

The Systems Biology Graphical Notation

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



Graphs are everywhere in biology

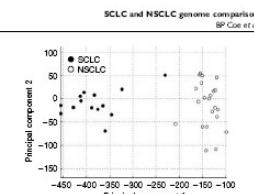
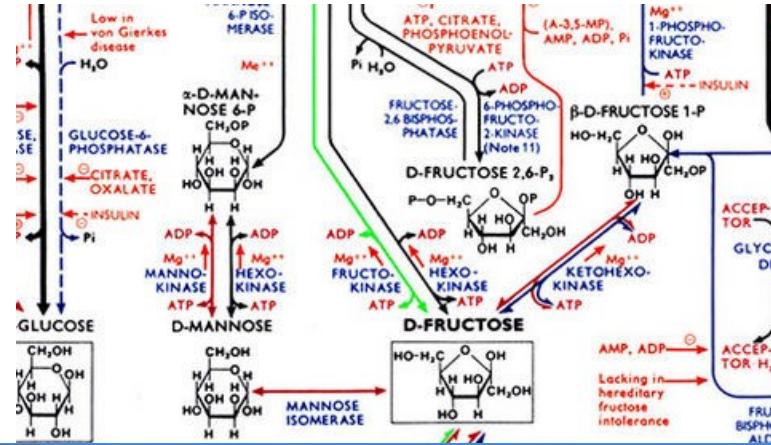
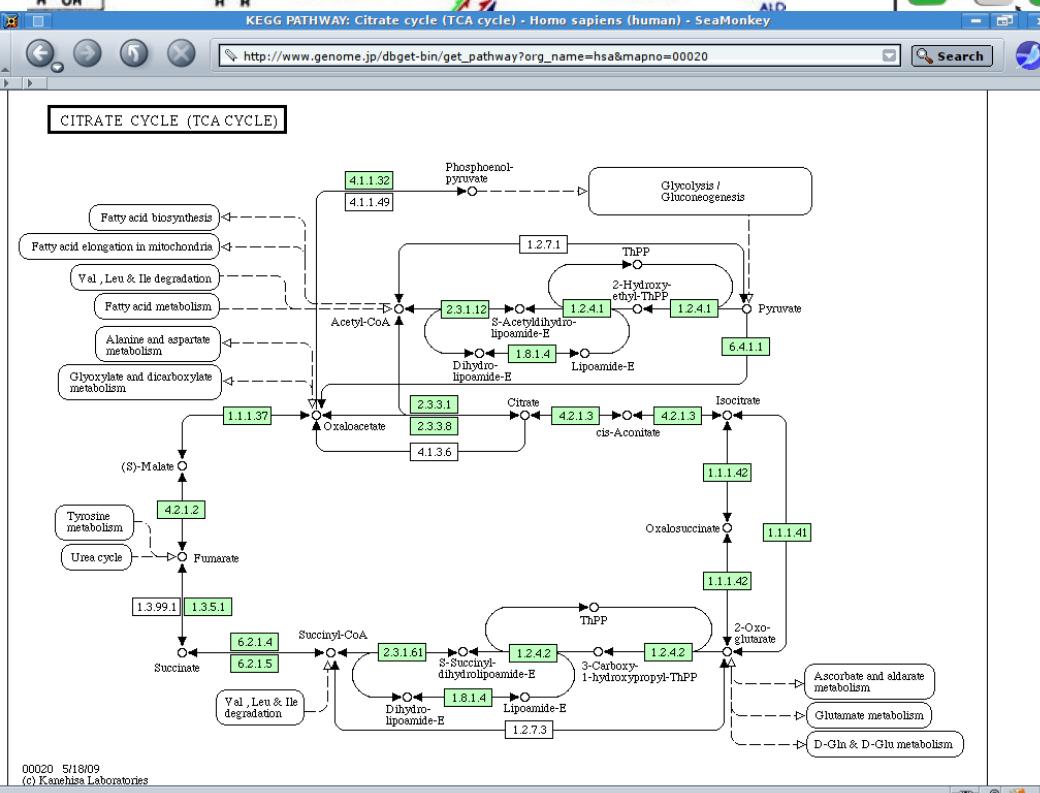
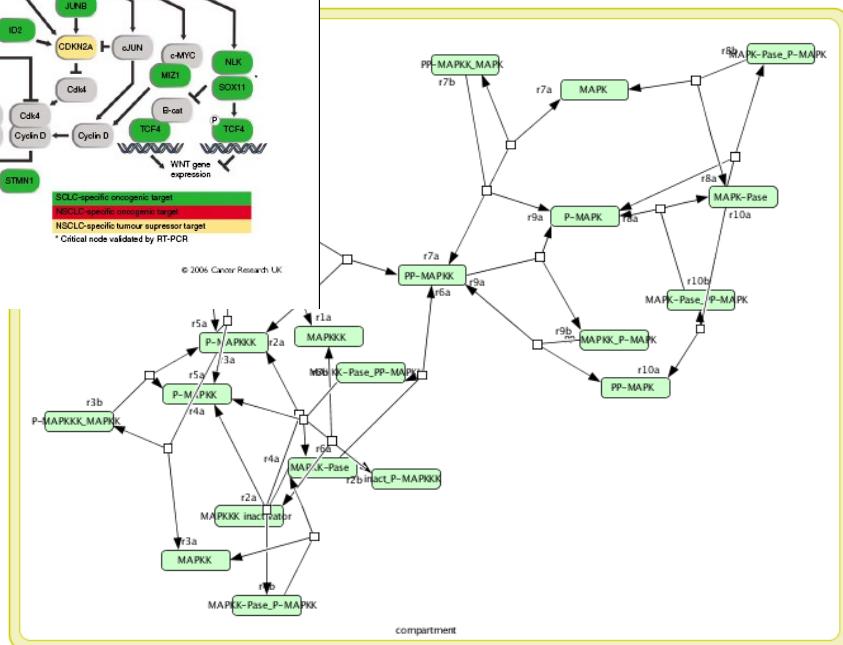
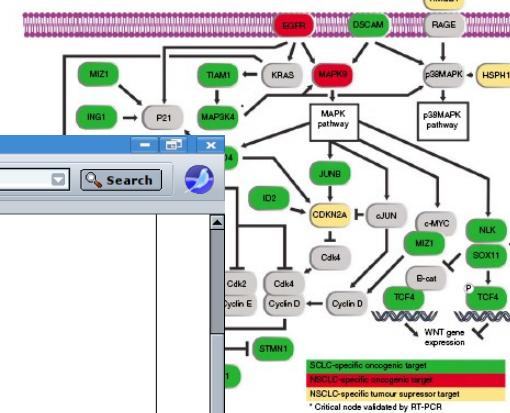
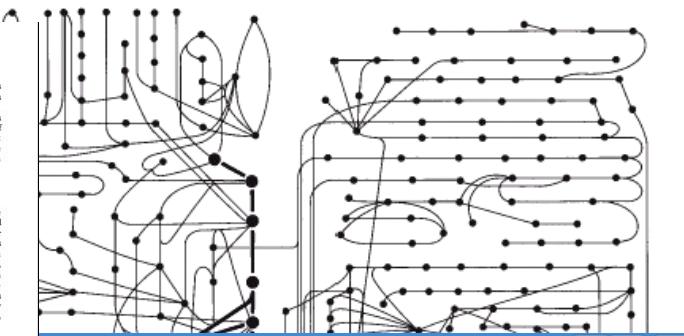


Figure 4 Contribution of copy number-induced gene expression differences to the SCLC and NSCLC phenotypes. Principal component analysis was performed utilising all 243 Affymetrix probe sets demonstrating expression differences as a result of copy number alterations. The SCLC samples are indicated by solid circles while the NSCLC samples are indicated by open circles. Strong separation of the SCLC and NSCLC cell lines along principal component 1 demonstrates the contribution of these genes to the differential phenotypes.

amplification in the NSCLC samples as well suggests that this gene may play an essential role in the development of lung cancer (Garnis *et al.* 2006).

It is noteworthy that a subset of the genomic similarities between the SCLC and NSCLC cell lines could be the result of adaptation to culturing conditions. Owing to this, the greatest insight into the biology of the clinical disease will be attainable through analysis of differences (rather than their similarities) in genomic alterations and gene regulation.

Regions of difference
 Through our analysis, numerous regions throughout the genome were determined to be differentially altered between the SCLC and NSCLC samples. This difference-based approach compensates for technical noise and thus provides a more robust analysis. These regions are most strongly linked to clinical disease. These regions range in size from whole chromosomes (chromosome 21) to discrete peaks kilobases in size (3q21). Using our stringent, multistep criteria (Fisher's exact test followed by additional thresholding), we detected several regions that differed strongly in their alteration status between the cell types; we refer to these as phenotype-specific copy number alterations (PSCNA). These included [p16q33-34] and



Ambiguity of usual representations

X → Y

Ambiguity of usual representations

X → 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

X → Y

X inhibits Y

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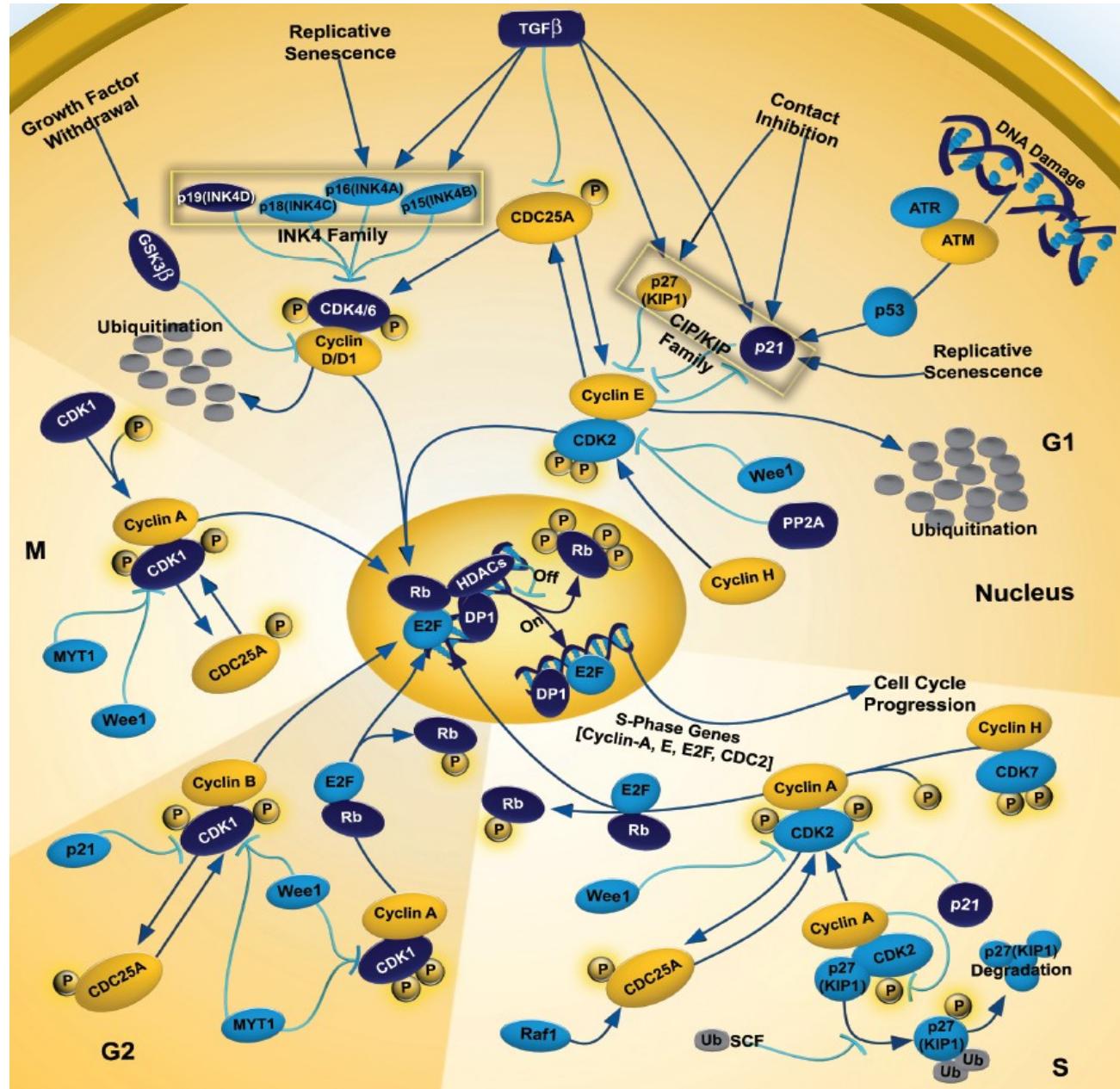
stimulates the expression of

catalyses the formation of

X inhibits Y



Can this be understood by biologists?



Can this be understood by biologists?

Stimulates? but ...
what exactly?

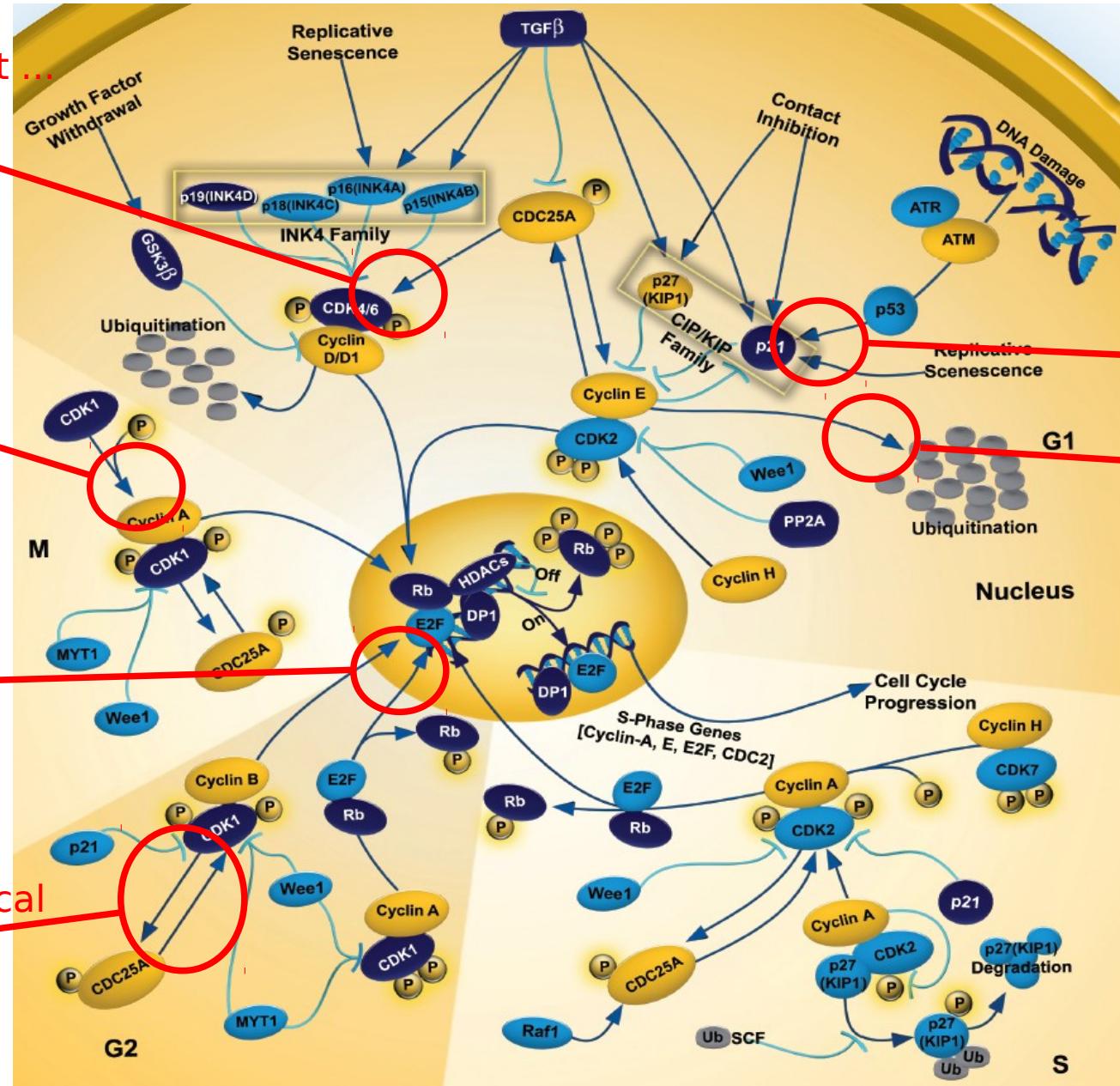
Associates into?

Translocates?

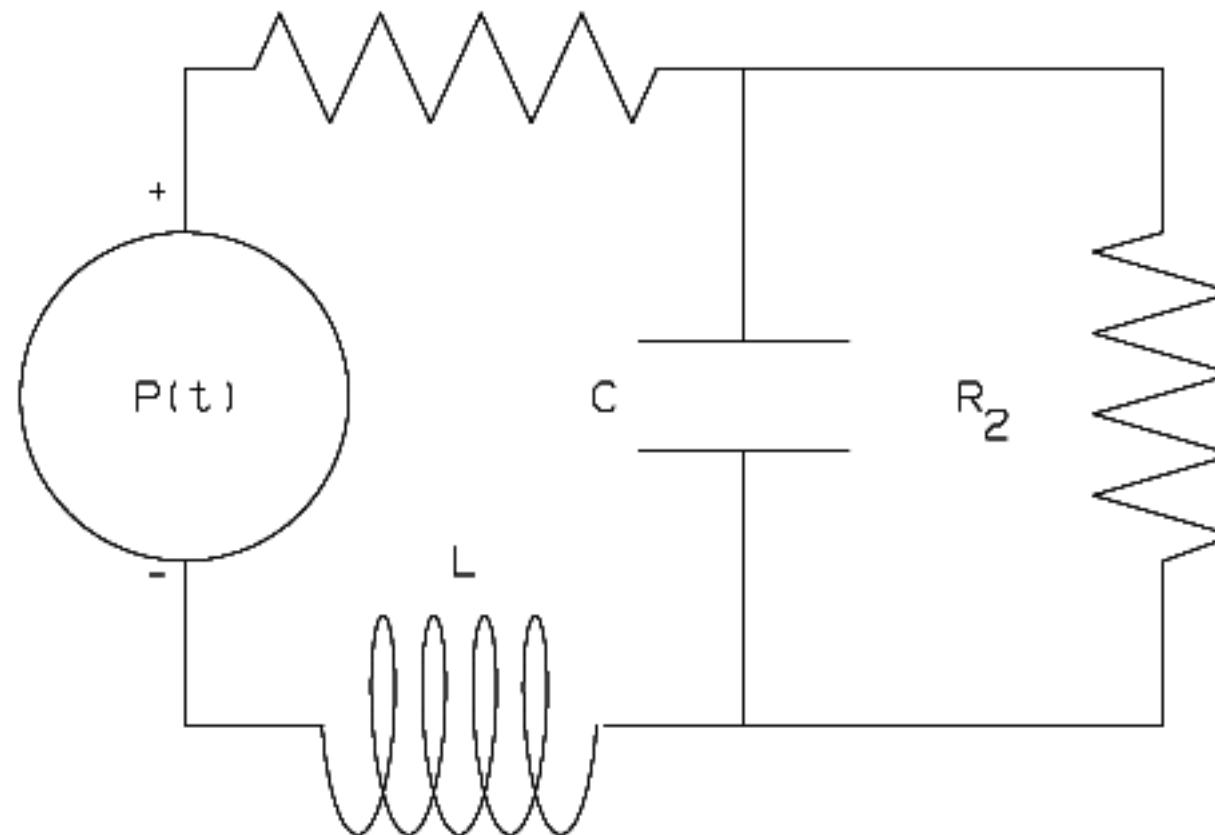
No idea. Reciprocal
stimulation?

Stimulates gene
transcription?

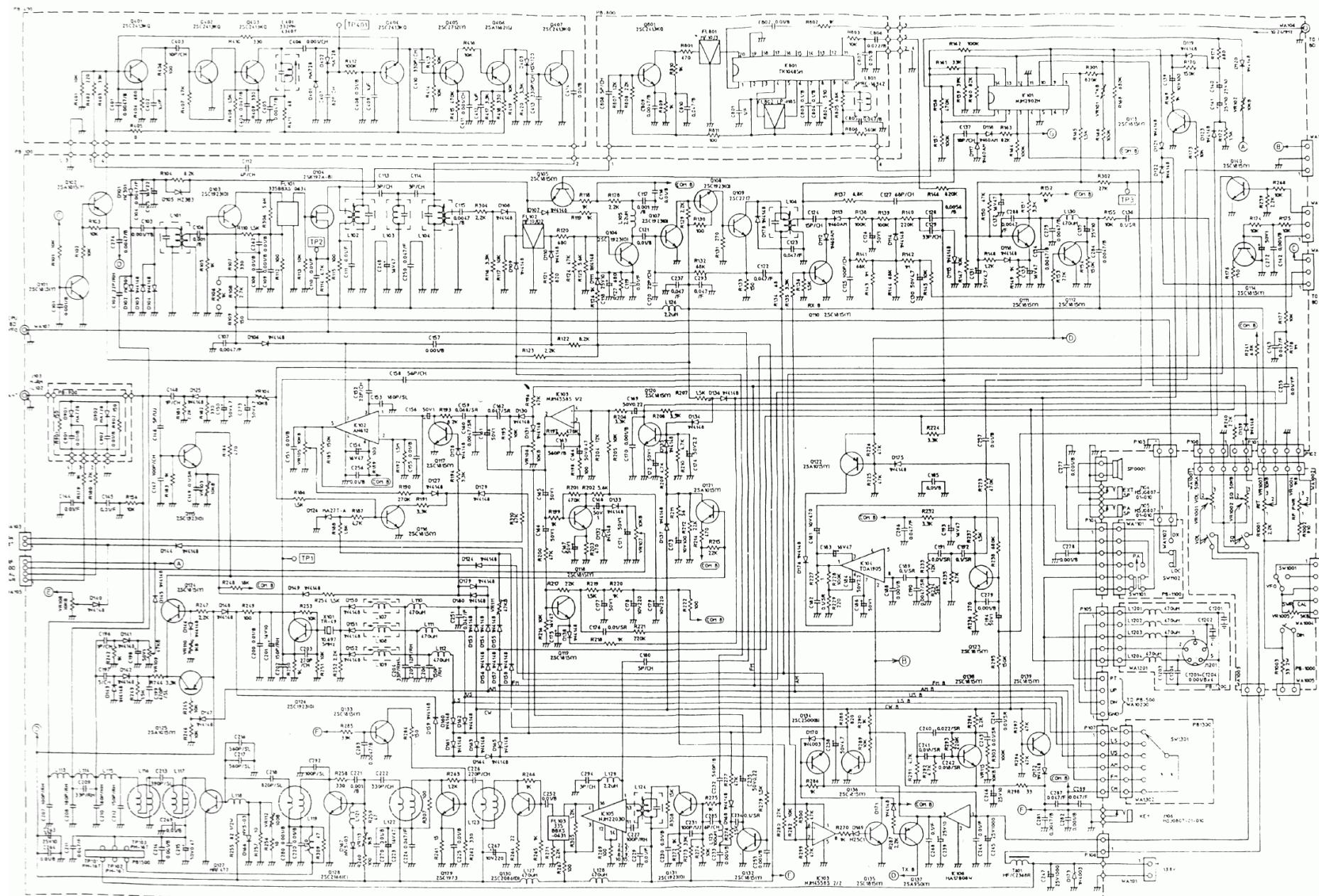
Is degraded?



Every engineer understands that



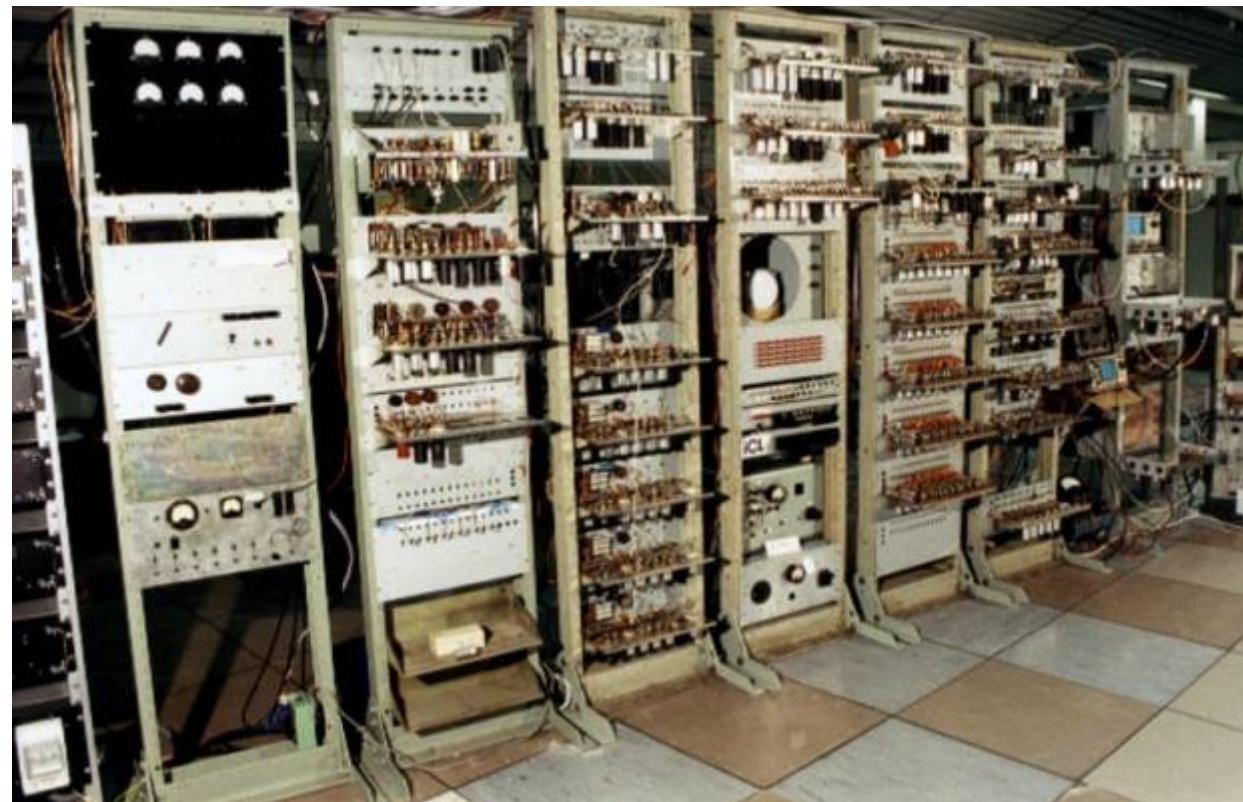
Or that



Date Integration in Life Sciences, 20-22 July 2009, Manchester

EMBL-EBI 

What did-those diagram bring?



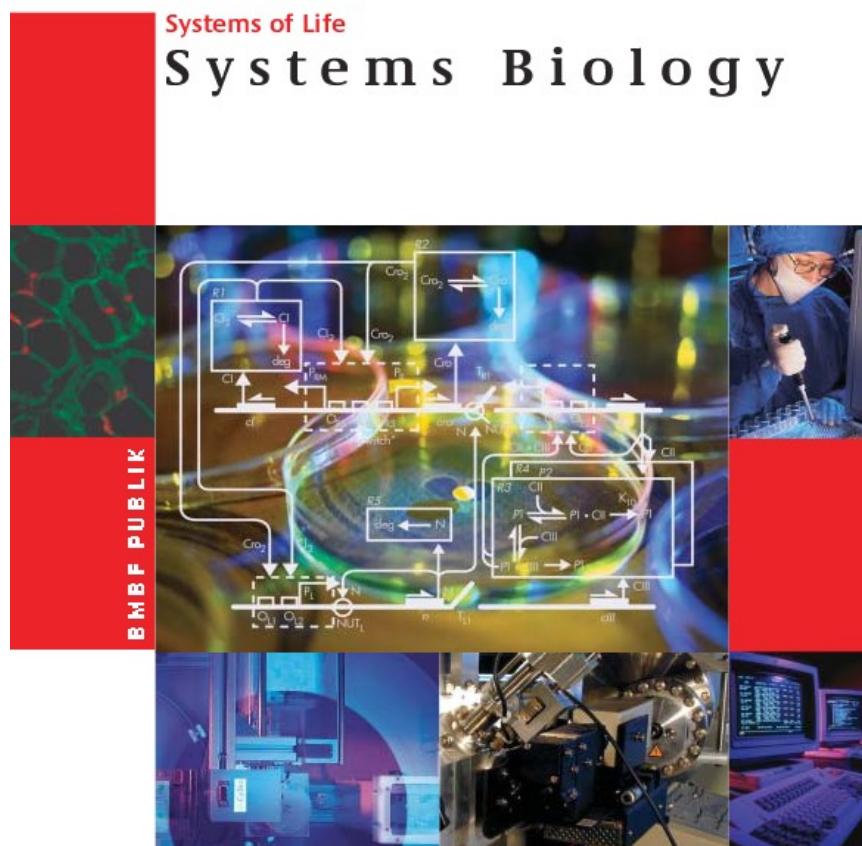
What did-those diagram bring?



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



Basic science



Systems of Life
Systems Biology

BMBF PUBLIK

The poster features a central diagram of a genetic circuit with various components labeled: R1, R2, R3, R4, R5, Cl, deg, N, P1, P2, P3, P4, T1, T2, CII, CIII, CIIII, and CIII. Arrows indicate interactions between these components. On the left, there is a fluorescence microscopy image showing green and red signals. On the right, a photograph shows a scientist in a blue lab coat and mask working at a bench. The bottom section shows two images: one of a robotic arm and another of a computer control panel.

Technology



EXTREME GENETIC ENGINEERING

An Introduction to Synthetic Biology

January 2007



- 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 Hucka², Huaiyu Mi^{3*}, Stuart Moodie⁴, Falk Schreiber^{5,6*}, Anatoly Sorokin⁷, Emek Demir⁸, Katja Wegner⁹, Mirit Aladjem¹⁰, Sarala M Wimalaratne¹¹, Frank T Bergman¹², Ralph Gauges¹³, Peter Ghazal^{4,21}, Kawaiji²², Hideya¹⁴, Lu Li¹, Yukiko Matsuoka¹⁵, Alice Villéger^{16,17}, Sarah E Boyd¹⁸, Laurence Calzone¹⁹, Melanie Courtot²⁰, Ugur Dogrusoz²¹, Tom Freeman²², Akira Funahashi²³, Samik Ghosh¹⁵, Akiya Jouraku²³, Sohyoung Kim¹⁰, Fedor Kolpakov²⁴, Augustin Luna¹⁰, Sven Sahle²⁵, Esther Schmidt¹, Steven Watterson^{4,22}, Guanming Wu²⁶, Igor Goryanin⁴, Douglas B. Kell^{17,27}, Chris Sander⁸, Herbert Sauro¹², Jacky L Snoep²⁸, Kurt Kohn¹⁰, Hiroaki Kitano^{15,29,30†}

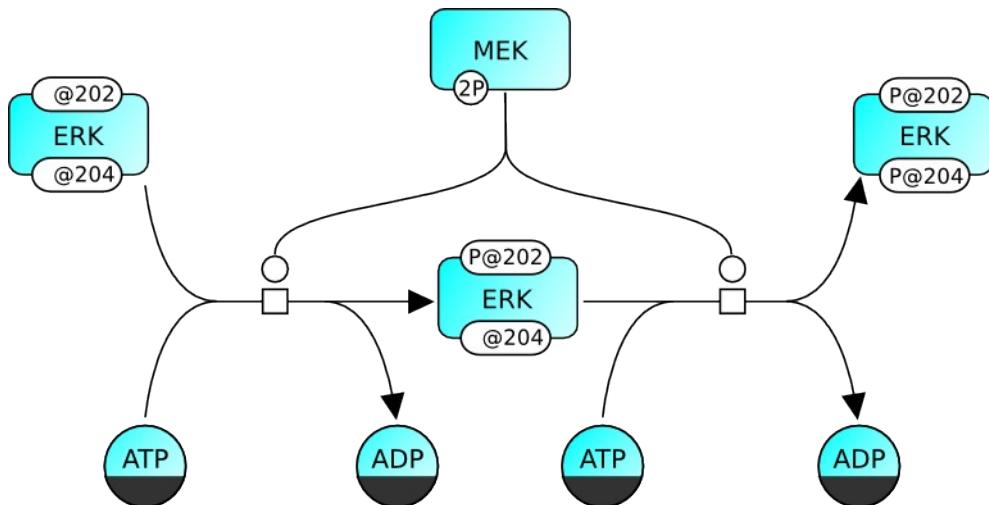
Nature Biotechnology, in the press

39 authors, 30 affiliations

- 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

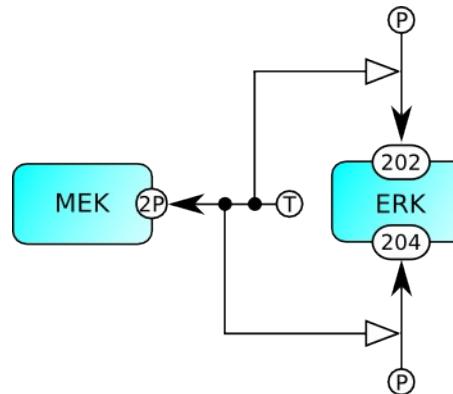
Graph trinity: three languages in one

Process diagrams



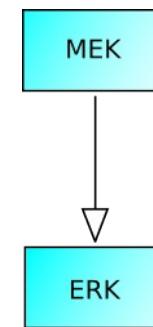
- Unambiguous
- Mechanistic
- Sequential
- Subject to combinatorial explosion

Entity Relationships diagrams



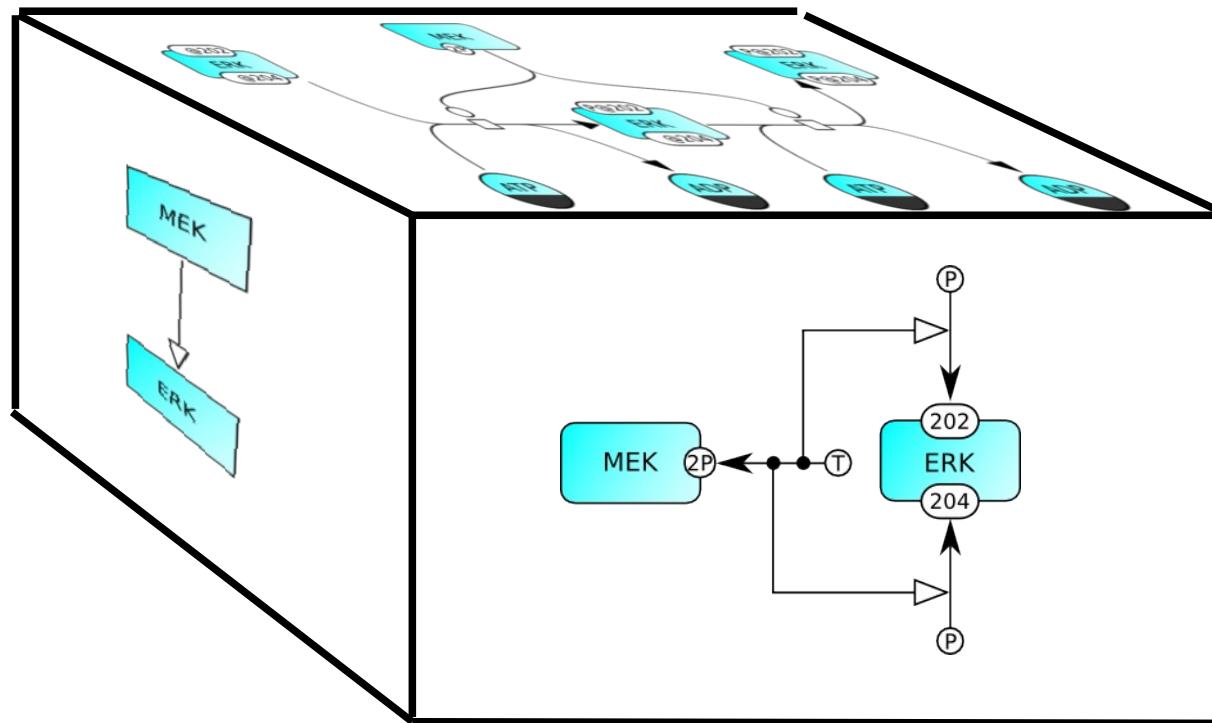
- Unambiguous
- Mechanistic
- Non-sequential
- Independence of relationships

Activity Flow diagrams

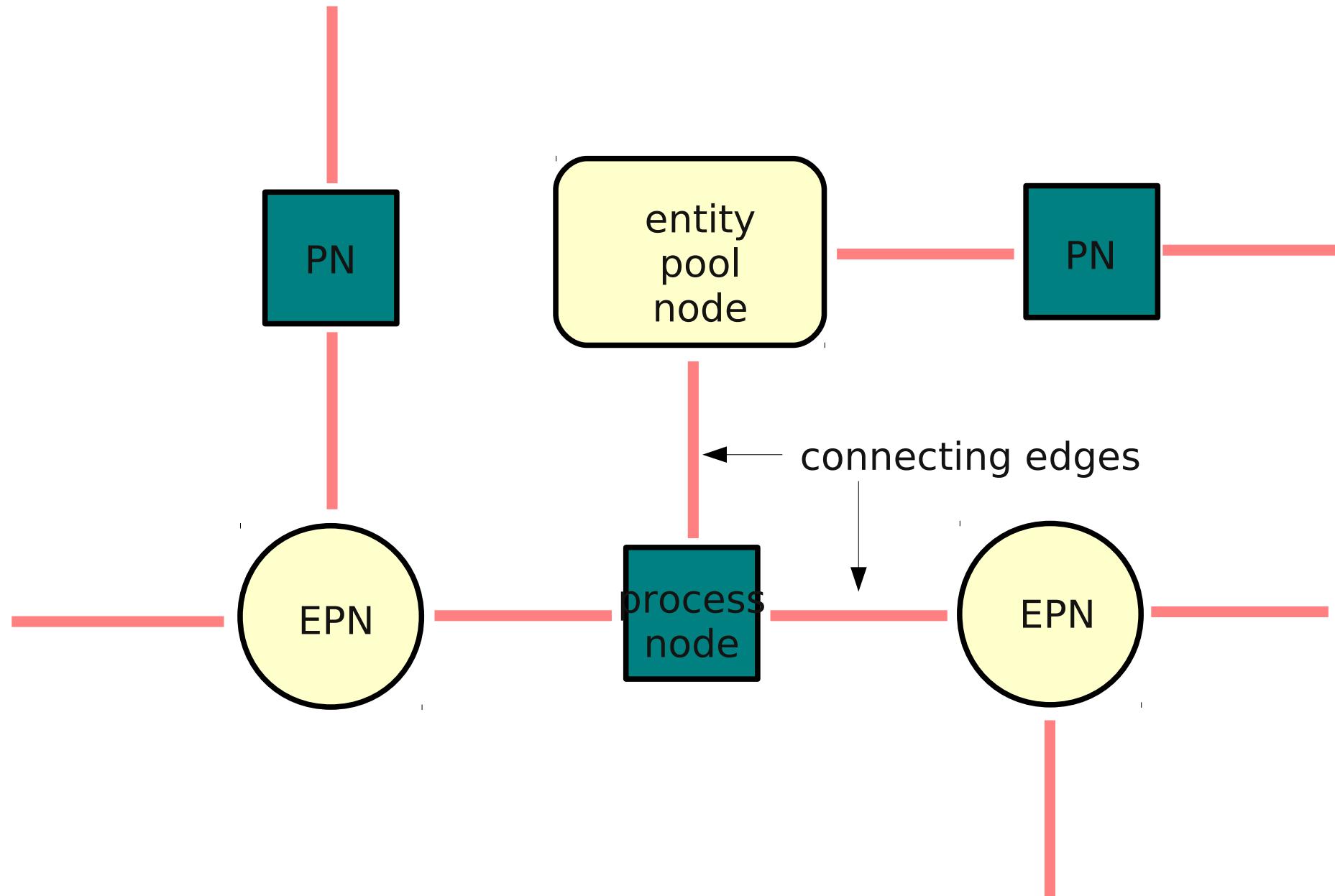


- Ambiguous
- Conceptual
- Sequential

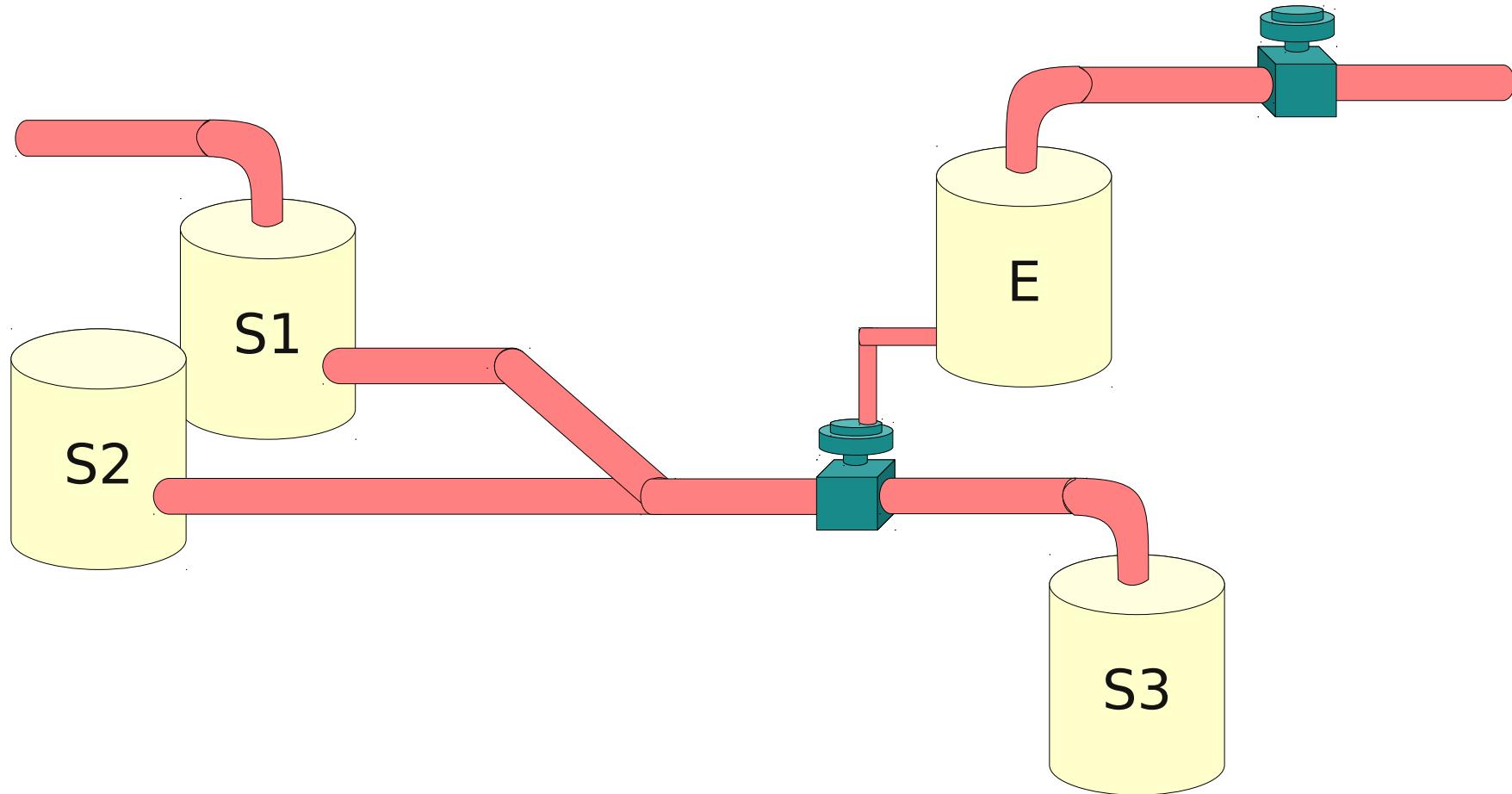
Three orthogonal projections of biology



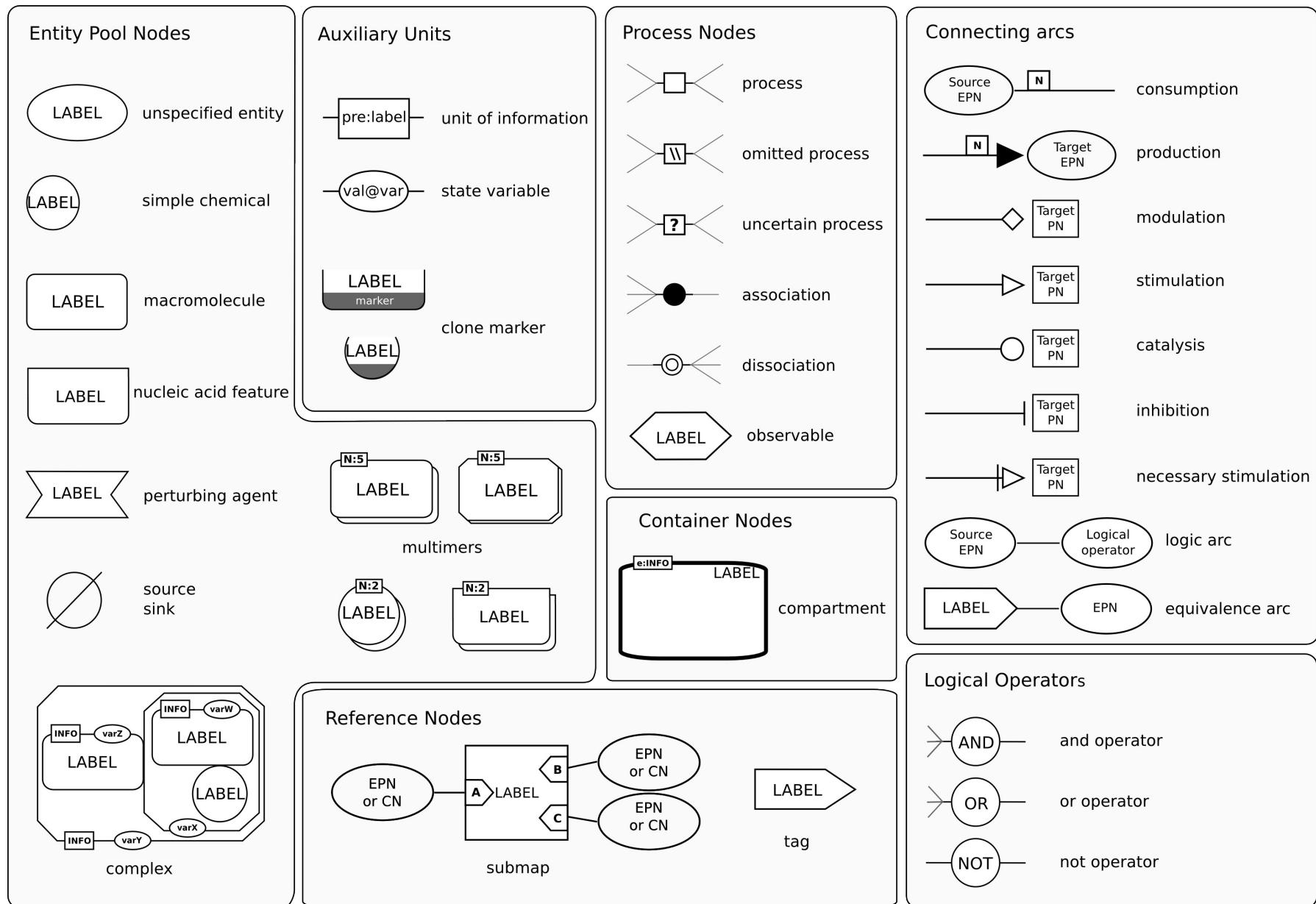
Process Diagrams are bipartite graphs



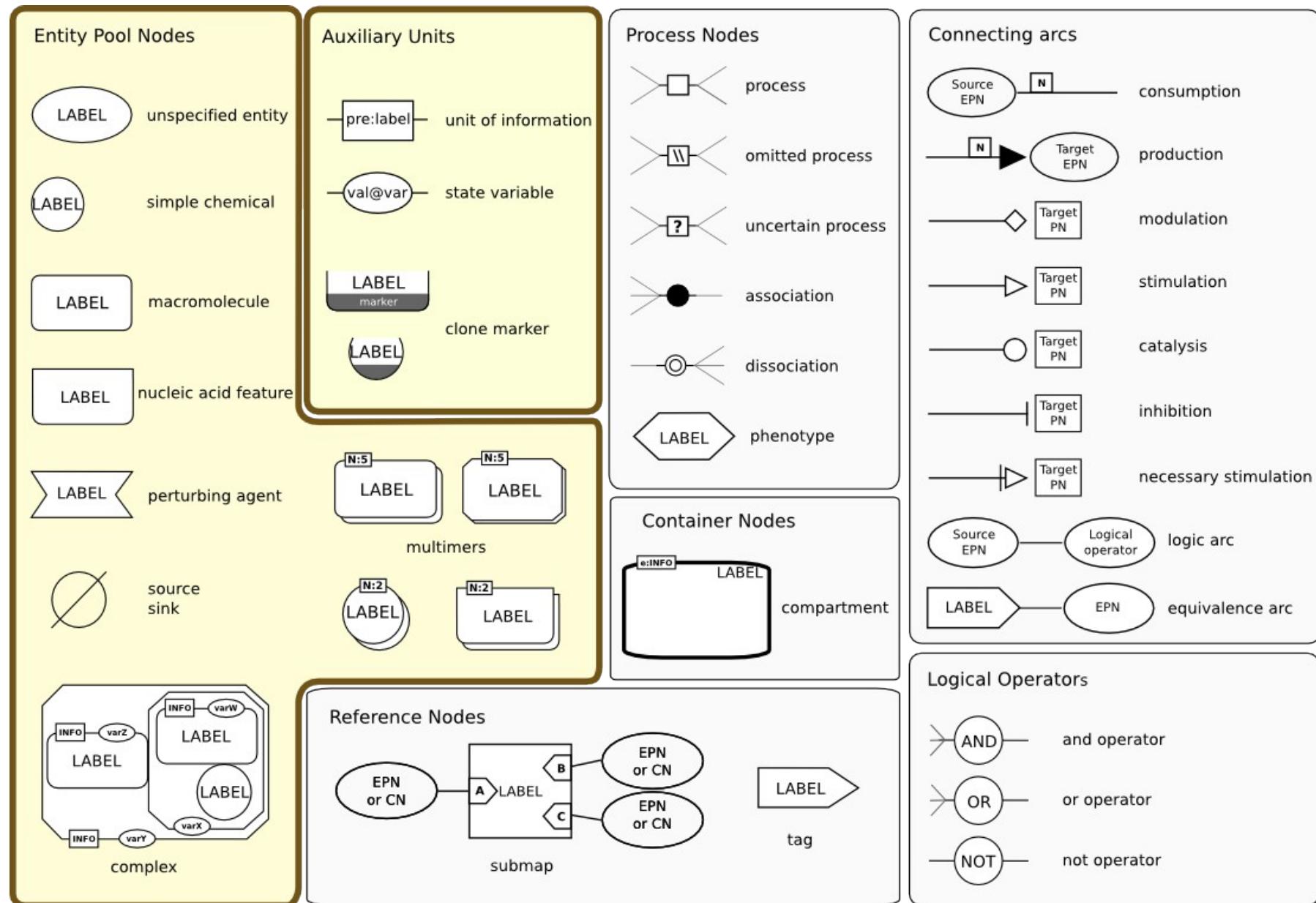
Process Diagrams can be viewed as pipelines



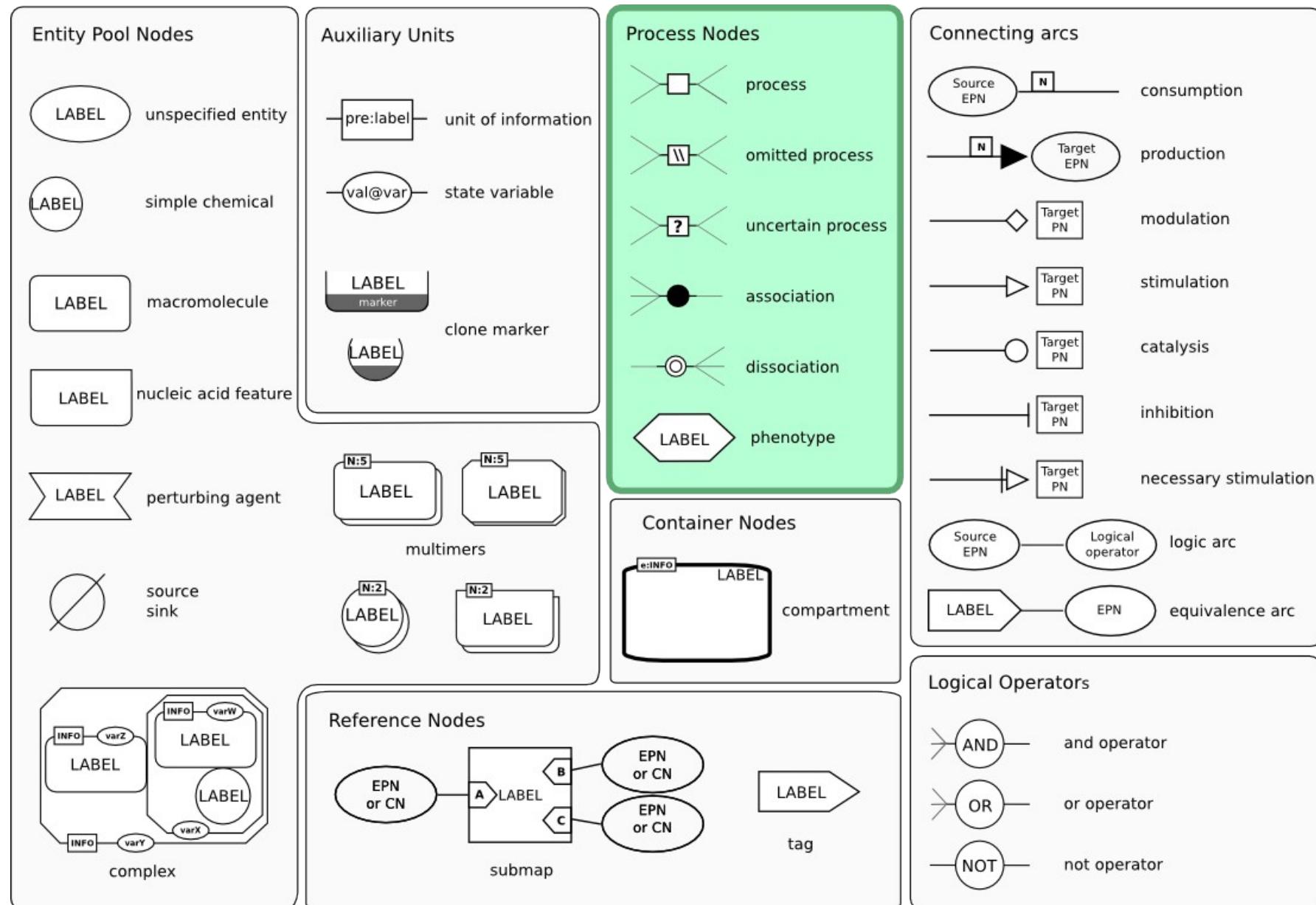
SBGN Process Diagram L1 reference card

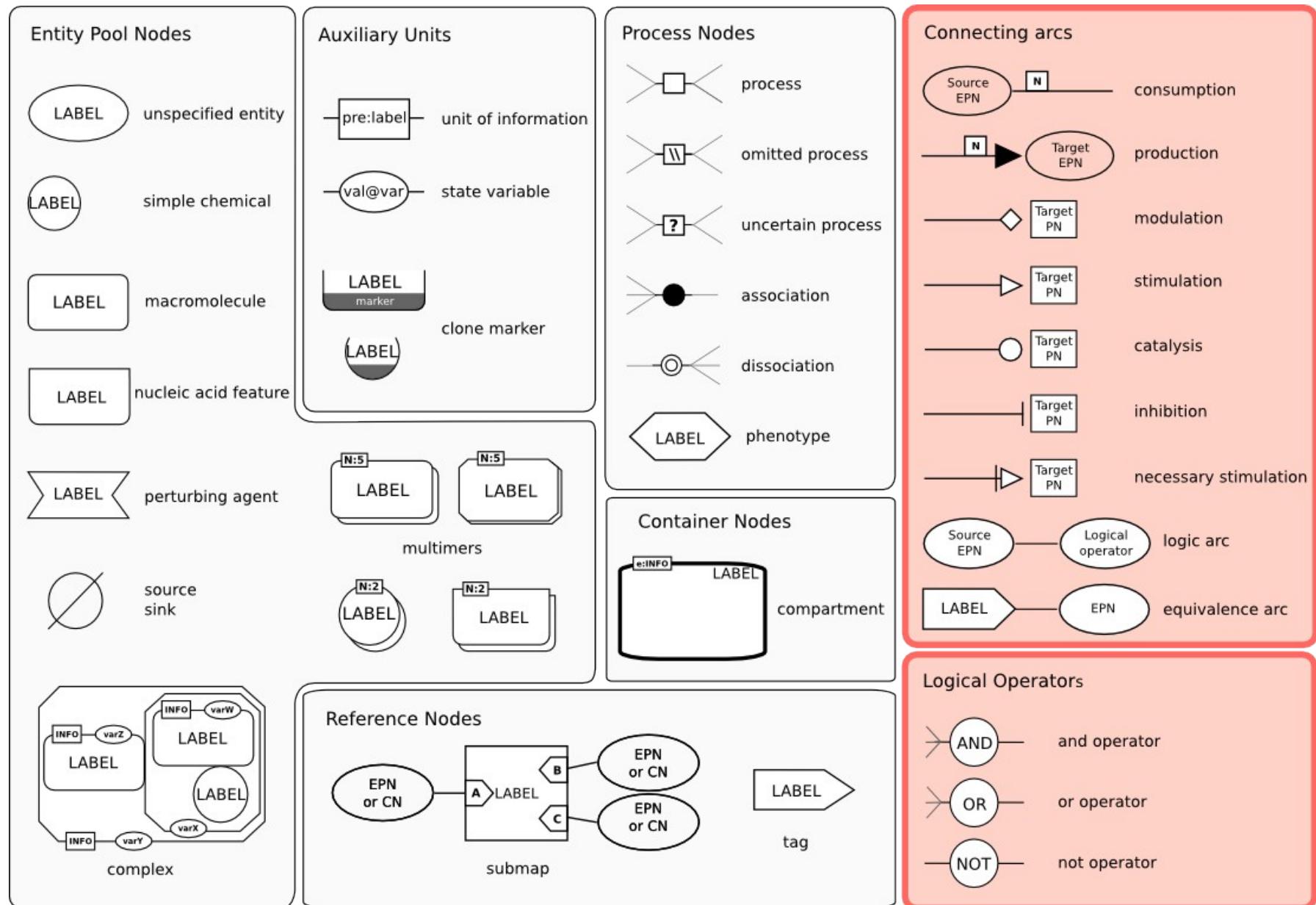


Entity Pool Nodes



Process Nodes



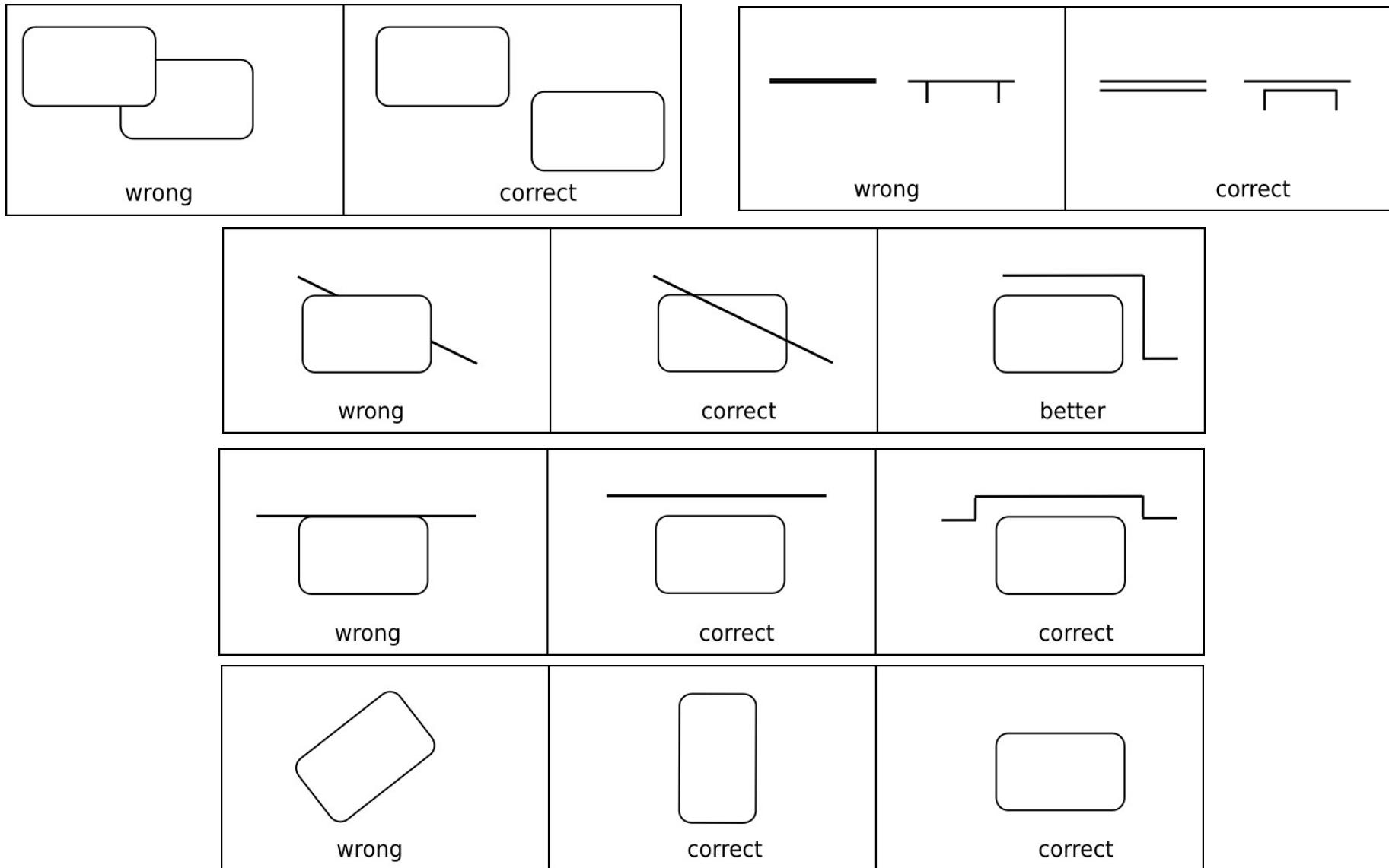


Syntax definition

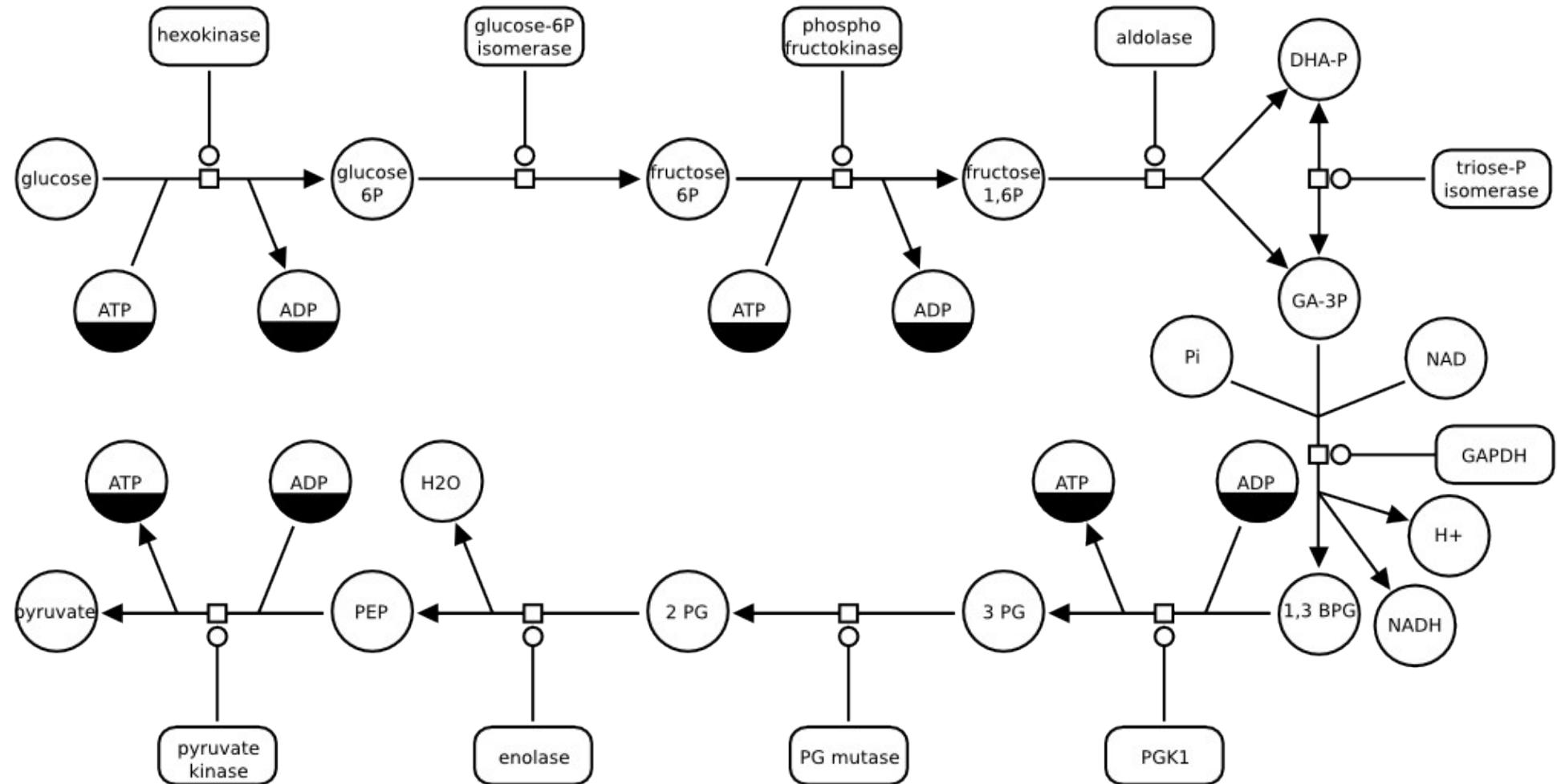
| <i>Arc\EPN</i> | <i>macromolecule</i> | <i>simple chemical</i> | <i>unspecified entity</i> | <i>multimer</i> | <i>complex</i> | <i>nucleic acid feature</i> | <i>tag</i> | <i>source/sink</i> | <i>perturbation</i> | <i>observable</i> | <i>submap</i> |
|------------------------|----------------------|------------------------|---------------------------|----------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

| <i>Arc\PN</i> | <i>transition</i> | <i>omitted process</i> | <i>uncertain process</i> | <i>association</i> | <i>dissociation</i> | <i>and</i> | <i>or</i> | <i>not</i> |
|------------------------|-------------------|------------------------|--------------------------|--------------------|---------------------|------------|-----------|------------|
| <i>consumption</i> | O | O | O | O | O(1) | | | |
| <i>production</i> | I | I | I | I(1) | I | | | |
| <i>modulation</i> | O | O | O | | | I(1) | I(1) | I(1) |
| <i>stimulation</i> | O | O | O | | | I(1) | I(1) | I(1) |
| <i>catalysis</i> | O | O | O | | | I(1) | I(1) | I(1) |
| <i>inhibition</i> | O | O | O | | | I(1) | I(1) | I(1) |
| <i>trigger</i> | O | O | O | | | I(1) | I(1) | I(1) |
| <i>logic arc</i> | | | | | | O | O | O(1) |
| <i>equivalence arc</i> | | | | | | | | |

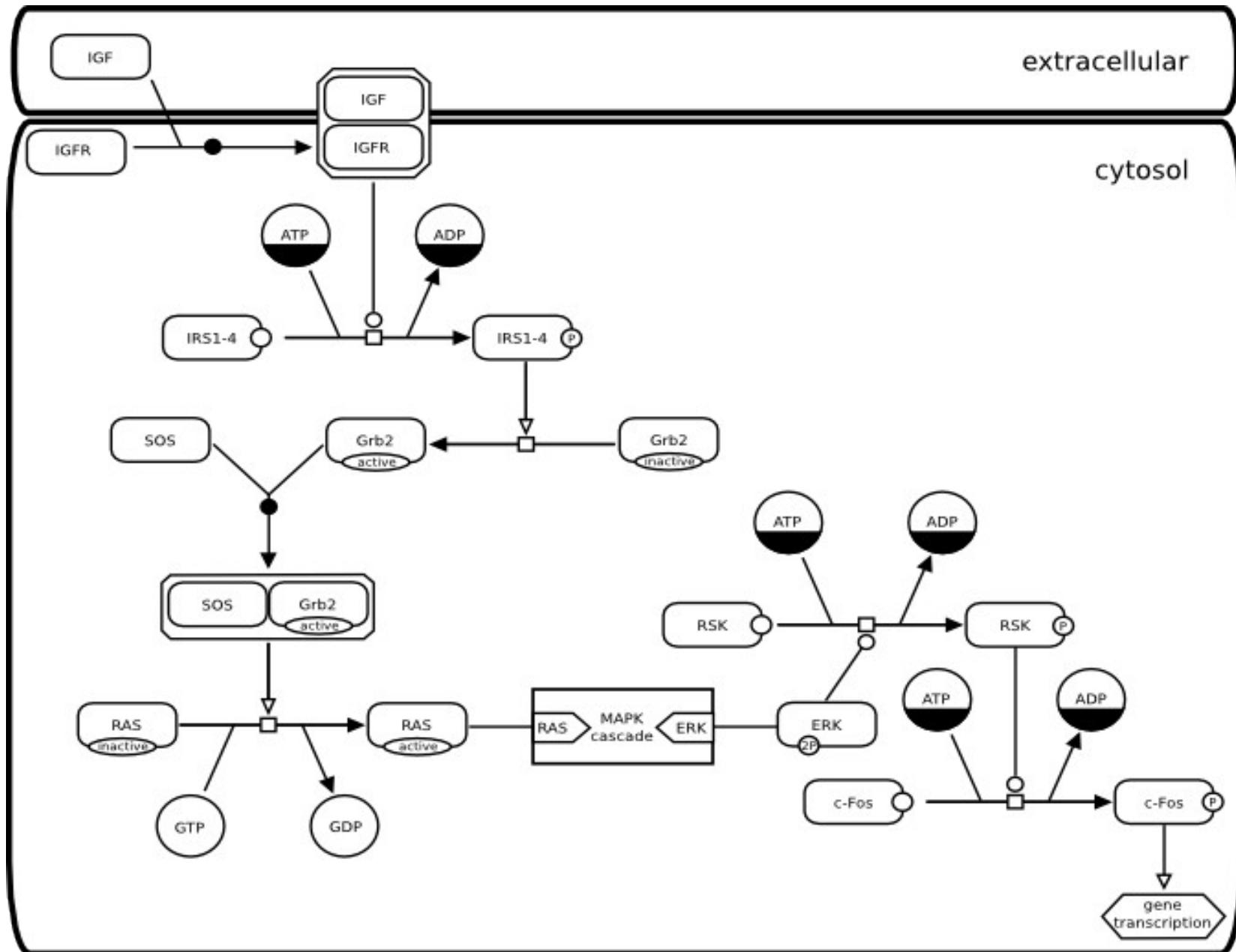
Layout constraints



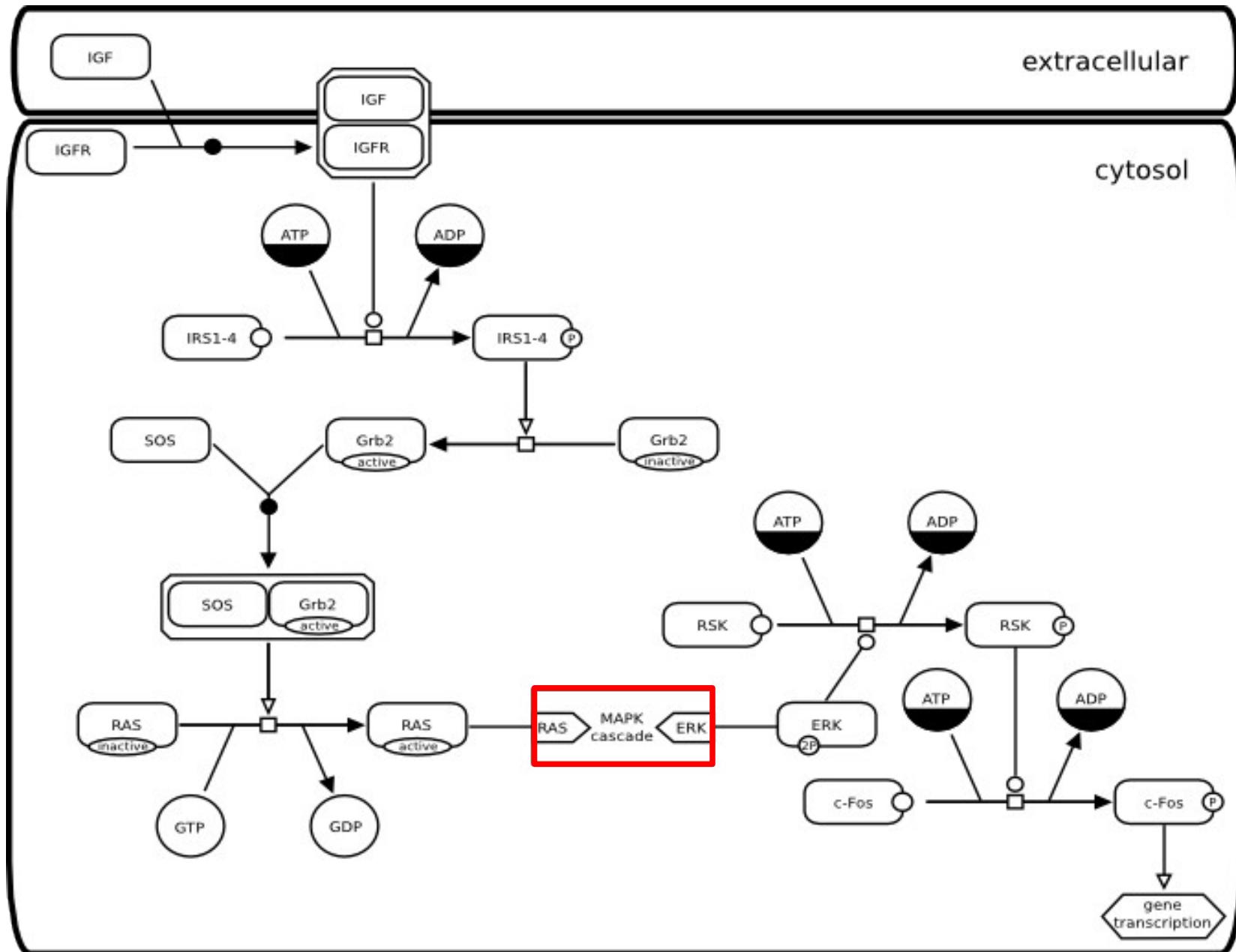
Metabolic network



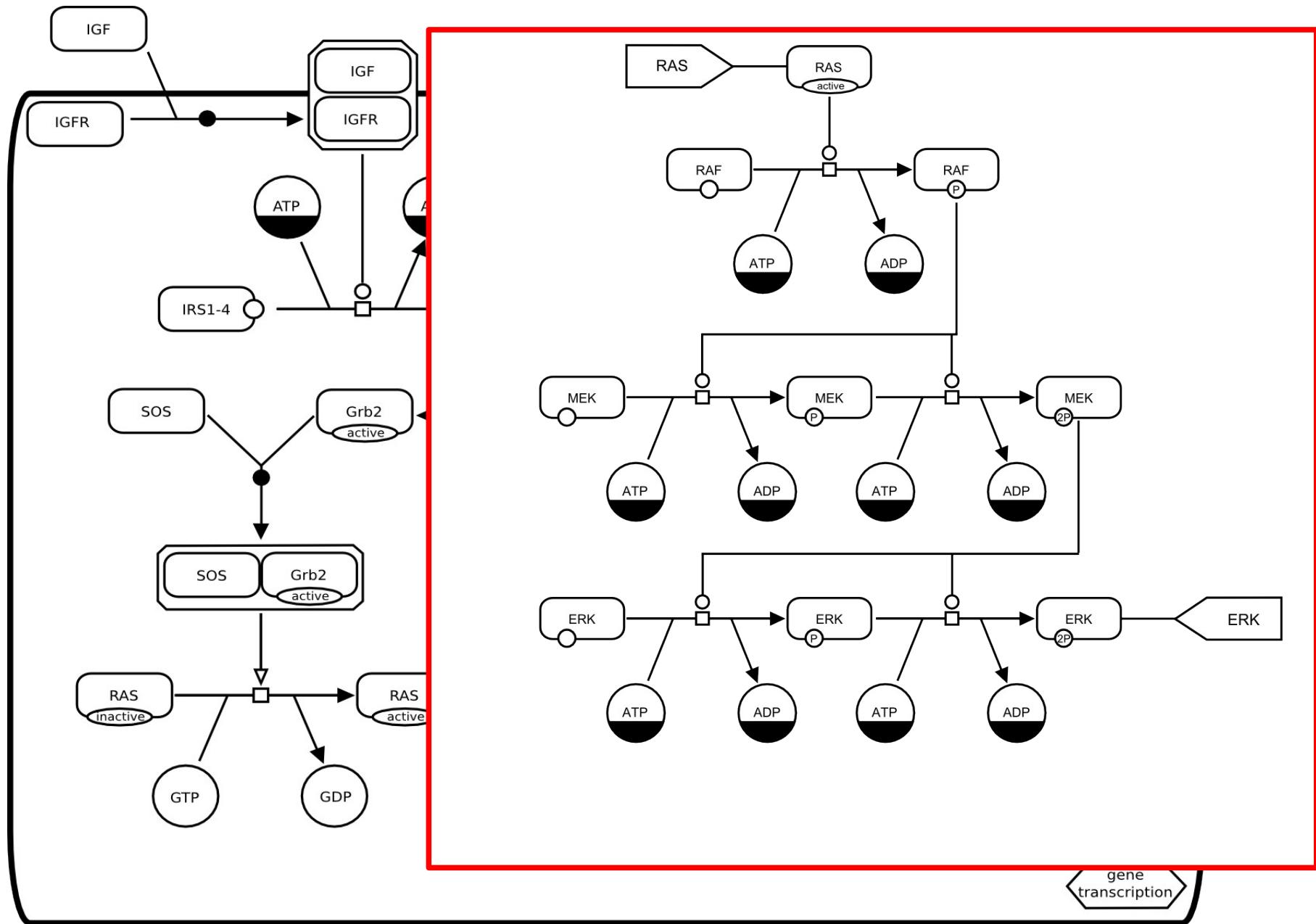
Signalling pathways



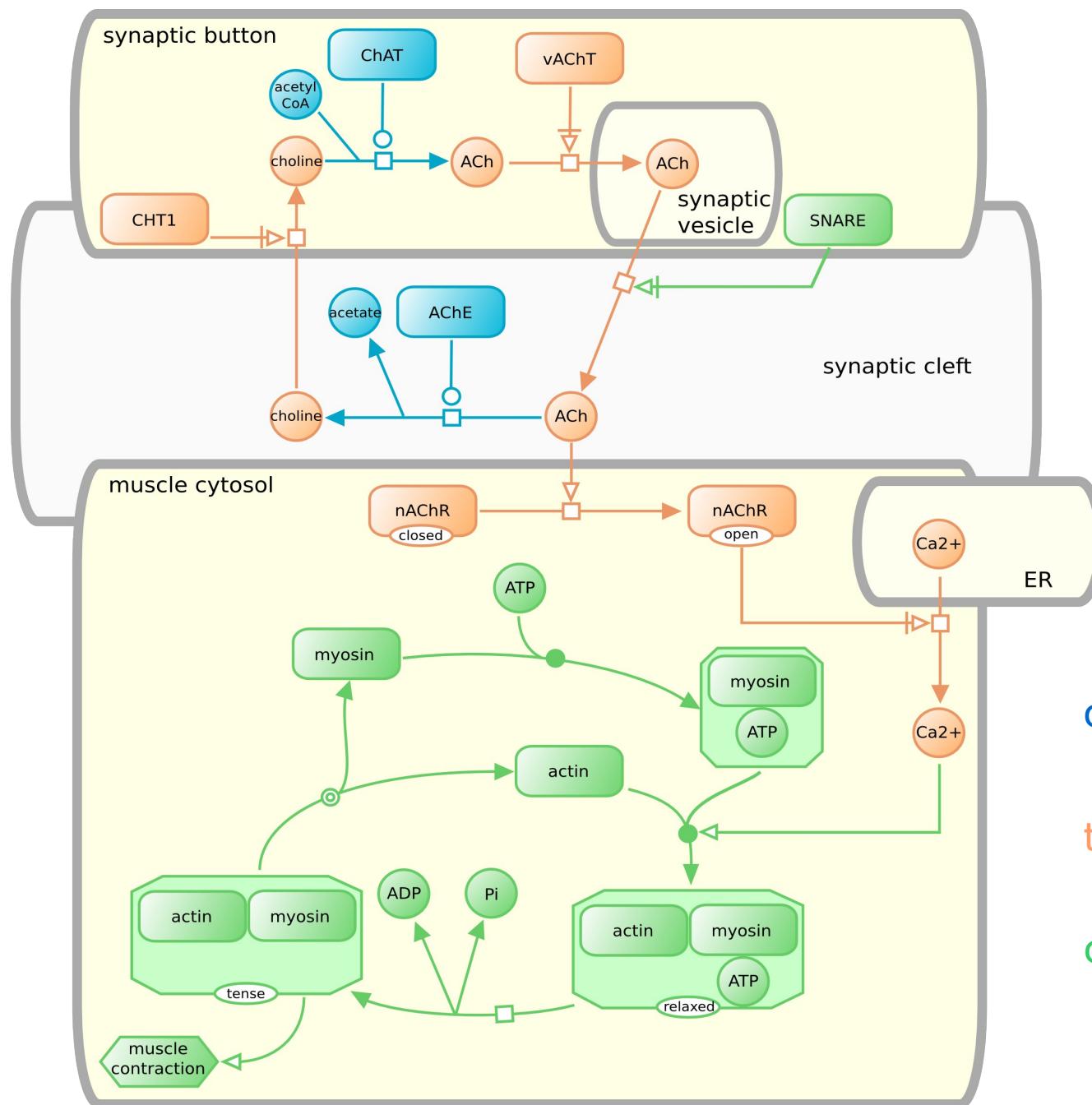
Submaps



Submaps



multi-cellular processes

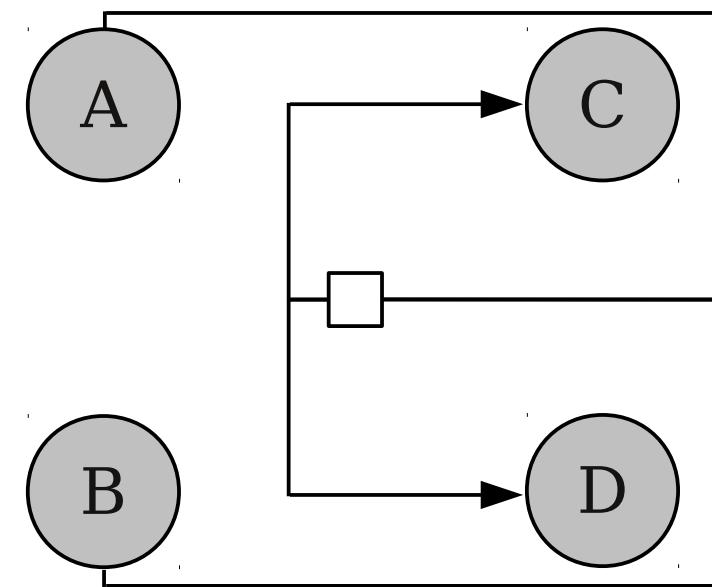
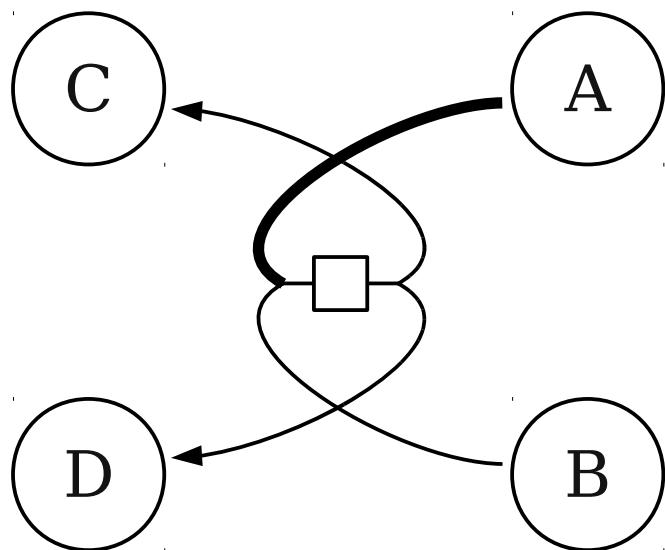
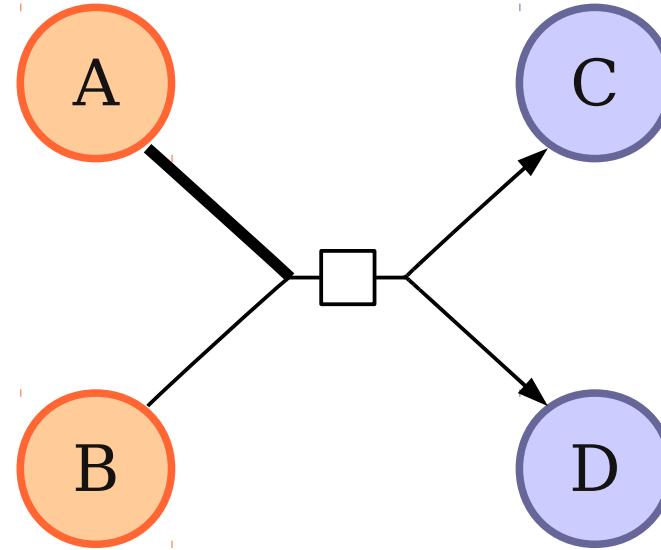
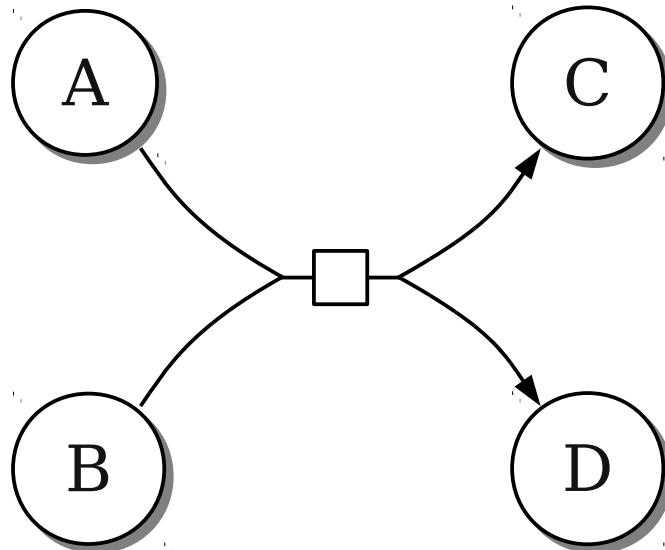


catalytic processes

transport processes

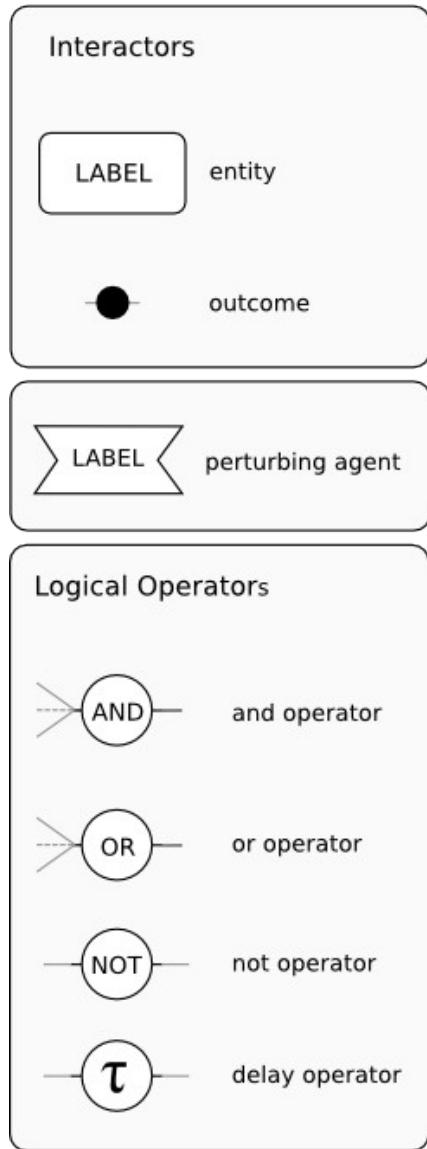
contractile proteins

All those diagrams are identical

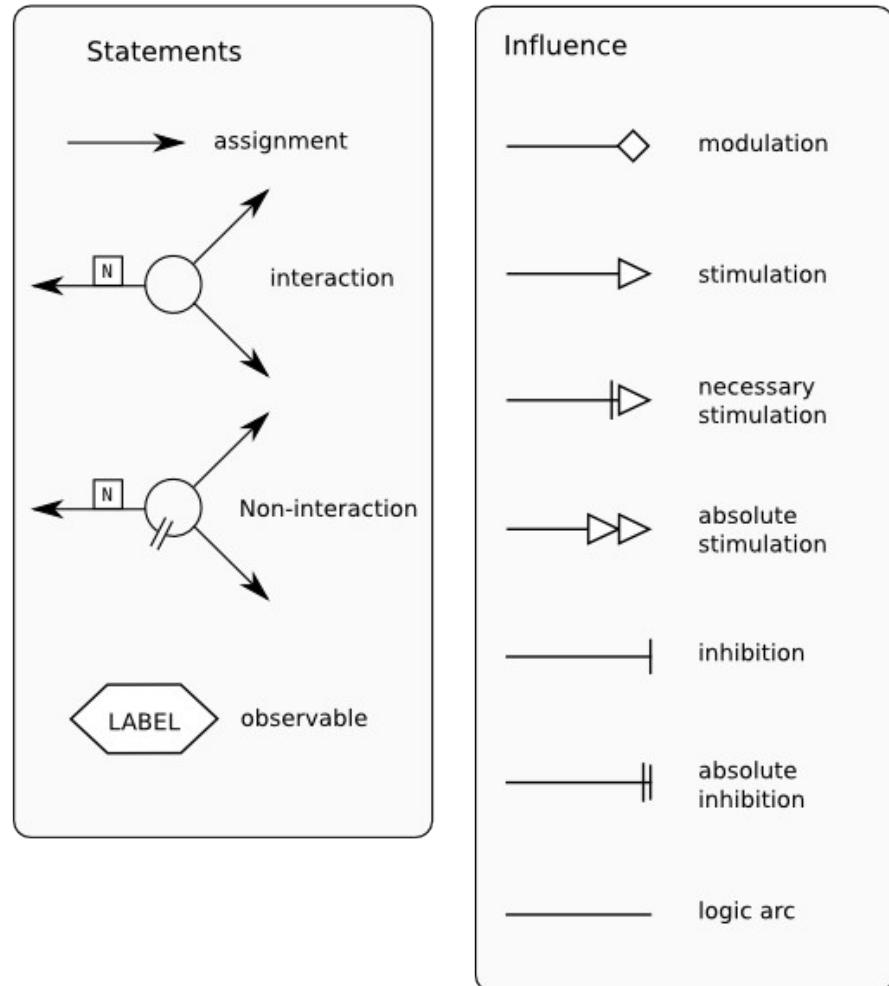


SBGN Entity Relationships L1 reference card

Entity Nodes

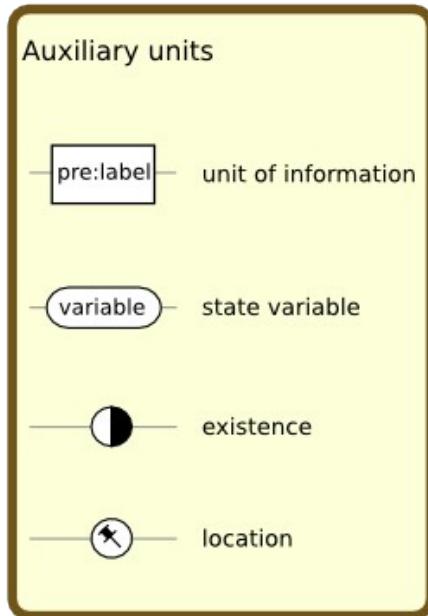
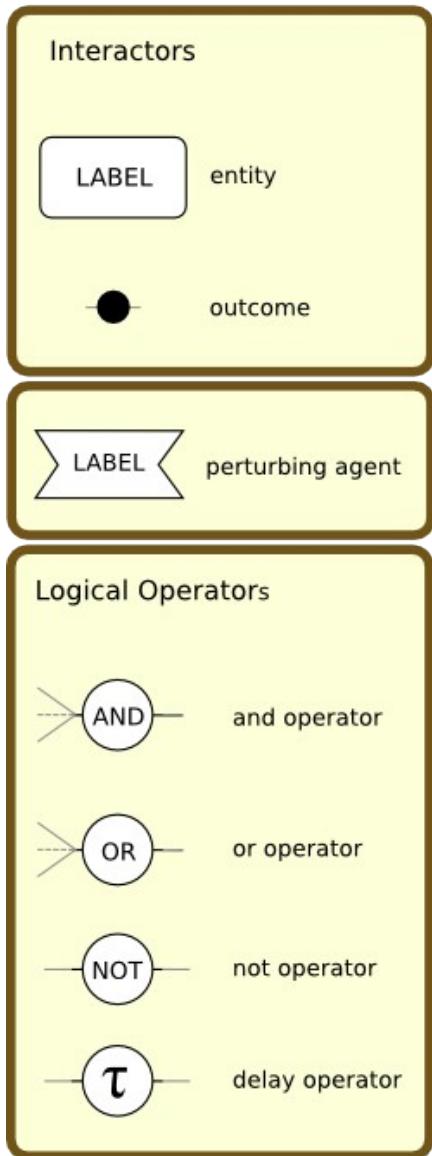


Relationship Nodes

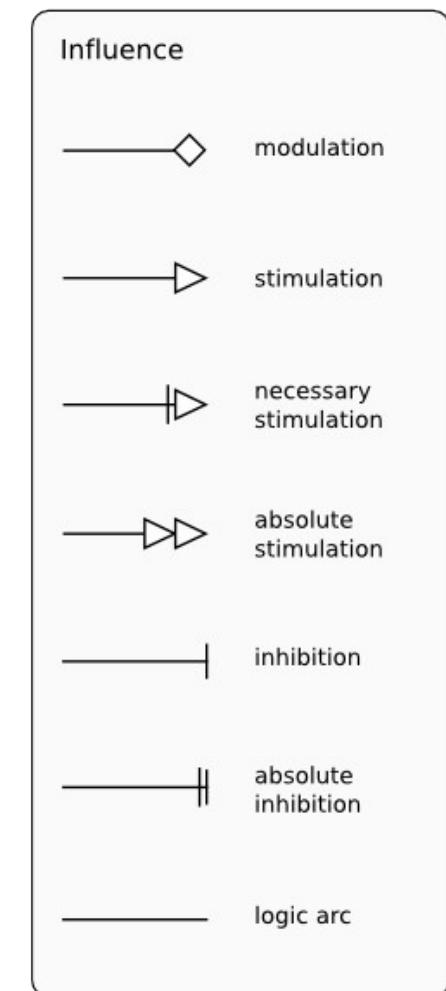
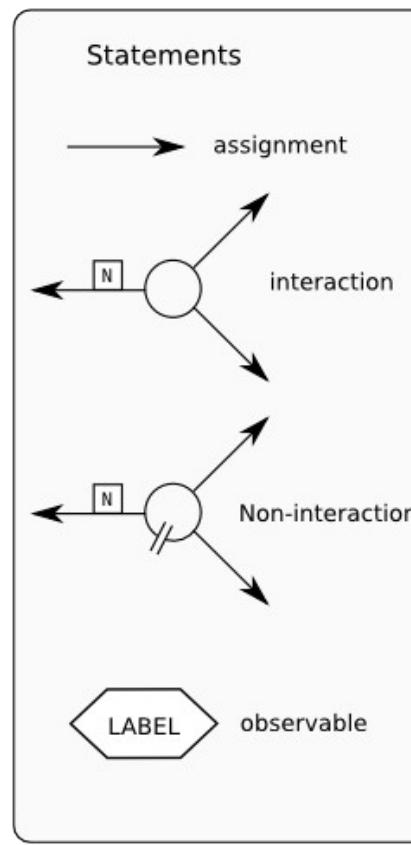


SBGN Entity Relationships L1 reference card

Entity Nodes

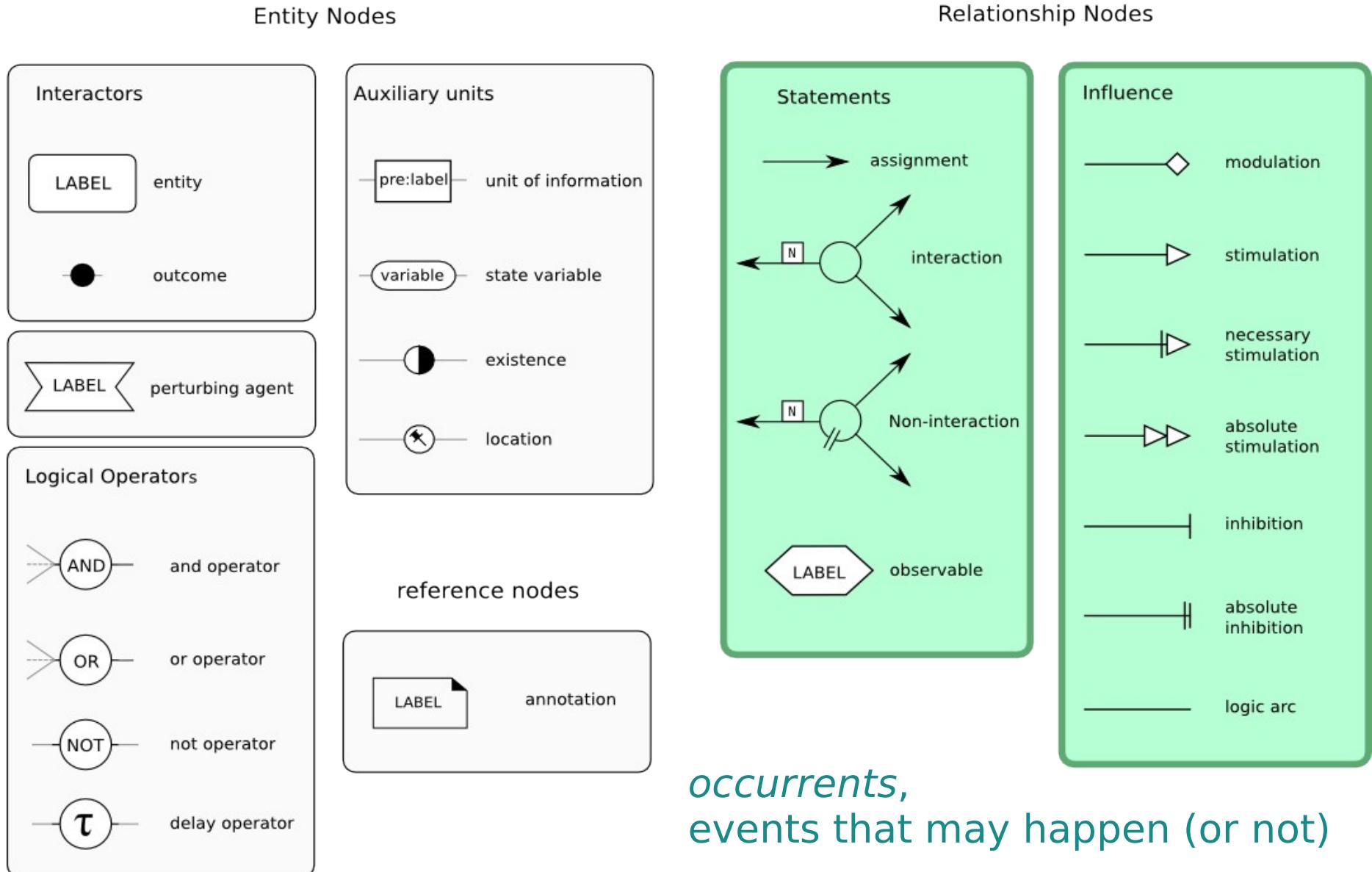


Relationship Nodes

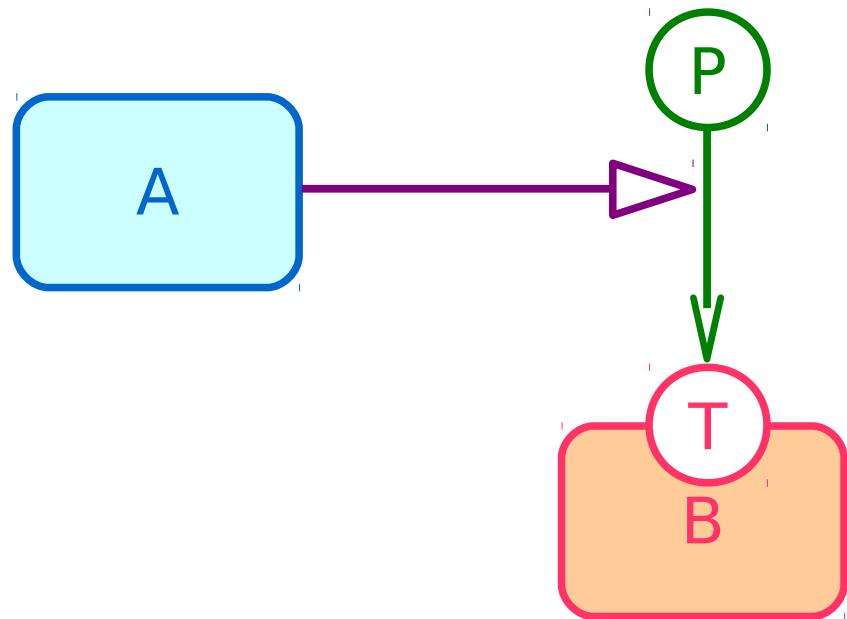


continuants,
things that exists (or not)

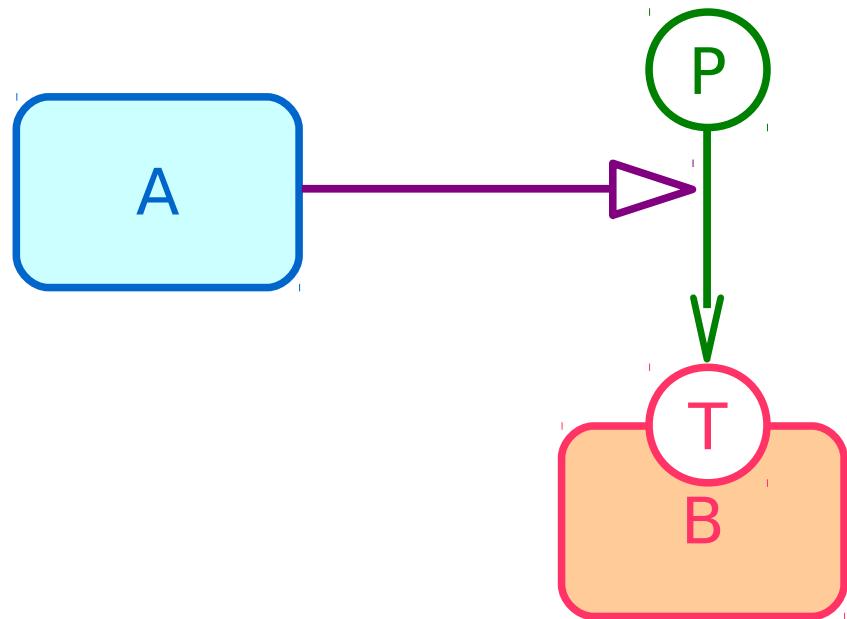
SBGN Entity Relationships L1 reference card



Entity Relationships can be viewed as rules

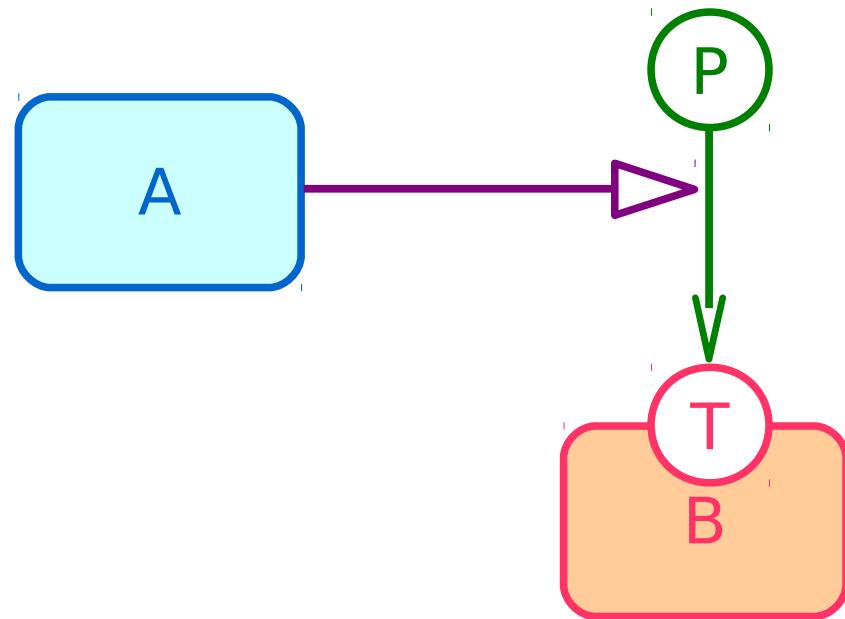


Entity Relationships can be viewed as rules



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

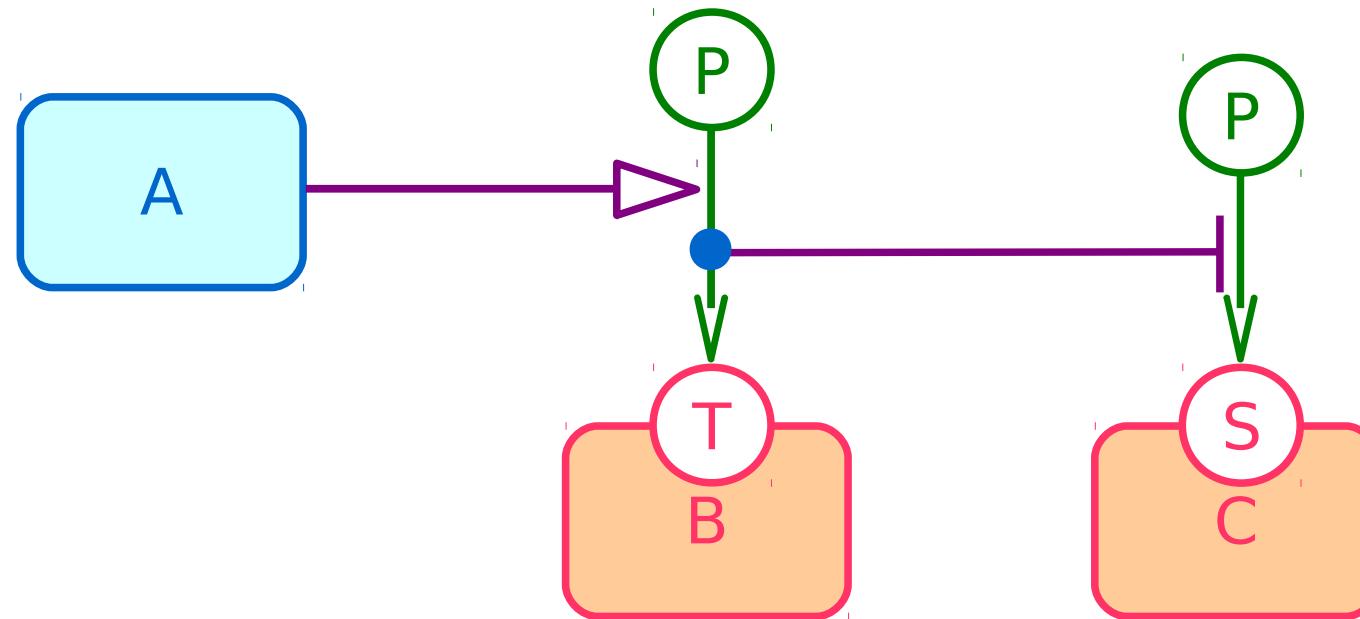
Entity Relationships can be viewed as rules



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)

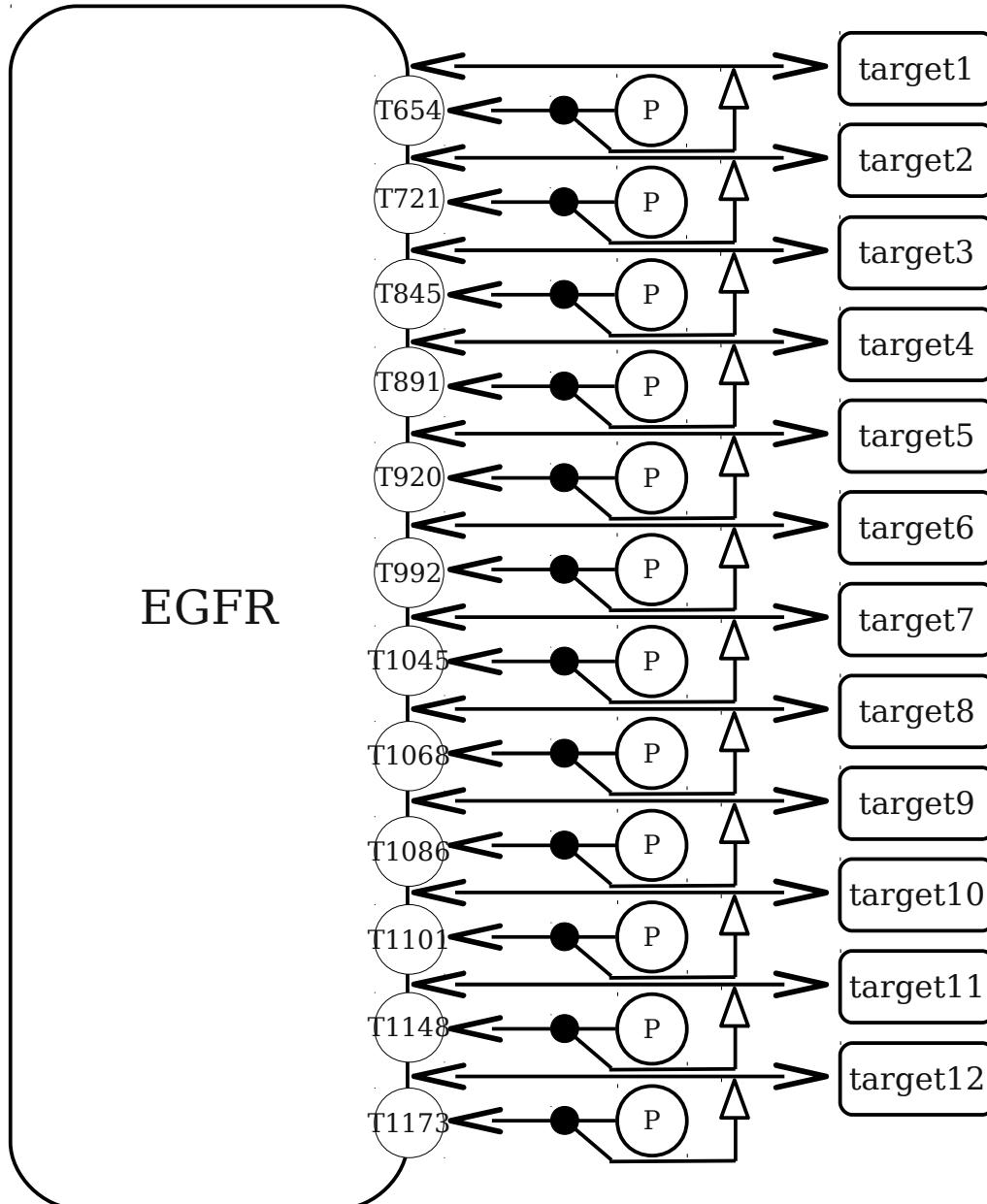
Entity Relationships can be viewed as rules



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

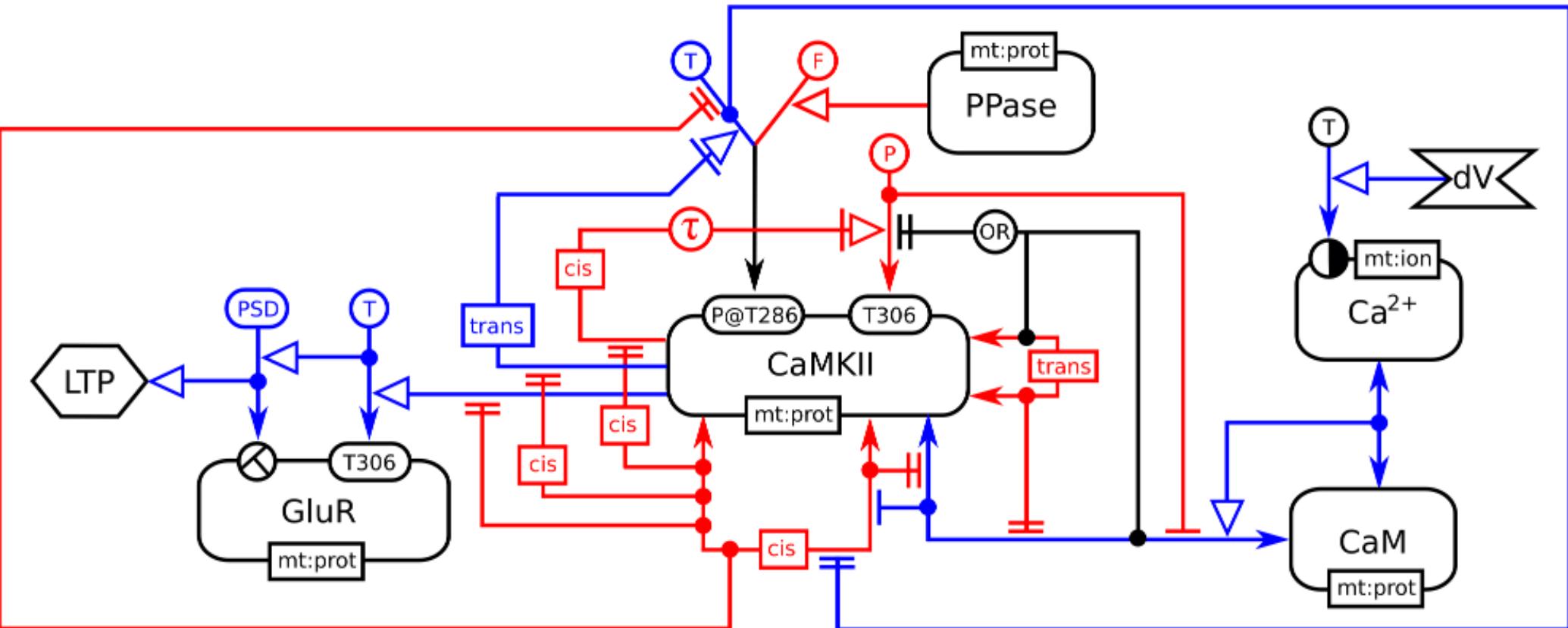
Multistate and combinatorial explosion



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

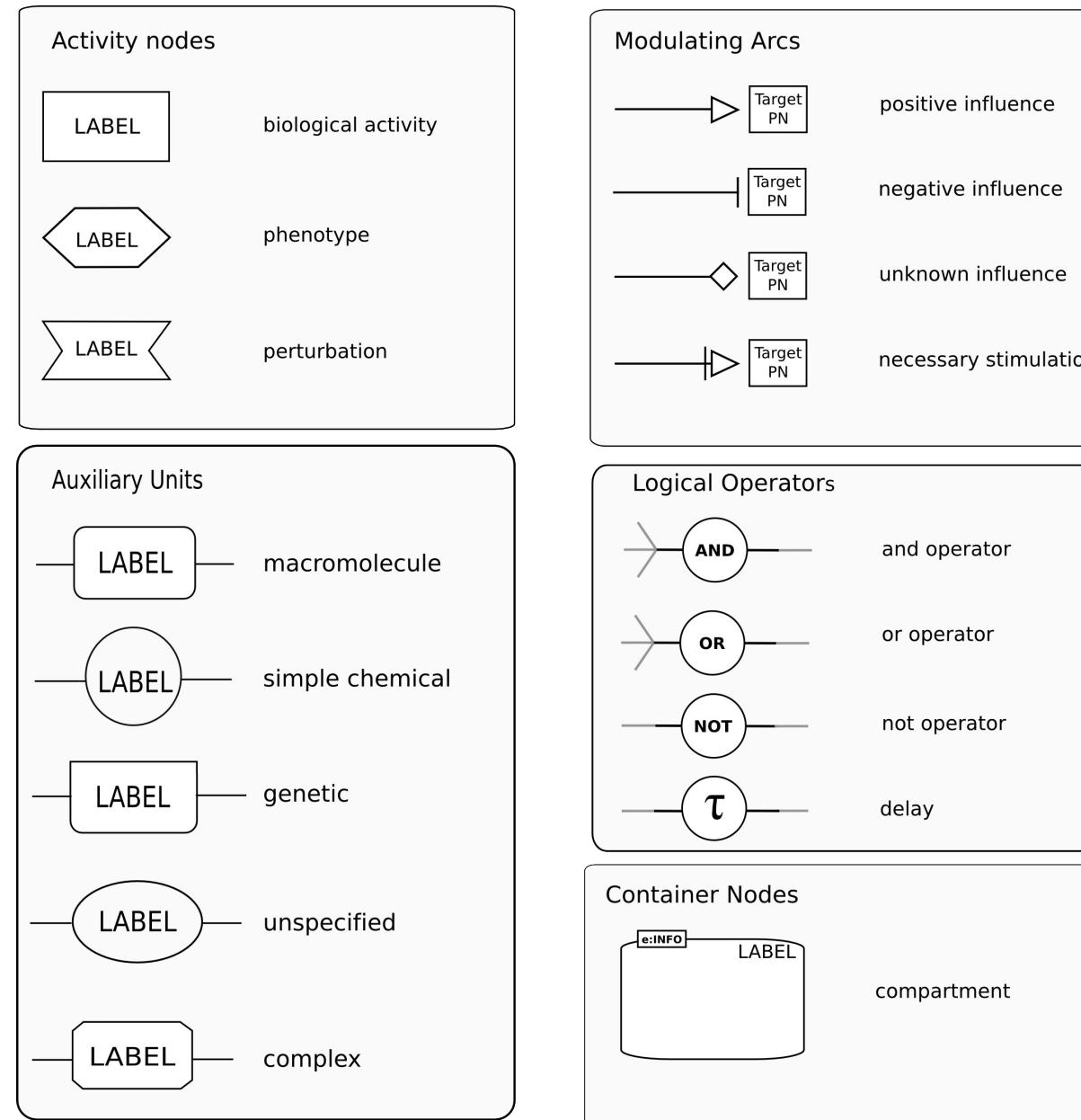
Example of Entity Relationships map



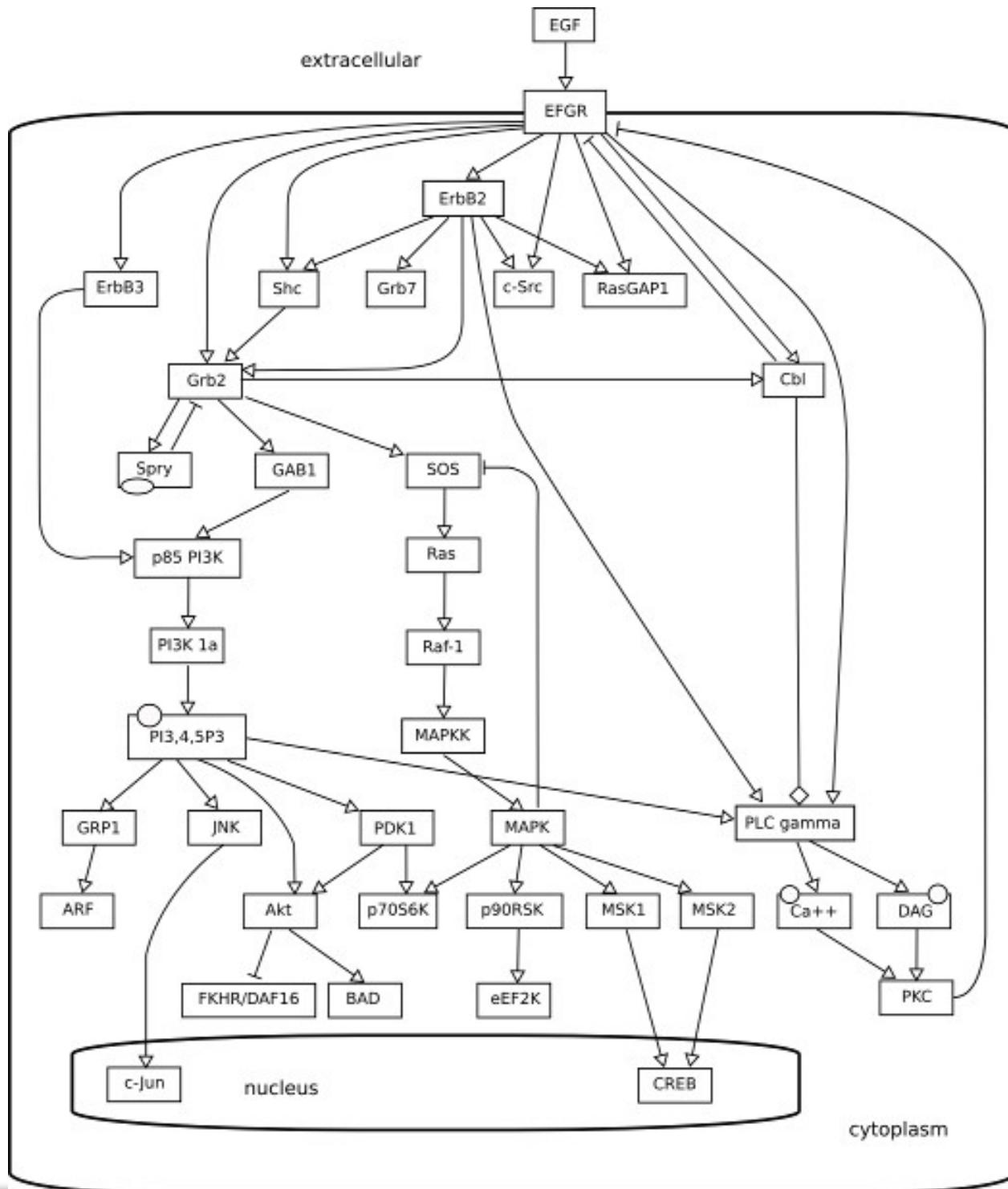
increases synaptic weight

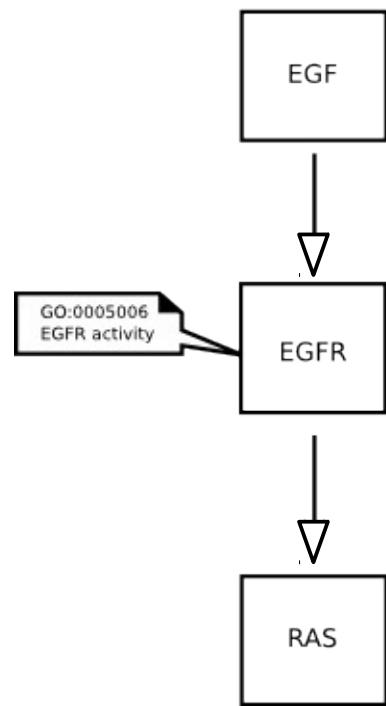
decreases synaptic weight

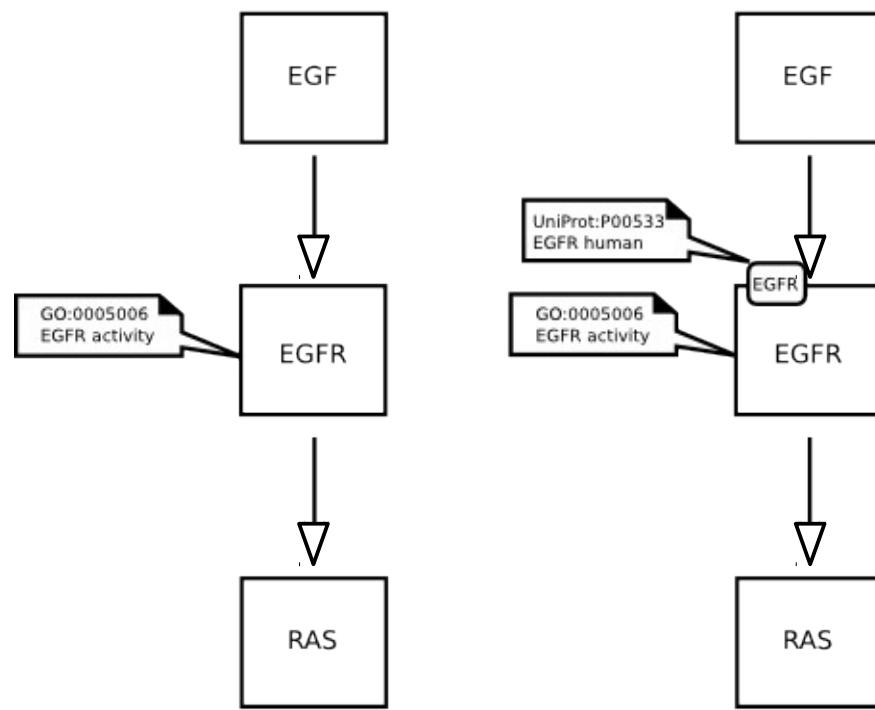
SBGN Activity Flow L1 reference card

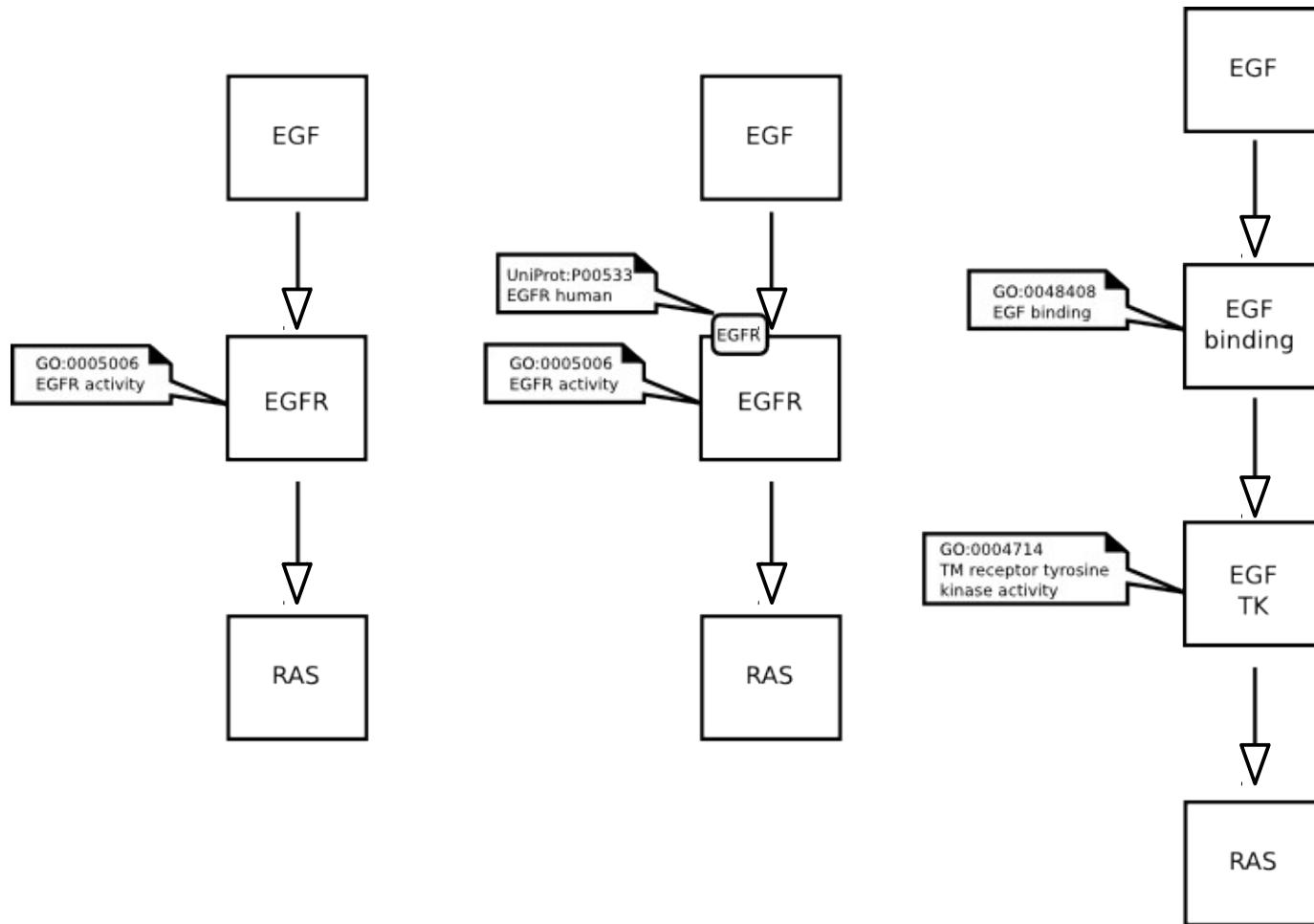


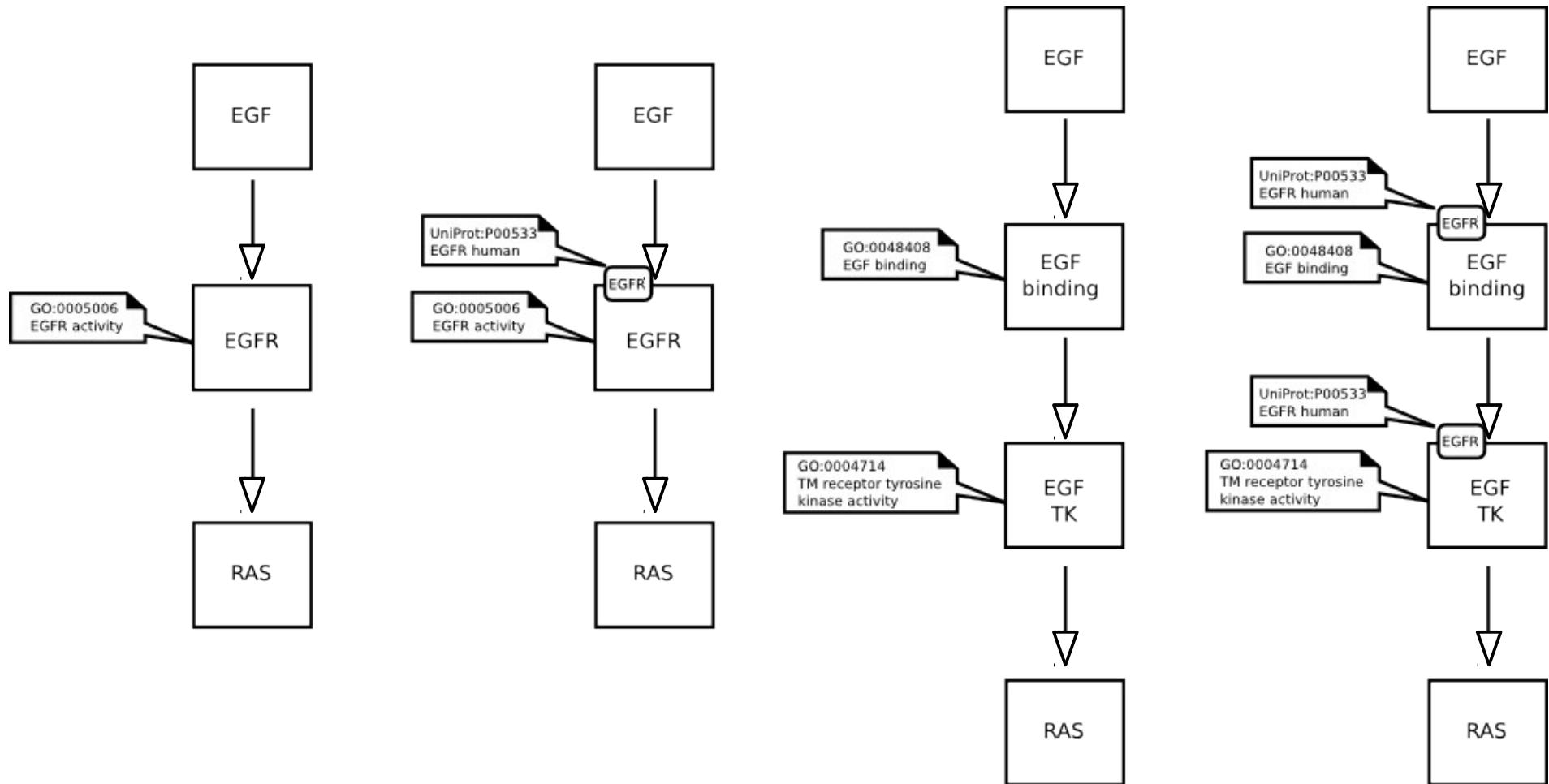
Example of Activity Flow map

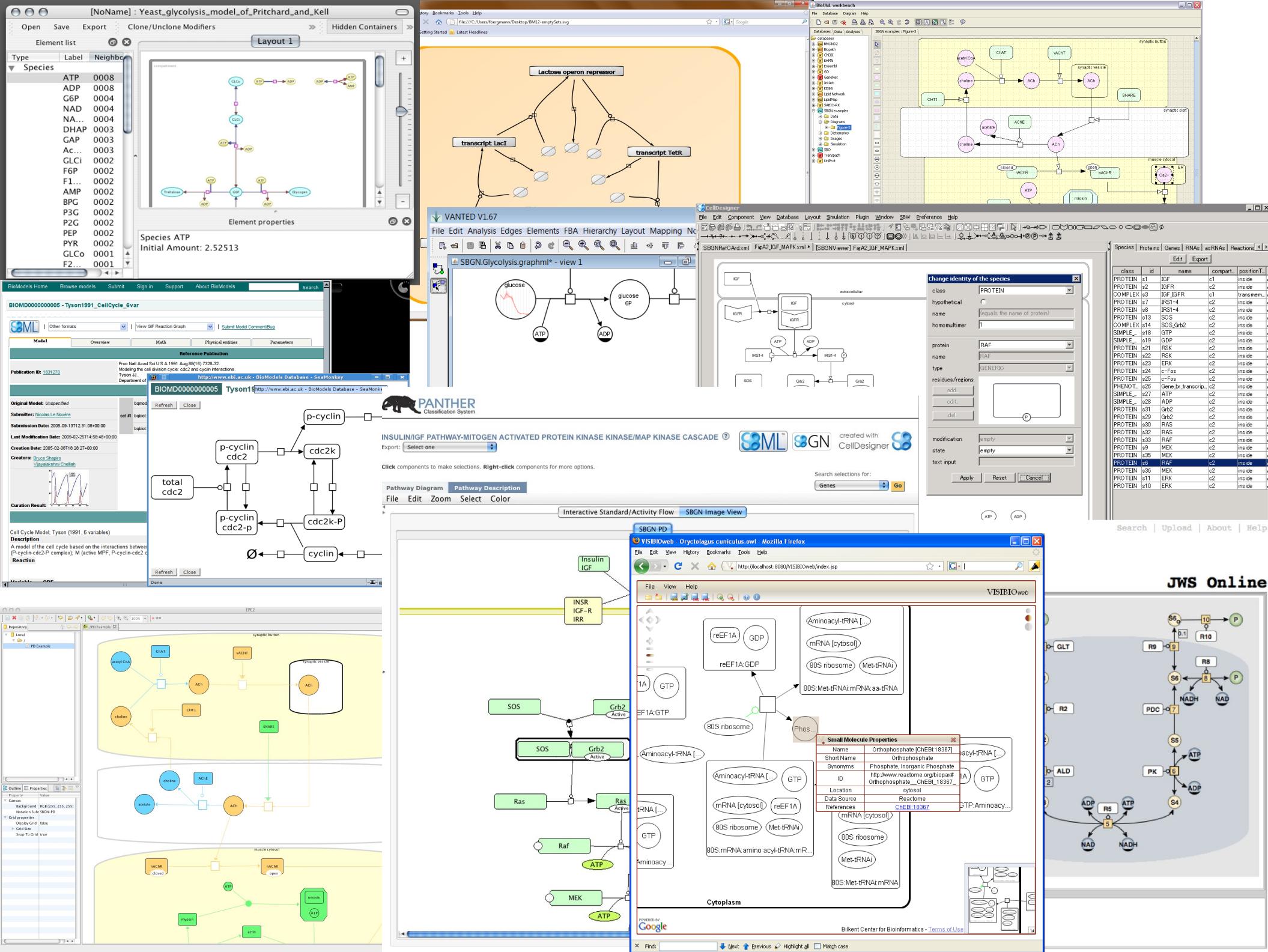


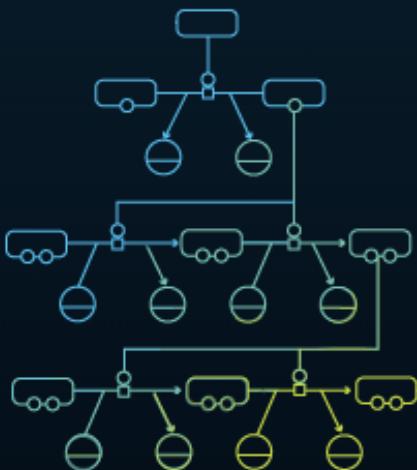












A Visual Notation for Network Diagrams in Biology

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!

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

