CMACS

Computational Modeling and Analysis for Complex Systems

2010 CMACS Workshop on Modeling Biological Systems

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Process Diagrams

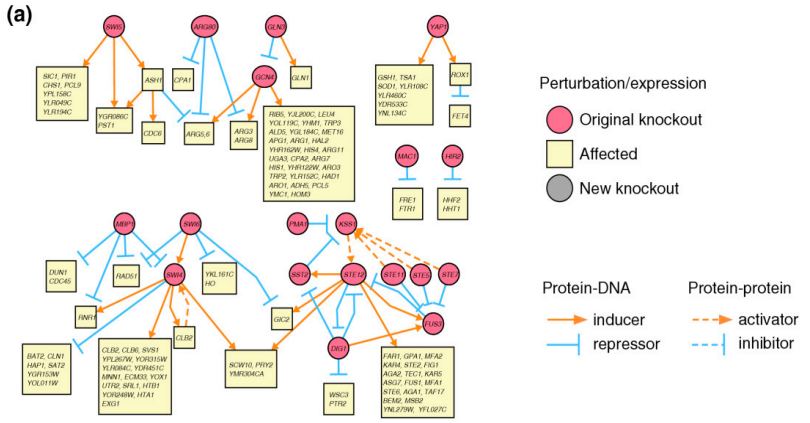
Napoleon Bonaparte

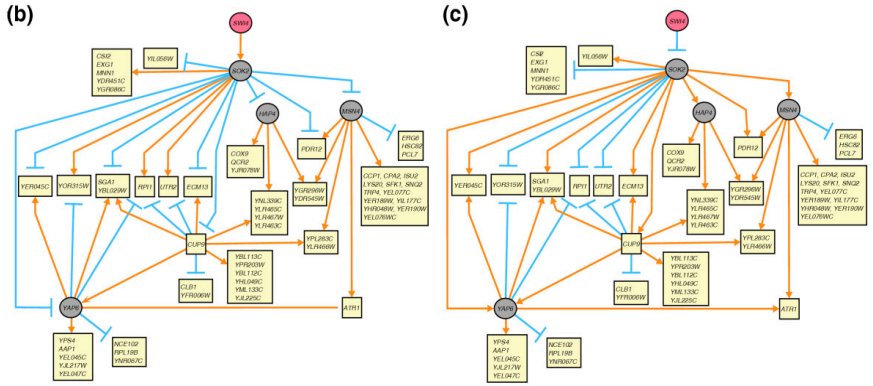
‘Un bon croquis vaut mieux qu’un long discours’
(A good sketch is better than a long speech)

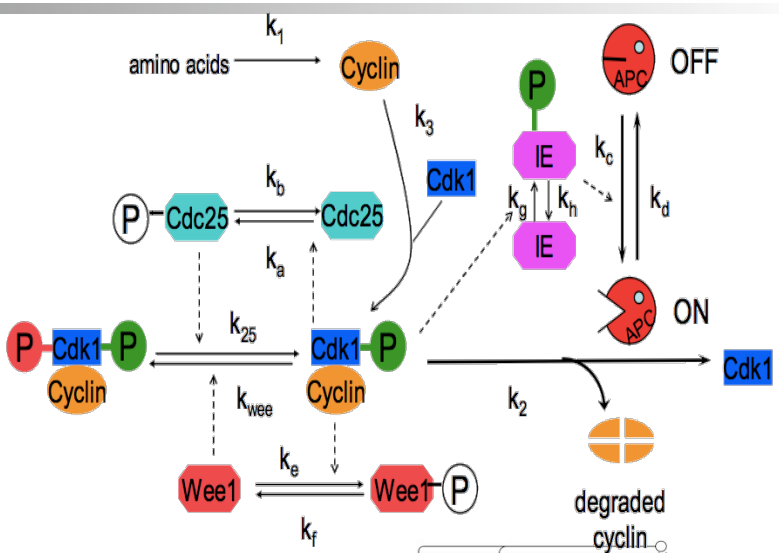
Diagrams are important

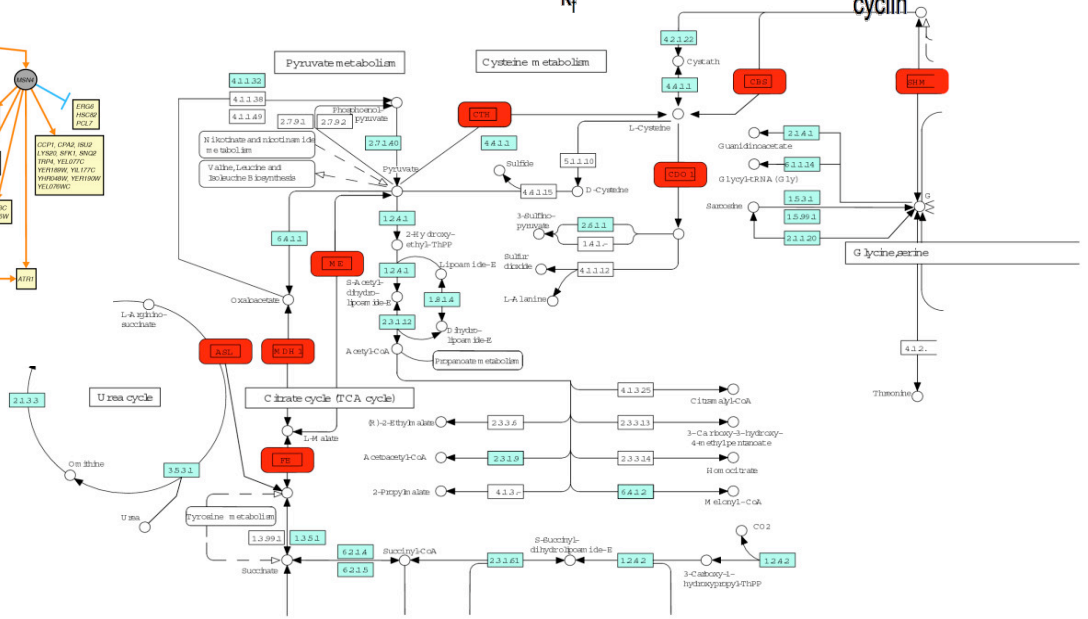
- They were already used by our cave-drawing ancestors..
- And are still widely used today..
- In many areas, like systems biology.

Diagrams in systems biology

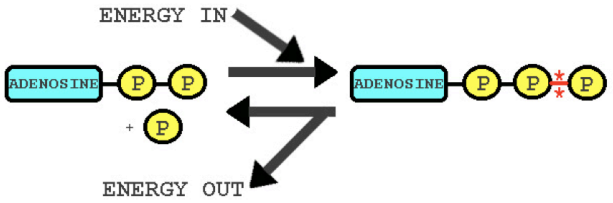








Diagrams can be ambiguous/ad hoc



From yesterday's lecture:

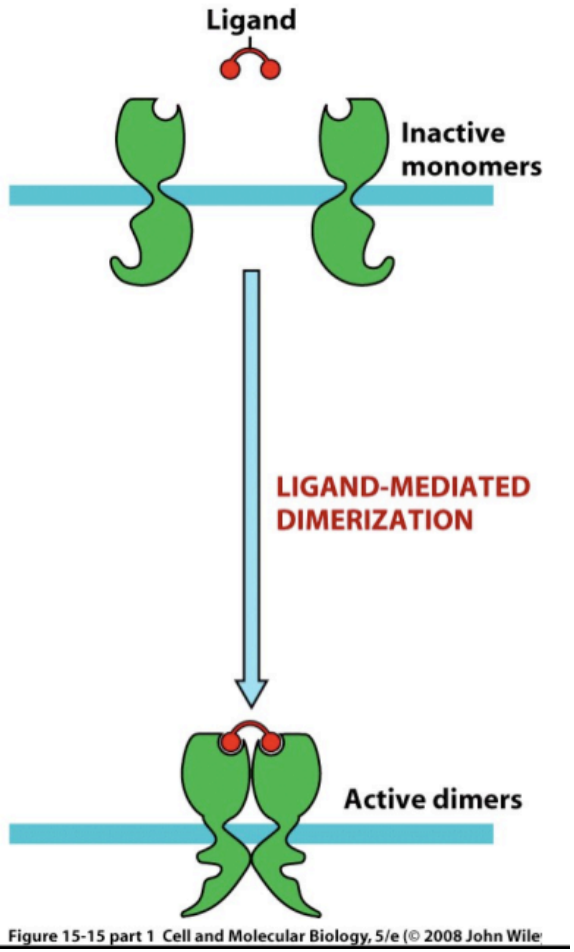


Figure 15-15 part 1 Cell and Molecular Biology, 5/e (© 2008 John Wile

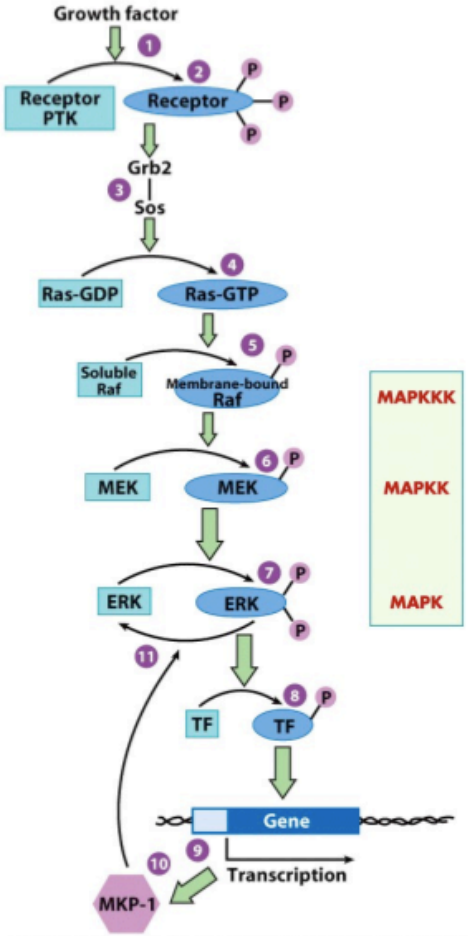
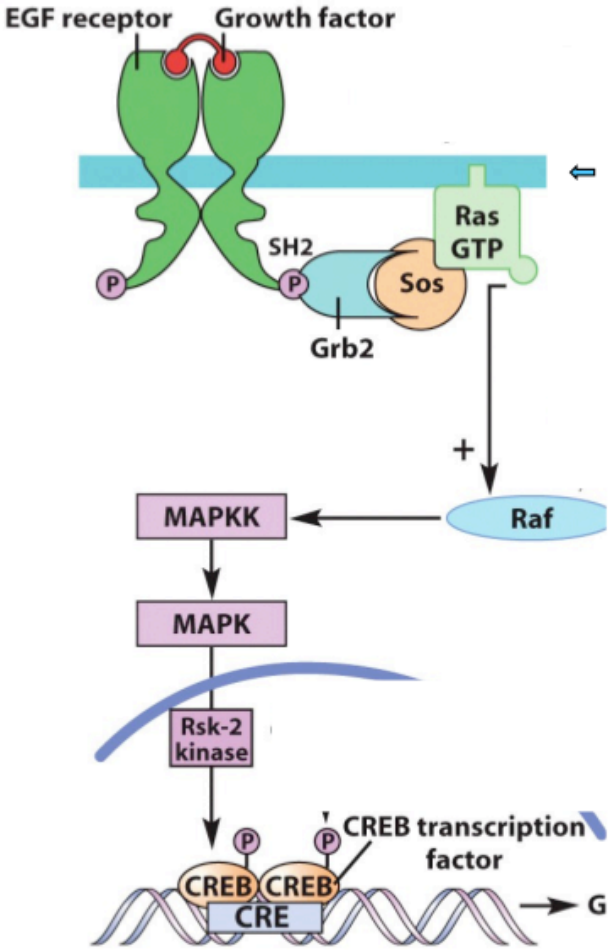


Figure 15-20 Cell and Molecular Biology, 5/e (© 2008 John Wiley & Sons)



But diagrams can be ambiguous/ad hoc

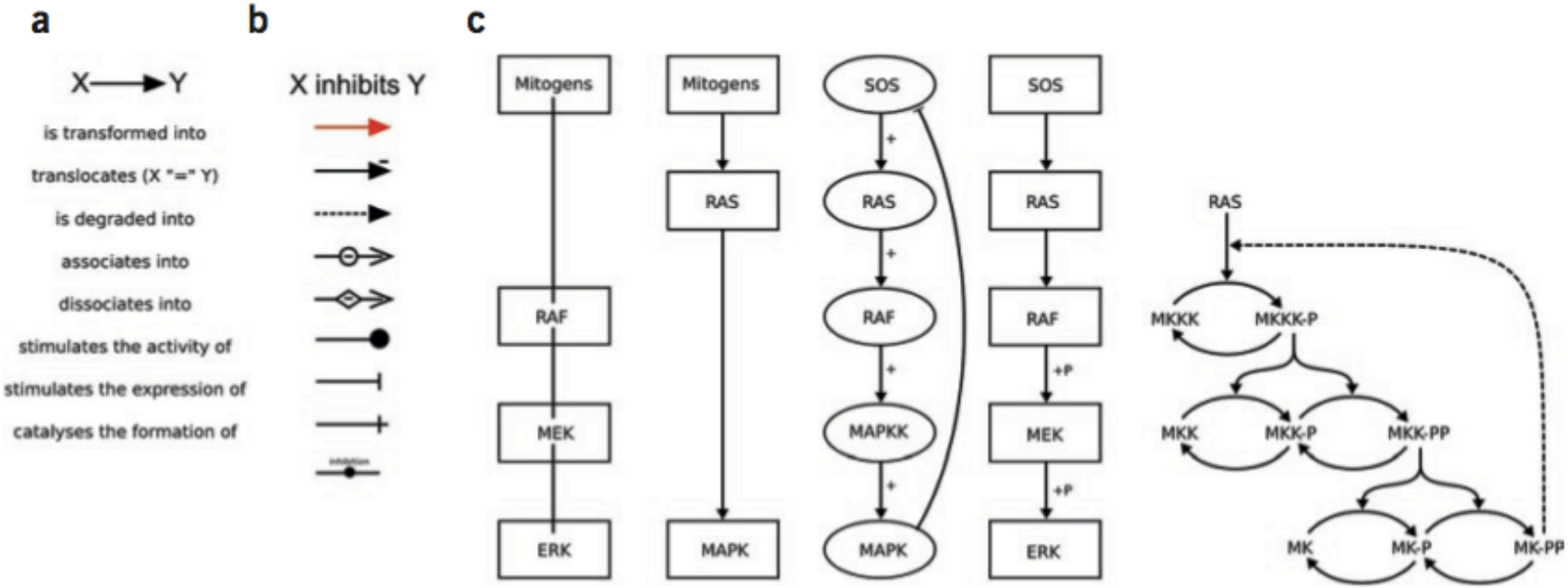
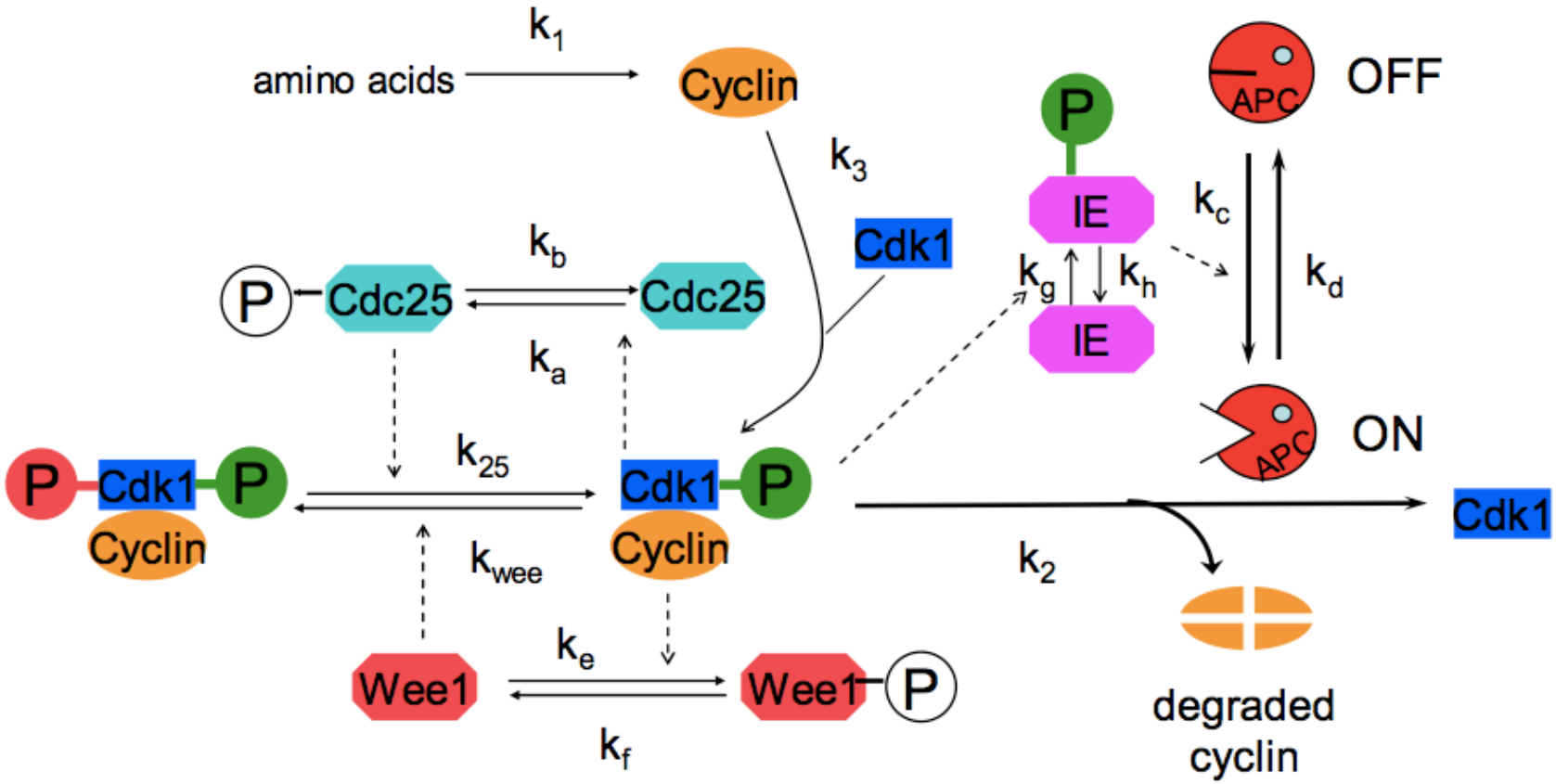


Figure 1 Inconsistency and ambiguity of current nonstandardized notations. (**a**) Eight different meanings associated with the same symbol in a chart describing the role of cyclin in cell regulations (http://www.abcam.com/ps/pdf/nuclearsignal/cell_cycle.pdf). (**b**) Nine different symbols found in the literature to represent the same meaning. (**c**) Five different representations of the MAP kinase cascade found in the scientific literature, depicting progressive levels of biological and biochemical knowledge. From left to right: relations[30], directionality of influence[31], directionality of effect[32], biochemical effect[33], chemical reactions[34]. In the last diagram, different instances of an identical arrowhead style represent catalysis, production and inhibition.

But diagrams can be ambiguous/ad hoc

The frog cell cycle:

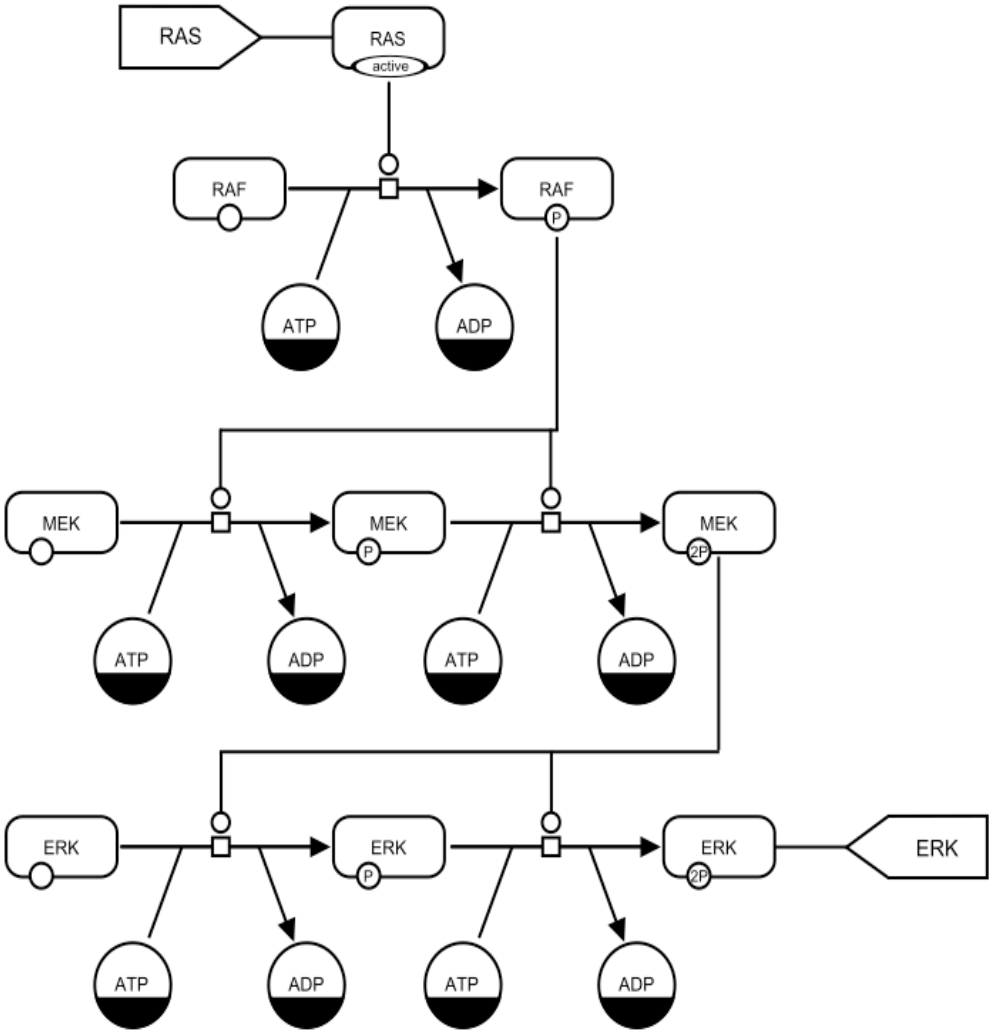


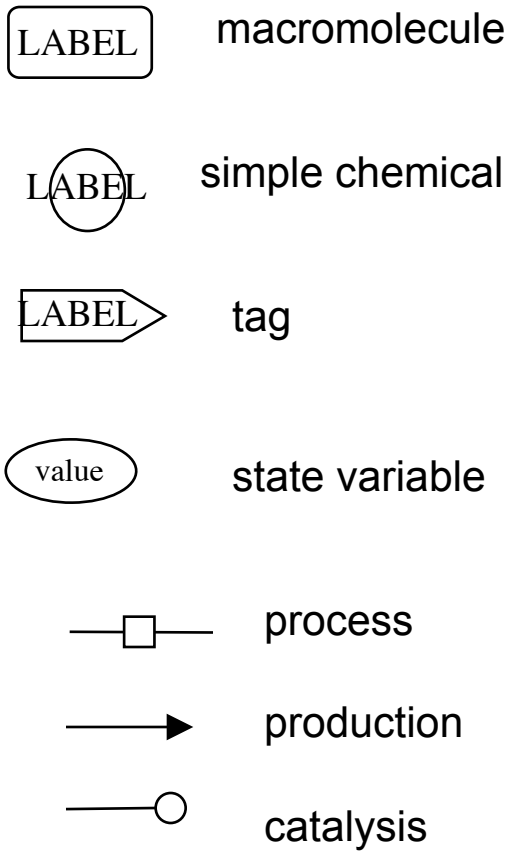
Systems Biology Graphical Notation (SBGN)

SGBN is a visual language designed to represents biochemical processes in a

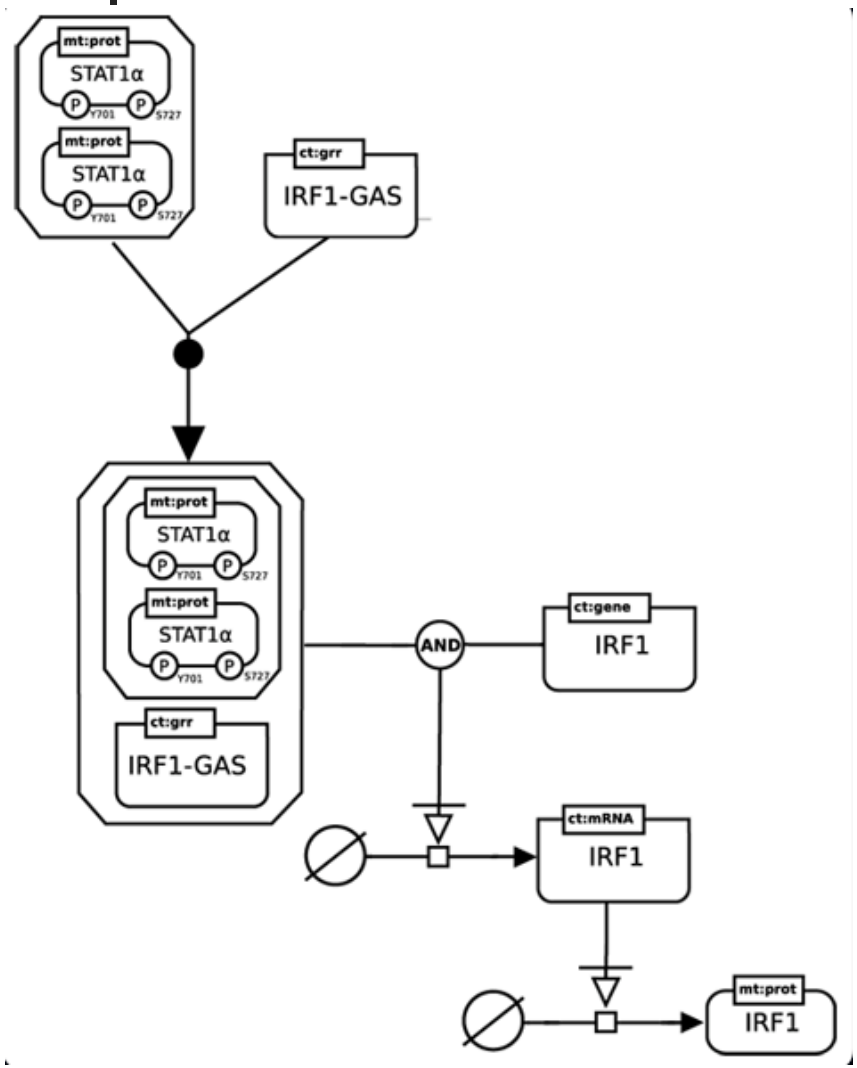
- *standard* and
- *unambiguous way.*

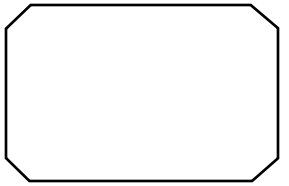
SBGN process language





SBGN process language

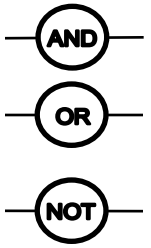




complex

LABEL — genetic entity

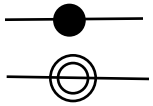
pre:label — unit of information



and operator

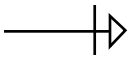
or operator

not operator



association

dissociation



necessary stimulation

source/sinc

Now its your turn… exercises

Draw the following reactions from Toy-Jim using the SBGN process diagram language:

- A ligand binds to a receptor.
- Two receptors, bound to ligands, form a dimer.
- An adaptor binds to a dimerized receptor.
- A kinase binds to the adaptor, which is bound to the dimerized receptor.
- Why is it hard to draw the entire Toy-Jim example in one picture using the SBGN language?

Now its your turn… exercises

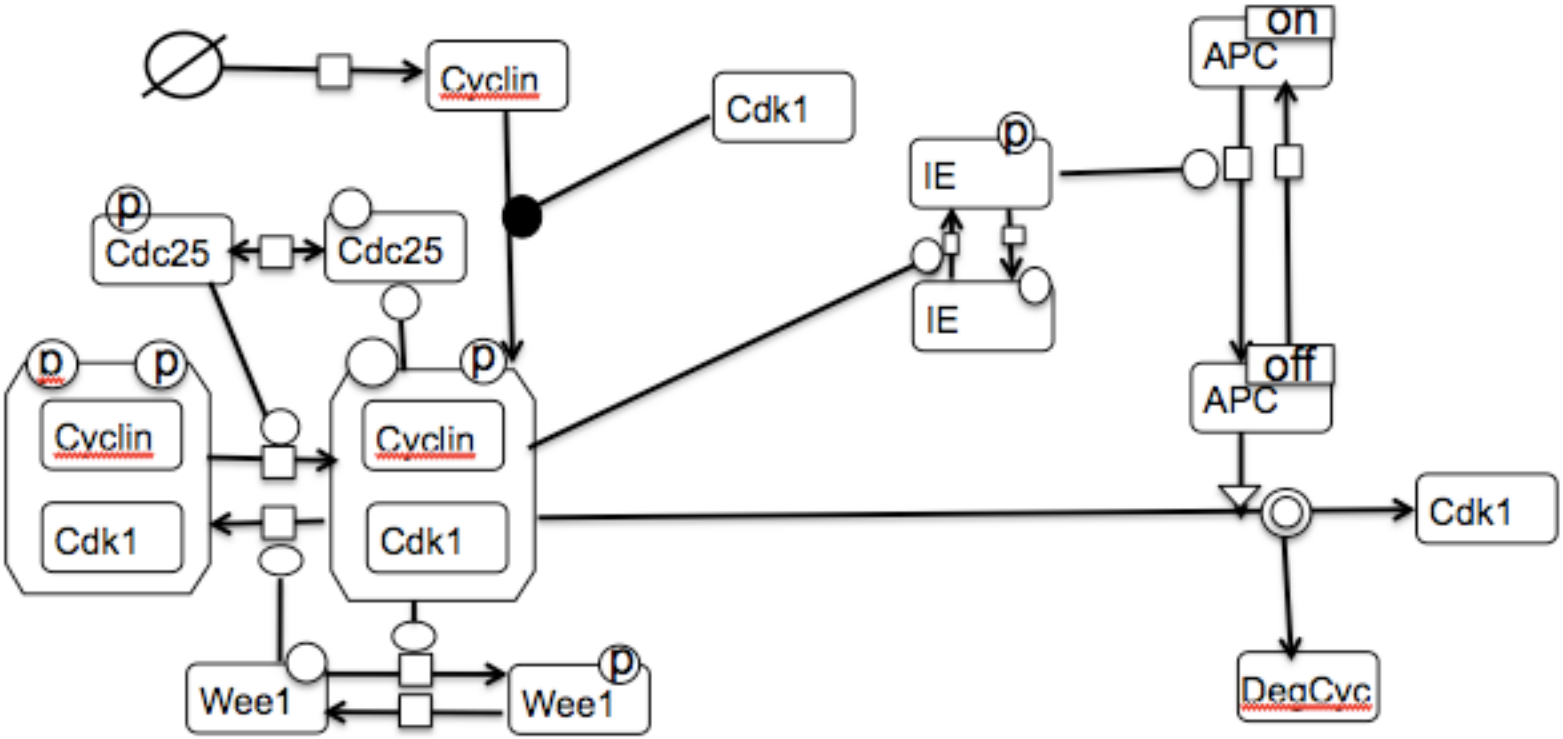
Redraw the frog cell cycle diagram using the SBGN process diagram language, assuming that:

- dotted arrows indicate catalysis,
- full arrows indicate production,
- all molecules are complex molecules,

and ignoring the reaction rates (k's).

How SBGN solves ambiguity

The frog cell cycle again..



Two more languages

SGBN consists of three languages:

- *Process diagram*

(represents all molecular processes)

- Entity relationship diagram

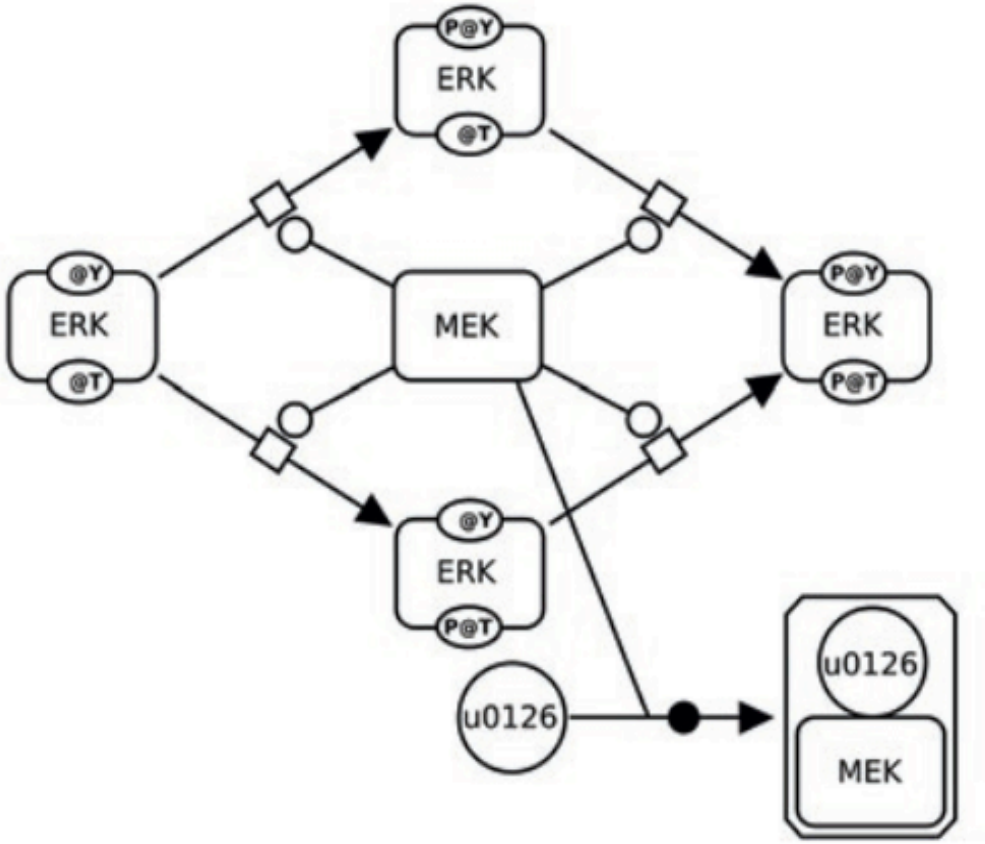
(describes influences that entities have upon each other's transformations)

- Activity flow diagram

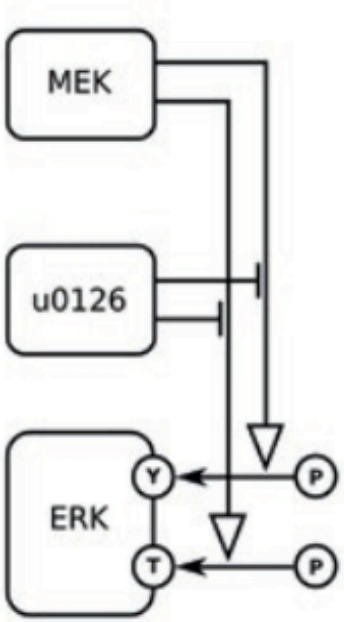
(ignores biochemical details)

The same process, three representations.

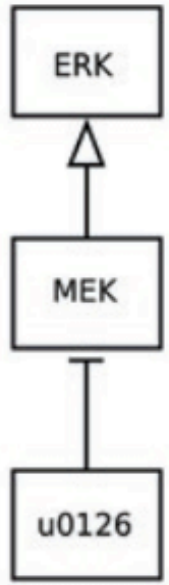
Process:



Entity relationship:



Activity flow:



SBGN: three languages

Comparison	Process	Entity relationship	Activity flow
Ambiguity	unambiguous	unambiguous	Ambiguous (in biochemical terms)
Level of description	Mechanistic descriptions of processes	Mechanistic description of relationships	Conceptual description of influences
Pitfalls	Explosion of states	Not easy to represent creation and destruction	Cannot represent assocation or dissocation
Advantages	Detailed, good for mechanistic processes	Good for signaling involving multistate entities	Good for functional genomics

SBGN: three languages

Can you think of other advantages or disadvantages?

Questions?

- References:

1. Le Novere et al. *The Systems Biology Graphical Notation.* Nature Biotechnology (vol 27 nr 8) August 2009.
2. sbgn.org
3. Sible and Tyson. *Mathematical modeling as a tool for investigation cell cycle control networks.* Methods (41) 2007.