

*Systems biology*

## An enhanced Java graph applet interface for visualizing interactomes

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**ABSTRACT**

**Summary:** We have developed several new navigation features for a Java graph applet previously released for visualizing protein–protein interactions. This graph viewer can be used to navigate any molecular interactome dataset. We have successfully implemented this tool for exploring protein networks stored in the Bioverse interaction database.

**Availability:** <http://bioverse.compbio.washington.edu/viewer>

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Modeling protein–protein interaction (PPI) networks as graphs with nodes and edges to depict proteins and their interactions is an important paradigm for systems analysis. The development of simple, intuitive interfaces to PPI and other molecular interaction networks is becoming increasingly important as these datasets grow exponentially. The ubiquity of web browsers on all modern computing platforms makes them the ideal interface to deploy such tools.

A Java applet to assist with the visualization of PPI data as interactive graphs was first released by Mrowka (2001). This tool was originally based on the Graph.java applet code distributed by Sun Microsystems. It utilizes a relaxation layout algorithm which attempts to prevent overlapping of nodes. It can run as a stand-alone applet or more commonly inside a Java-enabled web browser. Navigation of graphs is mediated by setting the desired neighborhood (depth) level and clicking on individual nodes. Double-clicking on nodes isolates the subgraph containing nodes of the specified neighborhood. A ‘freeze’ function is provided to halt the layout algorithm to aid visual analysis.

We have implemented feature improvements to this applet to enhance navigation (Fig. 1). We have added a simple search field to the toolbar which allows for asterisk-based wildcarding (i.e. S\* will show all nodes starting with S). The search feature can locate exact or similar node matches based on the identifiers used for node labels. Next, we added a sorted, enumerated list of functional groups in the drop-down menu. In our implementation, we employed Gene Ontology (GO) functional annotations for exploring PPI networks (Ashburner *et al.*, 2000). In practice, any functional annotation system can be used. An indication of the total number of nodes and edges present in the current graph is also displayed. In the graph

window, a color-coding scheme for edge weights has been implemented. These colors represent quartiles of interaction confidence values between 0.00 and 1.00 as stored in the Bioverse database (McDermott and Samudrala, 2003, 2004). The colors range from red (0.00–0.24), orange (0.25–0.49), yellow (0.50–0.74) to green (0.75–1.00). Finally, we added a right-click mouse feature, which in addition to expanding nodes, also opens hyperlinks to detailed protein records specific to a given node. This is based on URL forwarding and can be easily modified for hyperlinking to other destinations.

This updated graph viewer was used successfully as an interface to the Bioverse database which contains PPI data for more than 50 different organisms. We have used the viewer to depict contextual, as well as evolutionary, relationships between proteins. Contextual relationships are defined as physical interactions or functional linkages between proteins. Evolutionary relationships are based on sequence, structure and functional similarities. Our testing of this viewer indicates that it is effective in visualizing PPI networks, as well as any other molecular interactome. These can include genes, metabolites or other small molecules with pairwise interaction relationships. Gene interactions derived from microarray analysis, synthetic lethal screens or combinations with PPI data are some examples (Ideker *et al.*, 2001; Tong *et al.*, 2001). Such datasets can easily be adapted as input values.

This viewer is small, stable, multi-platform and simple to use. It can function as a stand-alone applet or be integrated into a web application. Detailed support information on the installation, usage and code development is available on our servers. In future versions, we plan to extend many of these interactive features into a server-based web application framework to provide more robust searching of PPI networks.

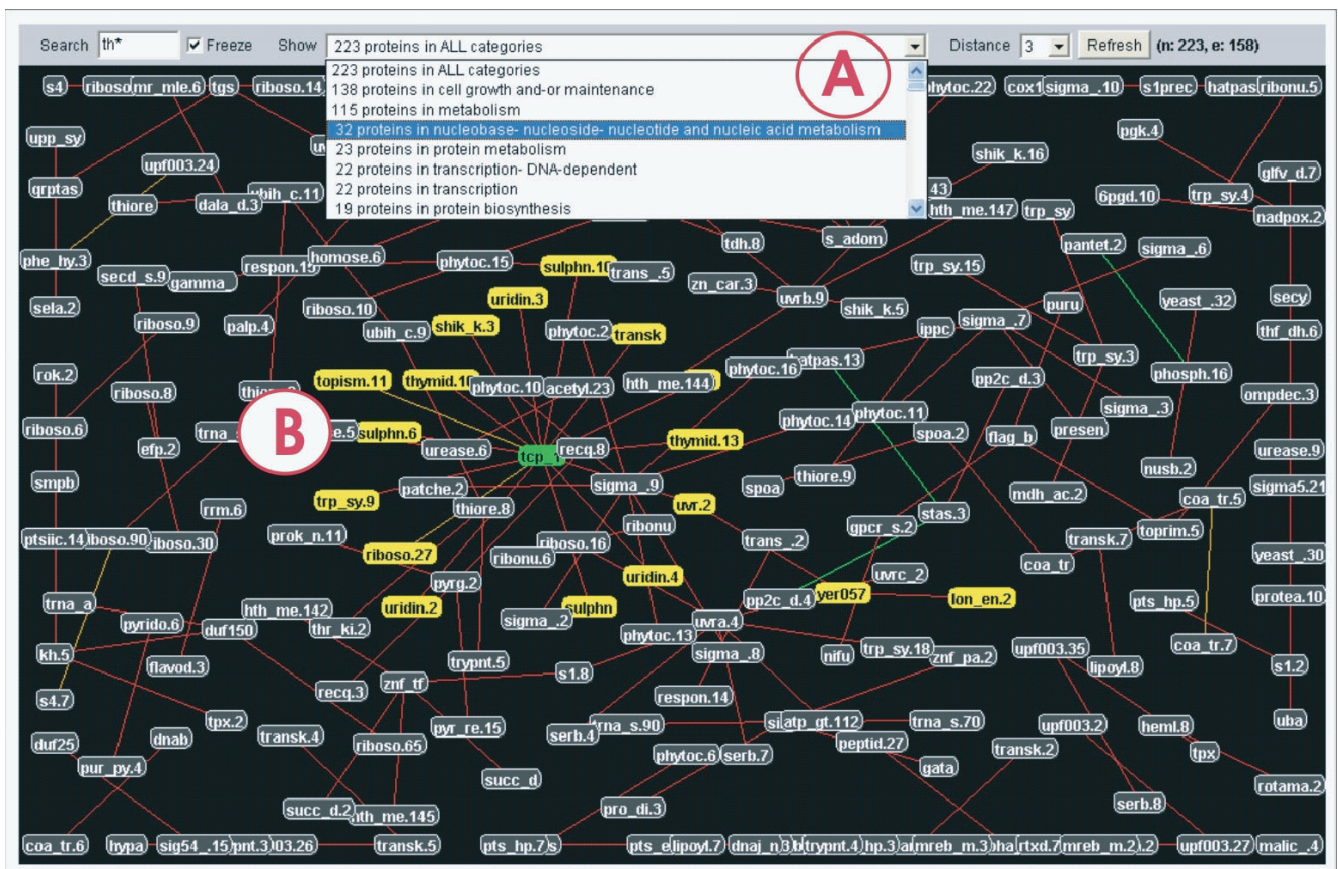
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**Fig. 1.** Enhanced Java graph viewer applet as integrated in the Bioverse framework. Here, the viewer is shown in the context of PPI data from *Bacillus subtilis* stored in the Bioverse database. (A) The tool bar. From left to right, this contains the search field, freeze button, drop-down functional group menu, depth selector (distance), refresh button and total counts of nodes and edges. Search terms can be exact matches or similar matches using asterisk wildcards. The drop-down menu enumerates the number of nodes for each functional group in reverse sort order. (B) Undirected, weighted edges are depicted by a color code for confidence values ranging from 0.00 to 1.00. The colors range from red (0.00–0.24), orange (0.250–0.49), yellow (0.50–0.74), to green (0.75–1.00). Clicking on a node will select it and expand its local neighbors according to the 'distance' setting in the toolbar. A selected node is green and its neighbors are yellow. Double-clicking a node will isolate the subgraph, removing unconnected nodes from the window. Right-clicking on a node will expand the node and bring up hyperlinked web pages pertinent to the node. In our case, the user is provided with a protein record page stored in the Bioverse database.

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