

BiNoM, a Cytoscape plugin for accessing and analyzing pathways using standard systems biology formats

Eric Bonnet

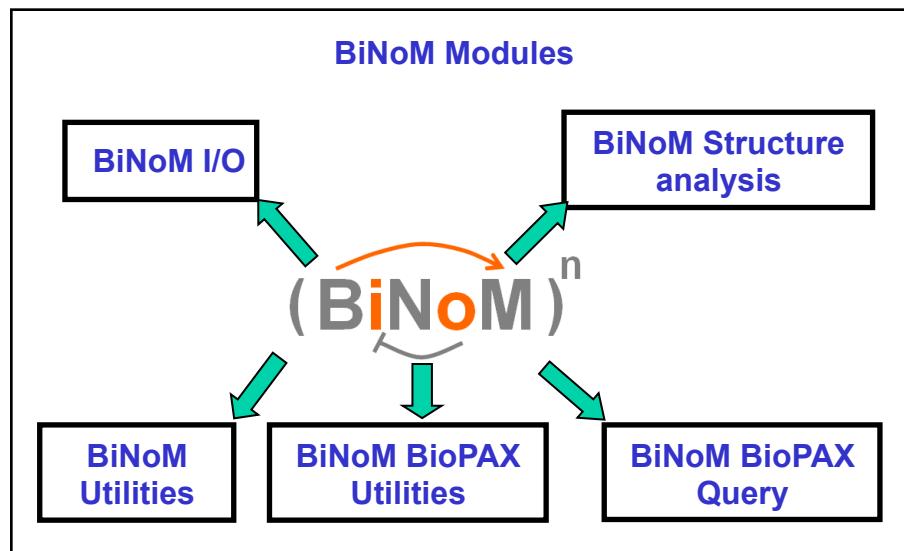
Computational Systems Biology of Cancer

Institut Curie - INSERM U900 - Mines ParisTech

<http://bioinfo.curie.fr/sysbio>

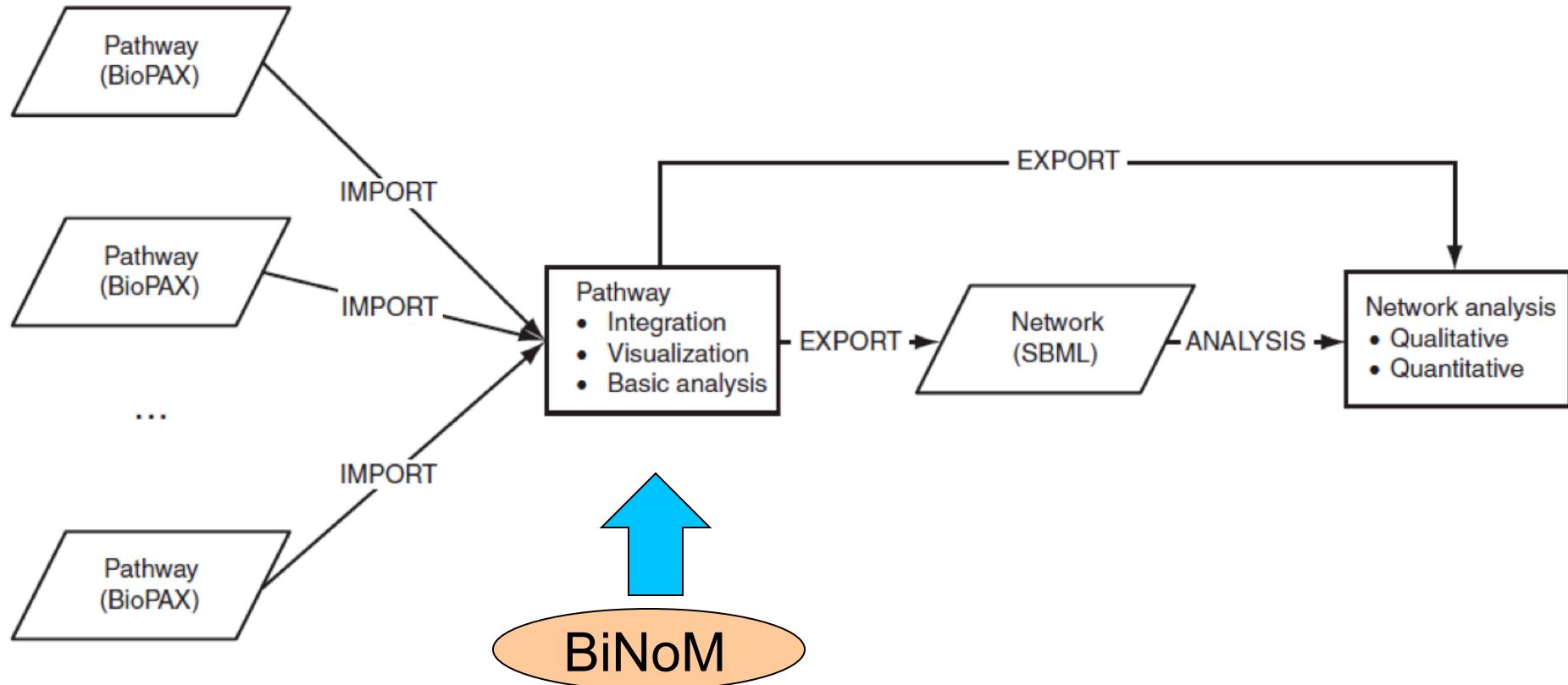
COMBINE 2012 – Toronto

BiNoM, a Biological Network Manager



- Facilitates the visualization and manipulation of biological networks.
- Supports standard systems biology formats (BioPAX, CellDesigner, etc.).
- Assists the user in the analysis of networks.
- Extracts specific information from databases such as Reactome.

BiNoM: a Cytoscape plugin for manipulating and analyzing biological networks. Zinovyev A, Viara E, Calzone L, Barillot E. Bioinformatics. 2008 Mar 15;24(6):876-7.

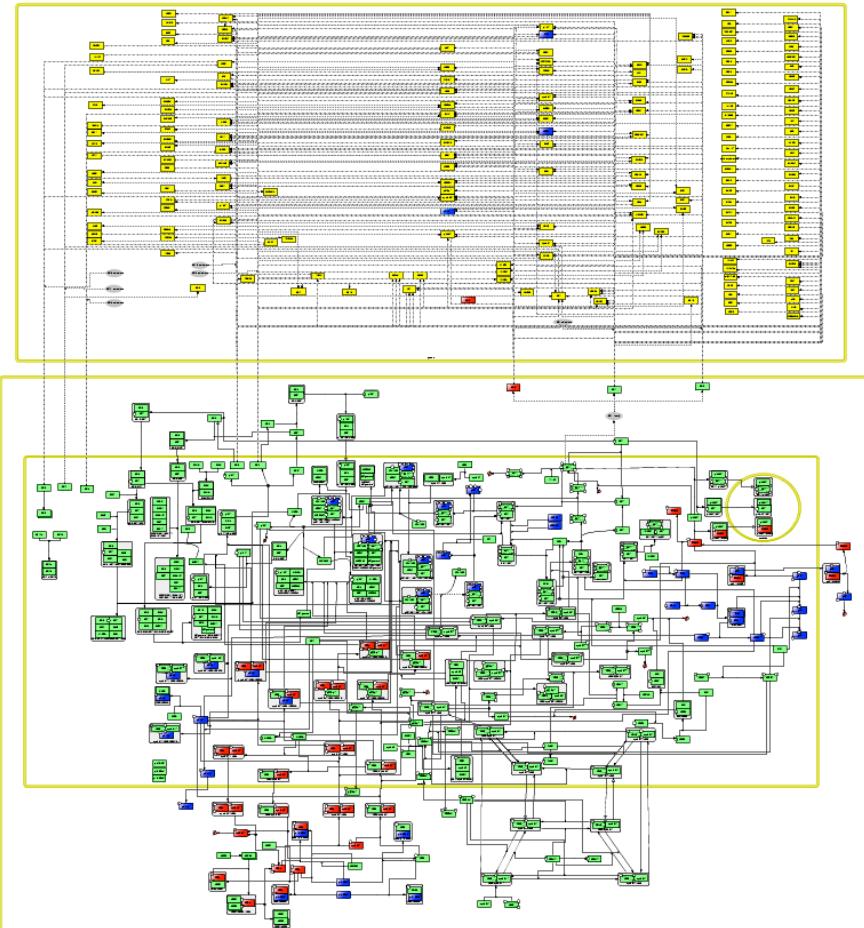


Use of data from public pathway databases for modelling purposes (from Bauer-Mehren et al., Pathway databases and tools for their exploitation: benefits, current limitations and challenges. 2009 Molecular Systems Biology 5:290).

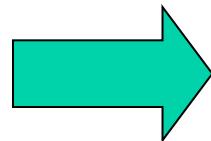
BiNoM typical scenarios

1. Import a CellDesigner diagram, manipulate, convert to BioPAX.
2. Import a CellDesigner diagram, analyze, decompose into modules, create a network modular view.
3. Import BioPAX file, extract a part, export to SBML, create a mathematical model.
4. Create a BioPAX file from simple factsheet text file.
5. Index huge BioPAX file (i.e., whole Reactome), make a query, save result as a smaller BioPAX file.

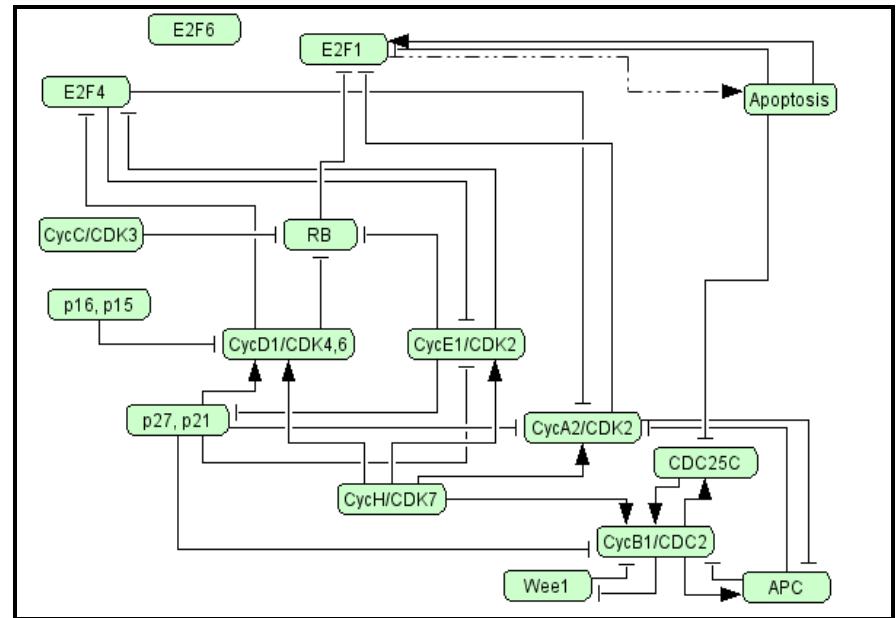
Knowledge extraction



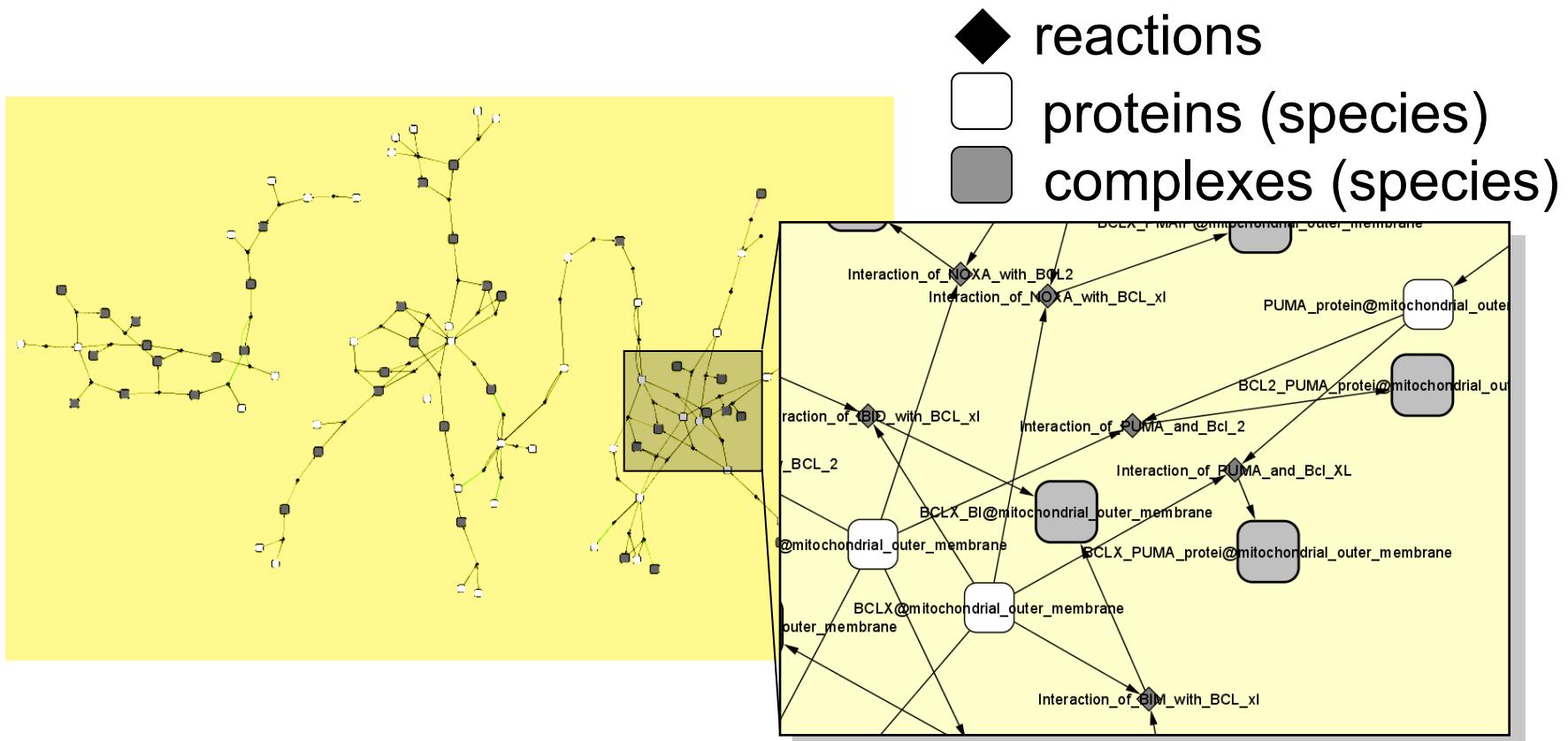
RB / E2F network, 70+ proteins,
160+ reactions, 350 publications



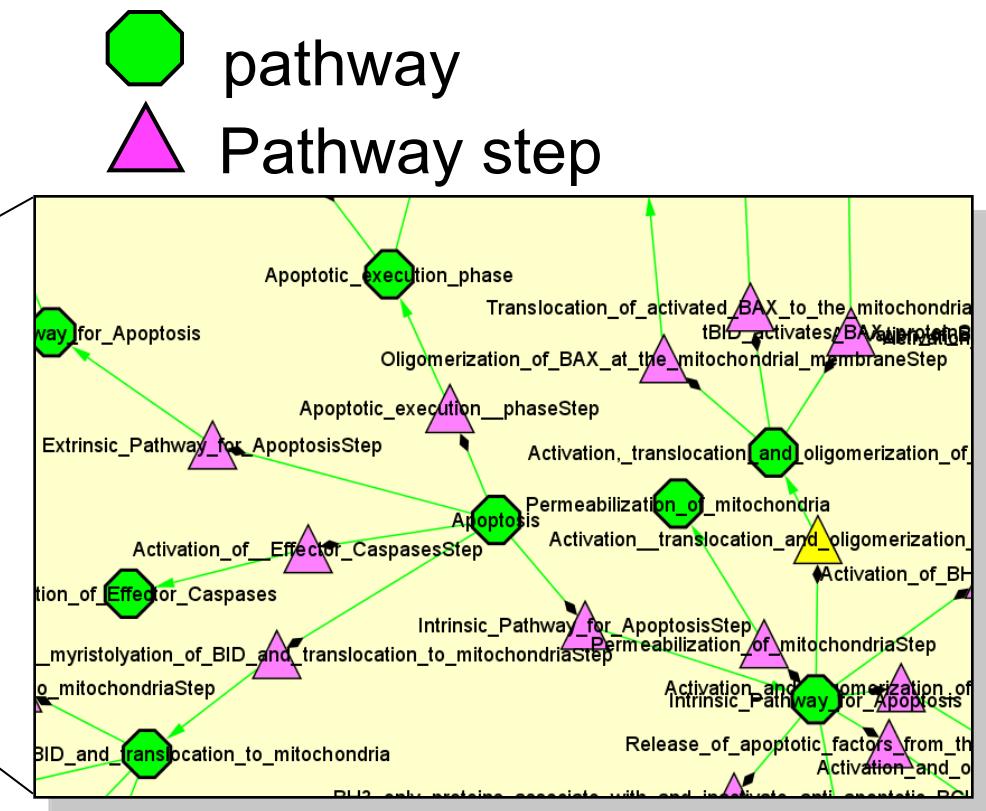
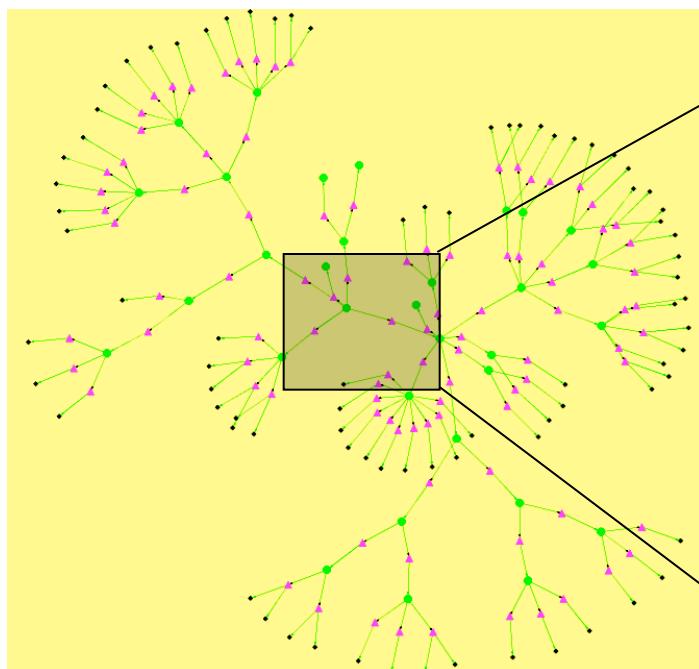
Modular representation



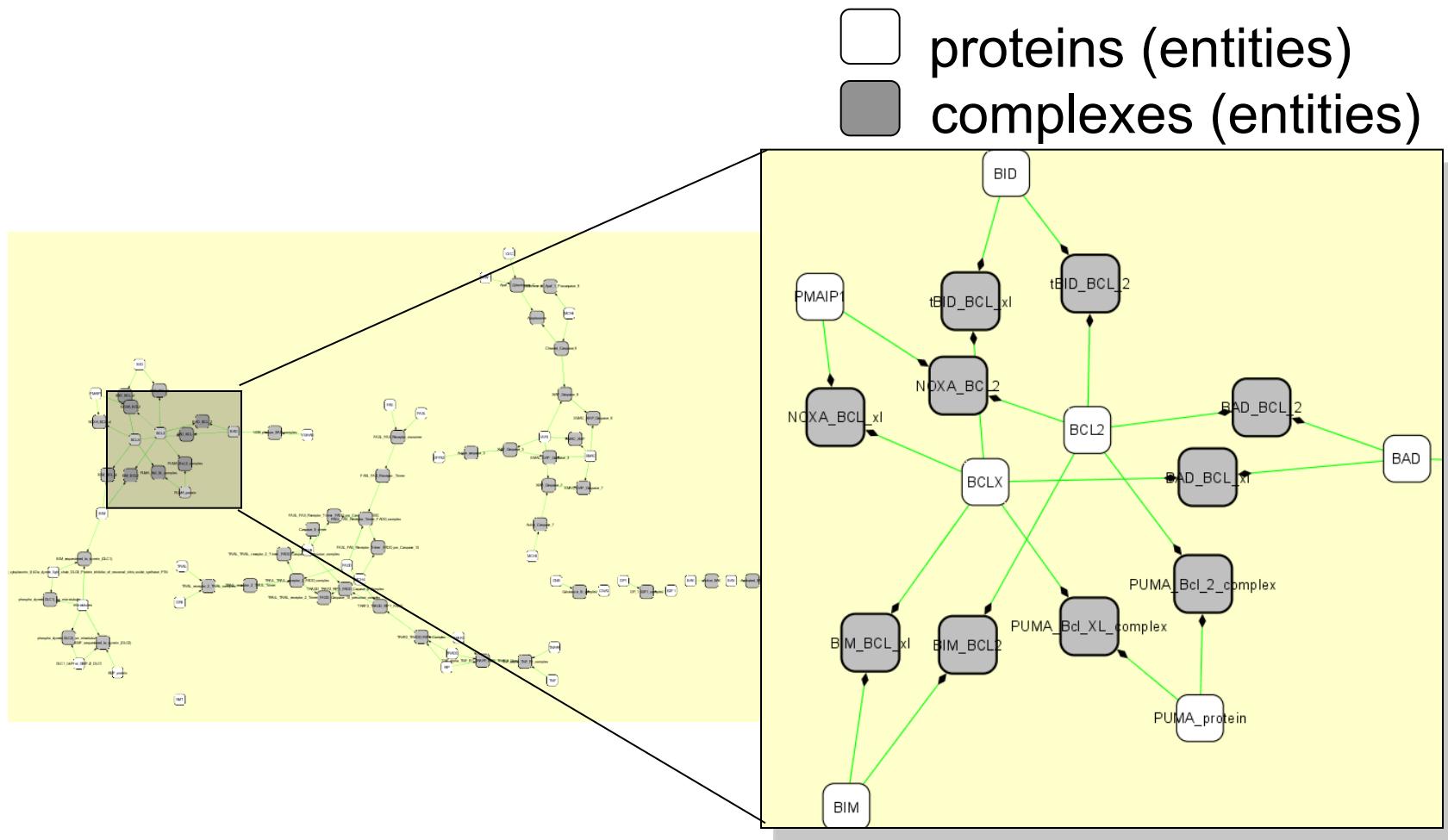
BioPAX -> Reaction Network

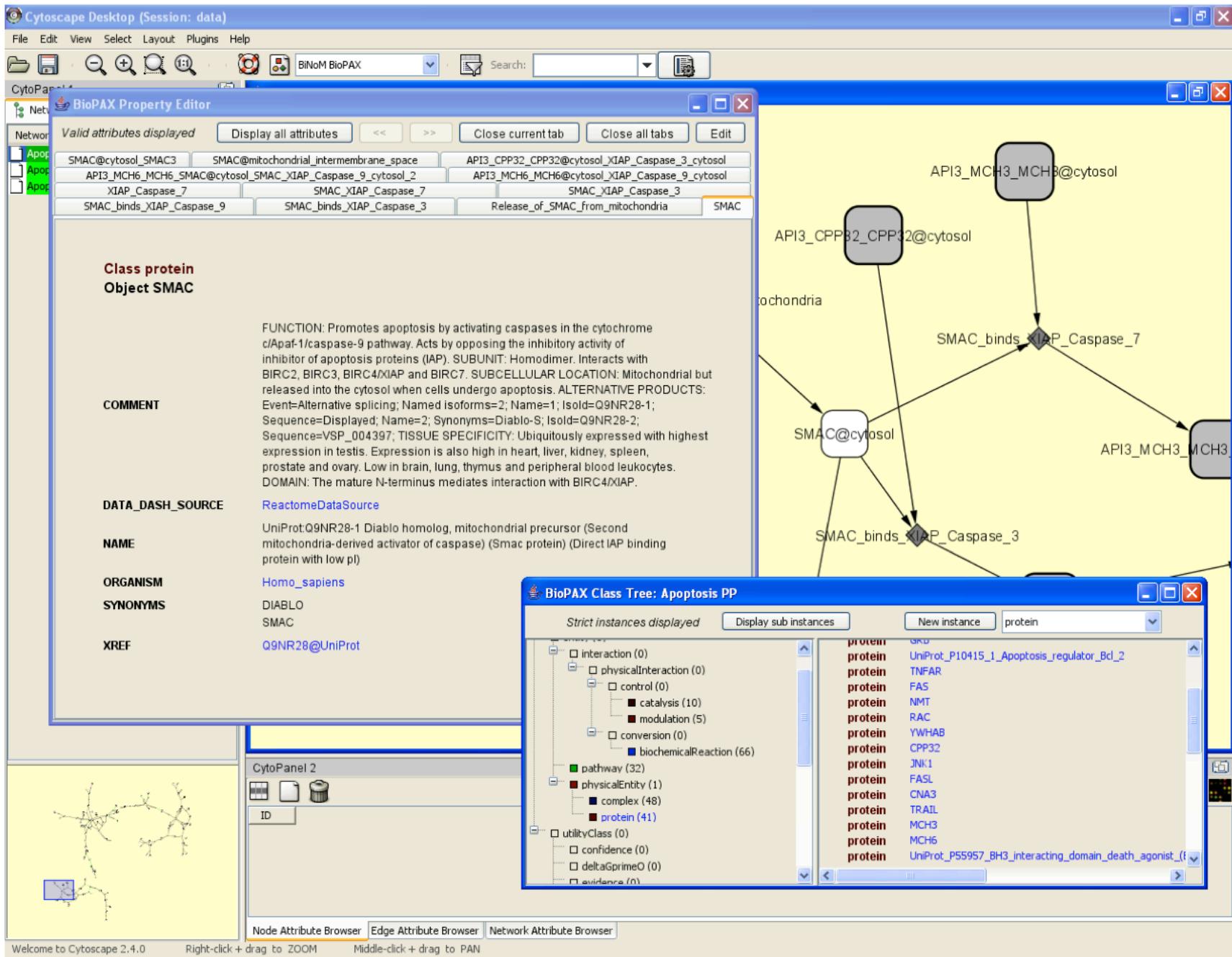


BioPAX -> Pathway Structure



BioPAX -> Protein Interactions





BiNoM v2.0 (2012): New functionalities

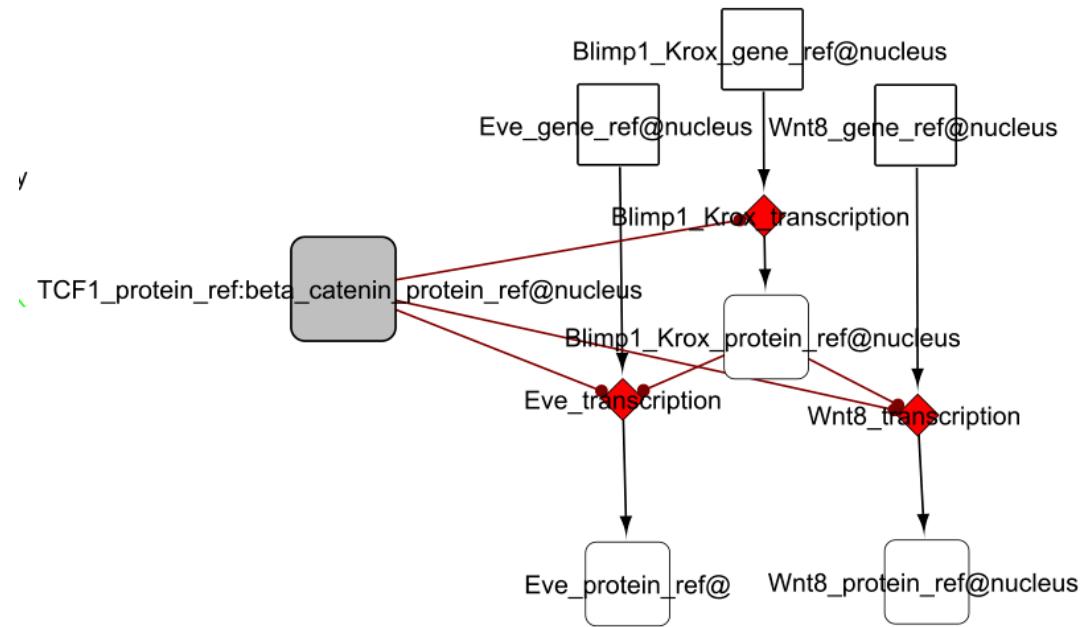
1. BioPAX level 3.0 support.
2. CellDesigner format 4.1 support.
3. Cytoscape 2.7.0+ support.
4. Pathway Quantification algorithm.
5. Minimal Cut Set algorithm.
6. Creation of interactive, “google maps” like molecular maps.

Support for BioPAX Level 3

- BioPAX is a standard language for representation of pathways.
- Latest specification (BioPAX level 3) released in 2010.
 - Metabolic pathways.
 - Signaling pathways.
 - Gene regulatory networks
 - Molecular interactions
 - Genetic interactions

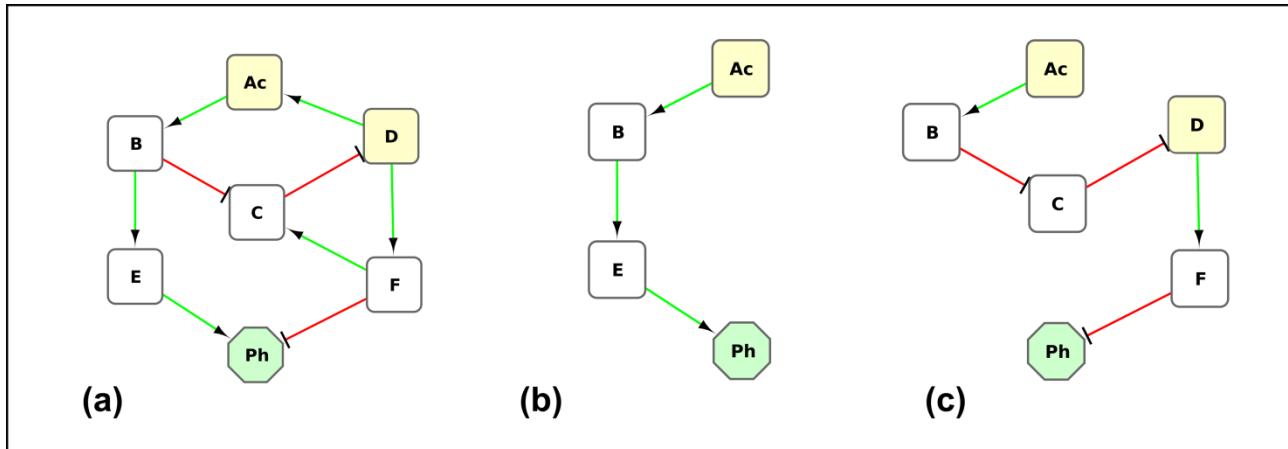


genetic-interaction



template-reaction Reaction Network

Pathway Influence Quantification (PIQuant)

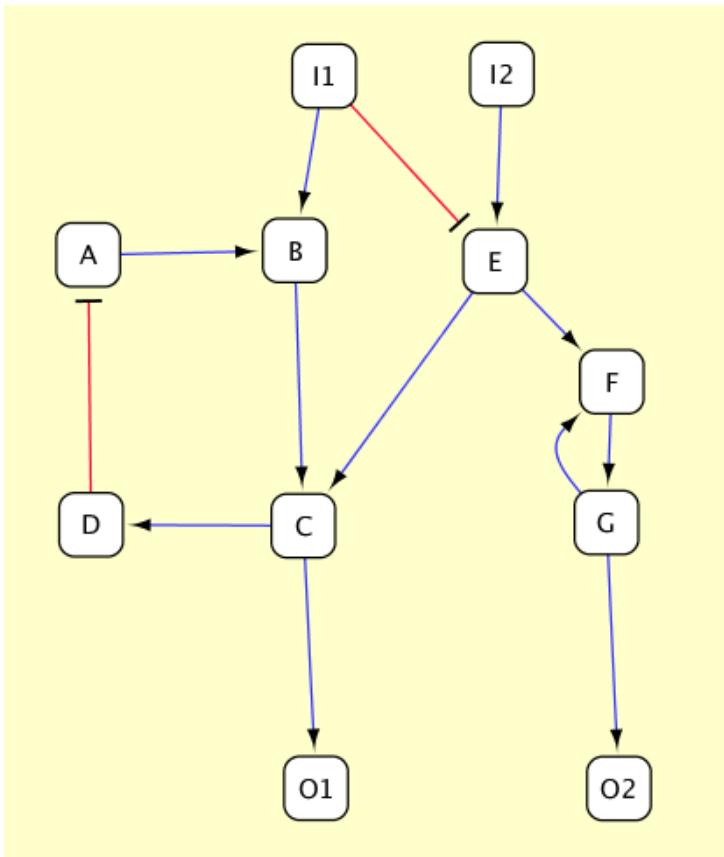


$$PIQuant_{Score} = \sum_{k=1}^q \alpha_k \sigma_k \frac{1}{\lambda_k}$$

Alpha: activity of the path
Sigma: sign of the path
Lambda: length of the path

$$PIQuant_{Score} = 2 \cdot 1 \cdot \frac{1}{3} + 2 \cdot (-1) \cdot \frac{1}{5} = 0.27$$

Minimal cut sets



- Influence graph G.
- Input nodes I₁, I₂.
- Output (target) nodes O₁, O₂.

I₁ → B → C → O₁
I₁ → E → C → O₁
I₂ → E → C → O₁

- Cut sets: {C}, {E, B}, {I₁, I₂}
- Minimal:
 - {E, C} is a cut set, but is not minimal.
- Application: define novel candidate drug targets.

MCS Algorithms

- Berge's algorithm (1989)
 - Based on hypergraph theory.
 - Do not scale well for networks 50+ nodes.

```
for  $i = 2, \dots, m$  do
    Find  $Tr(\mathcal{H}_{i-1})$ 
    Compute  $Tr(\mathcal{H}_i) = Min(Tr(\mathcal{H}_{i-1}) \cup \{\{v\}, v \in \mathcal{E}_i\})$ 
end for
Return  $Tr(\mathcal{H}_m)$ 
```

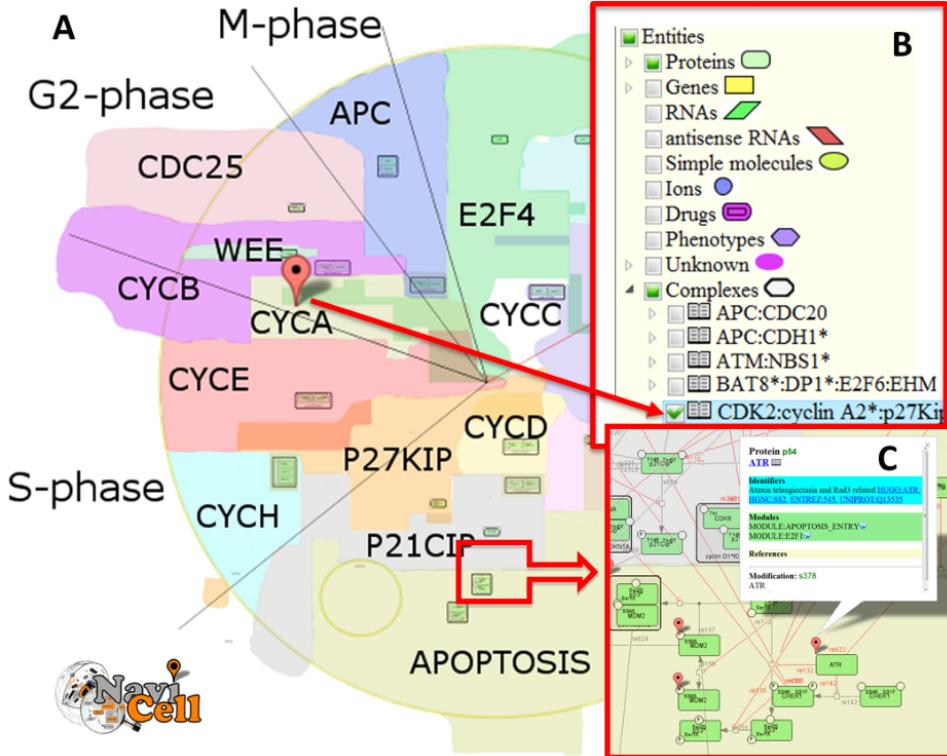
Algorithm 1: The algorithm of Berge

- Partial enumeration
 - Selection of a subset of nodes, by using a score based on path length and sign.
 - Enumerate subset of all possible solutions.
 - Check if they are cut sets and if they are minimal.



= Google map + Semantic zoom + Blog

Google map for browsing using semantic zooming



Blog for commenting

D

CDK2:cyclin A2*:p27Kip1*

Posted on 25 January 2012

Complex CDK2:cyclin A2*:p27Kip1* p24_p27_p73

Complex composition:

1. CDK2
2. cyclin A2*
3. p27Kip1*

CDK2:cyclin A2*:p27Kip1*@nucleus s740

Identifiers

CDK2:cyclin A2*/CDKN1B

Modules

MODULE:CYCLINA MODULE:P27KIP

References

Modifications: Participates in complexes:
In compartment: nucleus

1. CDK2:cyclin A2*:p27Kip1*@nucleus

Participates in reactions:

As Reactant or Product:

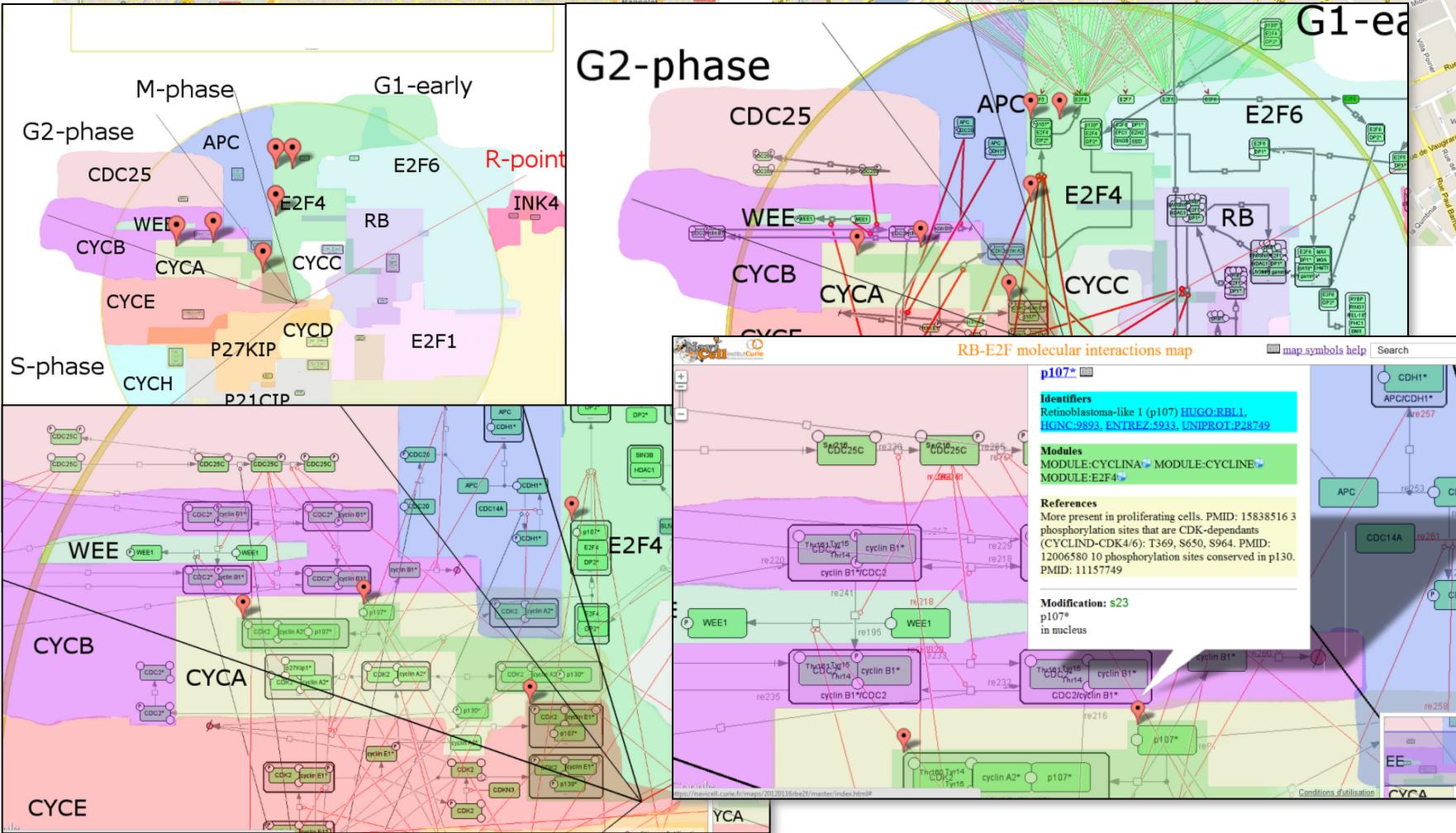
1. CDK2:cyclin A2* @nucleus + p27Kip1* @nucleus → CDK2:cyclin A2*:p27Kip1* @nucleus

As Catalyst:

Leave a reply



Semantic zooming



BiNoM v2.0

- Cytoscape plugin manager.
- <http://binom.curie.fr>
 - BiNoM jar file
 - BiNoM source code & doc
 - BiNoM manual (~100 pages)
 - BiNoM tutorial (book chapter)
 - BiNoM v1.0

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