

Using BioPAX Pathways for SBML Models with SyBiL

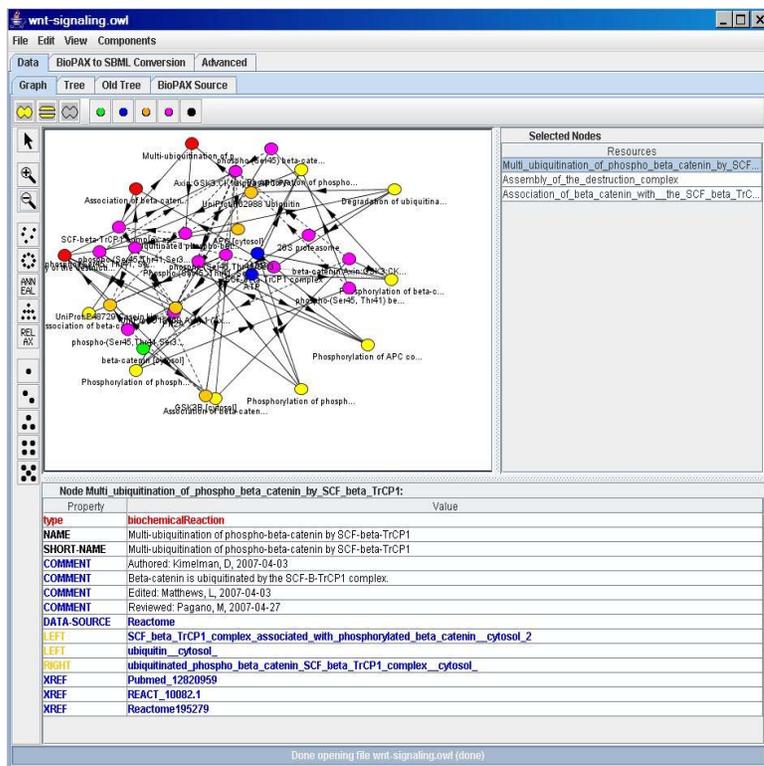
Oliver Ruebenacker, Ion I. Moraru, Michael L. Blinov
Center for Cell Analysis and Modeling
University of Connecticut Health Center

Systems Biology Linker (SyBiL, <http://vcell.org/biopax>) is a platform for the integration of knowledge in **Biological Pathway Exchange Format (BioPAX, <http://biopax.org>)** and models in **Systems Biology Markup-Language (SBML, <http://sbml.org>)**. BioPAX and SBML are community standards for exchange of pathway data and mathematical models, respectively.

Currently, **SyBiL** can visualize, analyze and query BioPAX data and convert BioPAX to SBML.

Visualization features a graph that displays different types of elements by different styles and colors and automatically groups or hides graph elements according to a level of detail chosen by the user. Levels of detail range from showing only reaction events to showing all substances including components of complexes and possible post-translational modifications. Selection of graph elements displays associated data. **Analyzing** and **querying** is based on SPARQL queries.

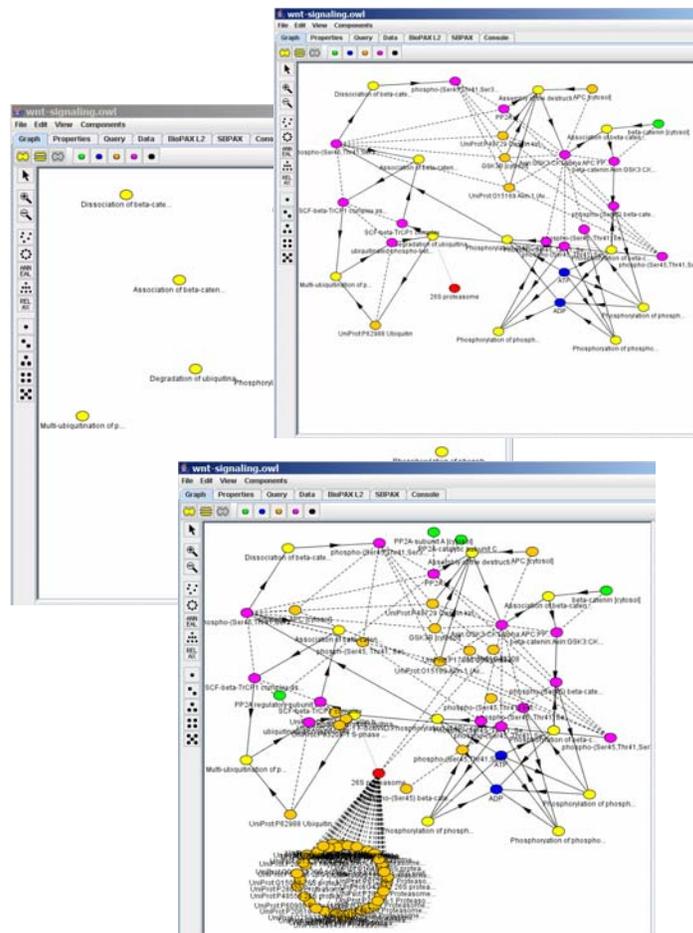
The BioPAX to SBML Conversion automatically performs all unambiguous mappings and allows user selections where the source data leaves ambiguities open. This includes identifying post-translational modifications and the geometrical layout of locations, to construct models runnable on simulators such as the Virtual Cell (<http://vcell.org>)



The screenshot shows the SyBiL interface with a network graph on the left and a detailed view of a reaction on the right. The reaction is:

Node Multi-ubiquitination of phospho_beta_catenin by SCF_beta_Trcp1:

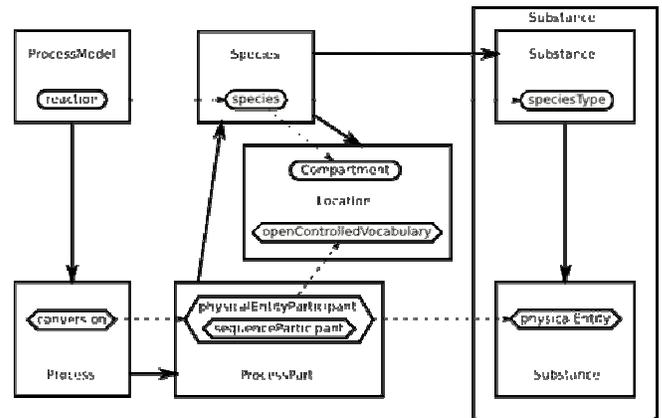
Property	Value
type	biochemicalReaction
NAME	Multi-ubiquitination of phospho-beta-catenin by SCF-beta-TrCP1
SHORT NAME	Multi-ubiquitination of phospho-beta-catenin by SCF-beta-TrCP1
COMMENT	Authors: Kimmelman, D., 2007-04-03
COMMENT	Beta-catenin is ubiquitinated by the SCF-B-TrCP1 complex.
COMMENT	Edited: Matthews, L., 2007-04-03
COMMENT	Reviewed: Pagano, M., 2007-04-27
DATA-SOURCE	Reactome
LEFT	SCF_beta_Trcp1_complex_associated_with_phosphorylated_beta_catenin_cytosol_2
LEFT	ubiquitin_cytosol
RIGHT	ubiquitinated_phospho_beta_catenin_SCF_beta_Trcp1_complex_cytosol
XREF	Pubmed_12820959
XREF	REACT_10082_1
XREF	Reactome195279



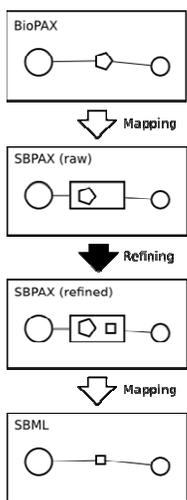
The two screenshots show the SyBiL interface displaying network graphs. The top screenshot shows a detailed graph with many nodes and edges, representing a complex biological pathway. The bottom screenshot shows a simplified graph with fewer nodes and edges, representing a higher level of detail or abstraction. The interface includes a menu bar (File, Edit, View, Components) and a toolbar with various icons for navigation and analysis.

With BioPAX focusing on universal, often qualitative statements and SBML on mathematical descriptions of specific scenarios, the meaning of central terms sometimes diverges between these two formats. For example, a reaction and a species type in SBML correspond most closely to a conversion and a physical entity in BioPAX, but multiple species types may correspond to one physical entity (in cases of post-translational modifications), or one species type may correspond to multiple physical entities (in cases of functionally equivalent substances).

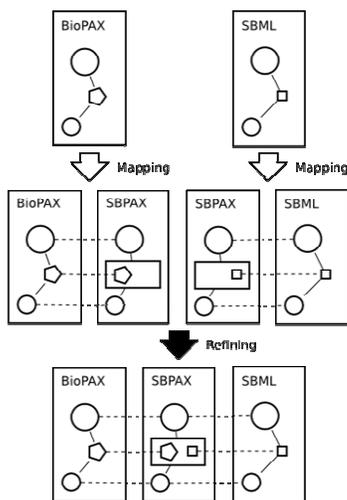
To integrate BioPAX and SBML, we developed a bridging ontology-based format **Systems Biological Pathway Exchange (SBPAX)**. The domain of SBPAX is the common subset of BioPAX and SBML, focusing on the structure of pathways (figure to the right). The expressive power of SBPAX is the common super set of BioPAX and SBML, offering sufficient flexibility to express any pathway structure expressible in BioPAX or SBML.



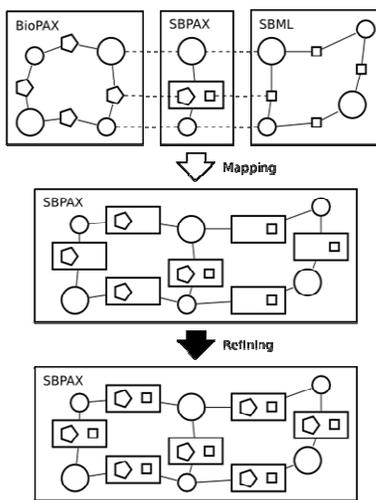
(a) Converting



(b) Gluing



(c) Merging



Integration tasks such as converting, gluing and merging data can be accomplished with the help of SBPAX by breaking them down into mapping and refinement steps (figure to the left). For conversion, data is mapped on-to-one from BioPAX or SBML to SBPAX. Then, the the data is refined within SBPAX by resolving ambiguities and adding other information. Once sufficiently refined, data can be mapped to a format different from the

original format, such as BioPAX and SBML. For gluing, we start with data in both BioPAX and SBML on the same pathway. After mapping, refinement includes identifying, which data from both sources describe the same things. The result is references between BioPAX and SBML elements describing the same things. For merging, start with multiple data sets in BioPAX or SBML, proceed like for gluing, and keep the refined SBPAX data, which constitutes a unified set of the originally separate data.

Based on the **Jena Semantic Web Framework for Java** SyBiL can easily be extended to integrate pathway data in any RDF/OWL-based formats.