

# The Systems Biology Graphical Notation



<http://www.sbgn.org/>



# What is SBGN?

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



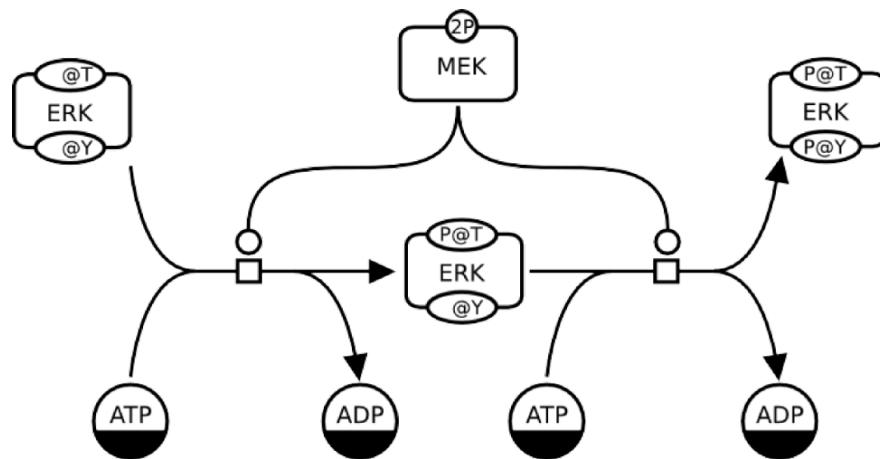
# What is SBGN?

- Three languages
  - Process Description → one state = one glyph
  - Entity Relationship → one entity = one glyph
  - Activity Flow → conceptual level



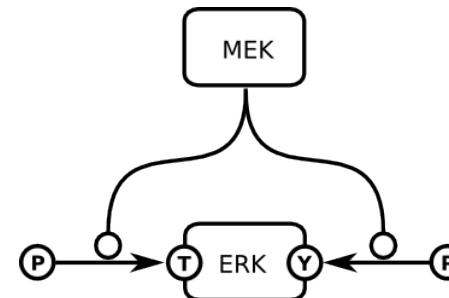
# Graph Trinity: Three Languages in One

## Process Description maps



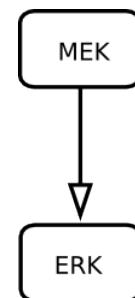
- ▶ Unambiguous
- ▶ Mechanistic
- ▶ Sequential
- ▶ Combinatorial explosion

## Entity Relationship maps



- ▶ Unambiguous
- ▶ Mechanistic
- ▶ Non-Sequential

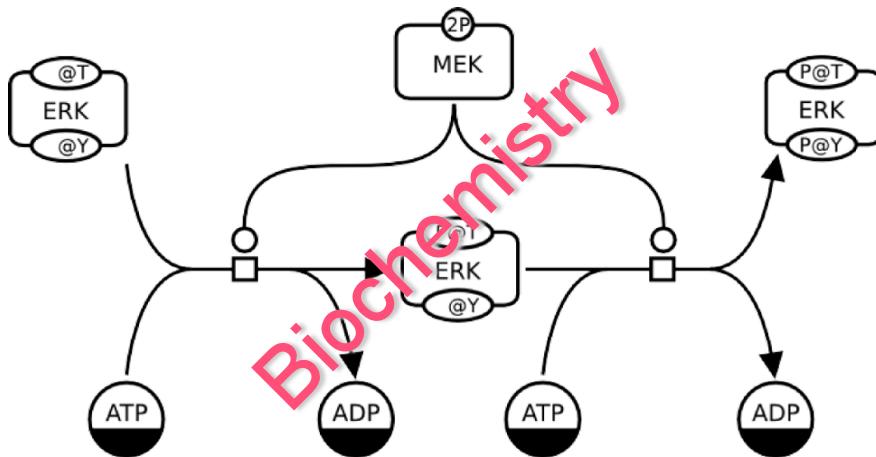
## Activity Flow maps



- ▶ Ambiguous (in sense of mechanism)
- ▶ Conceptual
- ▶ Sequential

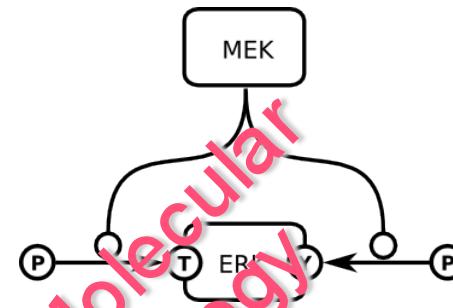
# Graph Trinity: Three Languages in One

## Process Description maps



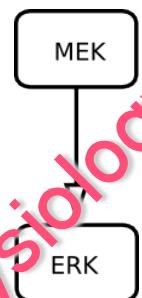
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## Entity Relationship maps



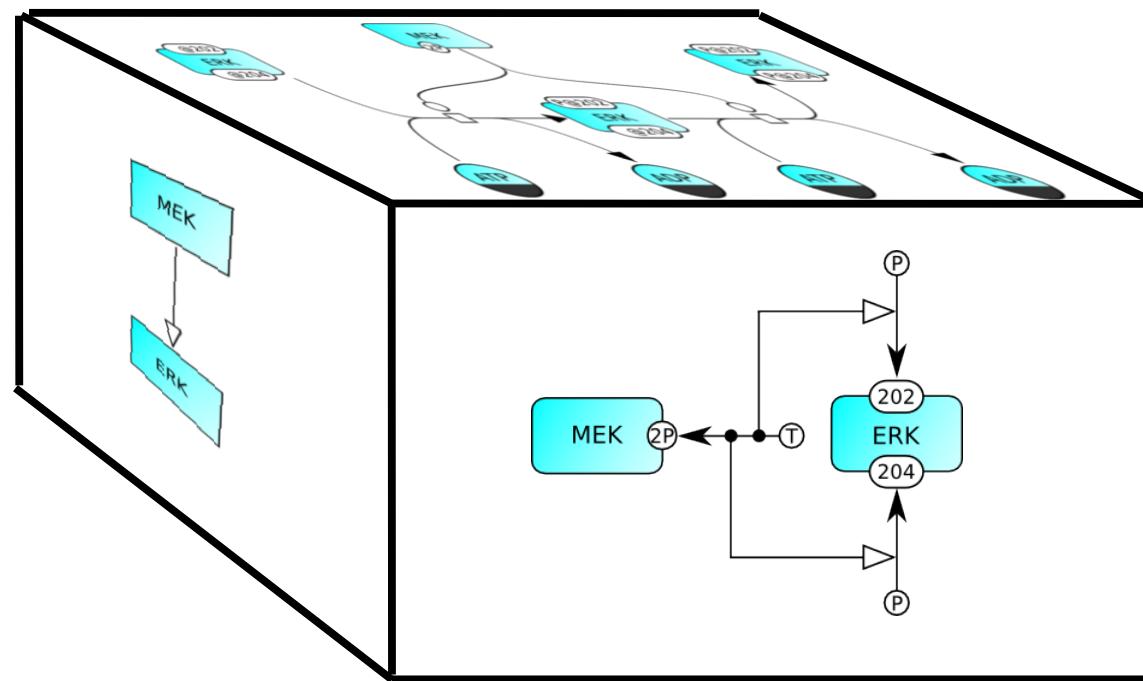
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## Activity Flow maps



- ▶ Ambiguous (in sense of mechanism)
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# Three Orthogonal Projections of Biology

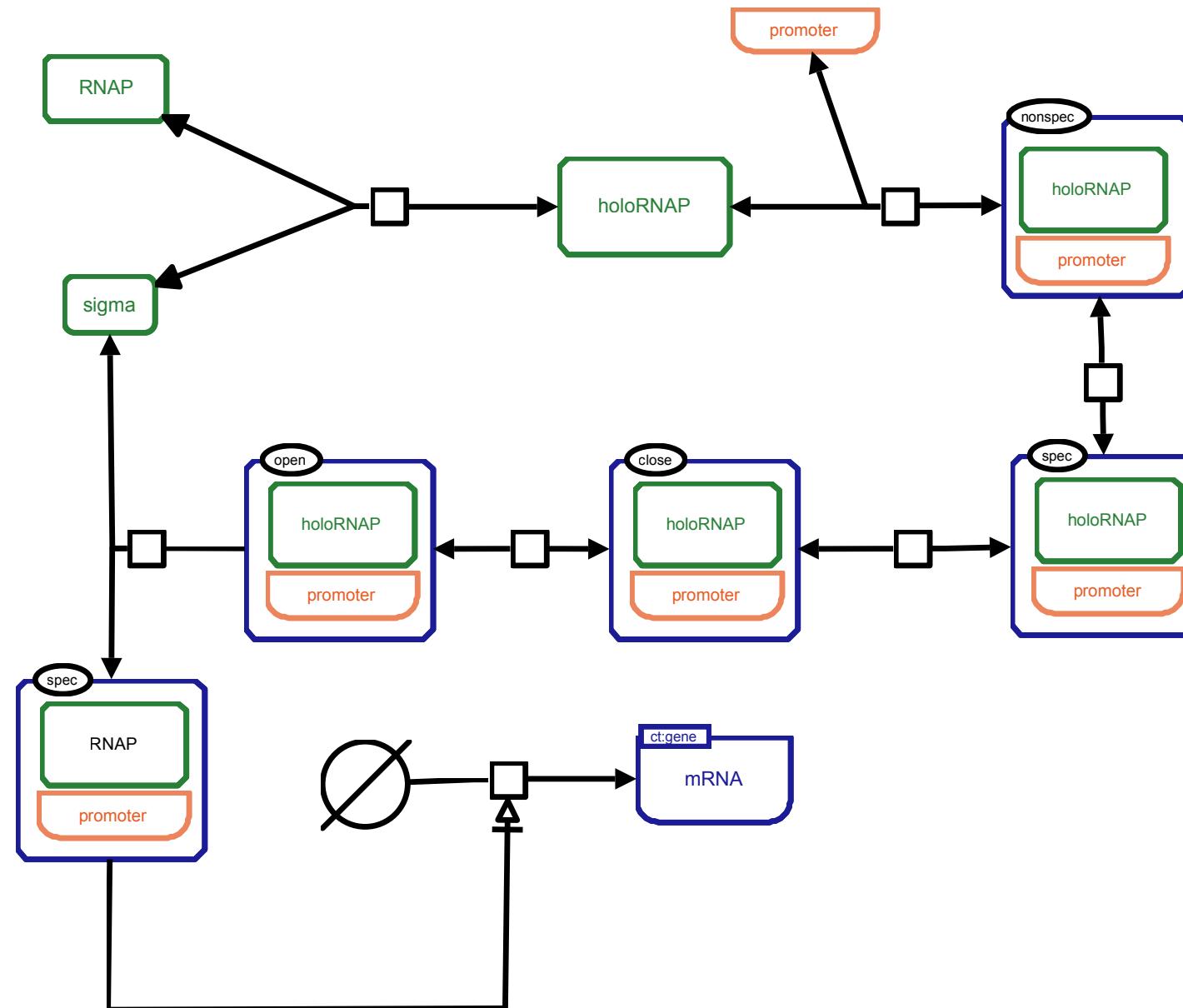


# SBGN

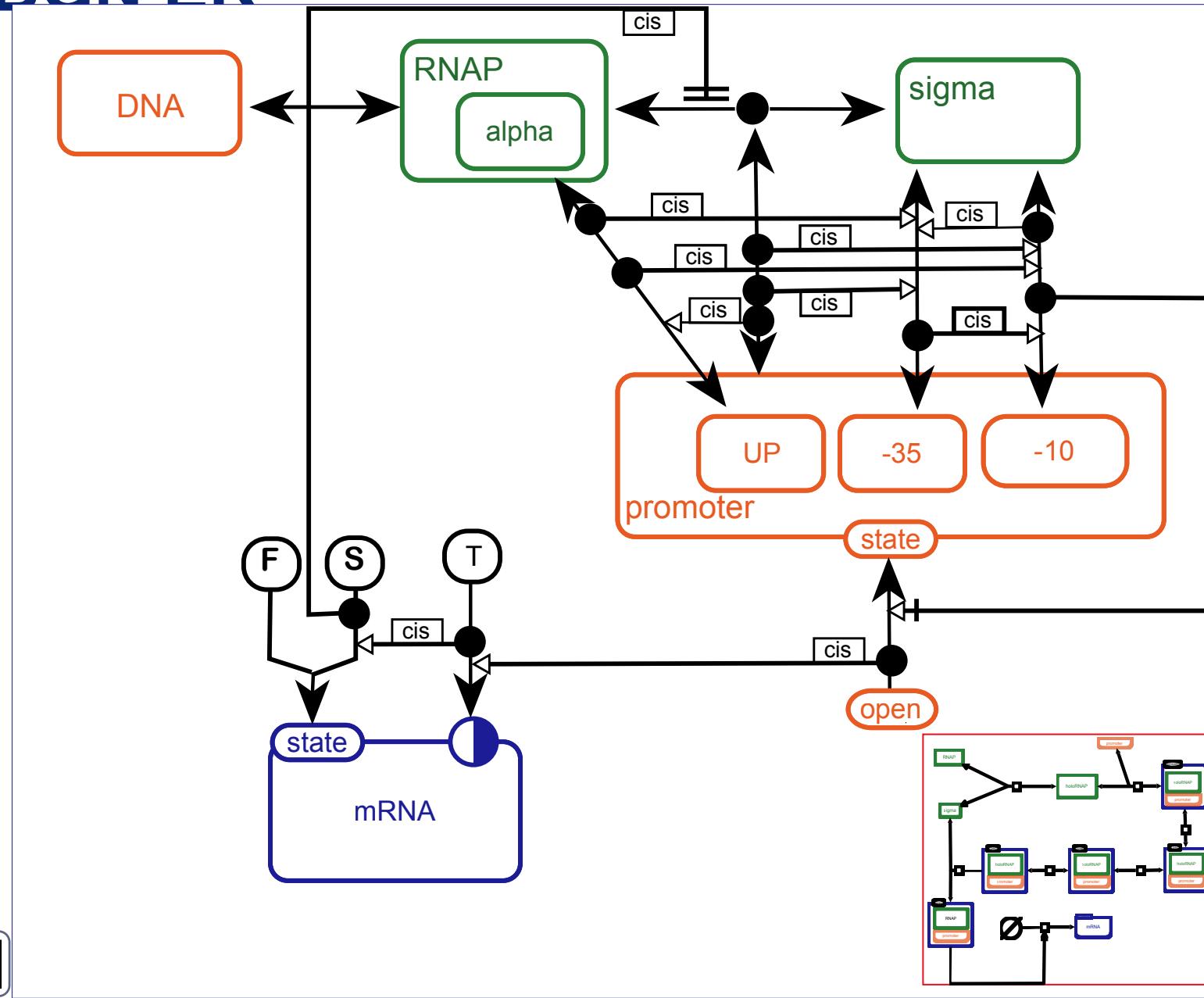
- Colour has no meaning
- Size has no meaning
- Meaning should be conserved upon
  - Scaling
  - Resolution
  - Relayout



# SBGN PD



# SBGN ER



# Strength and Weakness of SBGN-ER

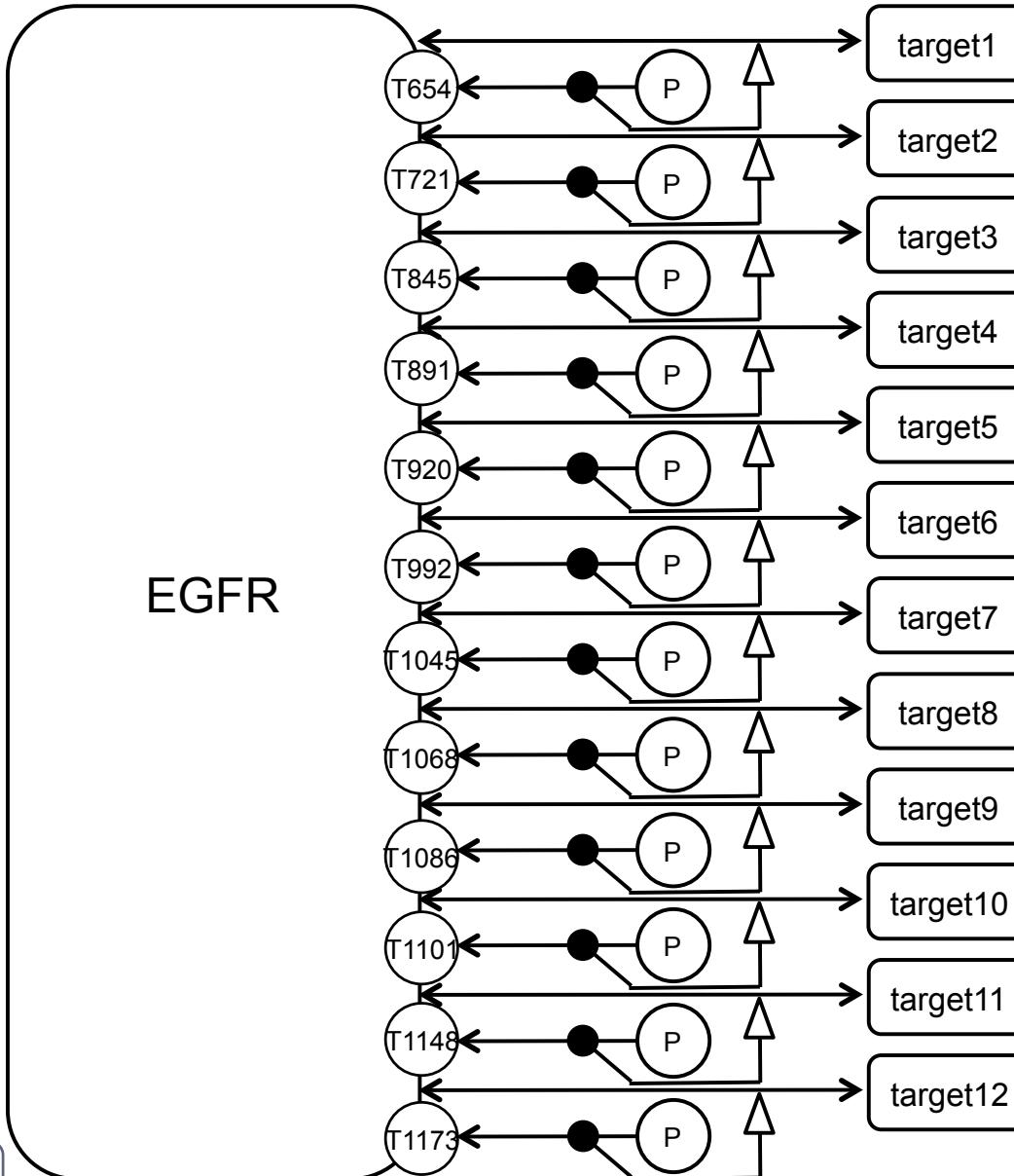
## Strength

- Statement based nature of ER helps in text annotation
- Close mapping to rule-based modeling
  - BNGL, kappa
- Handles combinatorial complexity naturally

## Weakness

- Difficult to read
- No timeline
- Difficult for validation and reasoning

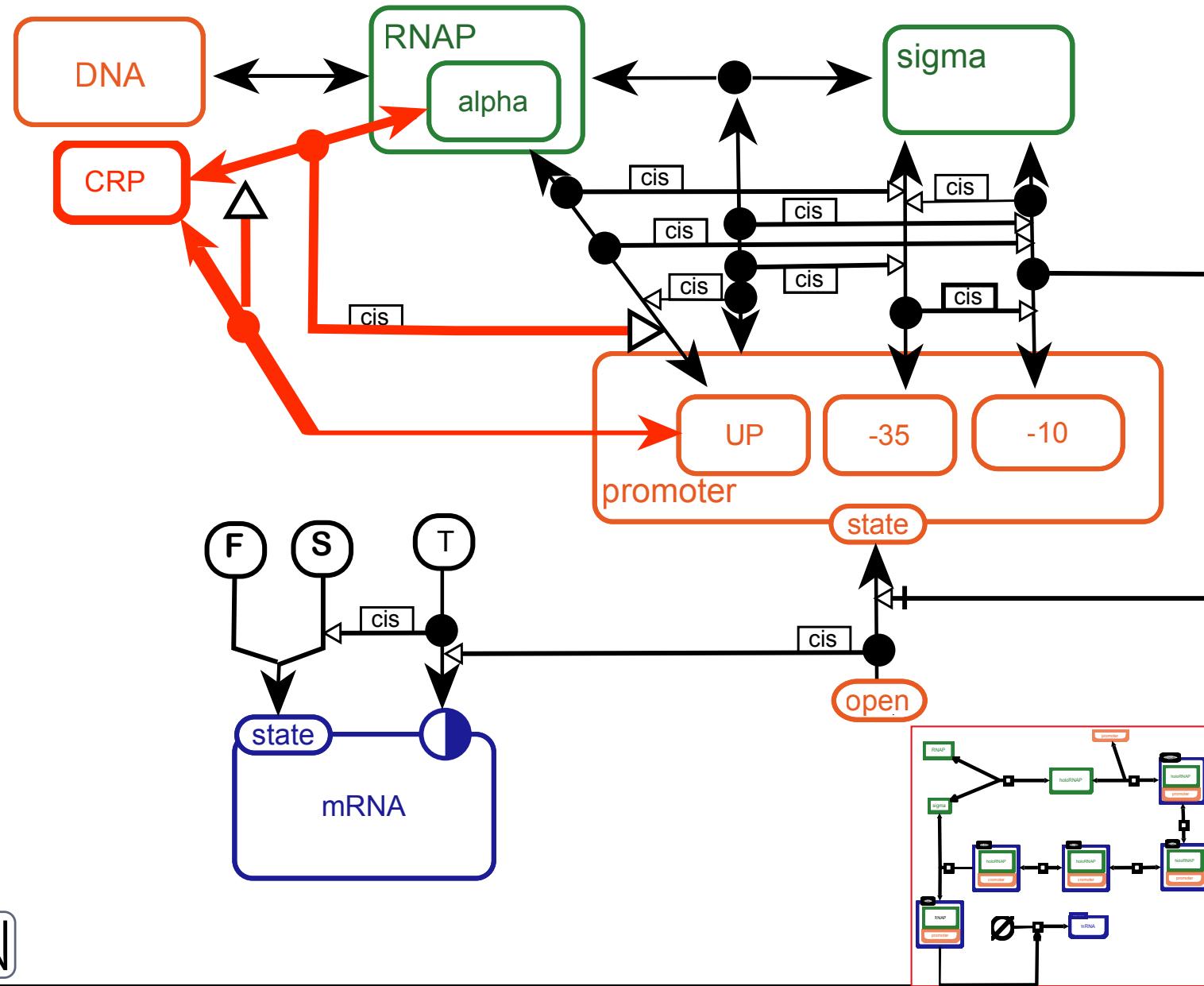
# Multistates and Combinatorial Explosion



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

# Compositionality of the diagram

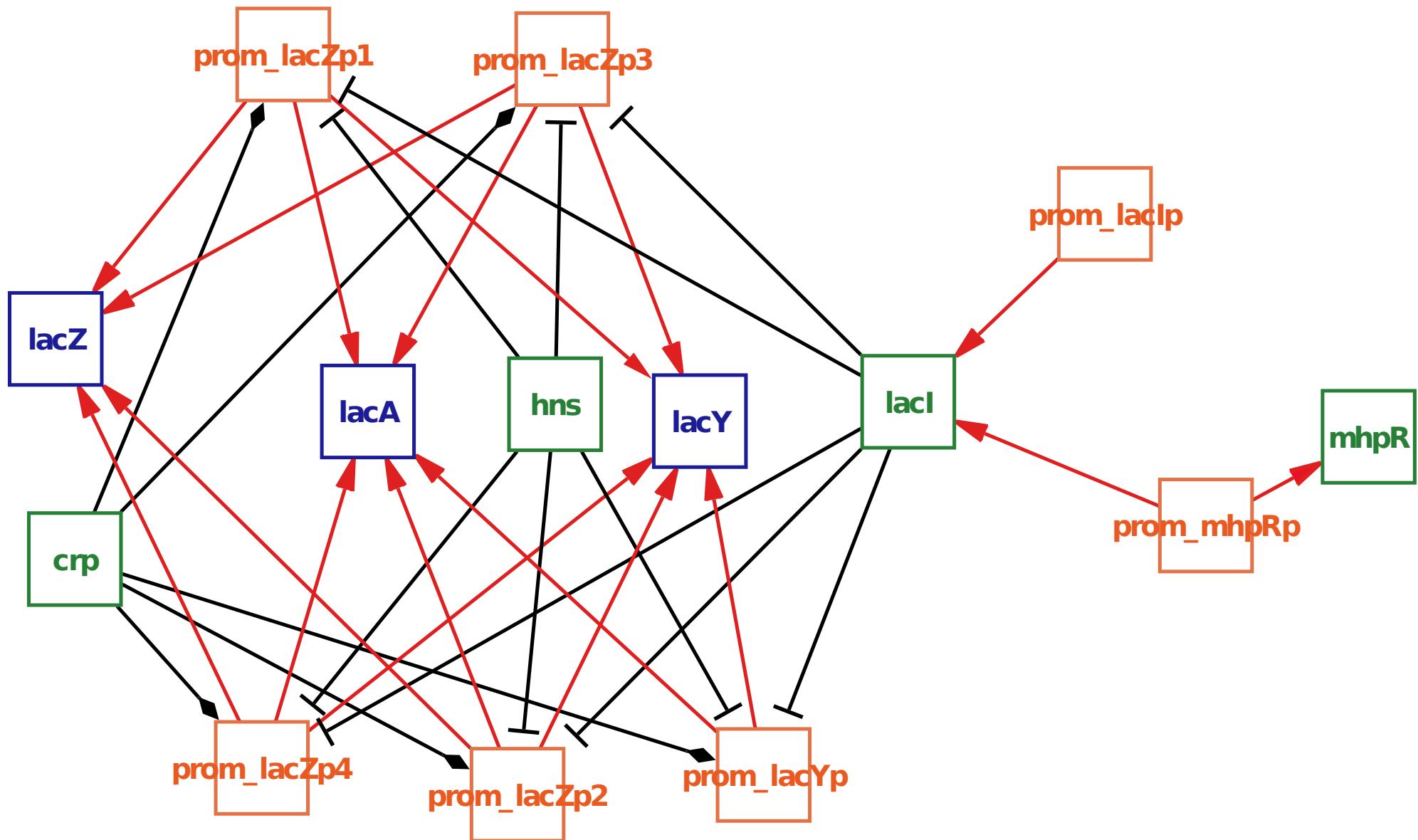


# SBGN Activity Flow

- SBGN activity flow diagram is similar to the way biologists draw signaling pathway
- It emphasizes on the influences exerted from one activity to another
- It is useful when the pathway knowledge is incomplete or irrelevant
- It allows modulatory arcs to directly link different activities
- It is familiar to biologists
- Highly ambiguous in description of mechanism

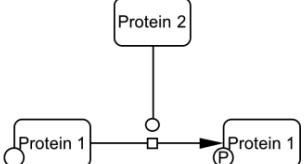
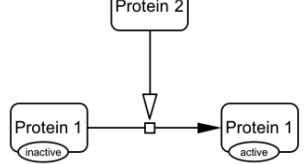
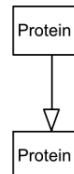
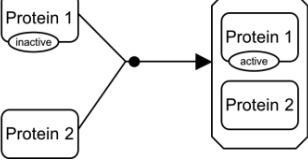
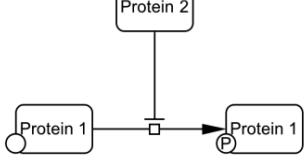
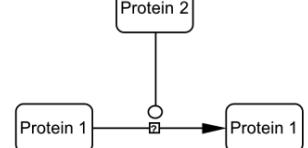
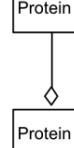
# Activity Flow: Abstraction

- Main concept is **Biological Activity**
  - Each node represents an activity, but not the entity
  - Multiple nodes can be used to represent activities from one entity (e.g., receptor protein kinase)
  - One node can be used to represent activities from a group of entities (e.g., a complex, generics etc.)



# Activity Flow Map is Ambiguous

- AF diagrams are ambiguous
- An AF diagram should be associated with either a PD or ER diagram, if possible
- Automatic conversion between PD and/or ER to AF is planned

Process Diagram	Activity Flow
 <p>Protein 2 catalyzes the transition of Protein 1 from non-phosphorylated form to phosphorylated form.</p>	
 <p>Protein 2 stimulates the conversion of Protein 1 from an inactive state to an active state.</p>	 <p>Protein 2 positively influences Protein 1.</p>
 <p>Inactive form of Protein 1 associates with Protein 2 to form a Protein 1/Protein 2 complex, and Protein 1 becomes active through the association.</p>	
 <p>Protein 2 inhibits the transition of Protein 1 from non-phosphorylated form to phosphorylated form.</p>	 <p>Protein 2 negatively influences Protein 1.</p>
 <p>Protein 2 catalyzes an unknown transition of Protein 1.</p>	 <p>Protein 2 influences Protein 1 with unknown mechanism.</p>

# Strength and Weakness of SBGN-AF

## Strength

- Similar to biological sketch drawings
- Compact

## Weakness

- Ambiguous
- Requires text or other diagram

# Documentation split

- Till last year there was technical Specification only
  - Too technical
  - Focused on tool developers
- It was decided to split documentation into two parts
  - Technical Specification: normative official description of the language
  - User Manual: description of the use of language to teach end users
- User Manual is available for SBGN PD

# Specification status update

- First draft of a user manual is available for SBGN PD Level 1 Version 1.3
  - [https://sourceforge.net/p/sbgn/code/HEAD/tree/ProcessDiagram/trunk/UserManual/sbgn\\_PD-level1-user.pdf](https://sourceforge.net/p/sbgn/code/HEAD/tree/ProcessDiagram/trunk/UserManual/sbgn_PD-level1-user.pdf)
- A first draft of SBGN PD Level 1 Version 2 is ready for review
  - [https://sourceforge.net/p/sbgn/code/HEAD/tree/ProcessDiagram/trunk/Specification/sbgn\\_PD-level1.pdf](https://sourceforge.net/p/sbgn/code/HEAD/tree/ProcessDiagram/trunk/Specification/sbgn_PD-level1.pdf)
- A draft of SBGN ER Level 1 Version 2 is available for review
  - [https://sourceforge.net/p/sbgn/code/HEAD/tree/EntityRelationship/trunk/sbgn\\_ER-level1.pdf](https://sourceforge.net/p/sbgn/code/HEAD/tree/EntityRelationship/trunk/sbgn_ER-level1.pdf)
- A draft of SBGN AF Level Version 1.1 is available for review
  - [https://sourceforge.net/p/sbgn/code/HEAD/tree/ActivityFlow/trunk/sbgn\\_AF-level1.pdf](https://sourceforge.net/p/sbgn/code/HEAD/tree/ActivityFlow/trunk/sbgn_AF-level1.pdf)



# Governance

- Editorial board



Tobias  
Czauderna



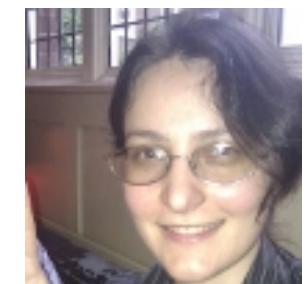
Stuart  
Moodie



Falk  
Schreibera



Anatoly  
Sorokin



Alice  
Villeger

- Scientific committee



# Changes in the Governance

- Editorial board
  - Step down
    - Emek Demir
    - Nicolas Le Novere
  - New editors
    - Stuart Moodie
    - Tobias Czauderna
- Scientific committee
  - New members
    - ♦ Falk Schreiber

# Survey

- Our aim is to gauge the levels of SBGN usage: what it is used for, what languages are used and to generally get feedback on what users like, don't like, or think can be improved.
- Form e-mail:
  - [http://www.sbgn.org/SBGN\\_Survey#Form\\_Email](http://www.sbgn.org/SBGN_Survey#Form_Email)
- Results so far
  - 39 responses
  - mEPN is most used notation
  - MIM is the second one

# Votes since COMBINE 2012

- Equivalence node

[edit ] "Do-you agree that we need a symbol to explicitly link generics and specifics depicted on the same map ?"

Choice	Votes	Fraction
yes	7	70%
no	0	0%
not sure	3	30%

# Votes since COMBINE 2012

- Equivalence node

[edit ] "Do you agree that the equivalence node must be a logical operator, and neither an entity pool node nor a process node ?"

Choice	Votes	Fraction
yes	8	80%
no	1	10%
not sure	1	10%

# Votes since COMBINE 2012

- Equivalence node

[edit ] "Do you agree that the arcs linking the equivalence symbol to the relevant EPN should be equivalence arcs ?"

Choice	Votes	Fraction
yes	8	80%
no	2	20%
not sure	0	0%

# Votes since COMBINE 2012

- Equivalence node

[edit ] " When do-you think the equivalence gate should be introduced ?"

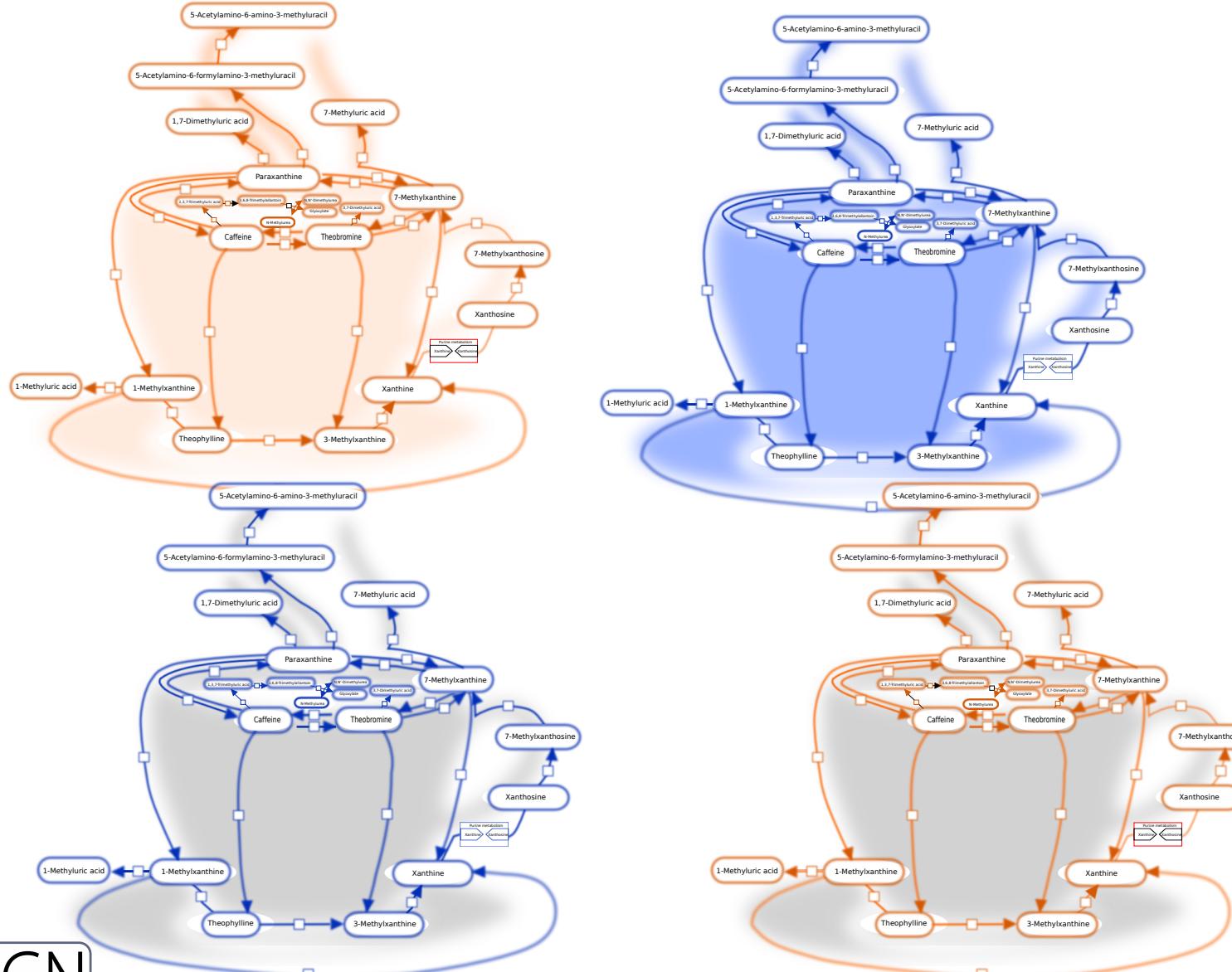
Choice	Votes	Fraction
In the forthcoming PD Level 1 Version 2	4	40%
In a subsequent version of PD Level 1	3	30%
In a future Level of the PD language	2	20%
Other (specify)	3	30%

# Acknowledgements

- **Visionary:** Hiroaki Kitano
- SBGN editors: *Nicolas Le Novère, Tobias Czauderna, Stuart Moodie, Falk Schreiber, Anatoly Sorokin, Alice Villéger, Emek Demir, Huaiyu Mi*
- All members of the SBGN community



# Ideas for T-shirt design



# **SBGN Issues to discuss**

*Brainstorming session*