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BiNoM: Cytoscape plugin for manipulating and analyzing biological networks

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ABSTRACT

BiNoM (BIological NetwOrk Manager) is a Cytoscape plugin which significantly facilitates usage and analysis of biological networks in standard systems biology formats. BiNoM implements full-featured BioPAX editor with method of "interfaces" for accessing BioPAX content, allowing to work with huge BioPAX files such as whole pathway databases. In addition, BiNoM allows to analyze networks created with CellDesigner software and convert them into BioPAX, and adds a rich set of operations to Cytoscape such as path and cycle analysis, clustering sub-networks, decomposition of network into modules, clipboard operations.

Availability: Last version of BiNoM together with documentation, source code and API is available at http://bioinfo.curie.fr/projects/binom

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1 INTRODUCTION

Importance of biological network knowledge standartisation and representation is widely accepted in systems biology community [1]. Several standards with different specializations such as SBML and BioPAX were proposed and actively promoted [2]. Standard for Graphical Notation in Systems Biology was proposed and implemented in CellDesigner software [3].

Cytoscape environment [4] is an open-source project aimed at creating universal and flexible biological network visualition tool. It attracted a loot of attention and collected large and active community around it due to possibility to extend its basic functionality with user-made plugins. A number of plugins are already developed and used in practice (see the list at http://cytoscape.org). In the recent versions of Cytoscape there is a possiblity to import BioPAX and SBML files, however, these capabilities remain limited to simple visualization of the file content.

BiNoM plugin (BiNoM stands for BIological NetwOrk Manager) was developed to facilitate manipulating files in BioPAX and SBML formats (including CellDesigner SBML extension). BiNoM allows to read, edit, extract parts, merge and save BioPAX object hierarchies. To support this function, a large set of tools is proposed for structural network analysis including path and cycle analysis, sub-networks clustering, decomposition into modules and clipboard operations. In addition, BiNoM supports conversion of CellDesigner files into BioPAX and BioPAX to SBML format. BiNoM was used in several projects on analyzing complex biological networks (for example, see [5]).

2 METHODS AND IMPLEMENTATION

To access the content of BioPAX file, BiNoM engine first maps it onto a graph, called *index*. Index represents the totality of BioPAX objects and their relations, however, with minimum information necessary only for their visual representation. The whole index is a highly connected graph which is usually not visualized explicitly, however, it can be stored as XGMML file (standard Cytoscape file format) and accessed independently. The user interacts with subgraphs extracted from the global index, called *BioPAX interfaces*. During BioPAX import operation, BiNoM proposes to generate three standard interfaces: Reaction Network (RN), Pathway Structure (PS) and Protein-protein Interaction (PP). These sub-graphs represent three different aspects of information contained in BioPAX file (see Fig. 1). For full description of BiNoM data model, go at the BiNoM web-site.

Reaction Network interface is a bi-partite graph in which there are two types of nodes: reactions (shown by diamonds on Fig. 1) and chemical species. They are connected by edges of different types (LEFT for reactants, RIGHT for reaction products, CATALYSIS and MODULATION for modifier chemical species). Pathway Structure interface represents the pathway structure contained in BioPAX. Here nodes can be of "pathway" and "pathway step" and "interaction" type. Protein-protein interactions BioPAX interface visualizes the formation of protein and other complexes and other protein-protein interactions described in the BioPAX file.

Starting from these subgraphs and using copy-paste operations proposed by BiNoM, graph merging and extracting graph parts, user can construct his own, arbitrary interface (see Fig. 2) to BioPAX. Any node or edge in the interface can be

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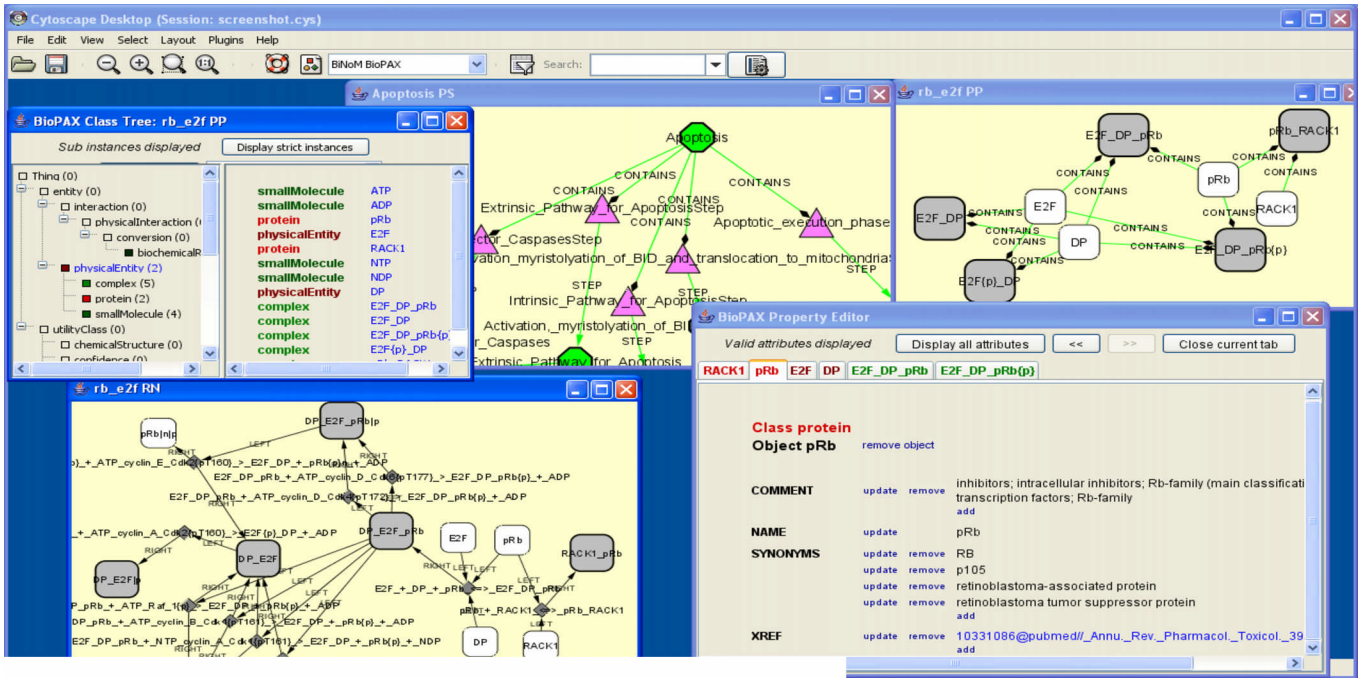

Fig. 1. BiNoM screenshot. Three standard BioPAX interfaces (RN, PS, PP), BioPAX property editor and BioPAX class tree dialog are shown.

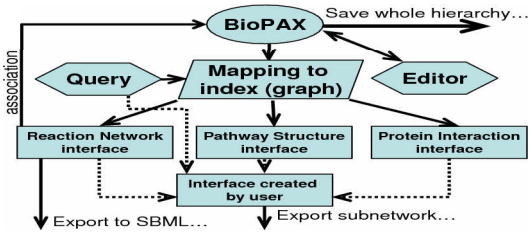

Fig. 2. Schema of working with BioPAX in BiNoM. Rectangles represent Cytoscape networks (interfaces) used to access BioPAX.

assigned one or several BIOPAX_URI attributes using which BiNoM can access and modify the content of BioPAX object hierarchy. To do it, the interface should be *associated* to a BioPAX file through BiNoM menu. After that, user can save the whole BioPAX hierarchy or export to a file only a part of BioPAX represented in the interface. When doing this, it is possible to merge the new information with already existing BioPAX file. Reaction Network interface can be exported to SBML format and serve as a first draft in creating pathway computational model. Any interface can be stored as XGMML file and used later. Moreover, the stored interface can be associated to a different BioPAX file provided that it uses the same system of URIs (universal resource identifiers).

If the BioPAX file is huge such as whole pathway database (as, for example, Reactome [6]), user can use BiNoM querying mechanism to extract part of the database and export it into a separate self-containing BioPAX file for further analysis. The querying mechanism converts Cytoscape into flexible local interface to local pathway database stored as a big BioPAX file. In the future development it is previewed to provide alternative ways of interacting with pathway databases.

An important part of BiNoM is the build-in library of graph analysis tools, including analysis of connected and strongly connected components, path analysis (finding shortest, suboptimal, all paths), modular decomposition of the network using node semantics, cycle analysis and subnetwork clustering, clipboard and some other operations.

Logic implementation in BiNoM code is completely decoupled from Cytoscape interface which allows to use BiNoM as independent biological graph analysis library. Using run-time object inspection in Java allows to reuse BiNoM code with practically any ontology schema, even completely different from BioPAX (for example, Systems Biology Ontology). BiNoM was tested with 2.3, 2.4 and 2.5 versions of Cytoscape.

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