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BiNoM: a Cytoscape plugin for manipulating and analyzing biological networks

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ABSTRACT

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

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 standardization and representation is widely accepted in the systems biology community [1]. Several standards with different specialties (e.g. SBML and BioPAX) have been proposed and are actively promoted in many softwares [2], such as CellDesigner in which the Systems Biology Graphical Notation standard (SBGN, http://sbgn.org) was proposed and implemented [3].

Cytoscape environment [4] is an open-source project aimed at creating universal and flexible biological network visualization tool. It attracted a lot 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 an option to import BioPAX and SBML files, however, these capabilities remain limited to a simple visualization of the file content.

BiNoM (BIological NetwOrk Manager) plugin 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 systems biology files. Together with this function, a large set of structure analysis tools is proposed. In addition, BiNoM supports conversion of CellDesigner to BioPAX and BioPAX to SBML formats. BiNoM was used in several projects on analyzing complex biological networks (for example, see [5]).

2 METHODS AND IMPLEMENTATION

The first guiding principle of BiNoM is to provide control in Cytoscape over the content of a systems biology file without complete conversion of the file into the Cytoscape internal format. Second, BiNoM aims at dissecting and reducing the complexity of the visual network presentation with help of a number of graph structural analysis methods, some of them taking into account the biological semantics connected to the graph elements.

To access the content of a file, the BiNoM engine first maps it onto a labeled directed graph, called *index*. Index represents the totality of objects and their relations, but with a minimum amount of information necessary for their visual representation. The whole index is a highly connected graph which is usually not visualized explicitly. The user interacts with subgraphs extracted from the global index, called *network interfaces*. For example, during BioPAX import operation, BiNoM proposes to generate three standard interfaces: Reaction Network (RN), Pathway Structure (PS) and Protein-Protein interaction (PP). These subgraphs represent three different aspects of information contained in BioPAX file (see Fig. 1). For full description of a BiNoM data model, go to the BiNoM web-site.

Starting from these subgraphs and using operations proposed by BiNoM such as copy-paste, graph merging and extracting graph parts, the user can construct his or her own arbitrary interface. Any node or edge in the interface can be assigned one or several URI attributes which BiNoM uses to access and modify the file content. To do so, the interface should be first *associated* to the file through BiNoM menu. After that, the user can save the whole object hierarchy or export to a file only a part of the content represented in

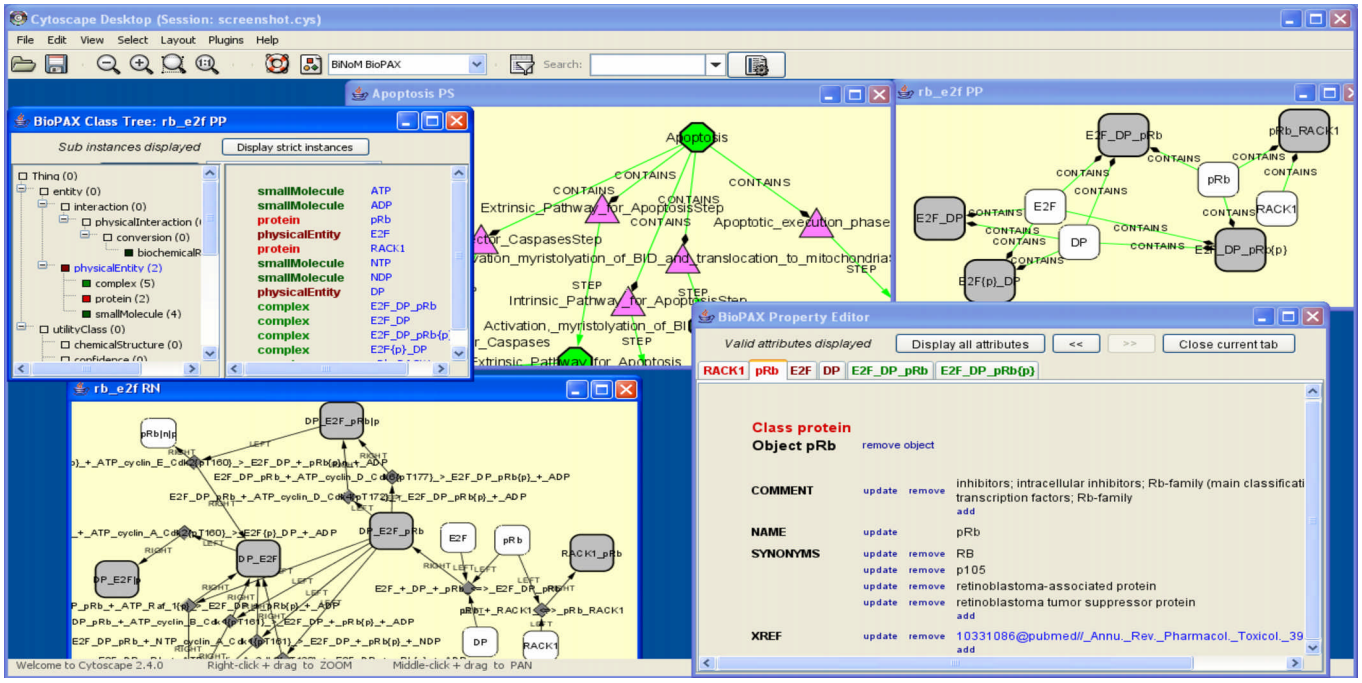

Fig. 1. BiNoM screenshot. Three standard BioPAX interfaces (RN, PS, PP), BioPAX property editor and BioPAX class tree dialog are shown.

the interface. When doing this, it is possible to merge the new information with already existing files. The BioPAX Reaction Network interface can be exported to SBML format and serve as a first draft for the creation of a pathway computational model. Any interface or the whole index can be stored as XGMML (standard labeled graph description format supported by Cytoscape) file and used later.

If the BioPAX file is huge such as a whole pathway database (e.g. Reactome [6]), the user can use the BiNoM querying mechanism to extract part of the database and export it into a separate self-containing BioPAX file for further analysis. This mechanism enables using Cytoscape viewer and a big BioPAX file as a pathway database with a flexible interface.

Simplification and analysis of the network representation are achieved by use of 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, subnetwork clustering and clipboard operations.

Logic implementation in BiNoM code is completely decoupled from Cytoscape interface. That way, BiNoM can be used as an independent biological graph analysis library. Using run-time object inspection in Java allows the reuse of 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 and with 3.* versions of CellDesigner.

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