flybase	FlyBase is the database of the Drosophila Genome Projects and of associated literature.
FMA	urn:miriam:obo.fma	The Foundational Model of Anatomy Ontology (FMA) is a biomedical informatics ontology. It is concerned with the representation of classes or types and relationships necessary for the symbolic representation of the phenotypic structure of the human body. Specifically, the FMA is a domain ontology that represents a coherent body of explicit declarative knowledge about human anatomy.
Gene Ontology	urn:miriam:obo.go	The Gene Ontology project provides a controlled vocabulary to describe gene and gene product attributes in any organism.

requirements for a MIRIAM-compliant data-type

- **Open access**
  Anybody can access any public data without restriction (no commercial licence; no login page etc.)
- **Atomicity**
  The granularity of the data distributed has to be appropriately selected (A database of “reactions” distributes reactions and not pathways) and consistent (e.g. classes or instances but not classes AND instances)
- **Identifier**
  An atomic data is associated to a unique and perennial identifier
- **Community recognition**
  The resource has to be “recognised” by the corresponding experimental community, be reasonably supported etc

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
URIs		
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+$
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

Resources health check (ALL - 107)

Up | Down | Probably Up | Unknown | All

Resource	Data type	State	Uptime
MIR:00100095	3DMET	up	98%
MIR:00100091	Aclame	up	98%
MIR:00100061	ArrayExpress	probably up	100%
MIR:00100060	arXiv	up	100%
MIR:00100008	BIND	unknown	0%
MIR:00100086	BioGRID	up	99%
MIR:00100006	BioModels Database	up	98%
MIR:00100107	BioModels Database	unknown	0%
MIR:00100101	BRENDA	unknown	0%
MIR:00100009	ChEBI	up	100%
MIR:00100030	CluSTr	up	67%
MIR:00100072	Database of Interacting Proteins	up	99%
MIR:00100010	DOI	up	100%
MIR:00100065	DOI	up	99%
MIR:00100011	Ensembl	up	54%
MIR:00100099	Entrez Gene	unknown	0%
MIR:00100001	Enzyme Nomenclature	up	99%
MIR:00100002	Enzyme Nomenclature	up	100%
MIR:00100003	Enzyme Nomenclature	up	100%
MIR:00100083	Evidence Code	up	100%
MIR:00100050	FlyBase	up	100%
MIR:00100097	FMA	up	99%
MIR:00100012	Gene Ontology	up	100%
MIR:00100013	Gene Ontology	up	99%
MIR:00100014	Gene Ontology	up	99%
MIR:00100015	Gene Ontology	up	100%
MIR:00100082	GEO	up	100%
MIR:00100079	HMDB	up	98%
MIR:00100104	HOVERGEN	unknown	0%
MIR:00100016	ICD	probably up	100%
MIR:00100017	IntAct	up	91%
MIR:00100018	InterPro	up	95%
MIR:00100071	IPI	up	100%
MIR:00100092	ISBN	up	100%
MIR:00100093	ISBN	up	98%
MIR:00100021	KEGG Compound	up	100%
MIR:00100035	KEGG Drug	up	100%
MIR:00100100	KEGG Genes	unknown	0%
MIR:00100036	KEGG Glycan	up	100%
MIR:00100020	KEGG Pathway	up	100%
MIR:00100022	KEGG Reaction	up	100%
MIR:00100090	Ligand Expo	up	98%

MIRIAM Resources

Health history: MIR:[redacted]

Health history of: MIR:[redacted]).

2009

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
January																															
February																															
March																															
April																															
May																															
June																															
July																															
August																															
September																															
October																															
November																															
December																															

Legend

- up and responsive
- probably up
- resource down
- state unknown
- no data available

Go back to the resource health details

Tools developing support for MIRIAM identifiers

- Data resources
  - BioModels Database (kinetic models)
  - PSI consortium (protein interactions)
  - Reactome (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)

Tools using MIRIAM identifiers

- Data resources
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  - Reactome (pathways)
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  - libSBML
  - SAINT (semar
  - SBML2BioPAX
  - SBML2LaTeX
  - SBMLeditor (n
  - SemanticSBM merging)
  - Snazer (Netw ations)
  - Systems Biolo (model design and simulation)
  - The Virtual Cell (Simulation)

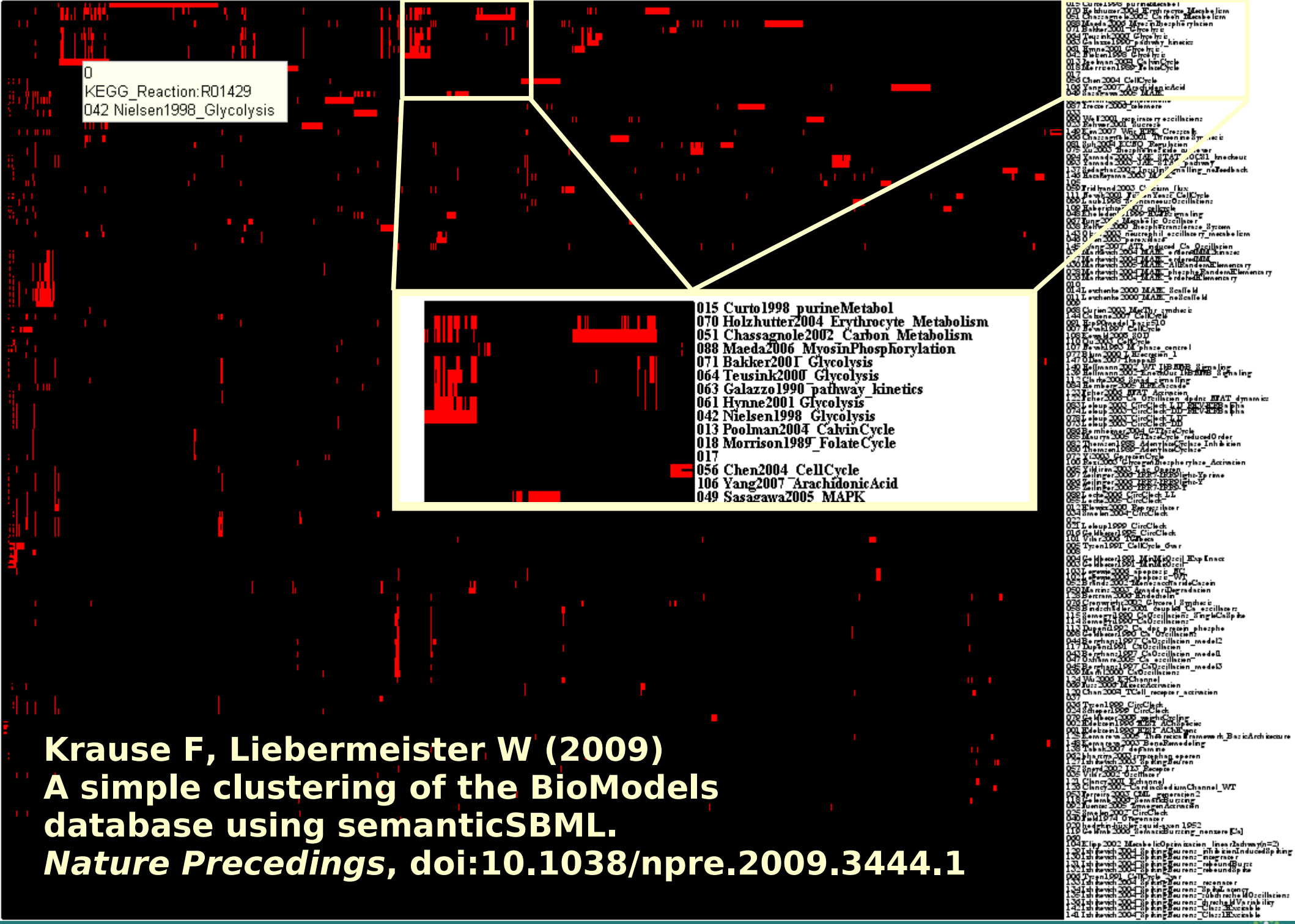
Application: whole-cell metabolic models

- Yeast Metabolic Model
  Herrgård M.J., Swainston N., Dobson P., Dunn W.B., Arga K.V., Arvas M., Blüthgen N., Borger S., Costenoble R, Heinemann M., Hucka M., Le Novère N., Li P., Liebermeister W., Mo M.L., Oliveira A.P., Petranovic D., Pettifer S., Simeonidis E., Smallbone K., Spasic I., Weichart D., Brent R., Broomhead D.S., Westerhoff H.V., Kırdar B., Penttilä M., Klipp E., Palsson B.Ø., Sauer U., Oliver S.G., Mendes P., Nielsen J., Kell D.B. (2008) A consensus yeast metabolic network reconstruction obtained from a community approach to systems biology. *Nature Biotechnology*, 26: 1155-1160.

  2152 species, 1857 reactions, 4861 MIRIAM annotations

- Human Metabolic Model

  4889 species, 8866 reactions, **66968** MIRIAM annotations



Krause F, Liebermeister W (2009)
A simple clustering of the BioModels database using semanticSBML.
***Nature Precedings*, doi:10.1038/npre.2009.3444.1**

Lack of biological semantics in SBML

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What are those?

("who" has been answered by MIRIAM annotations)

Do those affect/are affected by the reaction?

How should-I understand this?

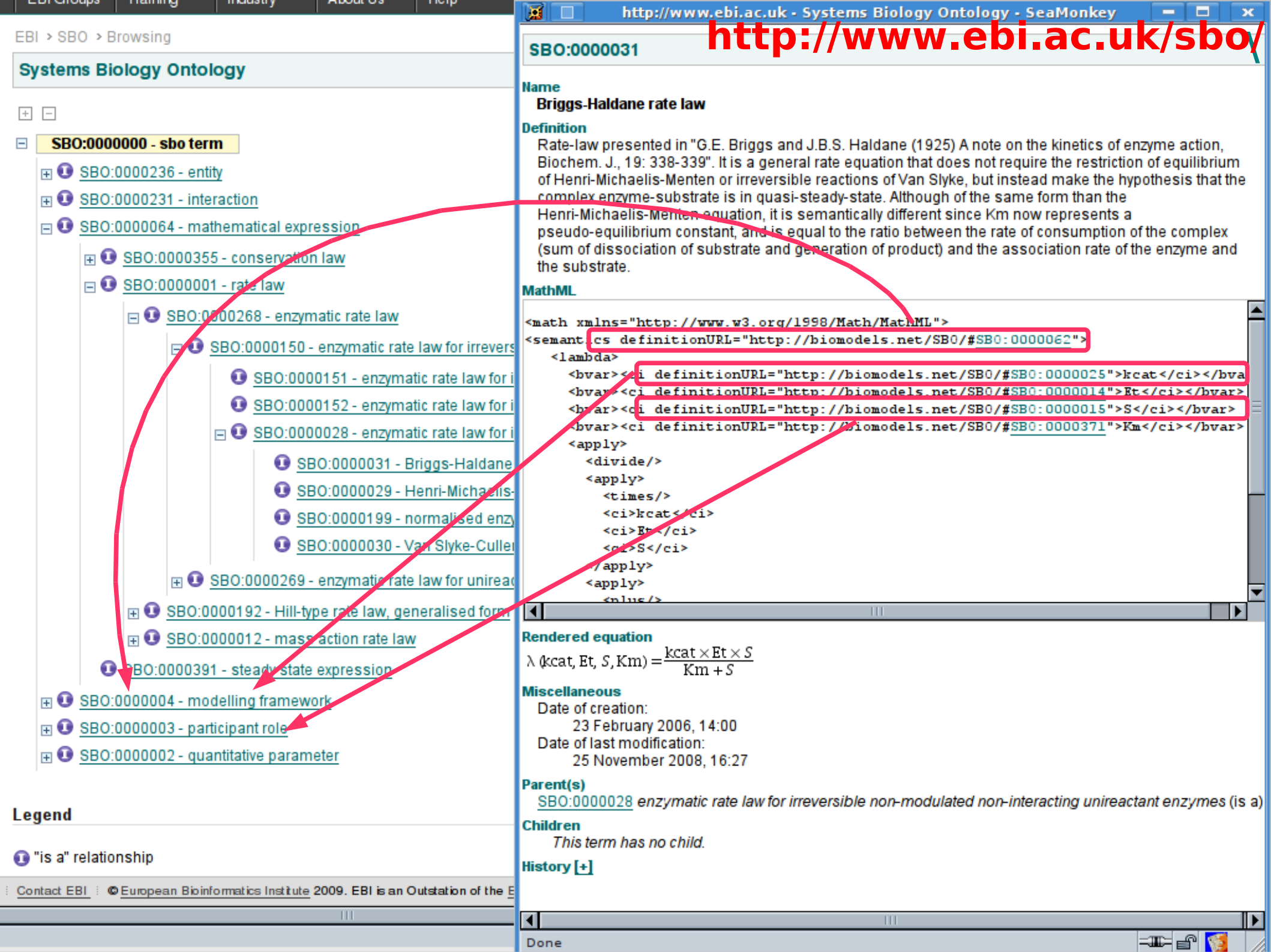
The Systems Biology Ontology

http://biomodels.net/sbo

Systems Biology Ontology vocabularies

- Entities, that is existing objects, whether functional or material, such as "macromolecule", or "channel".
- Roles of reaction participants, including terms like "substrate", "catalyst" etc.
- Parameter used in quantitative models. This vocabulary includes terms like "Michaelis constant", "forward unimolecular rate constant"etc. A term may contain a precise mathematical expression stored as a MathML lambda function. The variables refer to other parameters.
- Mathematical expressions. Examples of terms are "mass action kinetics", "Henri-Michaelis-Menten equation" etc. A term may contain a precise mathematical expression stored as a MathML lambda function. The variables refer to the other vocabularies.
- Modelling framework to precise how to interpret the rate-law. E.g. "continuous modelling", "discrete modelling" etc.
- Event type, such as "catalysis" or "addition of a chemical group".

Le Novère N., Courtot M., Laibe C. Adding semantics in kinetics models of biochemical pathways. *Proc 2nd Intl Symp Experimental Standard Conditions of Enzyme Characterizations* (2007), 137-153. Available at http://www.beilstein-institut.de/index.php?id=196


EBI > SBO > Browsing
Systems Biology Ontology
SBO:0000000 - sbo term
SBO:0000236 - entity
SBO:0000231 - interaction
SBO:0000064 - mathematical expression
SBO:0000355 - conservation law
SBO:0000001 - rate law
SBO:0000268 - enzymatic rate law
SBO:0000150 - enzymatic rate law for irrevers
SBO:0000151 - enzymatic rate law for i
SBO:0000152 - enzymatic rate law for i
SBO:0000028 - enzymatic rate law for i
SBO:0000031 - Briggs-Haldane
SBO:0000029 - Henri-Michaelis-
SBO:0000199 - normalised enzy
SBO:0000030 - Van Slyke-Culle
SBO:0000269 - enzymatic rate law for unireac
SBO:0000192 - Hill-type rate law, generalised form
SBO:0000012 - mass action rate law
SBO:0000391 - steady state expression
SBO:0000004 - modelling framework
SBO:0000003 - participant role
SBO:0000002 - quantitative parameter
Legend
"is a" relationship
Contact EBI
© European Bioinformatics Institute 2009. EBI is an Outstation of the E
http://www.ebi.ac.uk - Systems Biology Ontology - SeaMonkey
http://www.ebi.ac.uk/sbo/
SBO:0000031
Name
Briggs-Haldane rate law
Definition
Rate-law presented in "G.E. Briggs and J.B.S. Haldane (1925) A note on the kinetics of enzyme action, Biochem. J., 19: 338-339". It is a general rate equation that does not require the restriction of equilibrium of Henri-Michaelis-Menten or irreversible reactions of Van Slyke, but instead make the hypothesis that the complex enzyme-substrate is in quasi-steady-state. Although of the same form than the Henri-Michaelis-Menten equation, it is semantically different since Km now represents a pseudo-equilibrium constant, and is equal to the ratio between the rate of consumption of the complex (sum of dissociation of substrate and generation of product) and the association rate of the enzyme and the substrate.
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$\lambda(\mathrm{kcat}, \mathrm{Et}, S, \mathrm{Km}) = \frac{\mathrm{kcat} \times \mathrm{Et} \times S}{\mathrm{Km} + S}$
Miscellaneous
Date of creation:
23 February 2006, 14:00
Date of last modification:
25 November 2008, 16:27
Parent(s)
SBO:0000028 enzymatic rate law for irreversible non-modulated non-interacting unireactant enzymes (is a)
Children
This term has no child.
History [+]
Done

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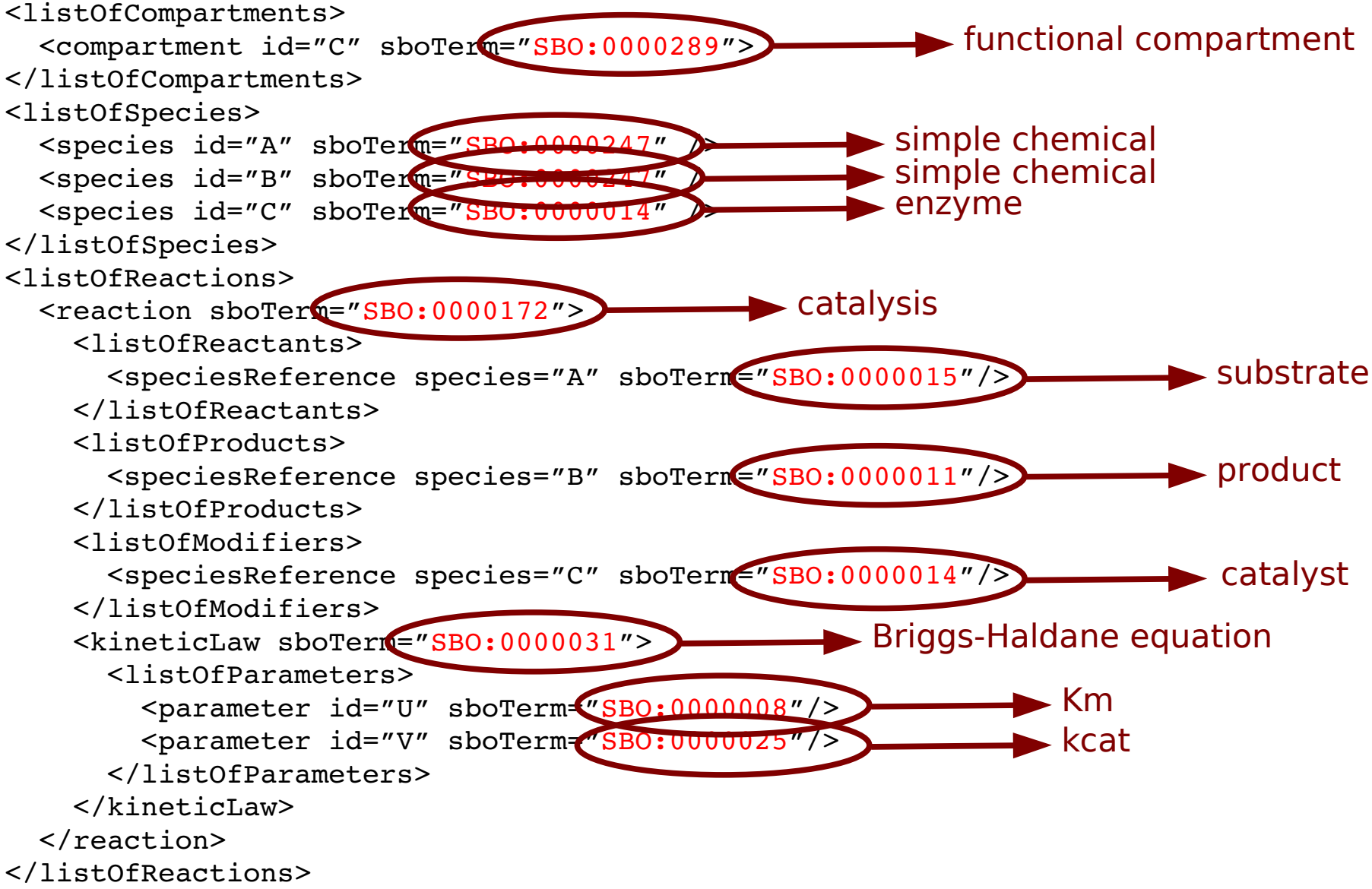
SBML and SBO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simple chemical
simple chemical
enzyme
catalysis
substrate
product
catalyst
Briggs-Haldane equation
Km
kcat

Conversion between modeling frameworks

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```

discrete simulator

$$v1 = \frac{(k_{-1} + V)}{U} \cdot [A] \cdot [C]$$

$$v2 = k_{-1} \cdot [D]$$

$$v3 = V \cdot [D]$$

continuous simulator

$$\nu = \frac{C \cdot V \cdot [A]}{(U + [A])}$$

SBML to BioPAX conversion using SBO

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```

GO annotation

Small molecule

Small molecule

Protein

catalysis

physicalEntityParticipant

physicalEntityParticipant

physicalEntityParticipant

http://www.biopax.org/

SBML to SBGN conversion using SBO

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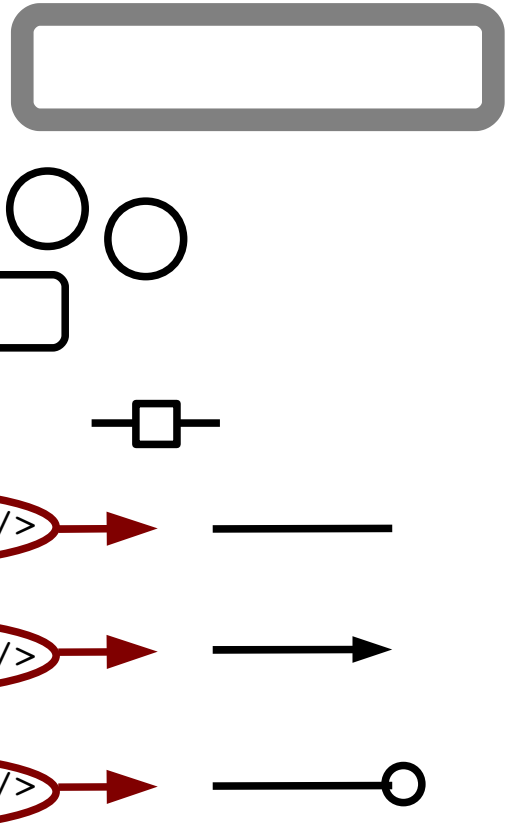

http://www.sbgn.org/

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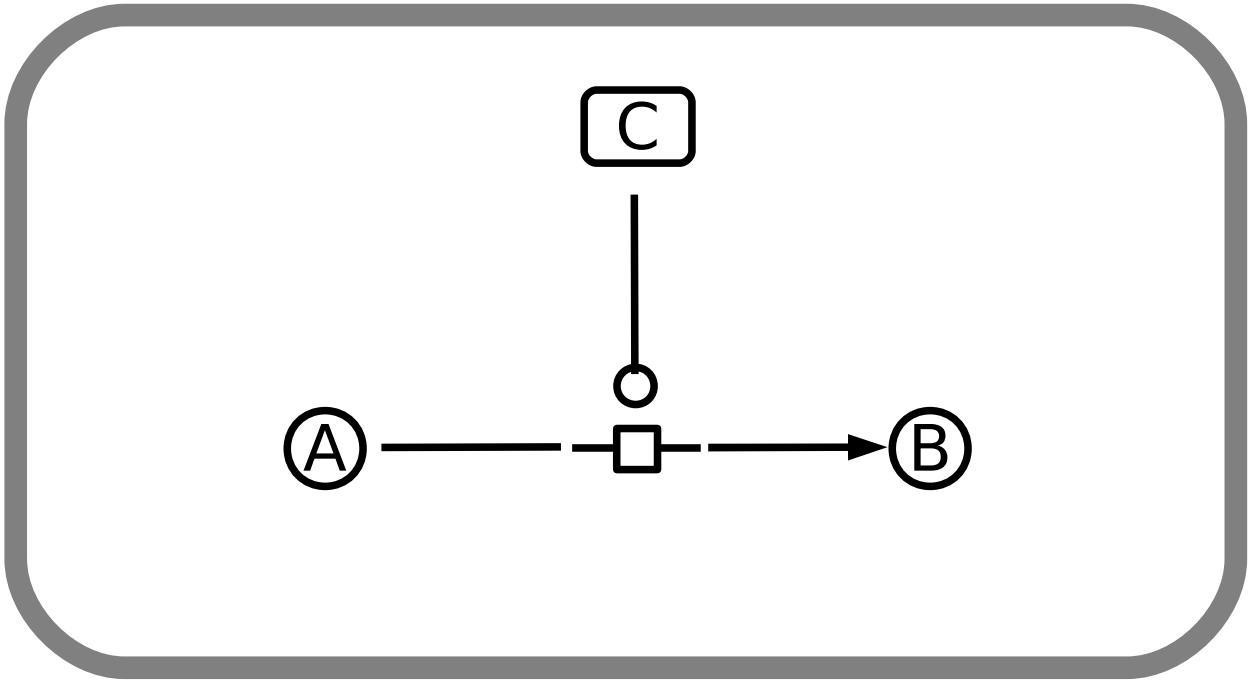


Systems Biology Ontology

https://sourceforge.net/projects/sbo

Tracker: Term request

List of suggested SBO term creations or modifications.

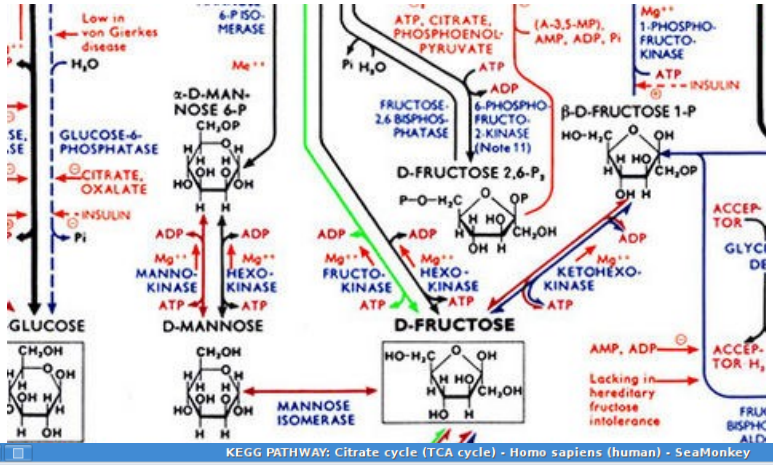
ID	Summary	Status	Opened	Assignee	Submitter	Priority
Assignee: Any **Status:** Any **Category:** Any **Group:** Any **Submitter:** **Keyword:** **Artifact ID:** Filter Reset **Permalink**						
2816343	growth and dilution	Open	2009-07-03	nobody	luen	5
2810944	Genetic enhancement	Open	2009-06-23	nobody	lenov	5
2810943	Genetic suppression	Open	2009-06-23	nobody	lenov	5
2810942	synthetic lethality	Open	2009-06-23	nobody	lenov	5
2799371	error in term 324 and 325	Closed	2009-06-01	nobody	luen	5
2790105	activator	Open	2009-05-11	nobody	wliebermeister	5
2790100	standard chemical potential	Open	2009-05-11	nobody	wliebermeister	5
2790038	products or geometric mean of kinetic constants	Open	2009-05-11	nobody	wliebermeister	5
2714265	Implicit Compartment	Closed	2009-03-26	nobody	fbergmann	5

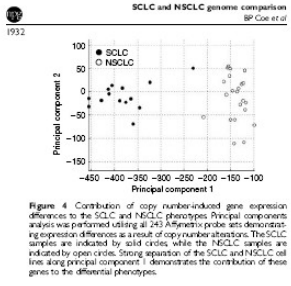
http://www.sbgn.org/

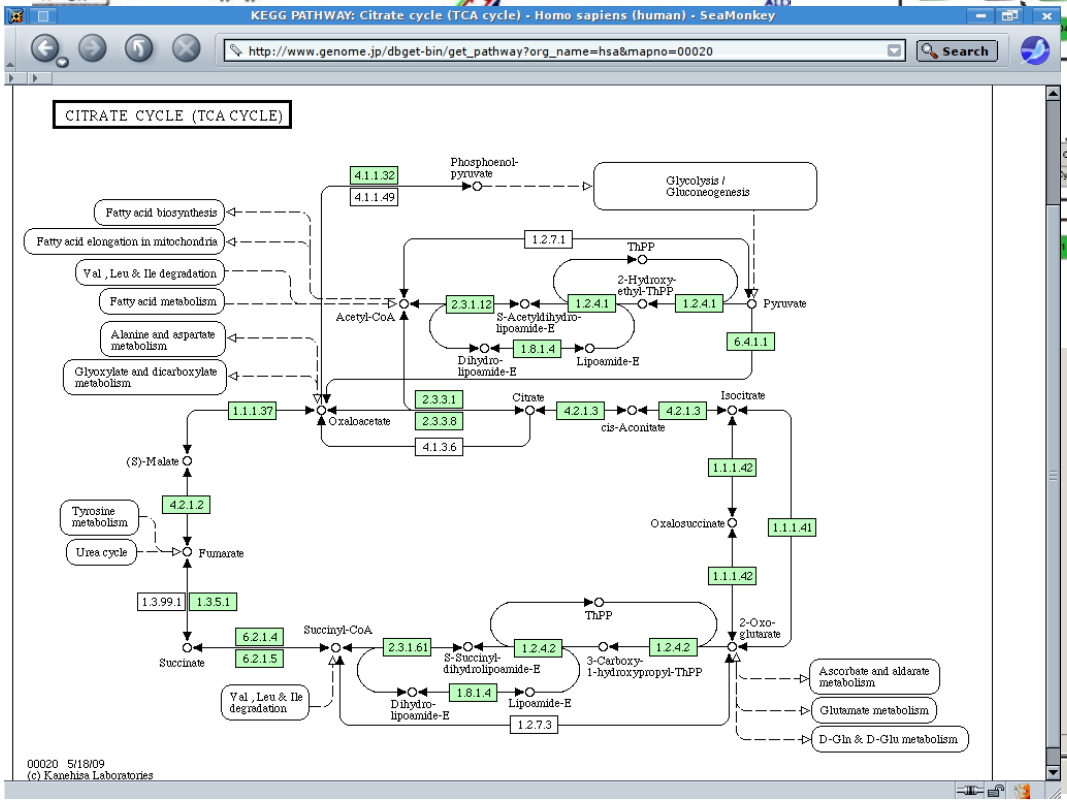
The Systems Biology Graphical Notation

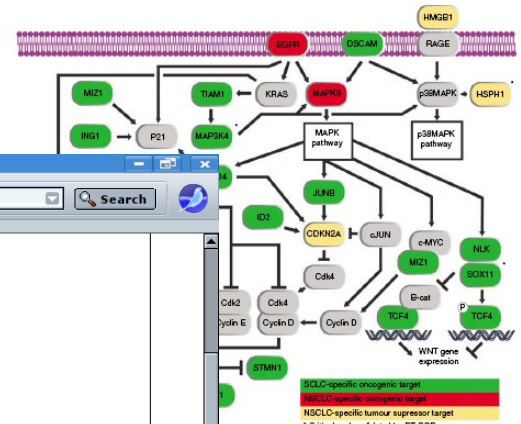
(on the behalf of SBGN editors, authors and contributors)

Graphs are everywhere in biology



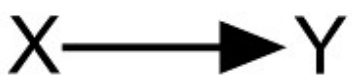






Ambiguity of usual representations

Ambiguity of usual representations



is transformed into

translocates (X "=" Y)

is degraded into

associates into

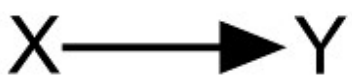
dissociates into

stimulates the activity of

stimulates the expression of

catalyses the formation of

Ambiguity of usual representations



X inhibits Y

is transformed into

translocates (X "=" Y)

is degraded into

associates into

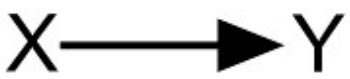
dissociates into

stimulates the activity of

stimulates the expression of

catalyses the formation of

Ambiguity of usual representations



is transformed into

translocates (X "=" Y)

is degraded into

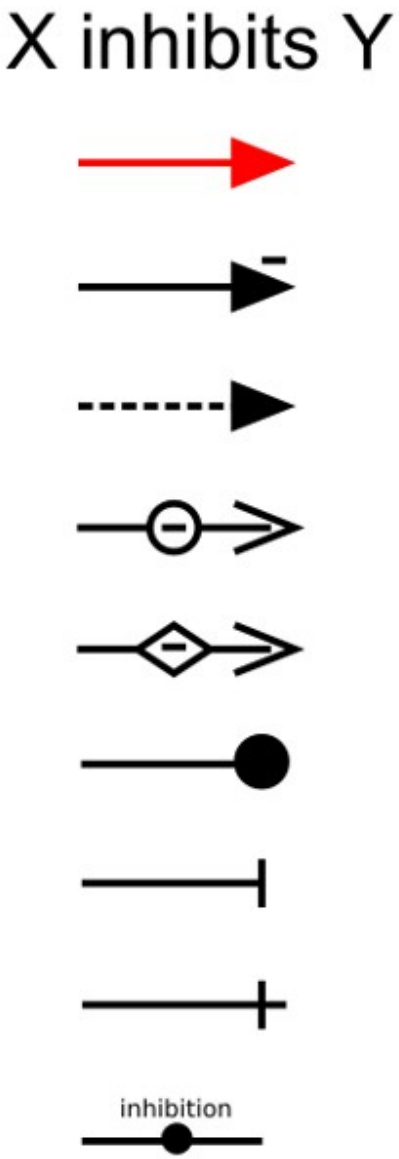
associates into

dissociates into

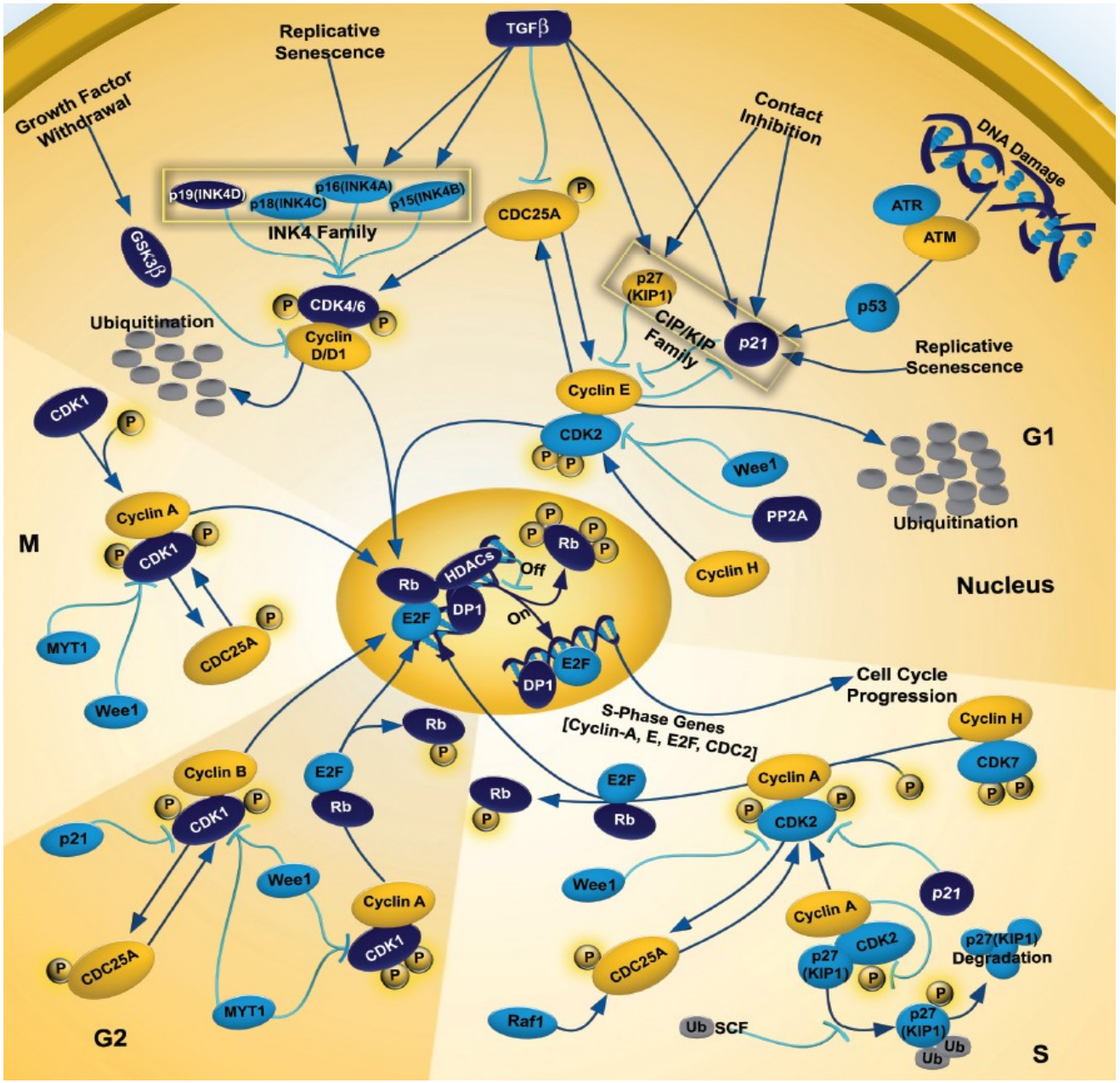
stimulates the activity of

stimulates the expression of

catalyses the formation of



Can-this be understood by biologists?



Can-this be understood by biologists?

Stimulates? but ... what exactly?

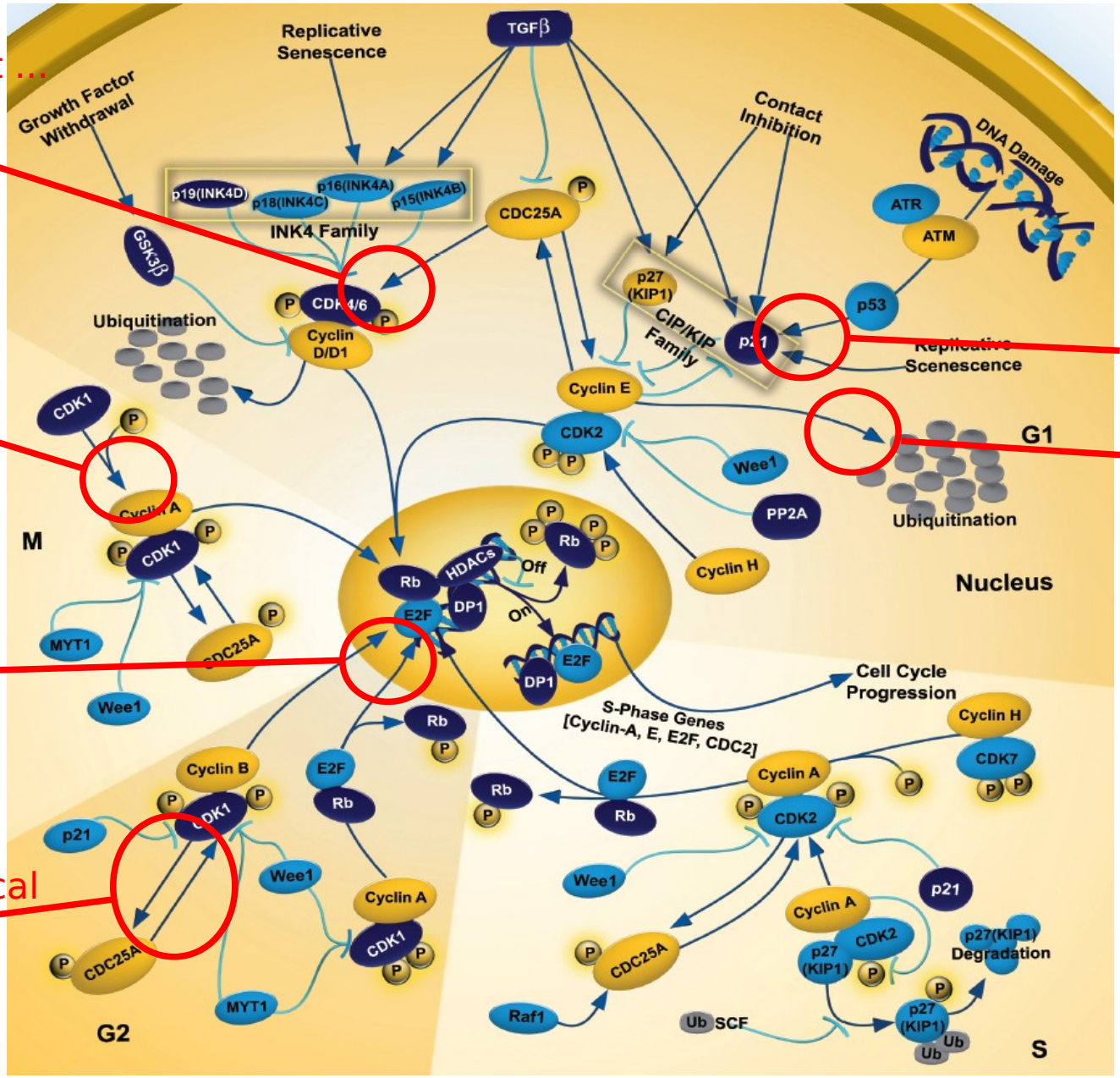
Associates into?

Translocates?

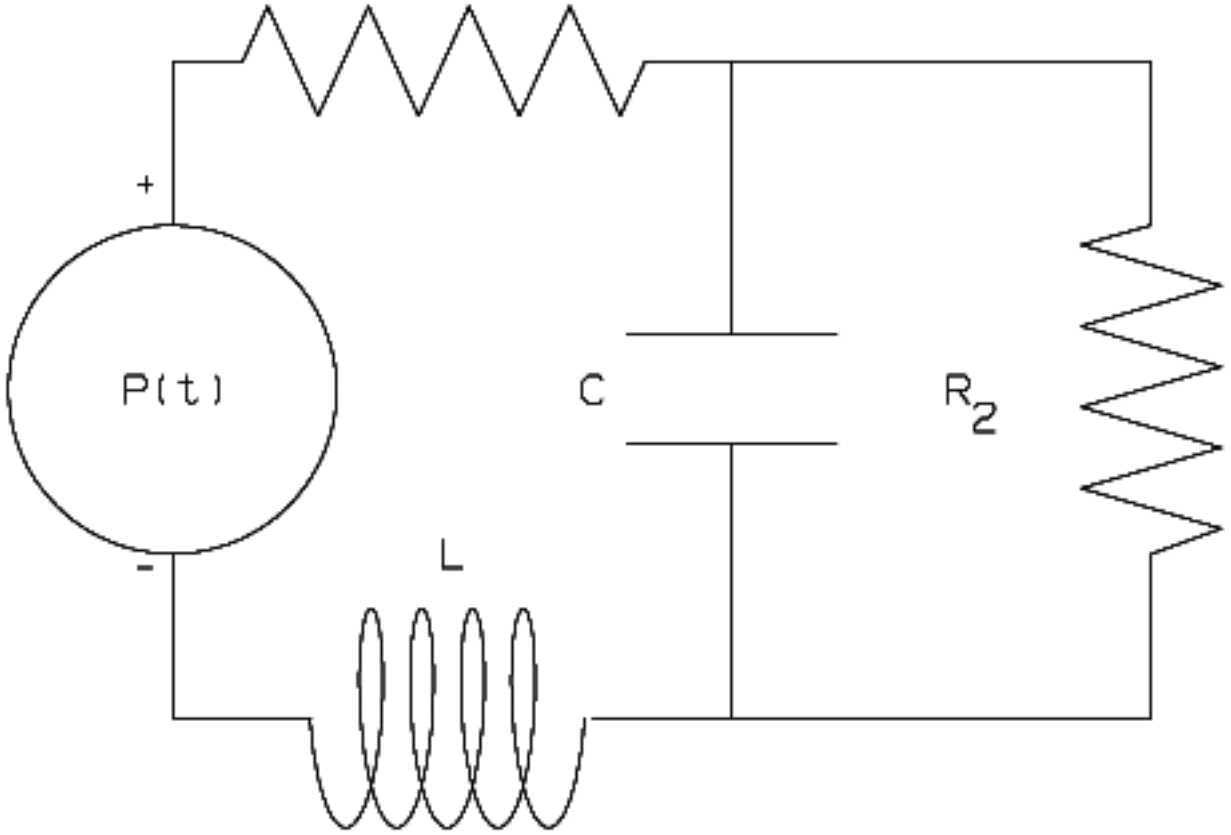
No idea. Reciprocal stimulation?

Stimulates gene transcription?

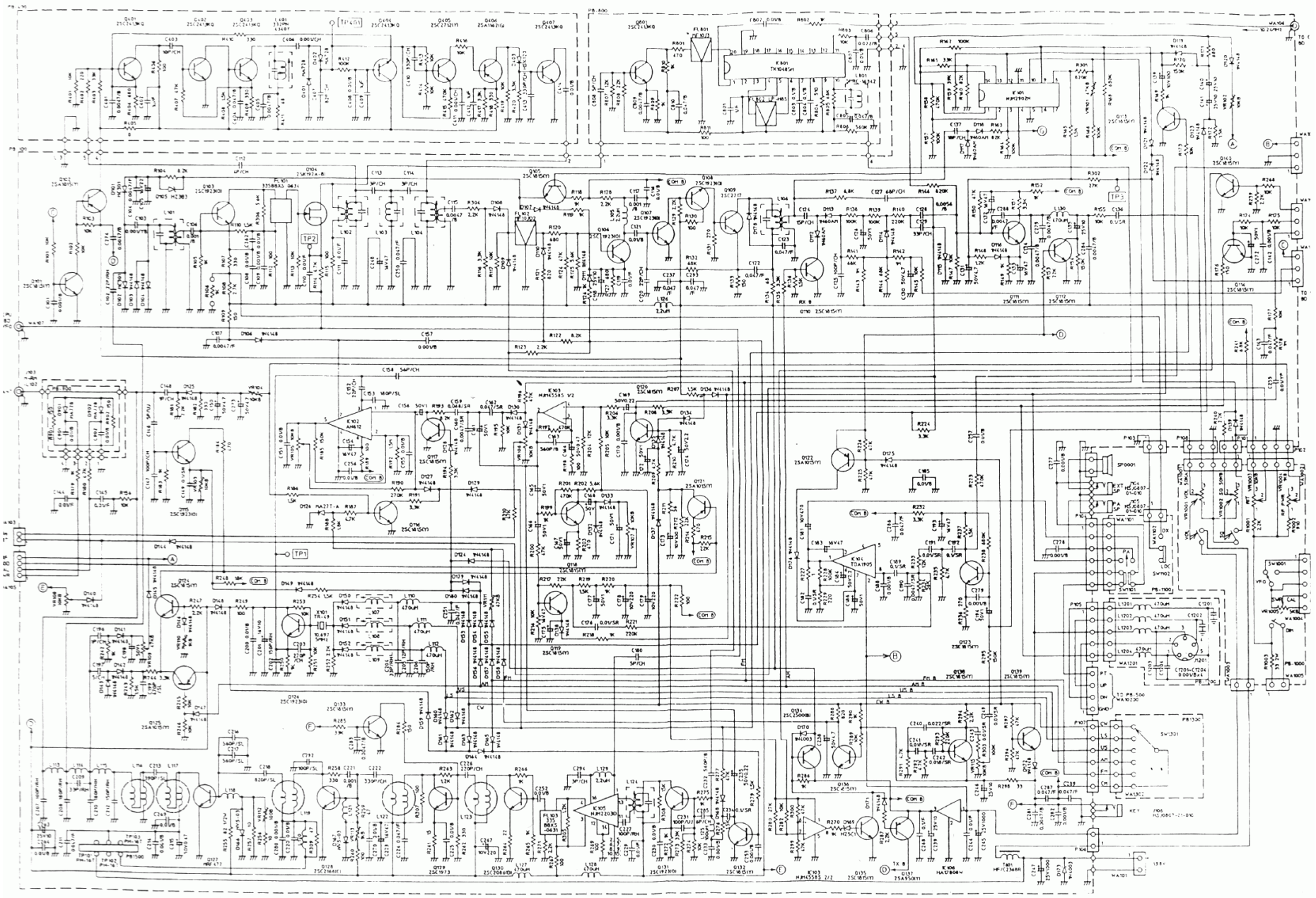
Is degraded?



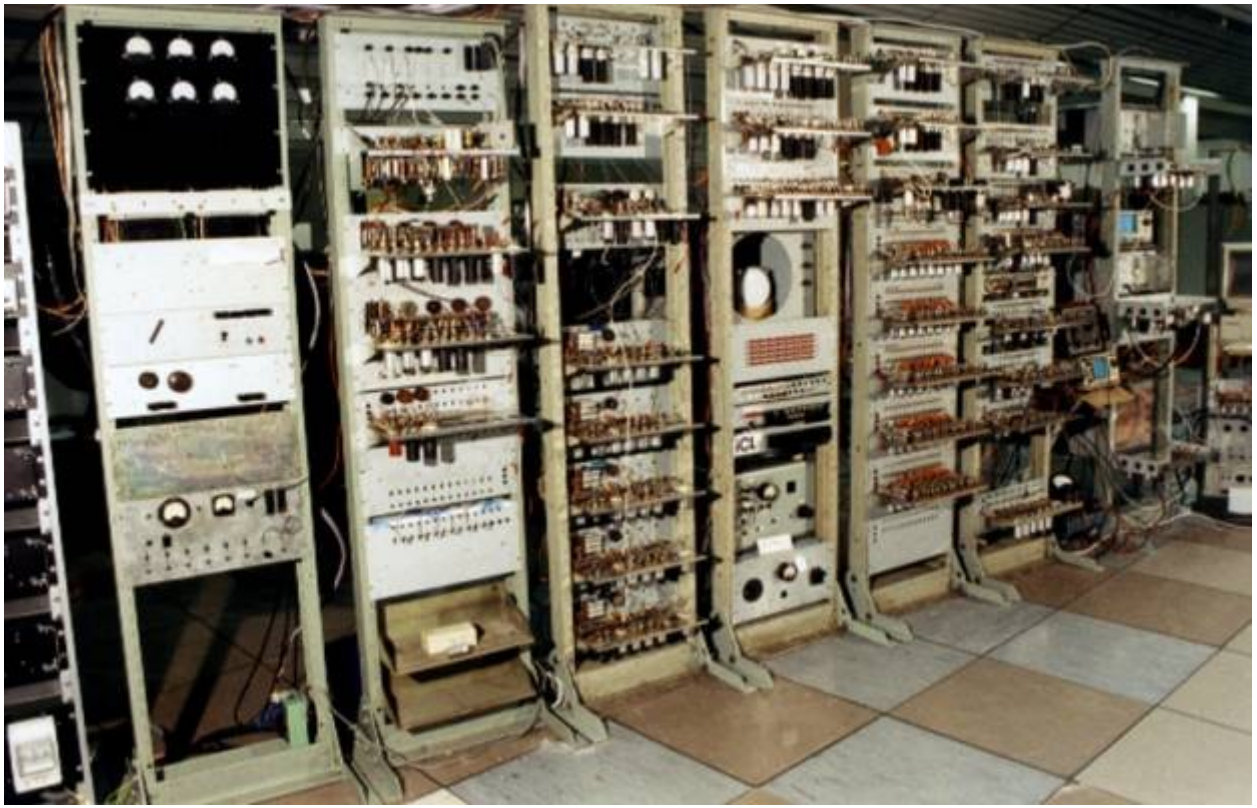
Every engineer understands that



Or that



What did-those diagram bring?

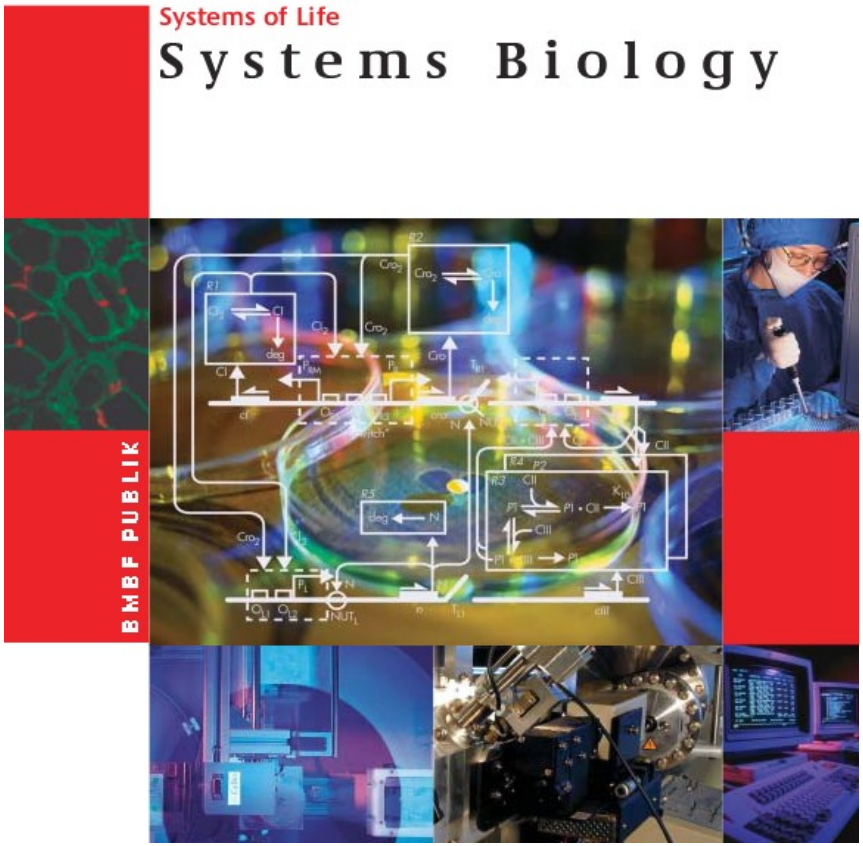


What did-those diagram bring?

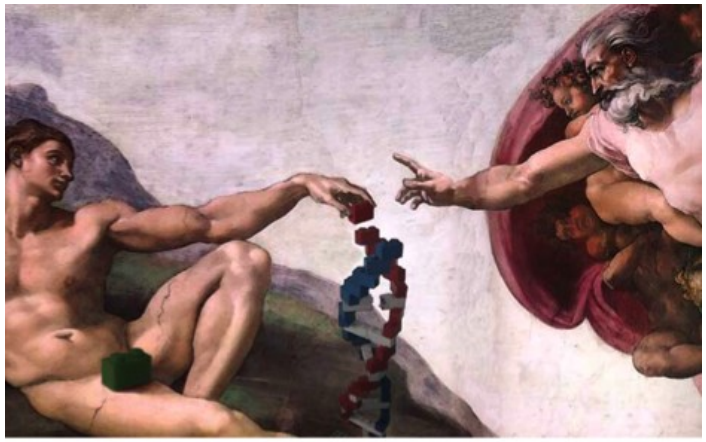
What do-we expect in modern (future) life scienc

Federal Ministry
of Education
and Research

Basic science



Technology



EXTREME GENETIC ENGINEERING

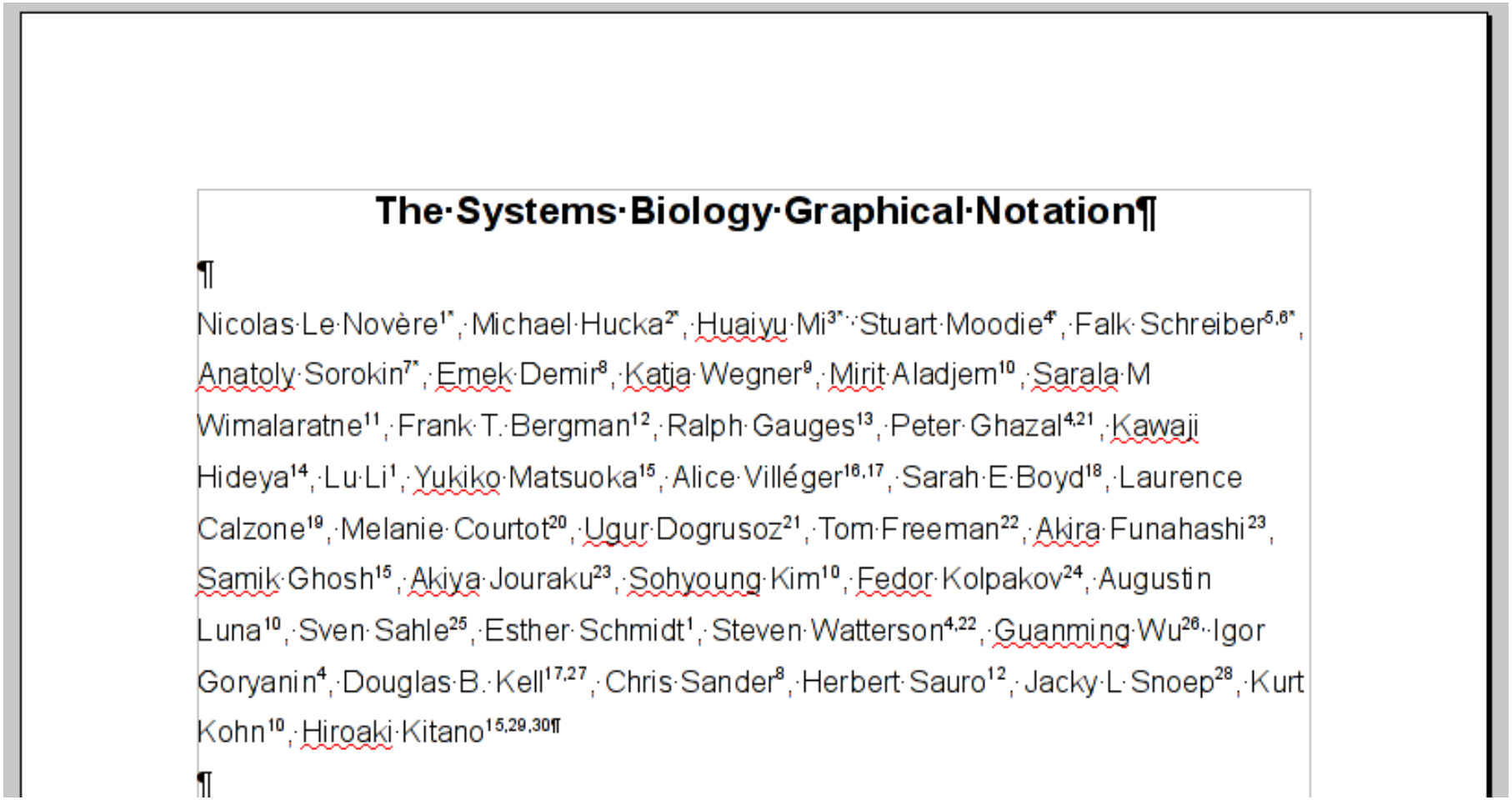
An Introduction to Synthetic Biology

etc group

January 2007

What is SBGN?

- A way to unambiguously describe biochemical and cellular events in graphs
- Limited amount of symbols ☞ Smooth learning curve
- Can graphically represent quantitative models, biochemical pathways, at different levels of granularity
- Developed over three years by a growing community



The·Systems·Biology·Graphical·Notation¶

¶

Nicolas·Le·Novère[1*],·Michael·Hucka[2*],·Huaiyu·Mi[3*],·Stuart·Moodie[4*],·Falk·Schreiber[5,6*],·Anatoly·Sorokin[7*],·Emek·Demir[8],·Katja·Wegner[9],·Mirit·Aladjem[10],·Sarala·M·Wimalaratne[11],·Frank·T.·Bergman[12],·Ralph·Gauges[13],·Peter·Ghazal[4,21],·Kawaji·Hideya[14],·Lu·Li[1],·Yukiko·Matsuoka[15],·Alice·Villéger[16,17],·Sarah·E·Boyd[18],·Laurence·Calzone[19],·Melanie·Courtot[20],·Ugur·Dogrusoz[21],·Tom·Freeman[22],·Akira·Funahashi[23],·Samik·Ghosh[15],·Akiya·Jouraku[23],·Sohyoung·Kim[10],·Fedor·Kolpakov[24],·Augustin·Luna[10],·Sven·Sahle[25],·Esther·Schmidt[1],·Steven·Watterson[4,22],·Guanming·Wu[26],·Igor·Goryanin[4],·Douglas·B.·Kell[17,27],·Chris·Sander[8],·Herbert·Sauro[12],·Jacky·L·Snoep[28],·Kurt·Kohn[10],·Hiroaki·Kitano[15,29,30]¶

¶

Nature Biotechnology, in the press

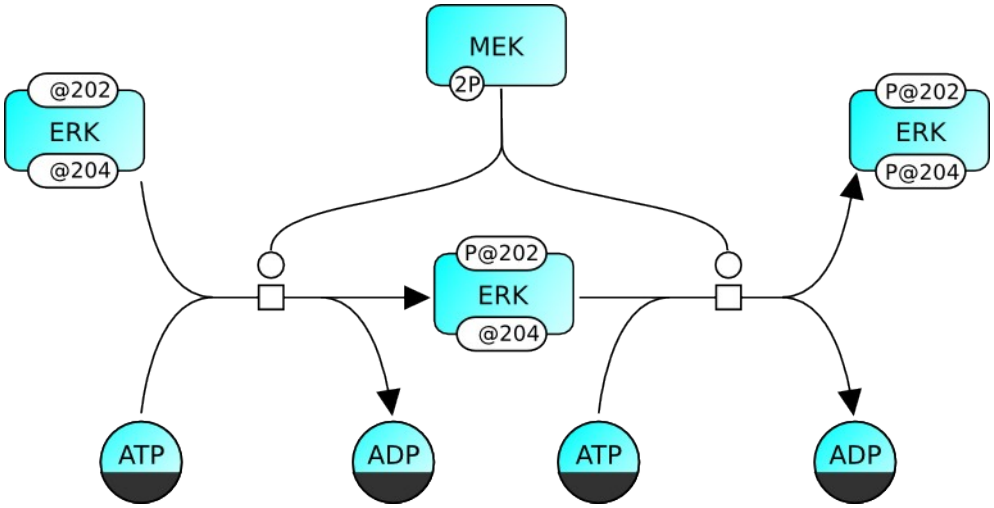
39 authors, 30 affiliations

What is SBGN?

- A way to unambiguously describe biochemical and cellular events in graphs
- Limited amount of symbols ☞ Smooth learning curve
- Can graphically represent quantitative models, biochemical pathways, at different levels of granularity
- Developed over three years by a growing community
- Three languages
  - Process Diagrams ☞ one state = one glyph, biochemical level
  - Entity Relationships ☞ one entity = one glyph, biochemical level
  - Activity Flow ☞ conceptual level

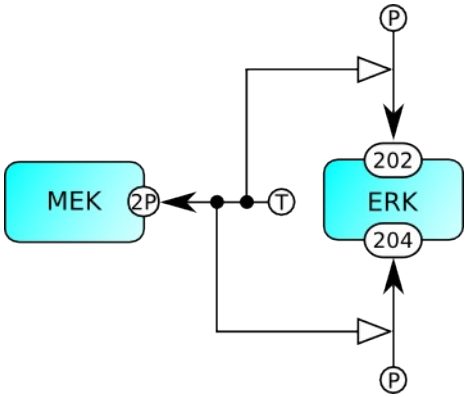
Graph trinity: three languages in one

Process diagrams



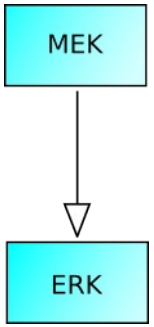
- Unambiguous
- Mechanistic
- Sequential
- Subject to combinatorial explosion

Entity Relationships diagrams



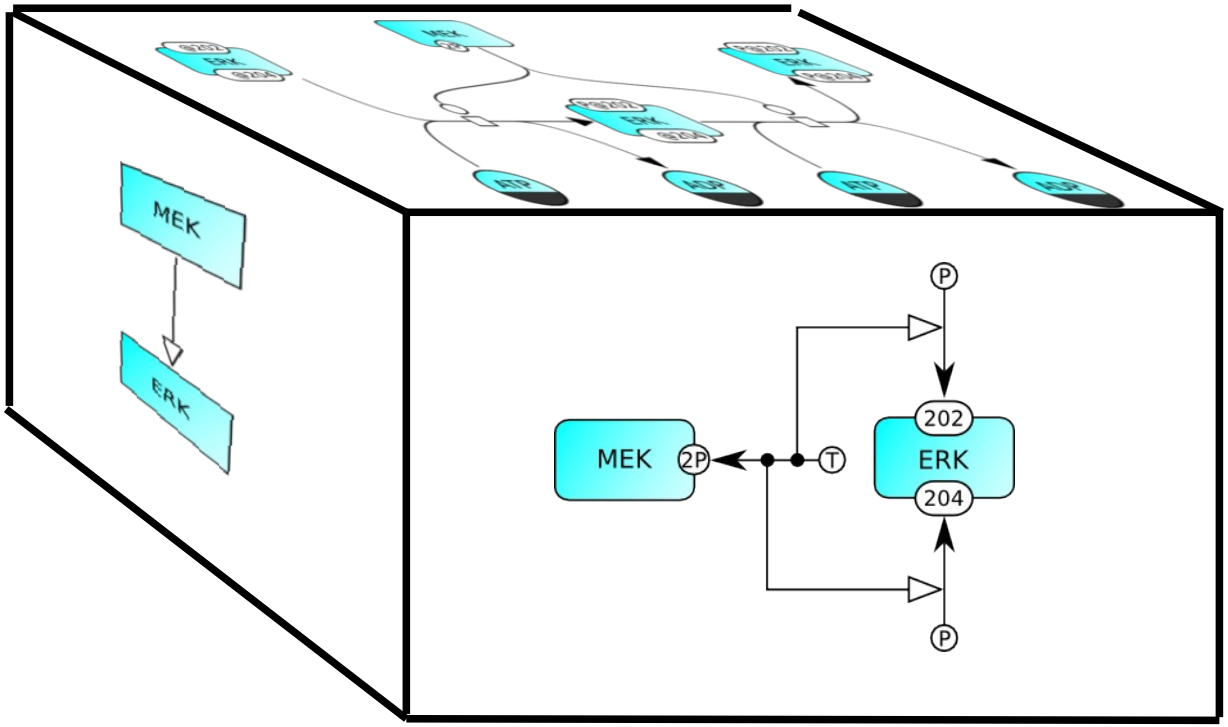
- Unambiguous
- Mechanistic
- Non-sequential
- Independence of relationships

Activity Flow diagrams

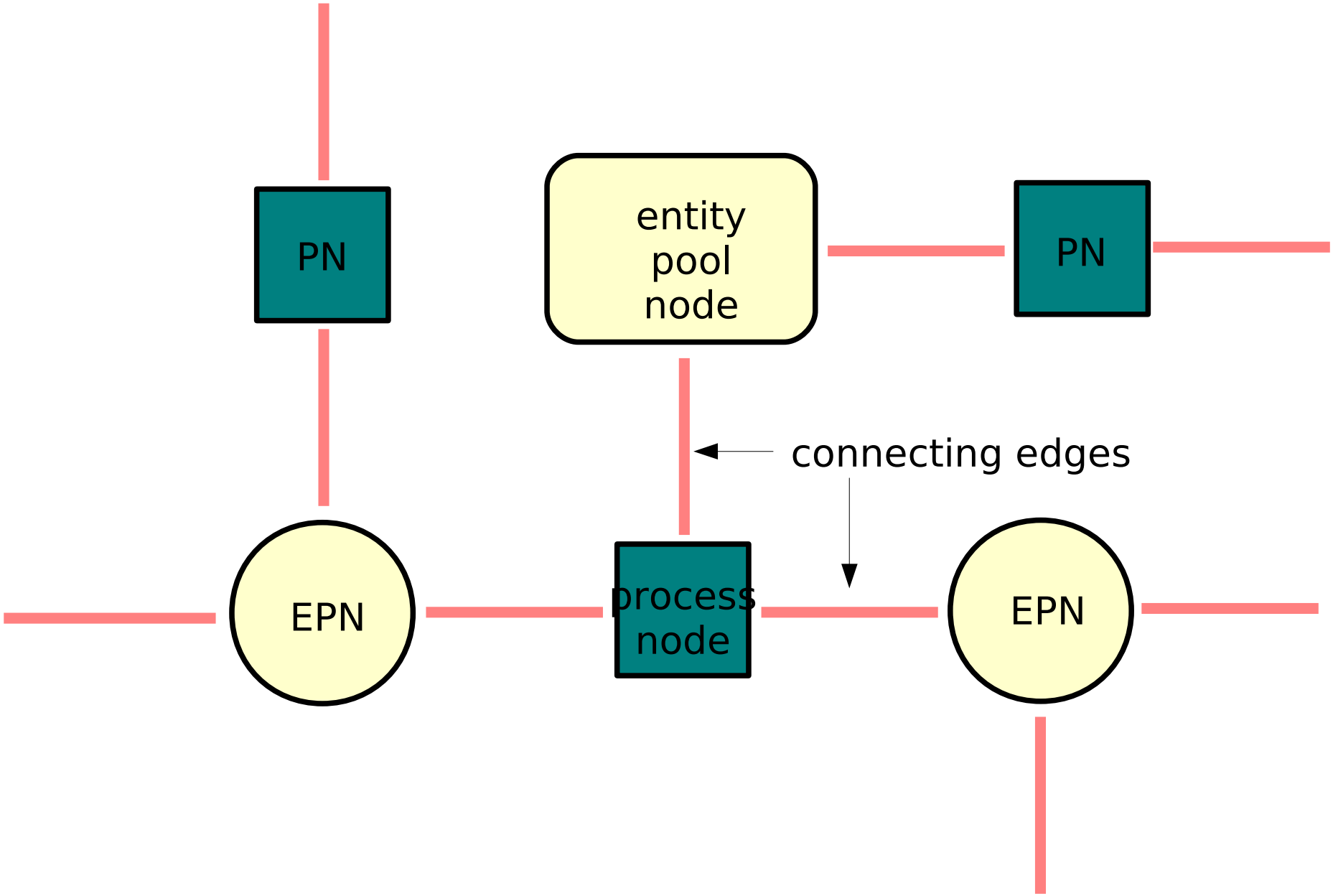


- Ambiguous
- Conceptual
- Sequential

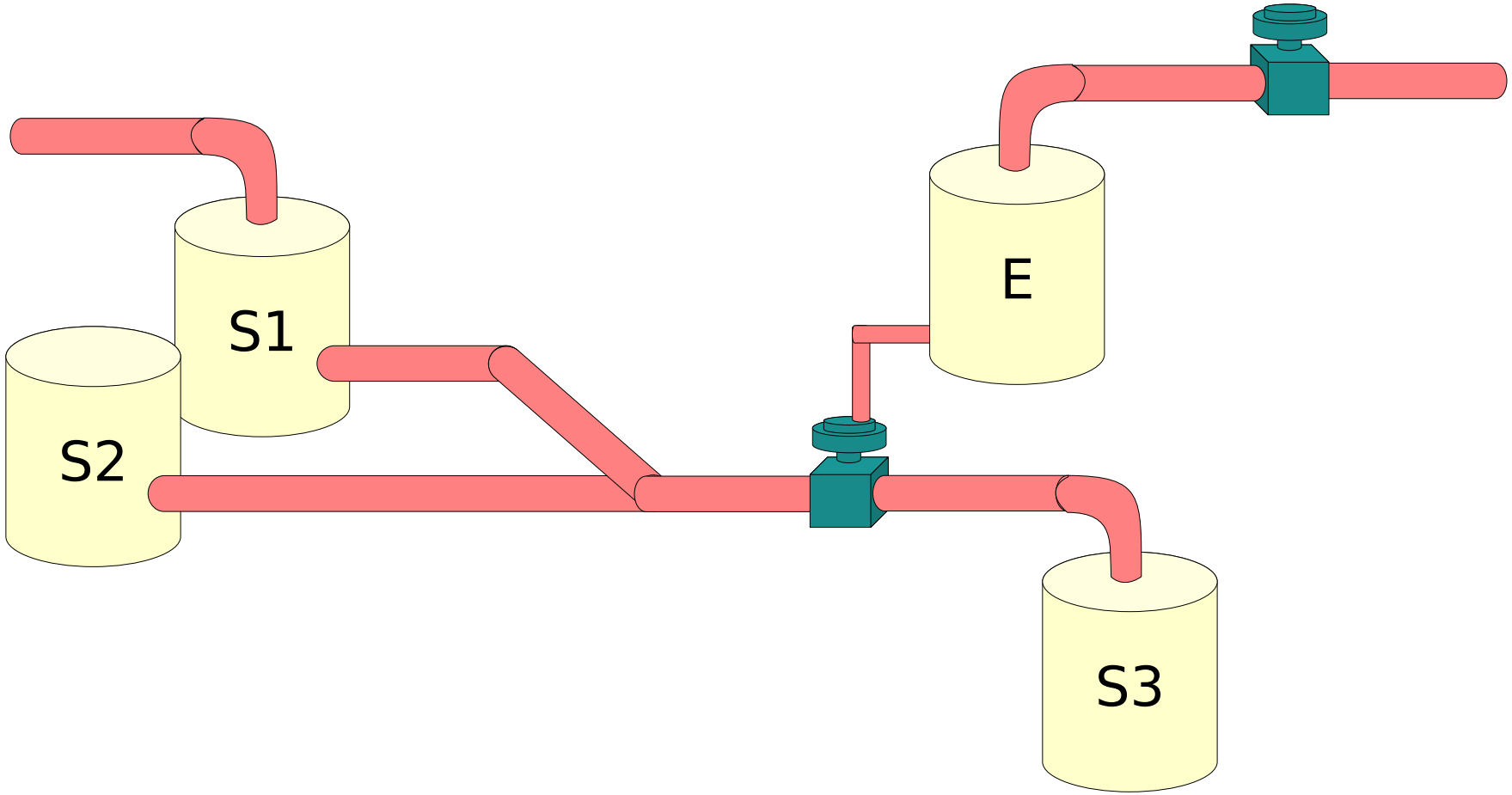
Three orthogonal projections of biology



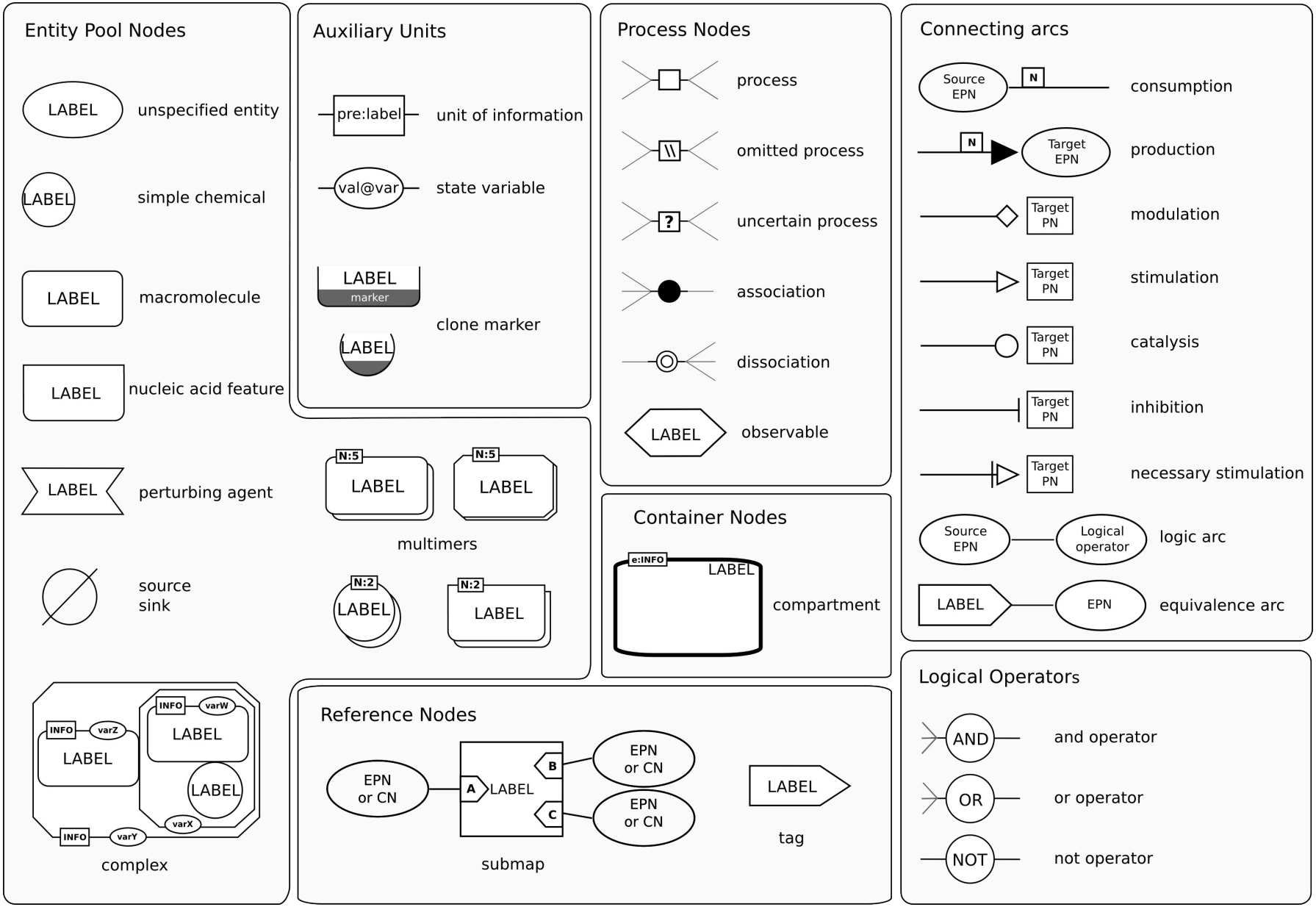
Process Diagrams are bipartite graphs



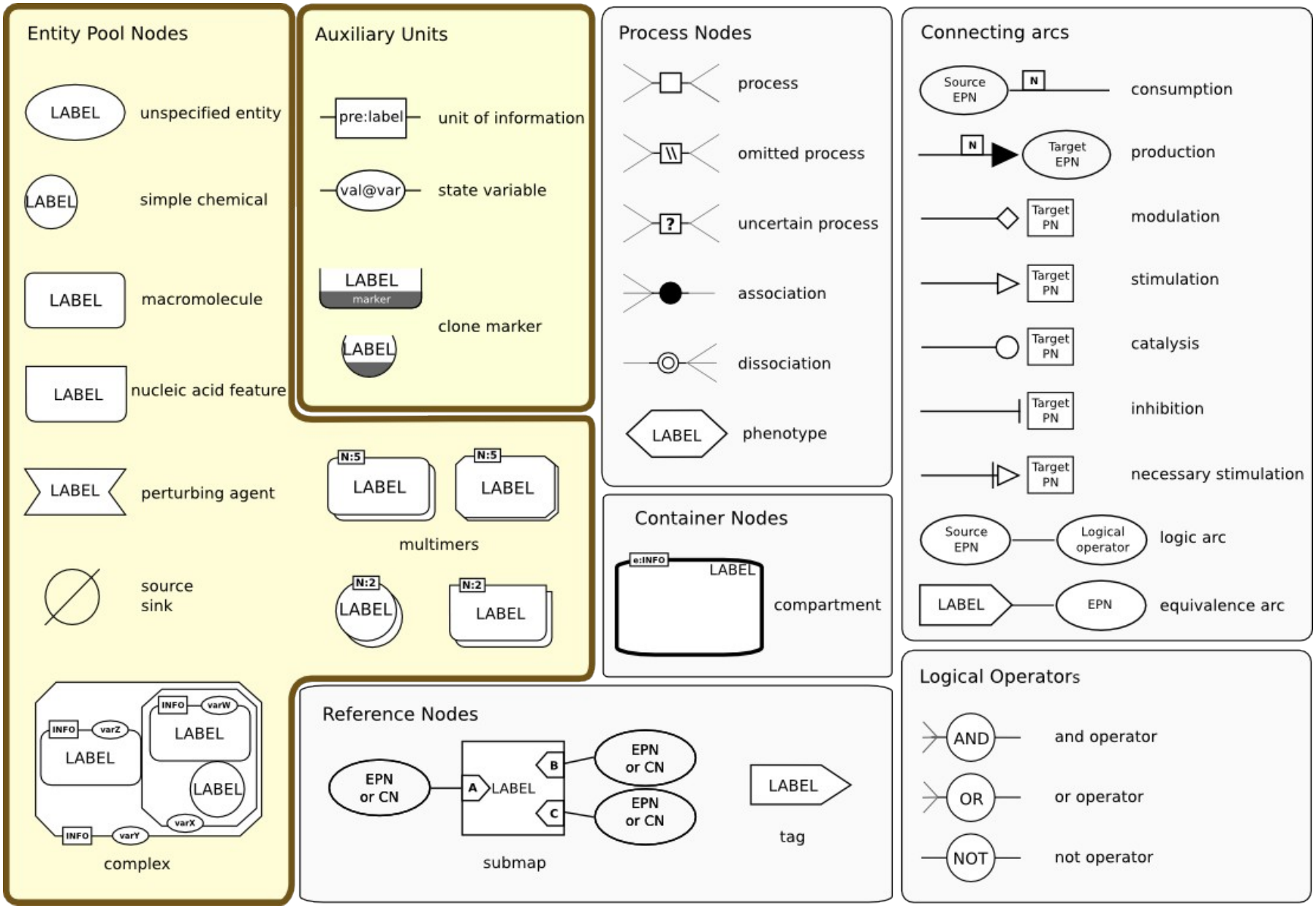
Process Diagrams can be viewed as pipelines



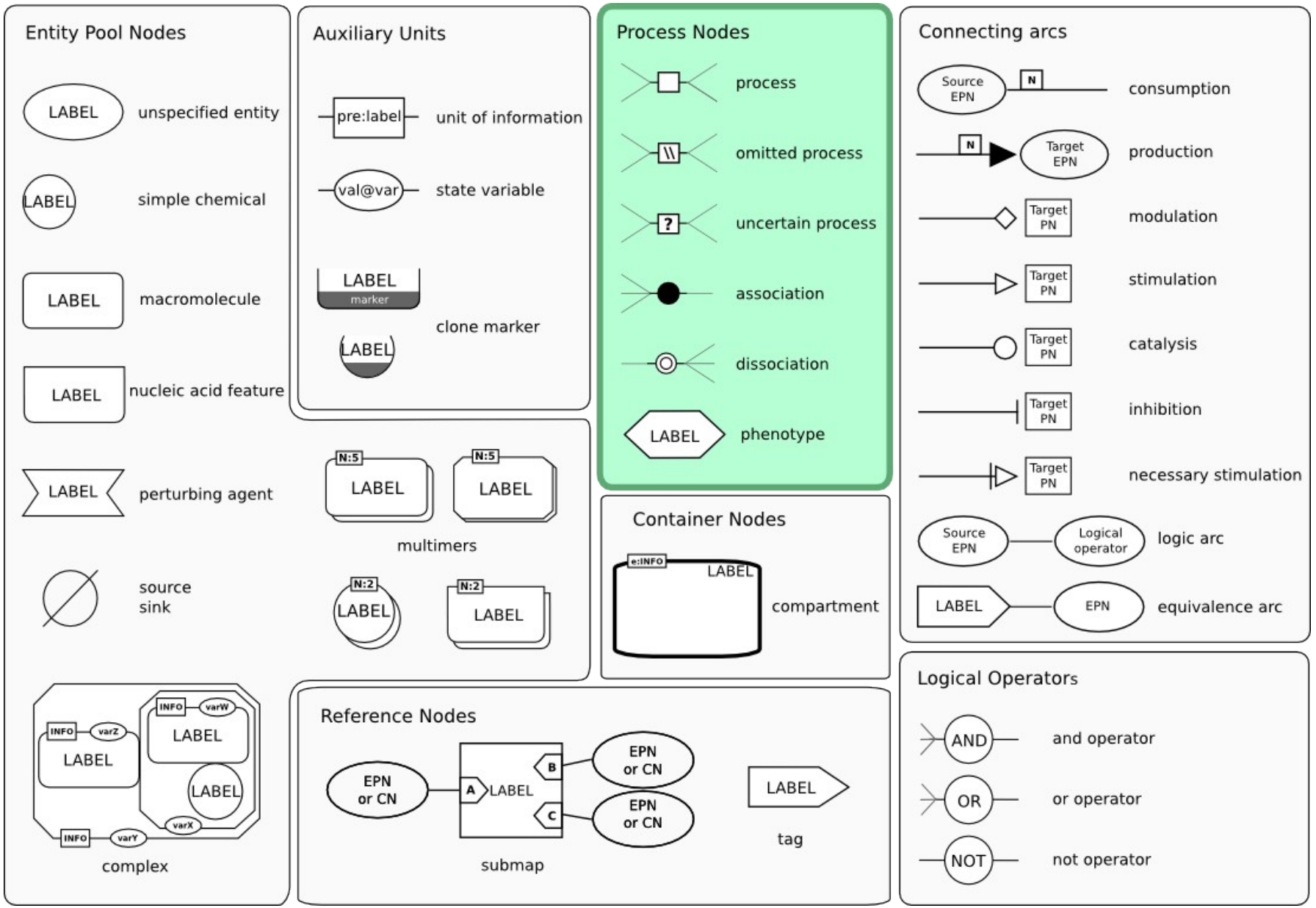
SBGN Process Diagram L1 reference card



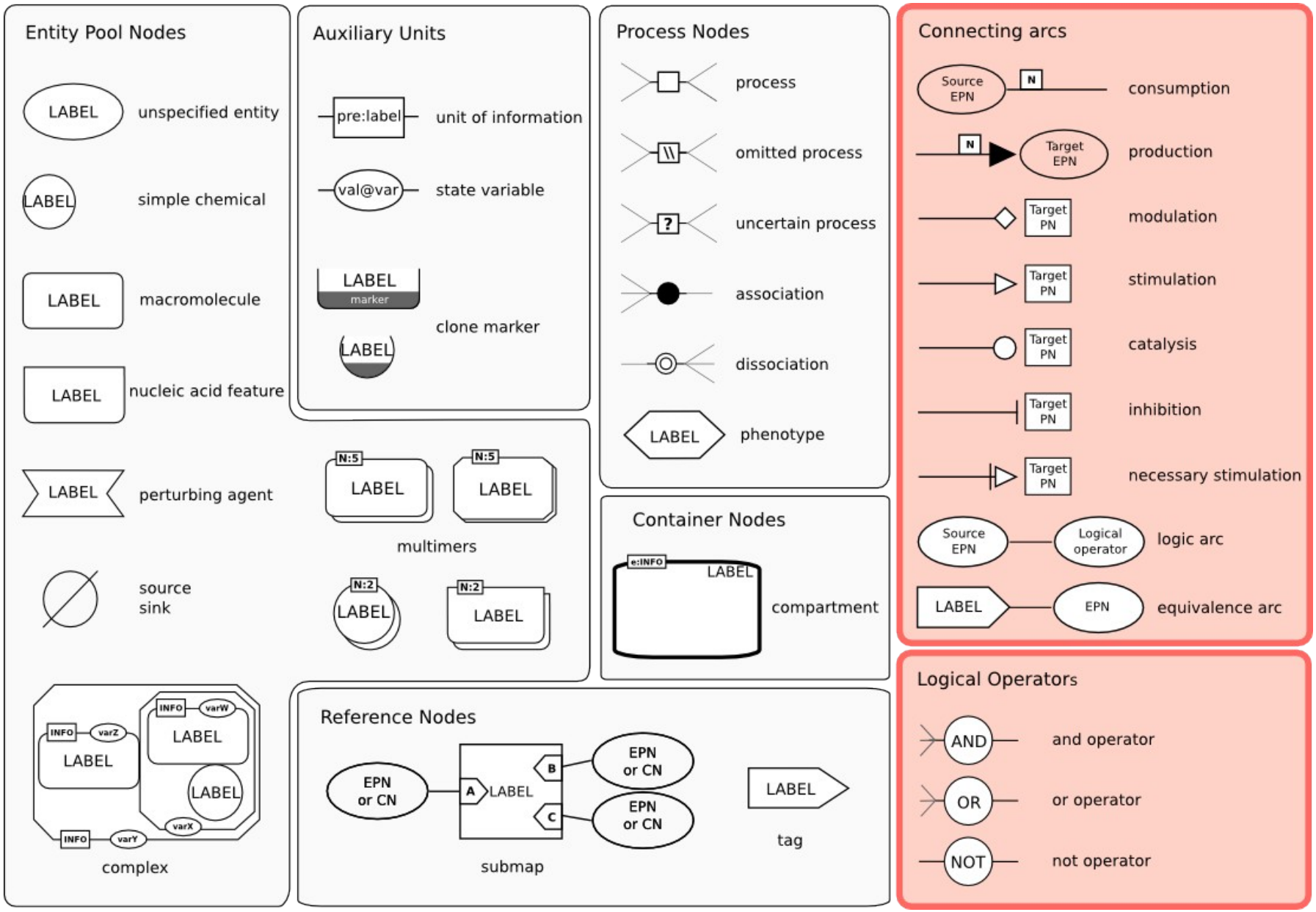
Entity Pool Nodes



Process Nodes



Edges

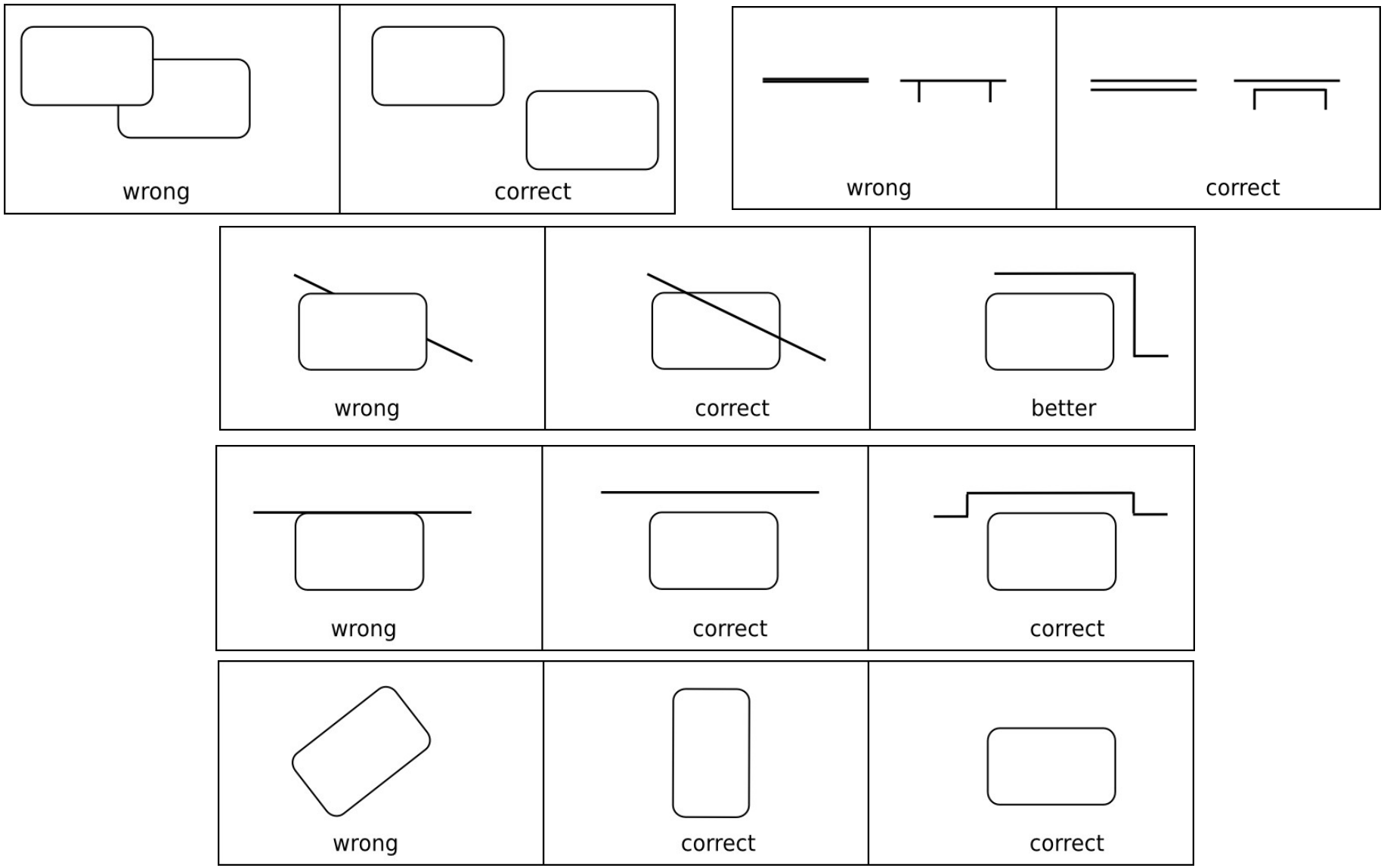

Entity Pool Nodes
LABEL
unspecified entity
LABEL
simple chemical
LABEL
macromolecule
LABEL
nucleic acid feature
LABEL
perturbing agent
source
sink
INFO
varZ
LABEL
INFO
varW
LABEL
LABEL
INFO
varY
varX
complex
Auxiliary Units
pre:label
unit of information
val@var
state variable
LABEL
marker
LABEL
clone marker
N:5
LABEL
N:5
LABEL
multimers
N:2
LABEL
N:2
LABEL
Process Nodes
process
omitted process
?
uncertain process
association
dissociation
LABEL
phenotype
Container Nodes
e:INFO
LABEL
compartment
Reference Nodes
EPN
or CN
A
LABEL
B
C
EPN
or CN
EPN
or CN
submap
LABEL
tag
Connecting arcs
Source
EPN
N
consumption
N
Target
EPN
production
Target
PN
modulation
Target
PN
stimulation
Target
PN
catalysis
Target
PN
inhibition
Target
PN
necessary stimulation
Source
EPN
Logical
operator
logic arc
LABEL
EPN
equivalence arc
Logical Operators
AND
and operator
OR
or operator
NOT
not operator

Syntax definition

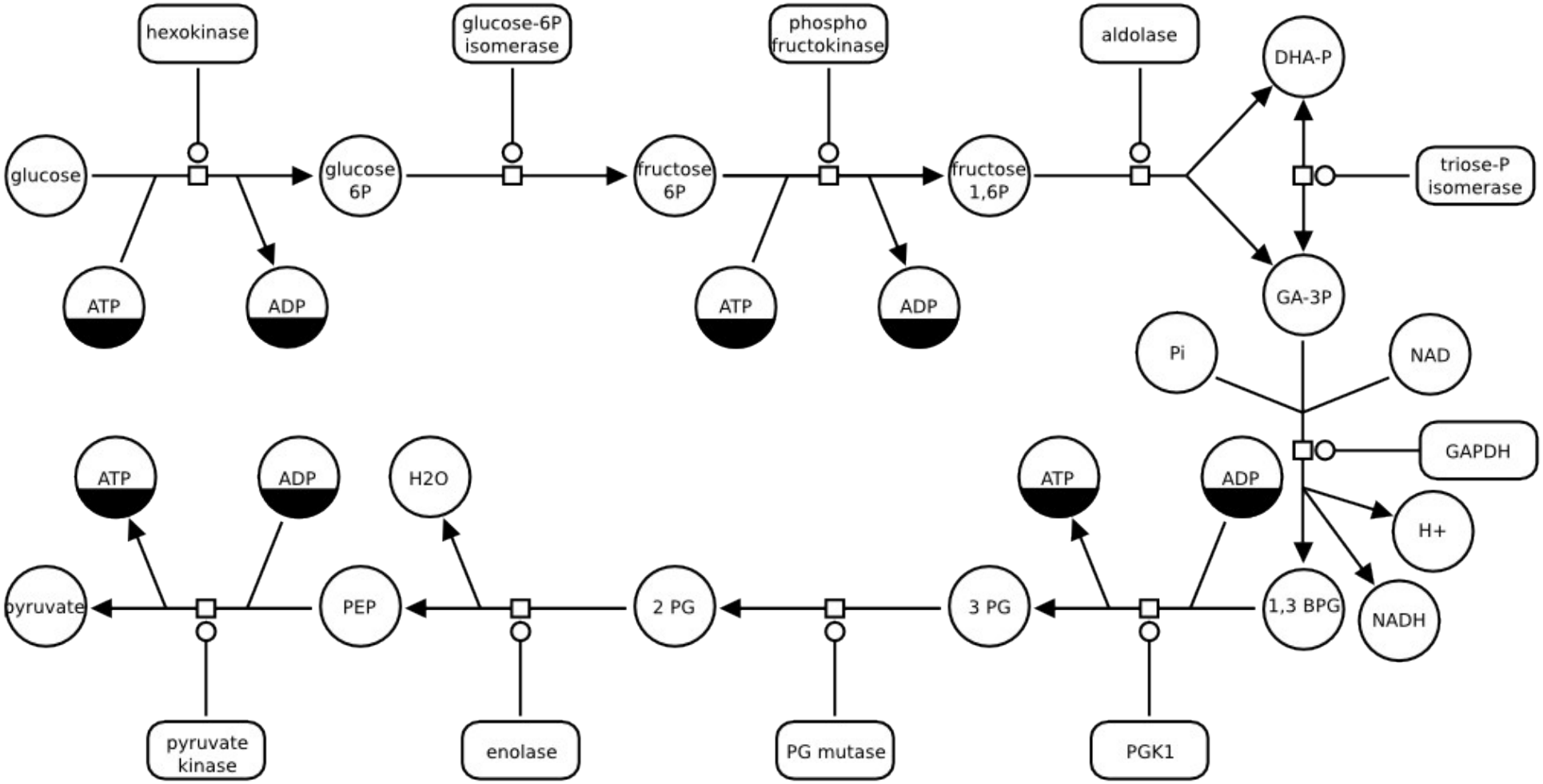
Arc\EPN	*macromolecule*	*simple chemical*	*unspecified entity*	*multimer*	*complex*	*nucleic acid feature*	*tag*	*source/sink*	*perturbation*	*observable*	*submap*
consumption	I	I	I	I	I	I		I			
production	O	O	O	O	O	O		O			
modulation	I	I	I	I	I	I			I	O	
stimulation	I	I	I	I	I	I			I	O	
catalysis	I	I	I	I	I				I	O	
inhibition	I	I	I	I	I	I			I	O	
trigger	I	I	I	I	I	I			I	O	
logic arc	I	I	I	I	I	I					
equivalence arc	I	I	I	I	I	I	O				O

Arc\PN	*transition*	*omitted process*	*uncertain process*	*association*	*dissociation*	*and*	*or*	*not*
consumption	O	O	O	O	O(1)			
production	I	I	I	I(1)	I			
modulation	O	O	O			I(1)	I(1)	I(1)
stimulation	O	O	O			I(1)	I(1)	I(1)
catalysis	O	O	O			I(1)	I(1)	I(1)
inhibition	O	O	O			I(1)	I(1)	I(1)
trigger	O	O	O			I(1)	I(1)	I(1)
logic arc						O	O	O(1)
equivalence arc								

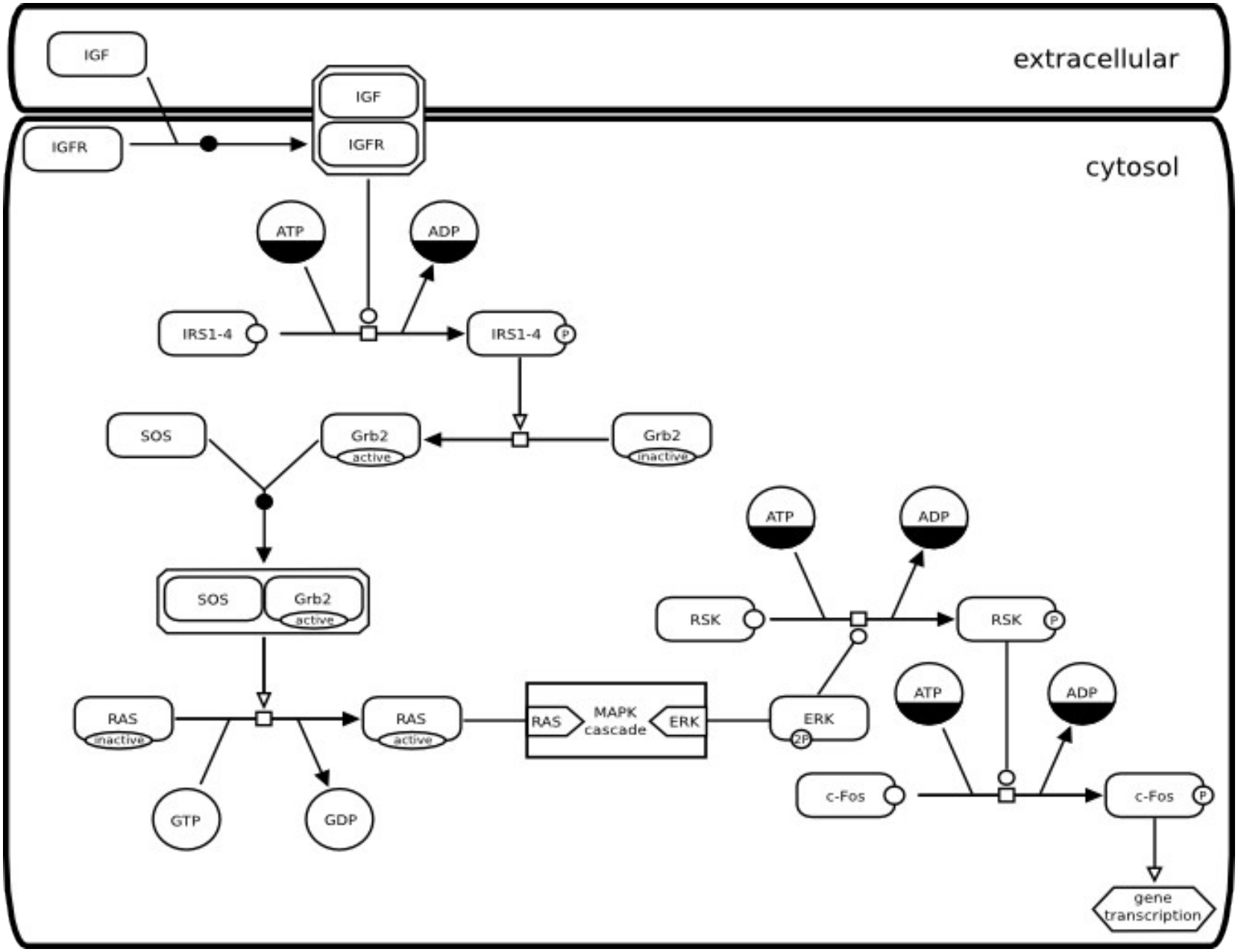
Layout constraints



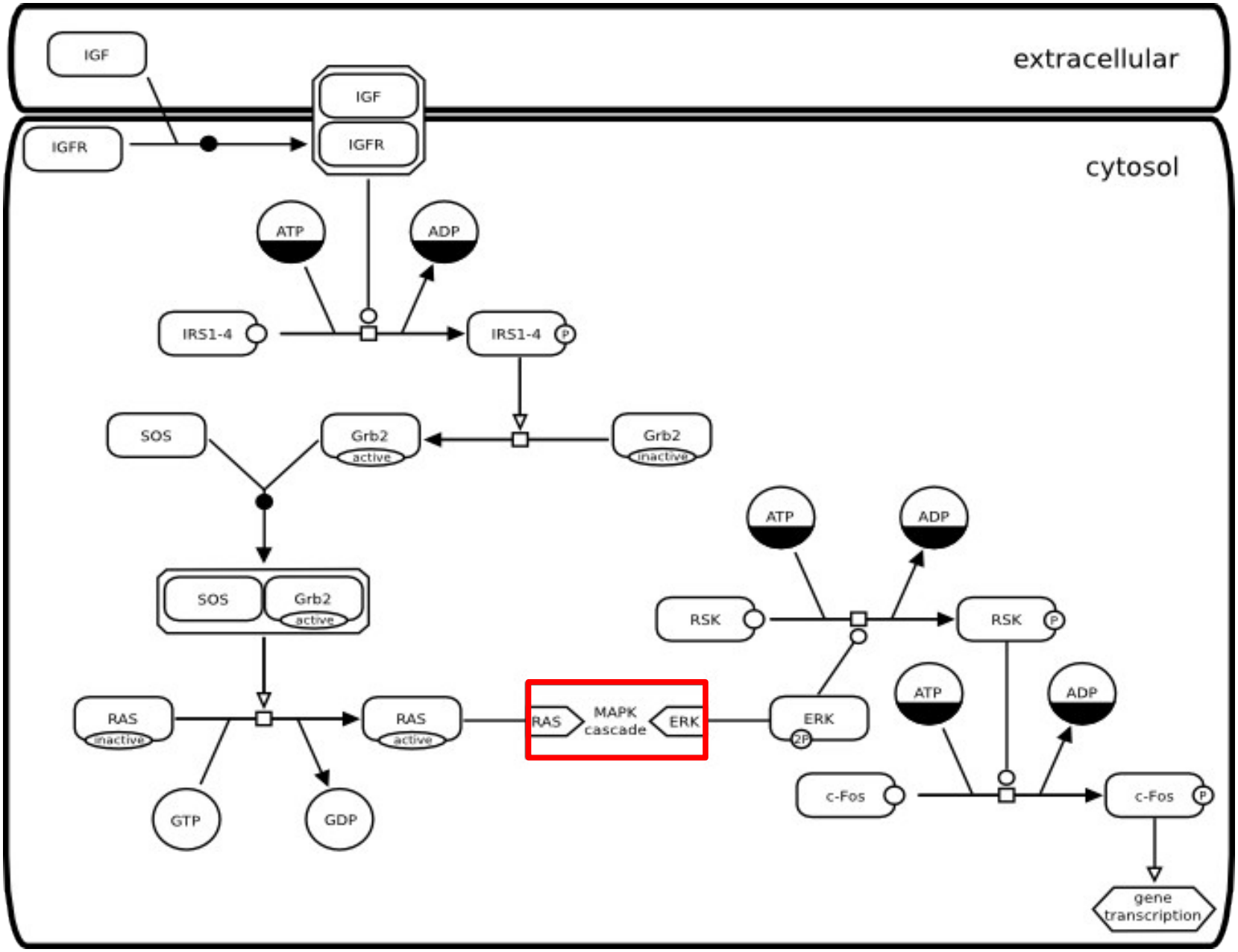
Metabolic network



Signalling pathways



Submaps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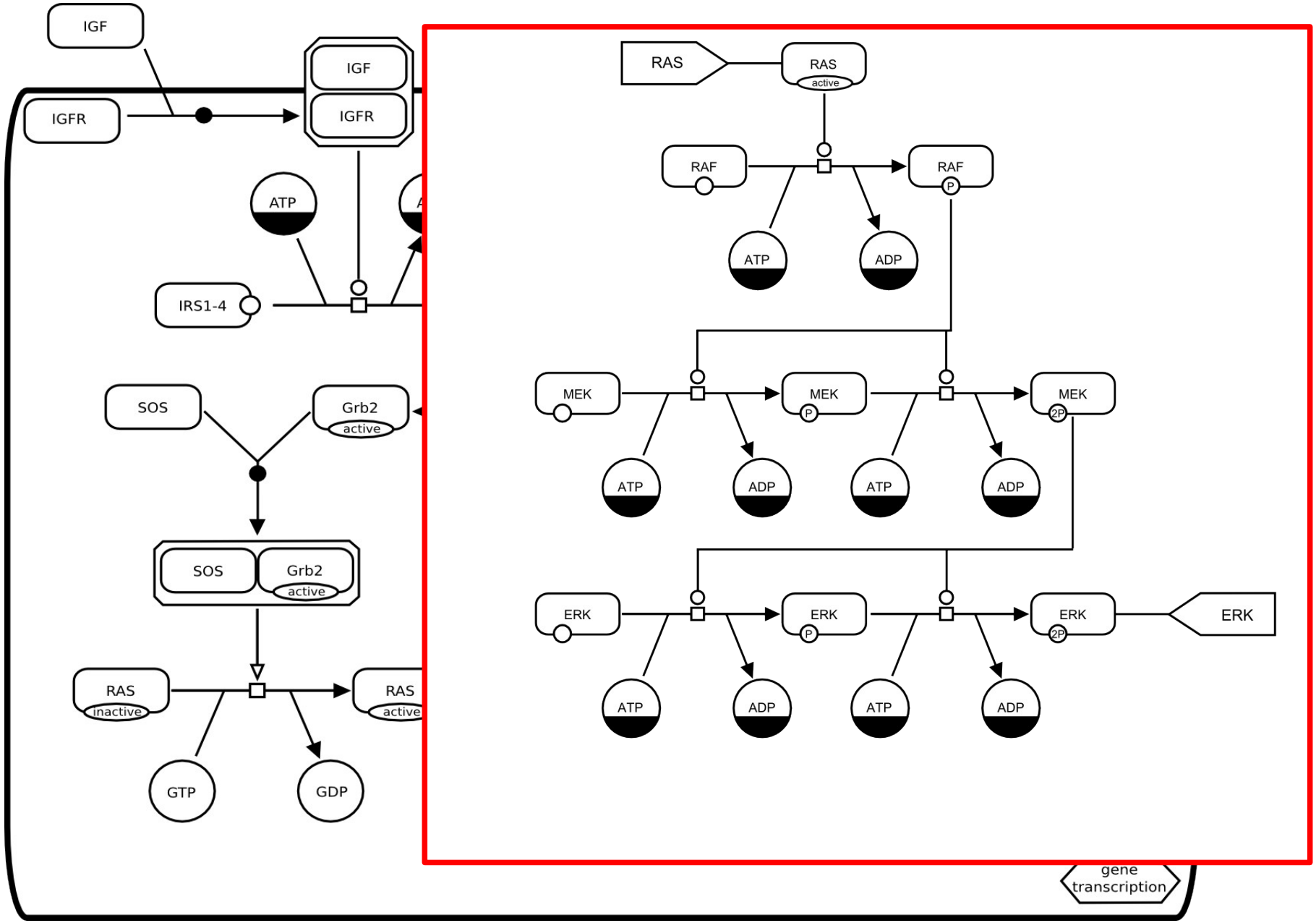
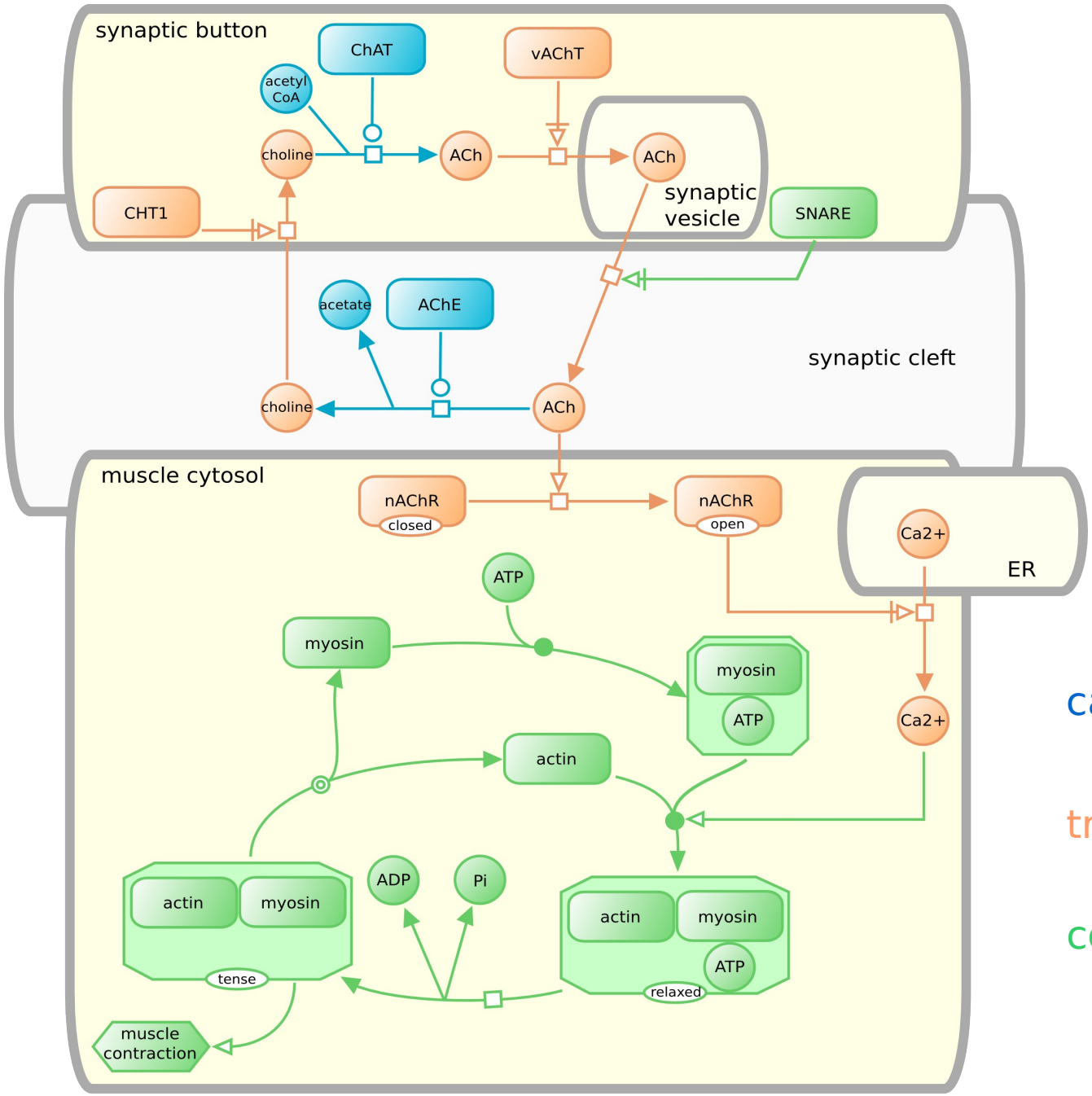
IGF
IGF
IGFR
IGFR
cytosol
ATP
ADP
IRS1-4
IRS1-4
P
SOS
Grb2
active
Grb2
inactive
SOS
Grb2
active
ATP
ADP
RSK
RSK
P
RAS
inactive
RAS
active
RAS
MAPK
cascade
ERK
ERK
2P
ATP
ADP
GTP
GDP
c-Fos
c-Fos
P
gene
transcription

Submaps


IGF
IGF
IGFR
IGFR
ATP
IRS1-4
SOS
Grb2
active
SOS
Grb2
active
RAS
inactive
RAS
active
GTP
GDP
RAS
RAS
active
RAF
RAF
P
ATP
ADP
MEK
MEK
P
MEK
2P
ATP
ADP
ATP
ADP
ERK
ERK
P
ERK
2P
ERK
ATP
ADP
ATP
ADP
gene
transcription

multi-cellular processes

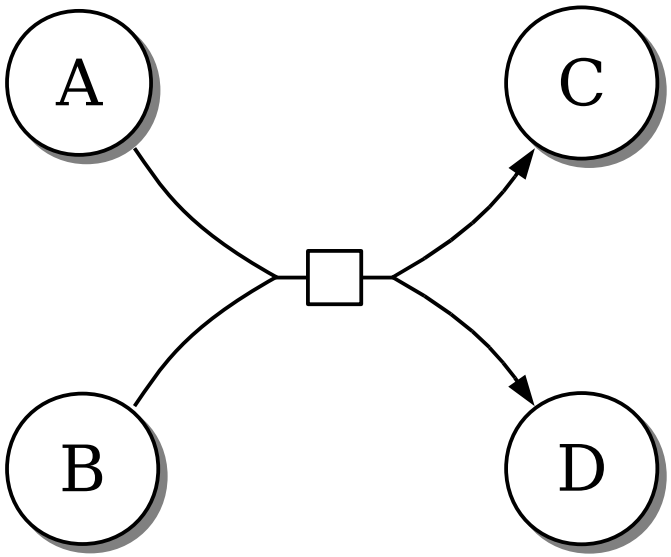


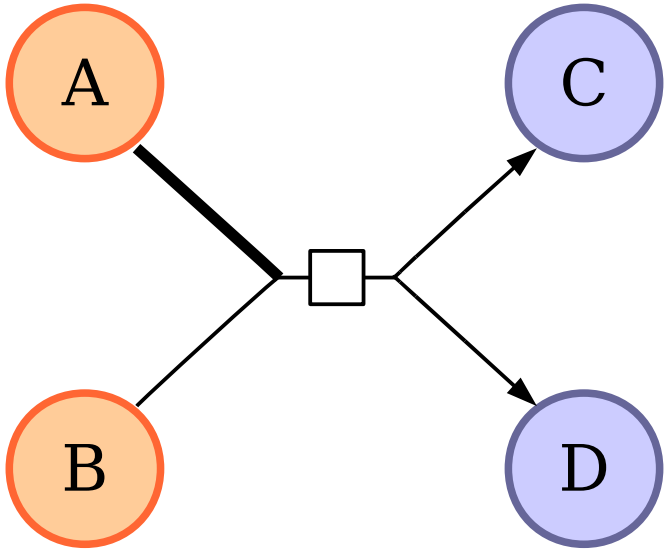
catalytic processes

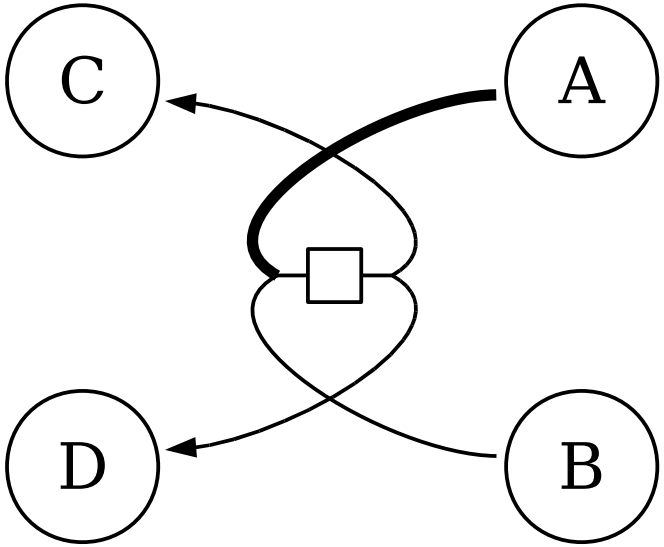
transport processes

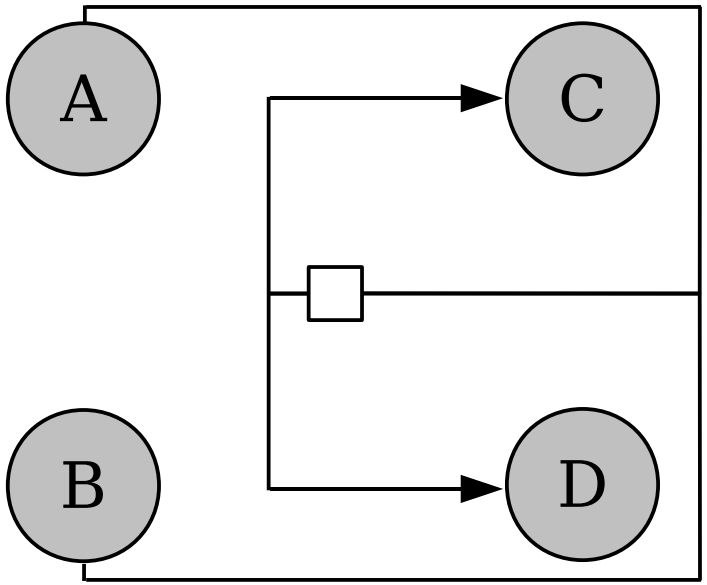
contractile proteins

All those diagrams are identical

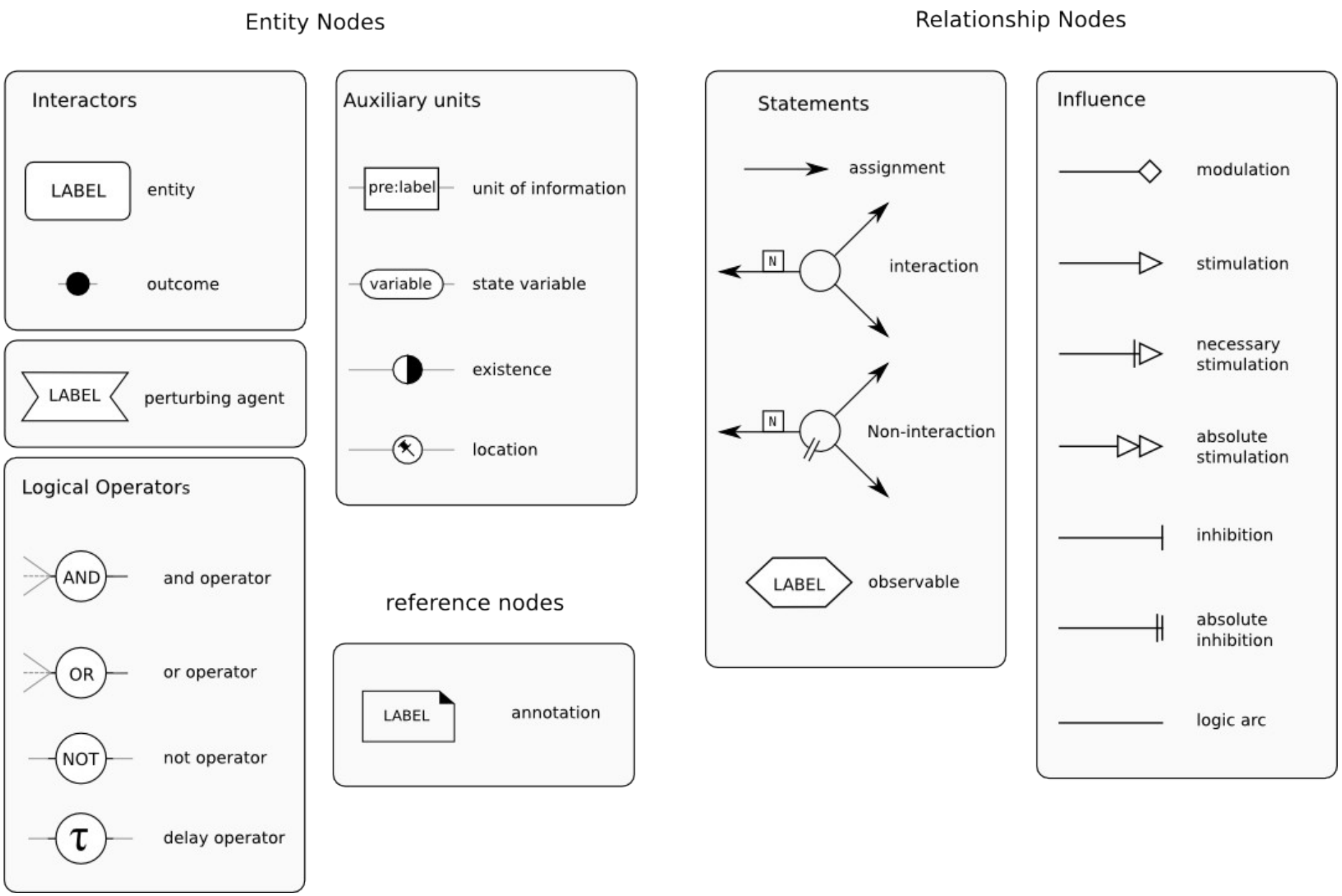




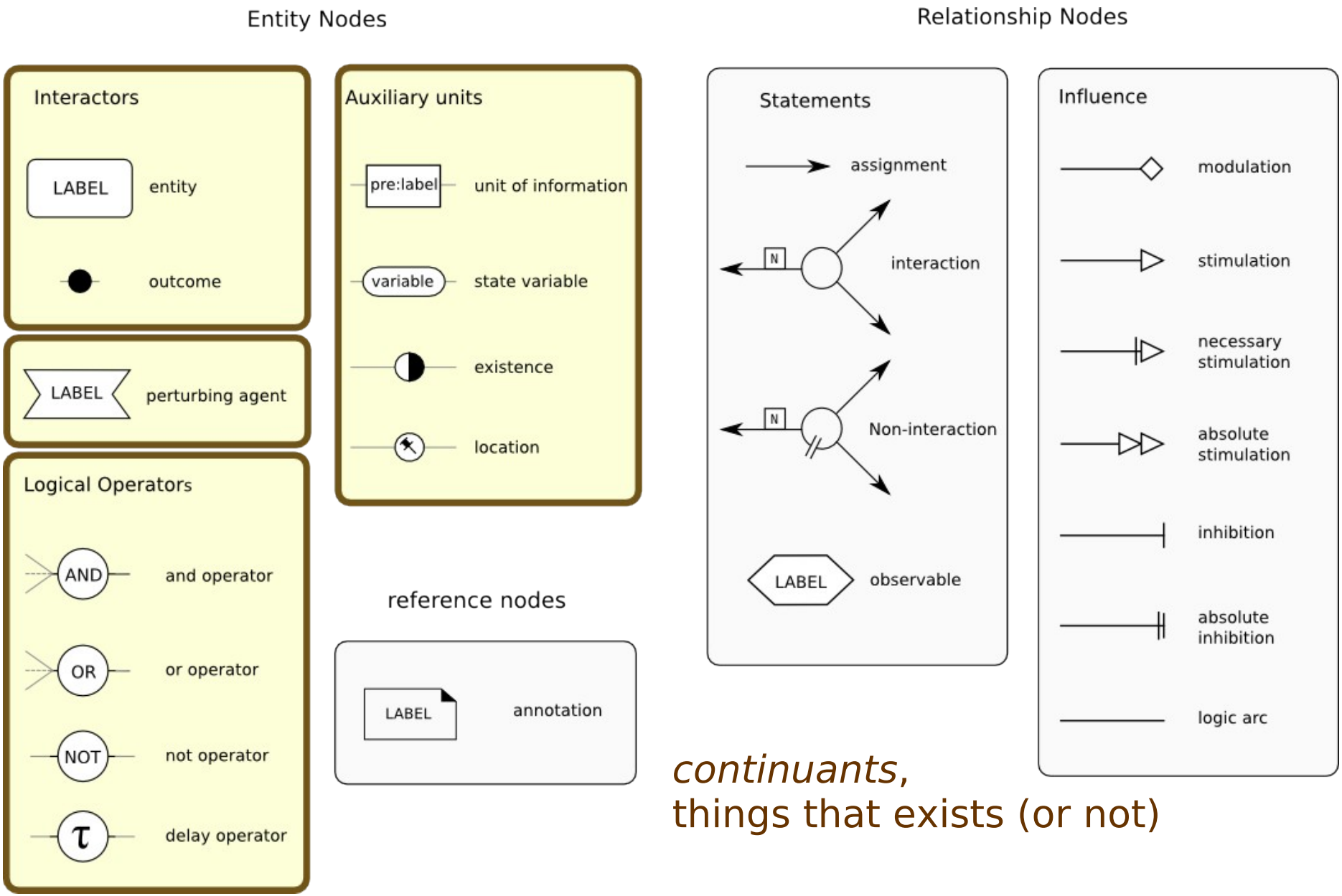




SBGN Entity Relationships L1 reference card

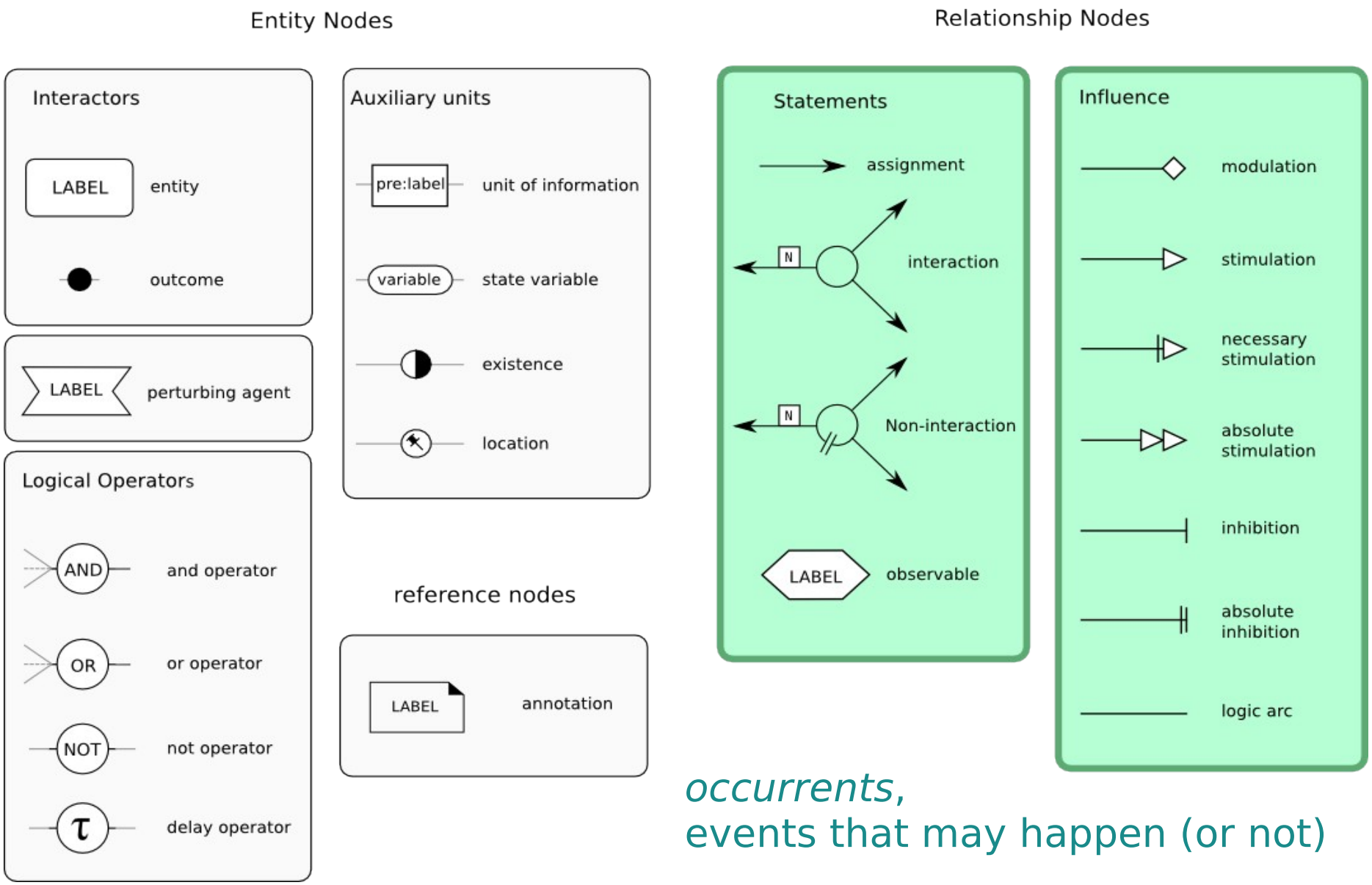


SBGN Entity Relationships L1 reference card



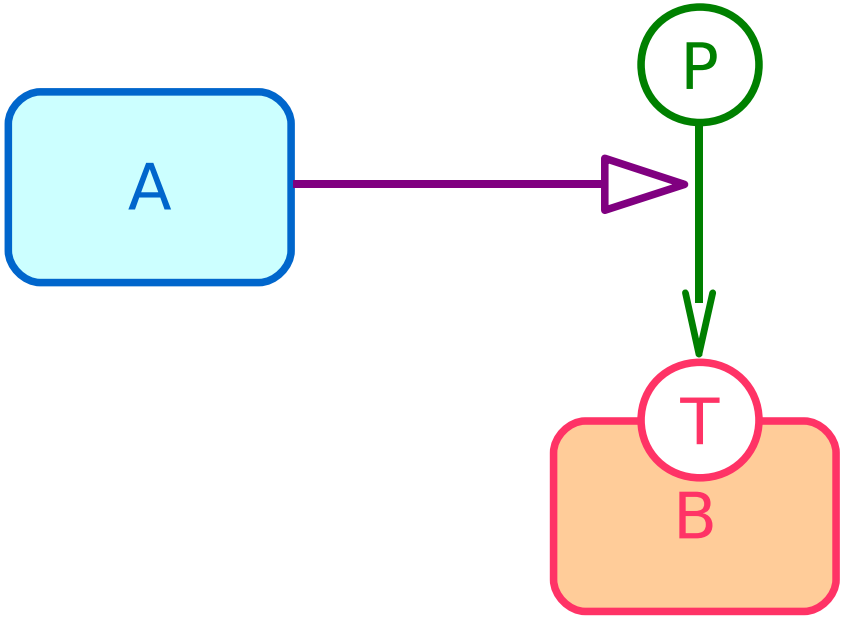
continuants,
things that exists (or not)

SBGN Entity Relationships L1 reference card

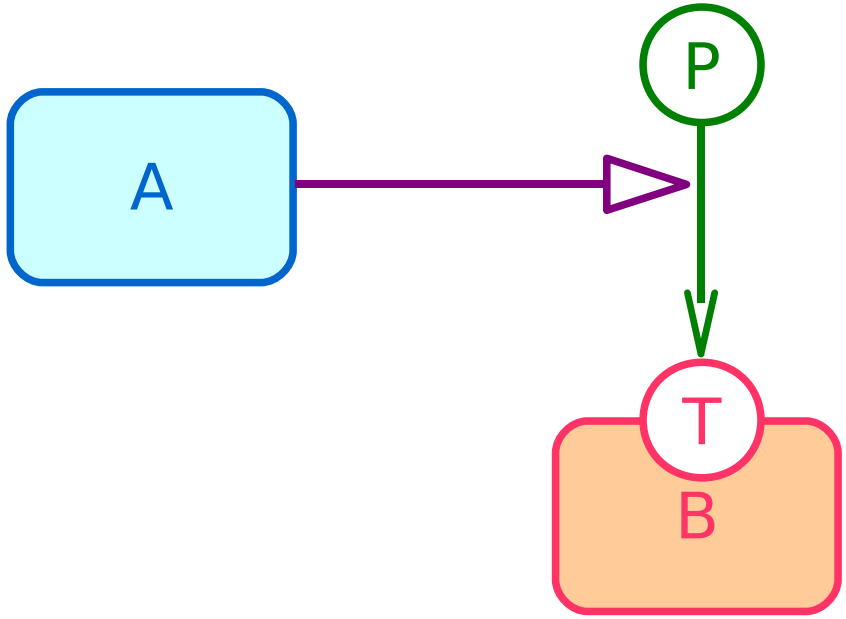


occurrents,
events that may happen (or not)

Entity Relationships can be viewed as rules

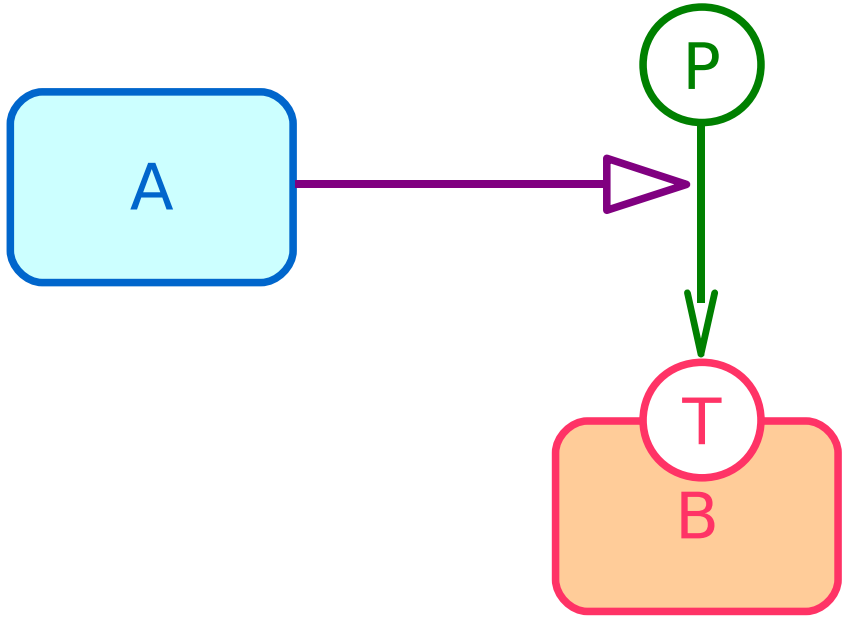


Entity Relationships can be viewed as rules



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

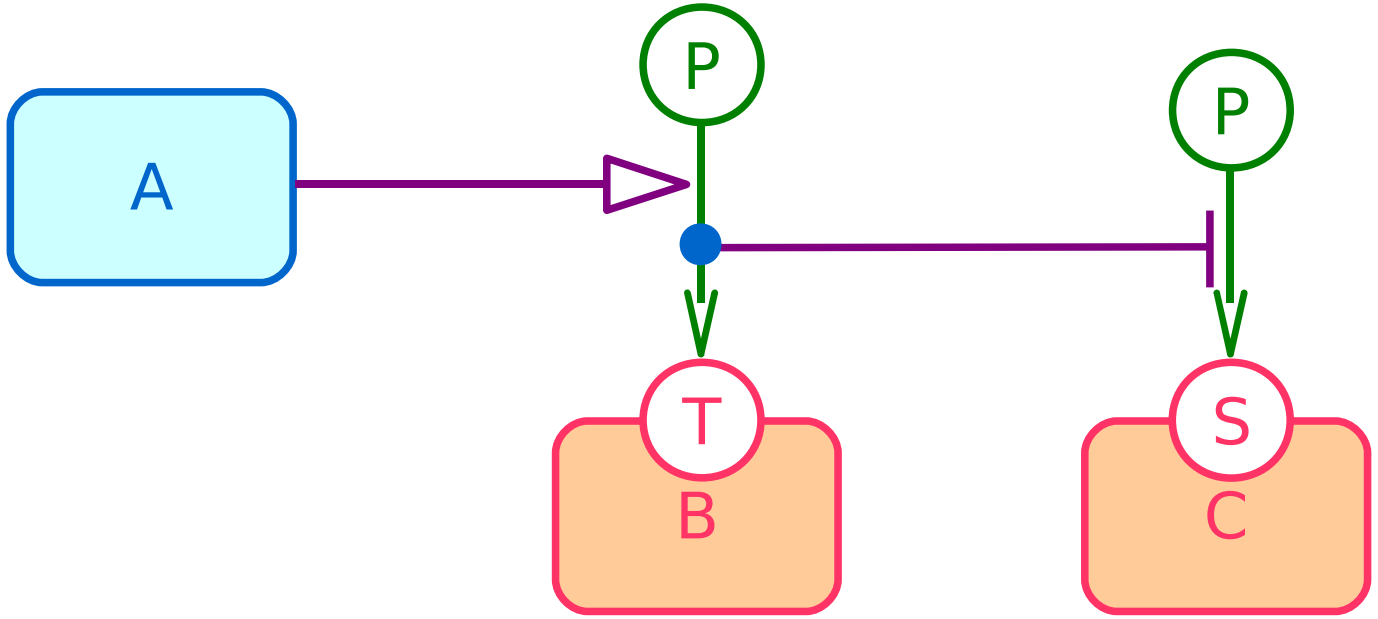
Entity Relationships can be viewed as rules



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)

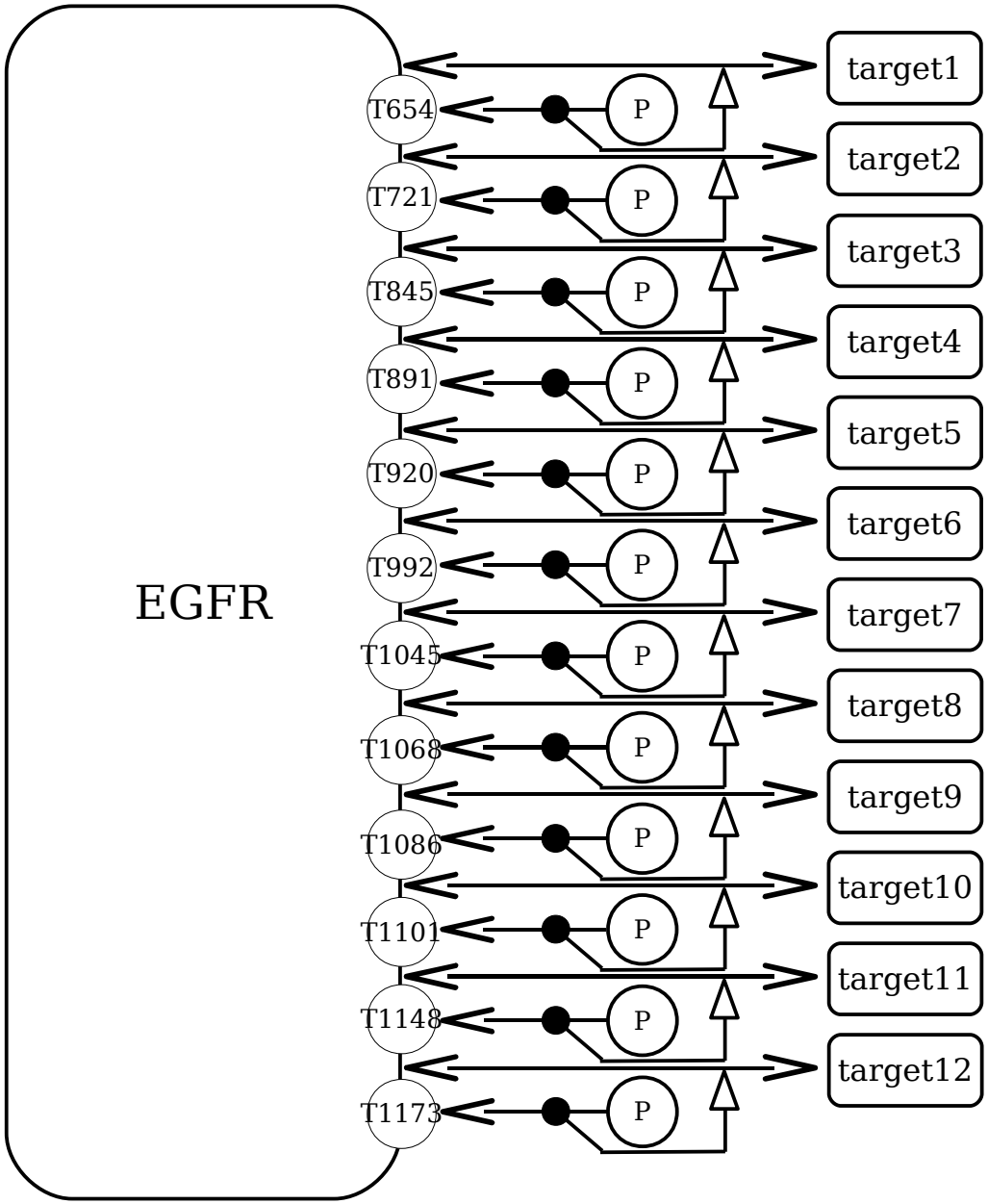
Entity Relationships can be viewed as rules



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

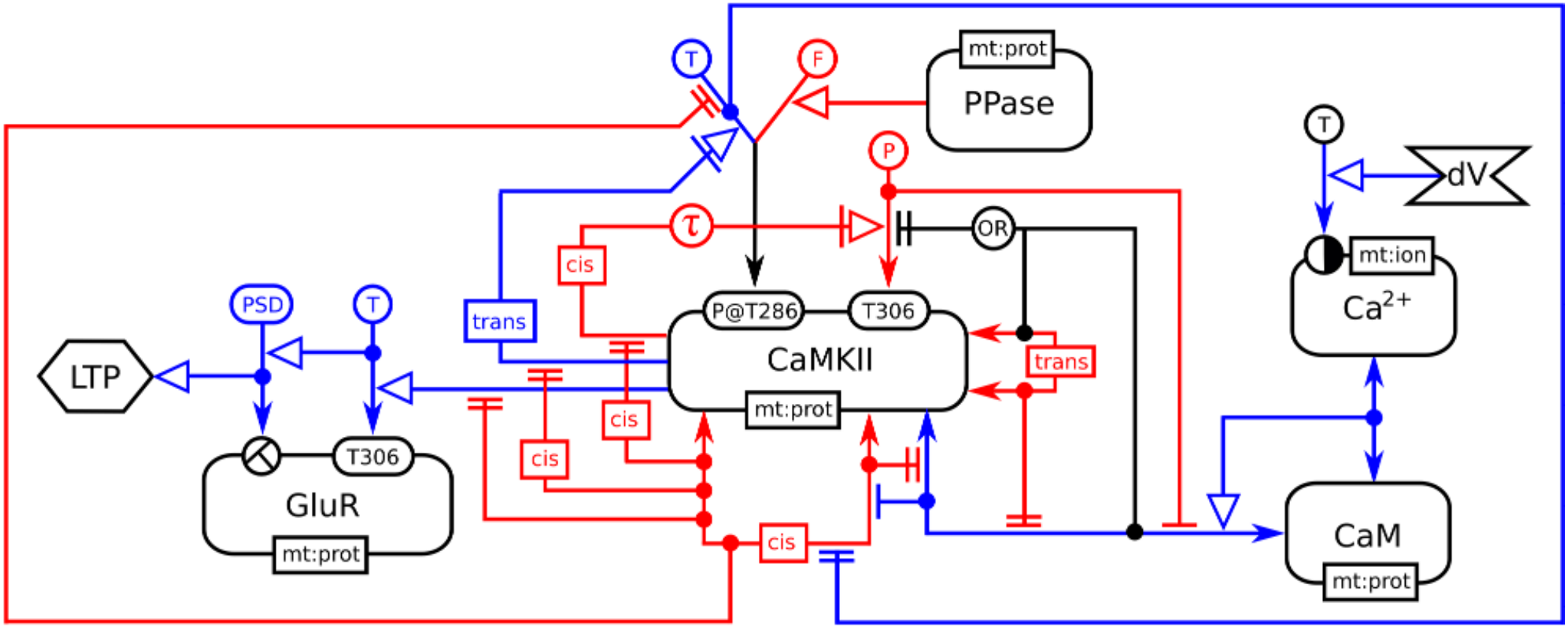
Multistate and combinatorial explosion



Process Diagram:
“once a state variable value,
always a state variable value”

2^{12} = 4096 states
(i.e. EPN glyphs) for EGFR
and 4096 complexes between
EGFR and targets

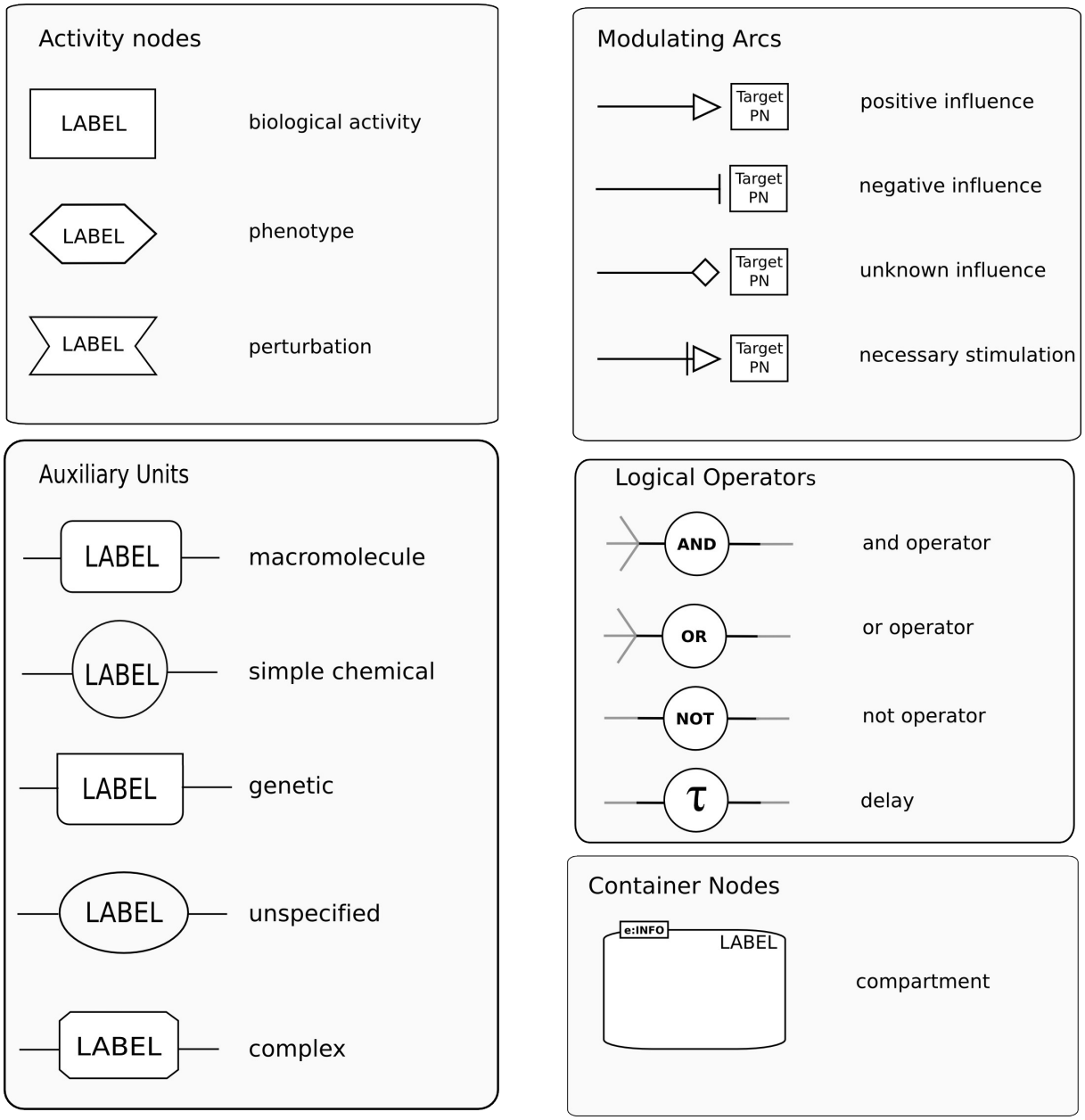
Example of Entity Relationships map



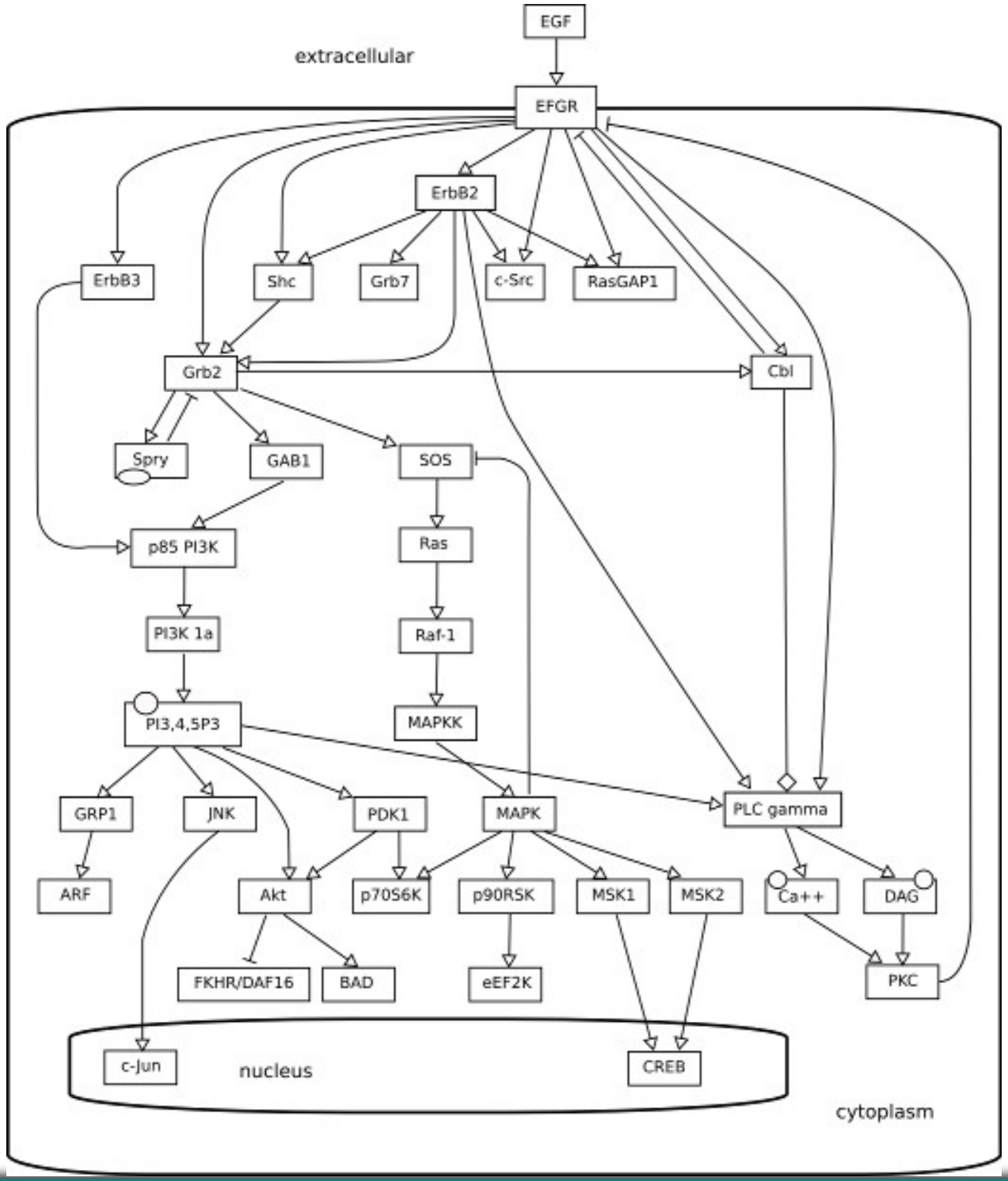
increases synaptic weight

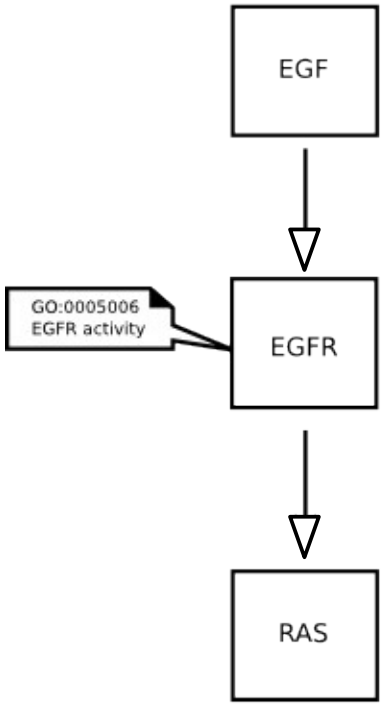
decreases synaptic weight

SBGN Activity Flow L1 reference card



Example of Activity Flow map

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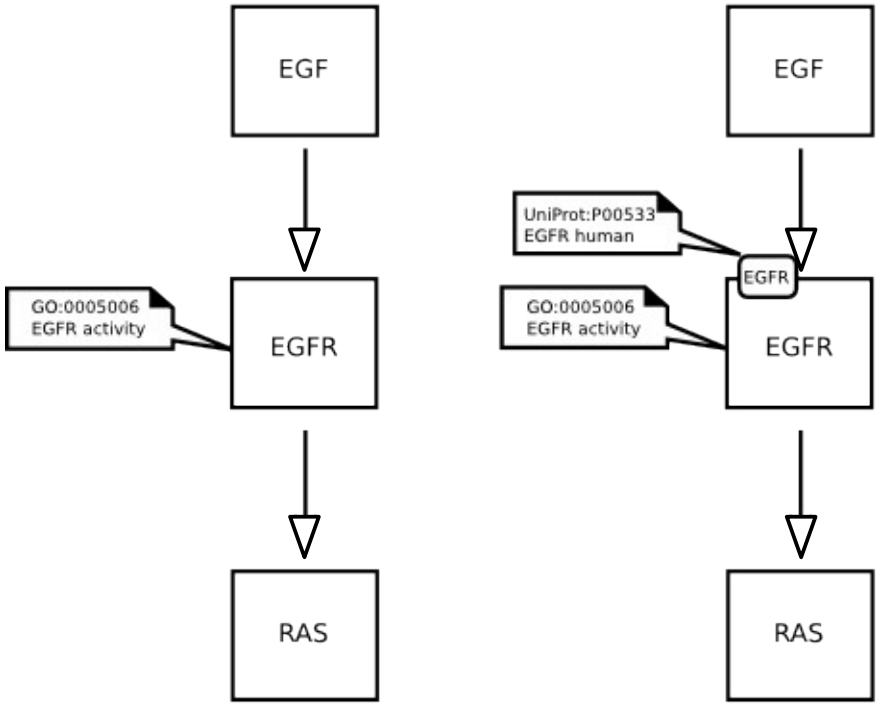
GO:0005006
EGFR activity
EGFR
RAS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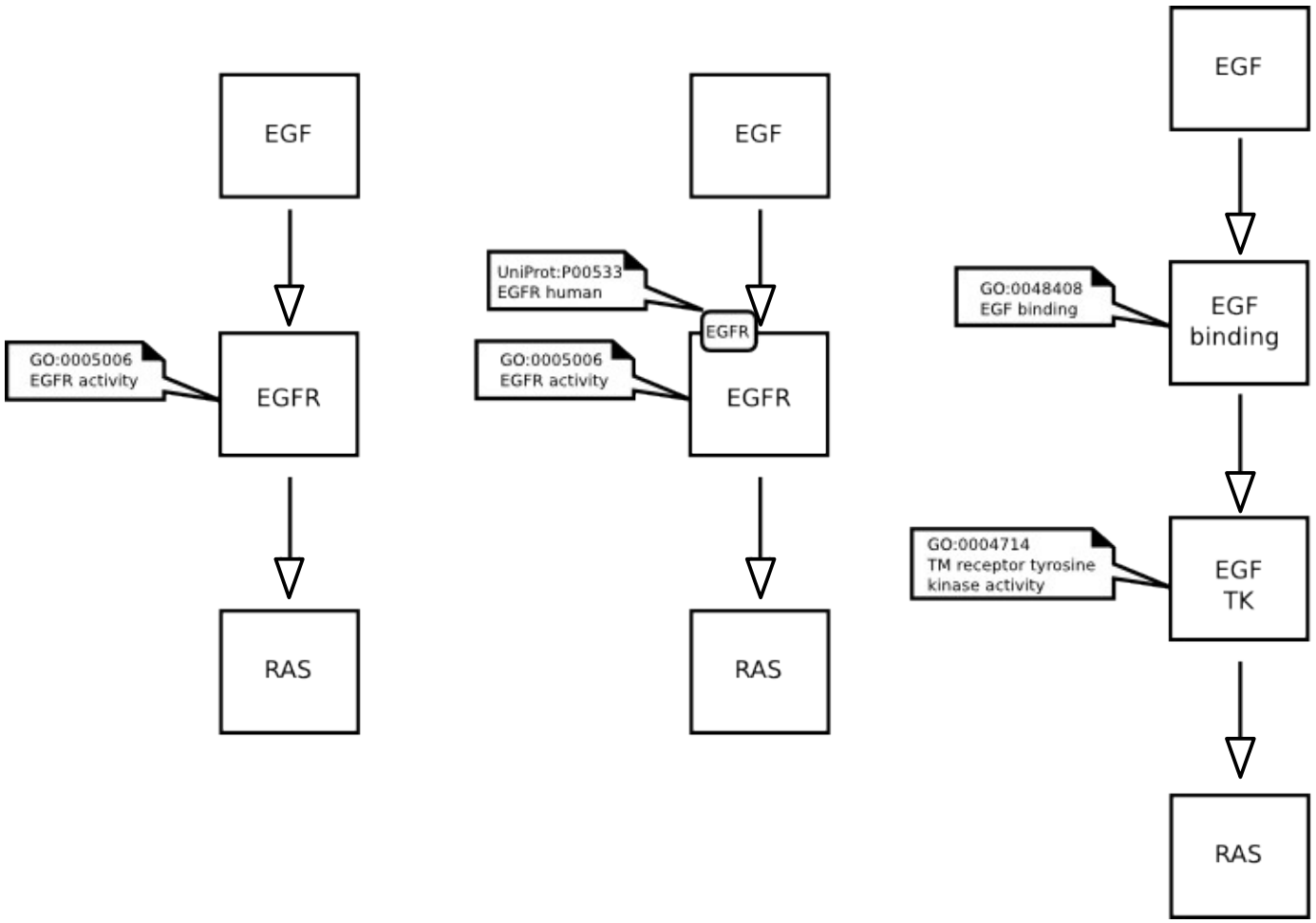
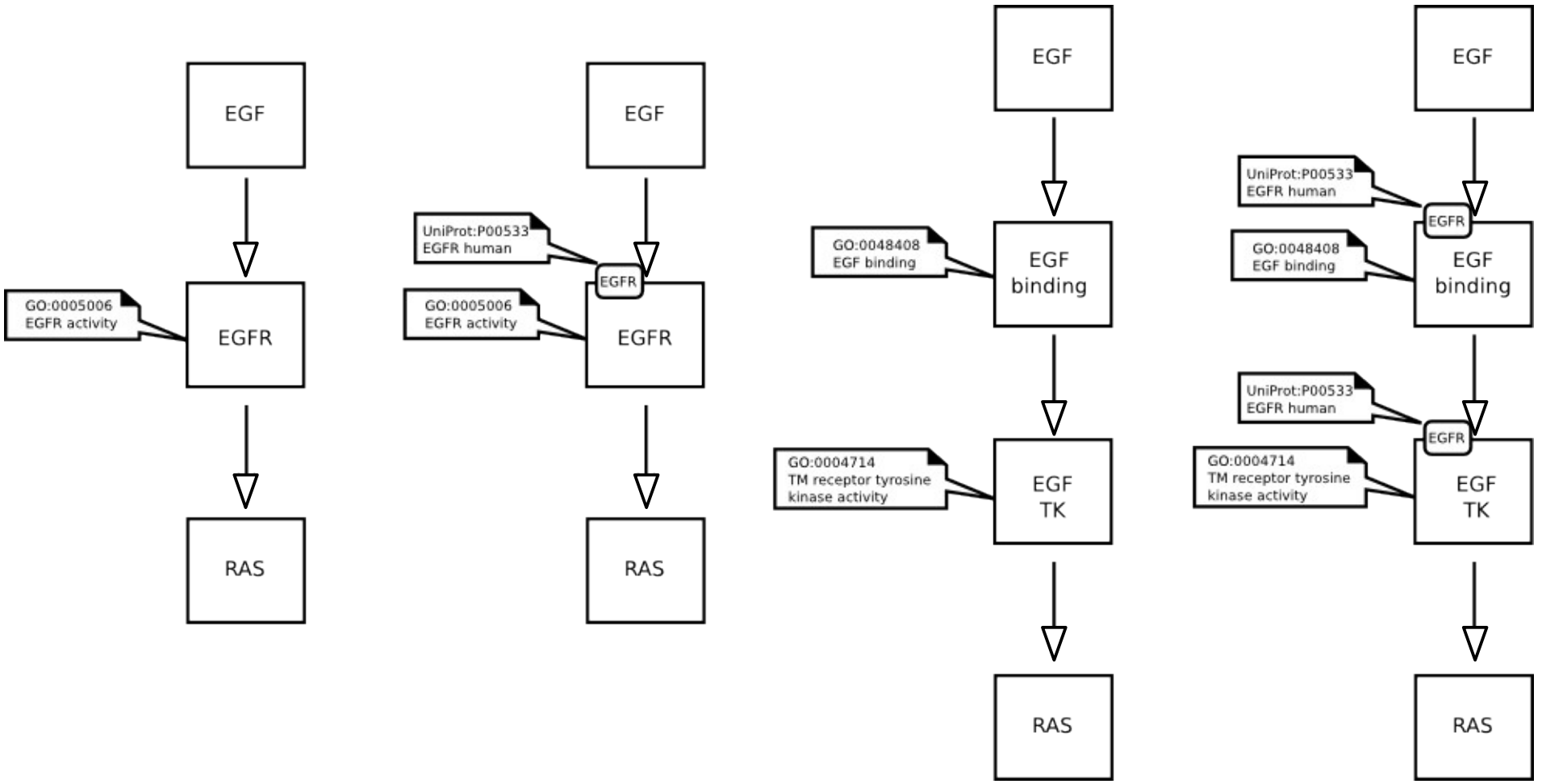
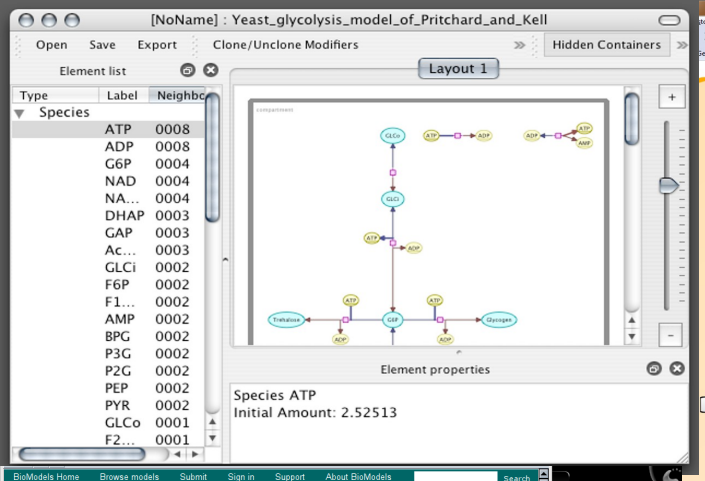
GO:0005006
EGFR activity
EGFR
RAS
EGF
UniProt:P00533
EGFR human
EGFR
GO:0005006
EGFR activity
EGFR
RAS


EGF
GO:0005006
EGFR activity
EGFR
RAS
EGF
UniProt:P00533
EGFR human
EGFR
GO:0005006
EGFR activity
EGFR
RAS
EGF
GO:0048408
EGF binding
EGF
binding
GO:0004714
TM receptor tyrosine
kinase activity
EGF
TK
RAS


EGF
GO:0005006
EGFR activity
EGFR
RAS
EGF
UniProt:P00533
EGFR human
EGFR
GO:0005006
EGFR activity
EGFR
RAS
EGF
GO:0048408
EGF binding
EGF
binding
GO:0004714
TM receptor tyrosine
kinase activity
EGF
TK
RAS
EGF
UniProt:P00533
EGFR human
EGFR
GO:0048408
EGF binding
EGF
binding
UniProt:P00533
EGFR human
EGFR
GO:0004714
TM receptor tyrosine
kinase activity
EGF
TK
RAS


[NoName] : Yeast_glycolysis_model_of_Pritchard_and_Kell
Open
Save
Export
Clone/Unclone Modifiers
Hidden Containers
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Layout 1
Type
Label
Species
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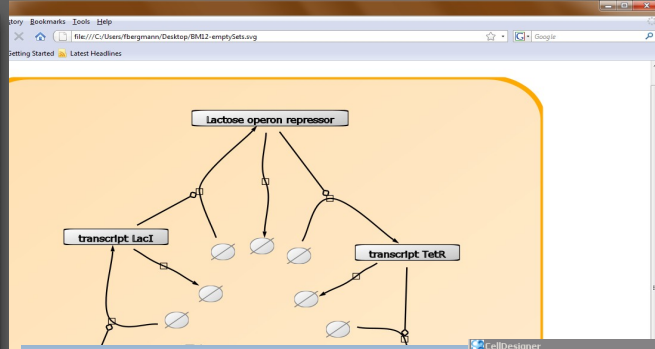
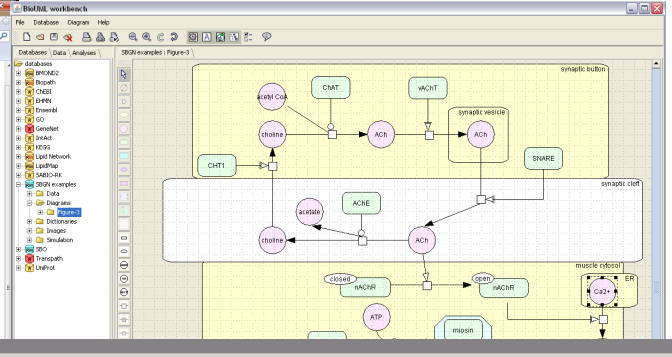
ADP 0008
G6P 0004
NAD 0004
NA... 0004
DHAP 0003
GAP 0003
Ac... 0003
GLCi 0002
F6P 0002
F1... 0002
AMP 0002
BPG 0002
P3G 0002
P2G 0002
PEP 0002
PYR 0002
GLCo 0001
F2... 0001
Element properties
Species ATP
Initial Amount: 2.52513


Lactose operon repressor
transcript LacI
transcript TetR


BioUML workbench
synaptic button
synaptic vesicle
synaptic cleft
muscle cytosol
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SNARE
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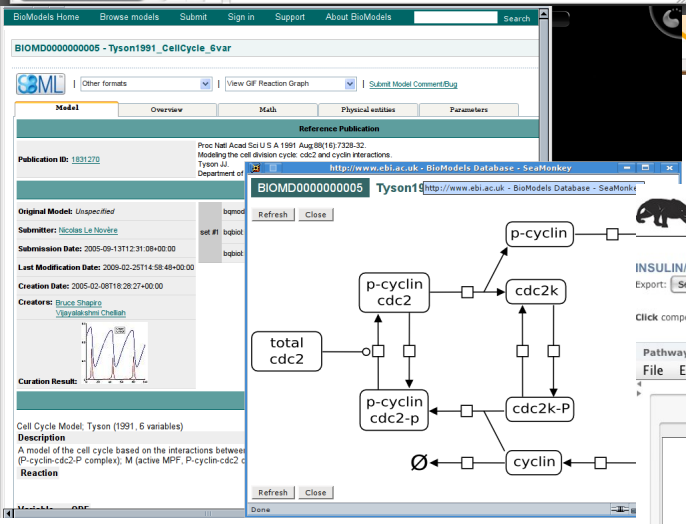
CHAT
VACHT
nAChR
closed
open
ATP
myosin
Ca2+
ER


BioModels Home
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Submit
Sign in
Support
About BioModels
BIOMD0000000005 - Tyson1991_CellCycle_6var
SBML
Model
Overview
Math
Physical entities
Parameters
Reference Publication
Publication ID: 1831270
Original Model: Unspecified
Submitter: Nicolas Le Novère
Submission Date: 2005-09-13T12:31:08+00:00
Last Modification Date: 2009-02-25T14:58:48+00:00
Creation Date: 2005-02-08T18:28:27+00:00
Creators: Bruce Shapiro
Vijayalakshmi Chelliah
Curation Result:
Cell Cycle Model; Tyson (1991, 6 variables)
Description
Reaction

BIOMD0000000005 Tyson19
http://www.ebi.ac.uk - BioModels Database - SeaMonkey
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Close
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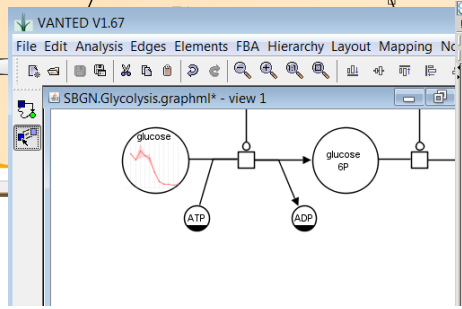
p-cyclin cdc2
cdc2k
total cdc2
p-cyclin cdc2-p
cdc2k-P
cyclin
Ø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glucose
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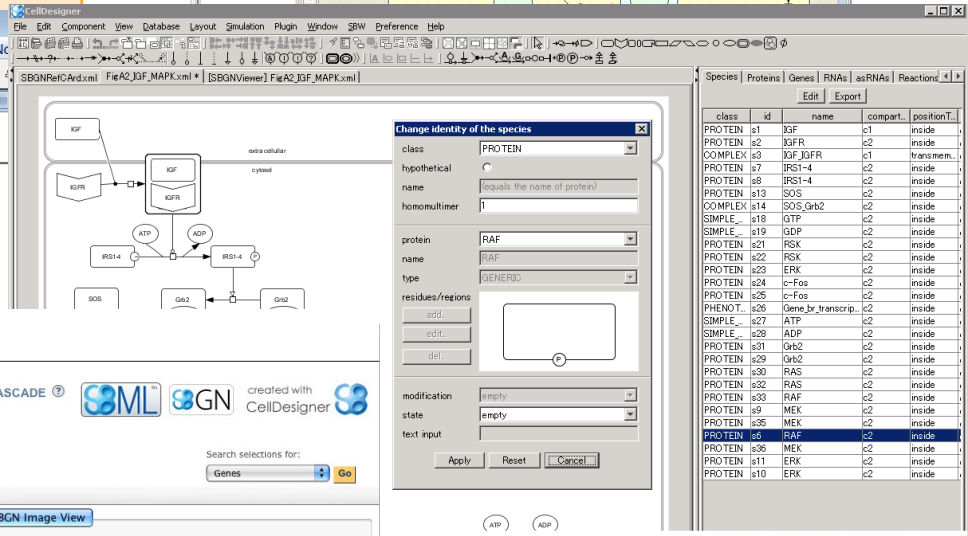
ATP
ADP


CellDesigner
File Edit Component View Database Layout Simulation Plugin Window SBW Preference Help
Change identity of the species
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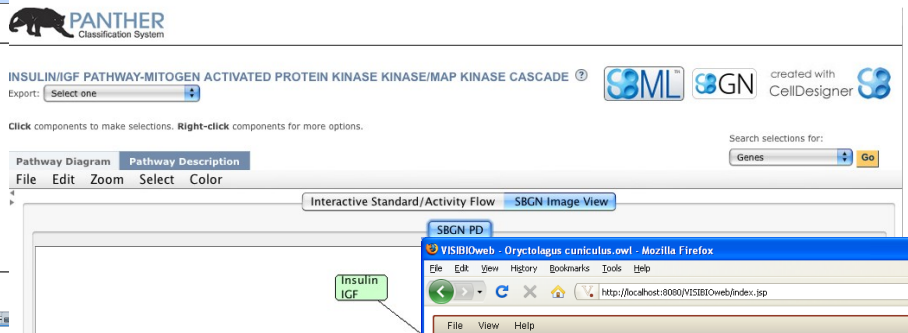
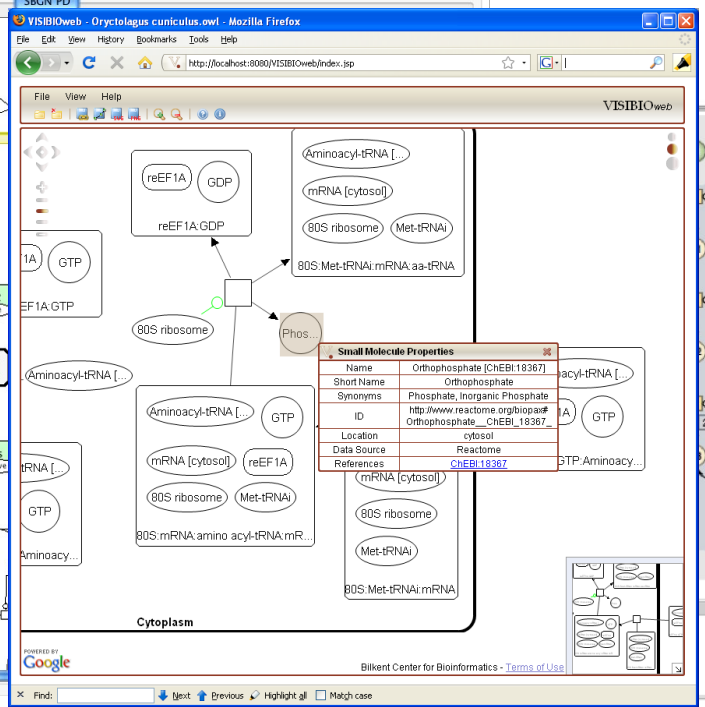
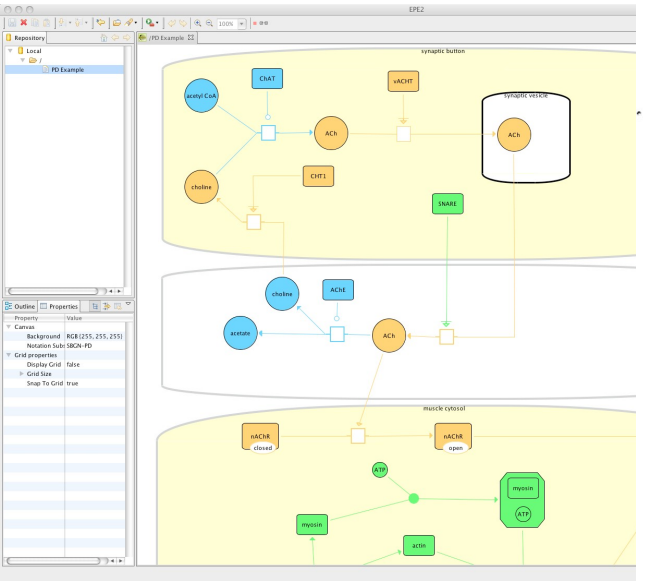
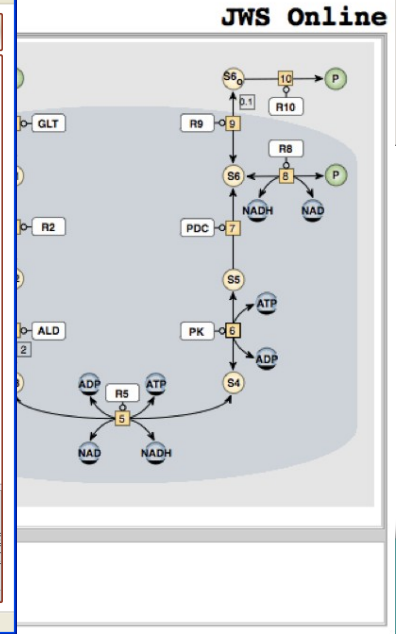
PROTEIN
hypothetical
name
homomultimer
protein
RAF
type
residues/regions
modification
state
empty
text input
Apply
Reset
Cancel
Species
Proteins
Genes
RNAs
asRNAs
Reactions
Edit
Export


PANTHER
Classification System
INSULIN/IGF PATHWAY-MITOGEN ACTIVATED PROTEIN KINASE KINASE/MAP KINASE CASCADE
Export:
Select one
SBML
SBGN
created with CellDesigner
Click components to make selections. Right-click components for more options.
Search selections for:
Genes
Go
Pathway Diagram
Pathway Description
File Edit Zoom Select Color
Interactive Standard/Activity Flow
SBGN Image View
SBGN PD
Insulin IGF
INSR IGF-R IRR
SOS
Grb2
Active
Ras
Raf
ATP
MEK
ATP


VISIBIOweb - Oryctolagus cuniculus.owl - Mozilla Firefox
http://localhost:8080/VISIBIOweb/index.jsp
File View Help
VISIBIOweb
reEF1A
GDP
reEF1A:GDP
Aminoacyl-tRNA [...
mRNA [cytosol]
80S ribosome
Met-tRNAi
80S:Met-tRNAi:mRNA:aa-tRNA
GTP
EF1A:GTP
Phos...
Small Molecule Properties
Name Orthophosphate [ChEBI:18367]
Short Name Orthophosphate
Synonyms Phosphate, Inorganic Phosphate
ID http://www.reactome.org/biopax#Orthophosphate__ChEBI_18367_
Location cytosol
Data Source Reactome
References ChEBI:18367
80S:mRNA:amino acyl-tRNA:mR...
80S:Met-tRNAi:mRNA
Cytoplasm
Bilkent Center for Bioinformatics - Terms of Use
Find: Next Previous Highlight all Match case

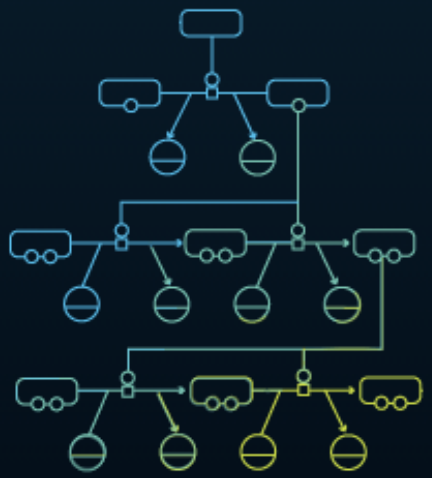

EPE2
synaptic button
synaptic vesicle
muscle cytosol
ChAT
vAChT
ACh
CHT1
choline
SNARE
AChE
acetate
nAChR
closed
open
mysin
actin
ATP


JWS Online
Search | Upload | About | Help
GLT
R9
R8
S6
NADH
NAD
R2
PDC
S5
ALD
PK
ATP
ADP
S4
R5
NAD
NADH

SBGN Systems Biology Graphical Notation

http://www.sbgn.org/

Home | Documents | Forums | Community | Events | About | Google Site Search..



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 diagrams of biochemical and cellular processes studied in systems biology.

Standardizing the diagrammatic notation is crucial for more efficient and accurate transmission of biological knowledge between different research communities in the expanding field of systems biology. Notations traditionally used by researchers and software have been informal, idiosyncratic and highly variable. Until SBGN, there has been no standard agreed-upon convention defining precisely how to draw biochemical interaction diagrams in a regular and systematic way that helps readers interpret them consistently and unambiguously.

SBGN defines a comprehensive set of symbols with precise semantics, together with detailed syntactic rules defining their use and how diagrams are to be interpreted. By standardizing the visual notation, SBGN can serve as a bridge between different communities in research, education, publishing, and more. The real payoff will come when researchers are as familiar with the notation as electronics engineers are familiar with the notation of circuit schematics. If researchers are saved the time and effort required to familiarize themselves with different notations, they can spend more time thinking about the biology being depicted.

On this site, you can browse some example diagrams to get a feeling for SBGN, read the SBGN specification documents, 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.

SBGN News

(23 Aug.'08) The first **SBGN Process Diagrams Level 1** specification is out! Download the specification and tell us what you think!

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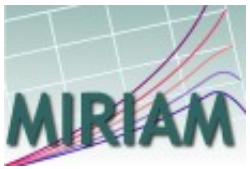
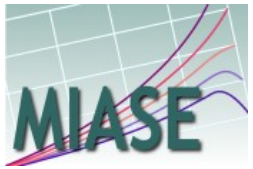
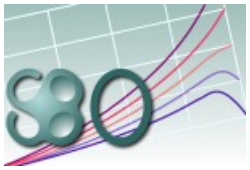
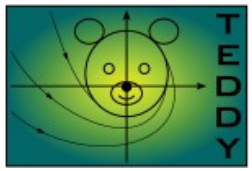
Future SBGN meetings

- 5th SBGN forum
  - 02-03 September 2009,
  - San Francisco
  - “Satellite” of ICSB 2009
- 4rd SBGN hackathon (SBGN 5.5)
  - 21-23 April 2010
  - Wittenberg
- 6th SBGN forum (provisional)
  - October 2010
  - Edinburgh
  - Satellite of ICSB 2010
- 5rd SBGN hackathon (SBGN 6.5)
  - Spring 2011, Bethesda, USA

Complete mosaic of standards

	Model definition	Simulation experiment	Numerical results
Minimal requirements			?
implemented by			
Data-models		SED-ML	SBRML
add meaning			
Ontologies			

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The whole community participating to SBGN meetings, and mailing-lists

NEDO

bbsrc biotechnology and biological sciences research council

NIGMS

EMBL