PIVOT: Protein Interactions VisualizatiOn Tool

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ABSTRACT

Summary: PIVOT is a visualization tool for protein-protein interactions. It allows the user to create personal datasets of interactions by combining information from private and public data sources. The user can gradually access the interactions' data using a clear interactive map that is focused on the researcher's protein of interest, and is reshaped and expanded in response to his/her queries. It also offers several visual enhancements and intelligent queries that help the user efficiently study it. PIVOT allows the user to search the interactions dataset for paths connecting proteins that are expected to cooperate. The user can also employ PIVOT to predict unknown interactions among proteins, based on interactions among their homologous proteins in other species.

Availability: Freely available for academic users, at http://www.cs.tau.ac.il/~rshamir/pivot

Contact: niro@post.tau.ac.il

Supplementary Information: A demonstration video clip is available at http://www.cs.tau.ac.il/~rshamir/-pivot/Demo.avi

FEATURES

The growing popularity of genome-wide experiments and the volumes of data they yield call for tools that provide visual scrutiny of the data, and enable a researcher to focus on the observations relevant to his/her protein of interest. Central protein-protein interactions databases, as well as companies that develop technologies for large-scale interactions research, offer accompanying visualization tools that present the data as a graph, thus allowing researchers to review many interactions simultaneously, e.g., JDIP, BIND Viewer, Curagen's PathCalling, Hybrigenics' PIMViewer (see list of website references). PIVOT is a novel software tool that unlike most current visualization tools allows combining interactions data from various sources including private observations, and facilitates graph-theory algorithms to explore the relationships among distant proteins (see *Datasets*, *Linking Distant Proteins* below).

Visualization: The main window (Figure 1) displays a graph whose nodes are proteins and edges are interactions. Any protein marked with a red dot has additional interactions that are currently not displayed. Those can be added to the map by double-clicking the protein. Functional annotation is displayed for each map protein when the user points the mouse cursor at it, aiding the initial interpretation of the map. Each protein is
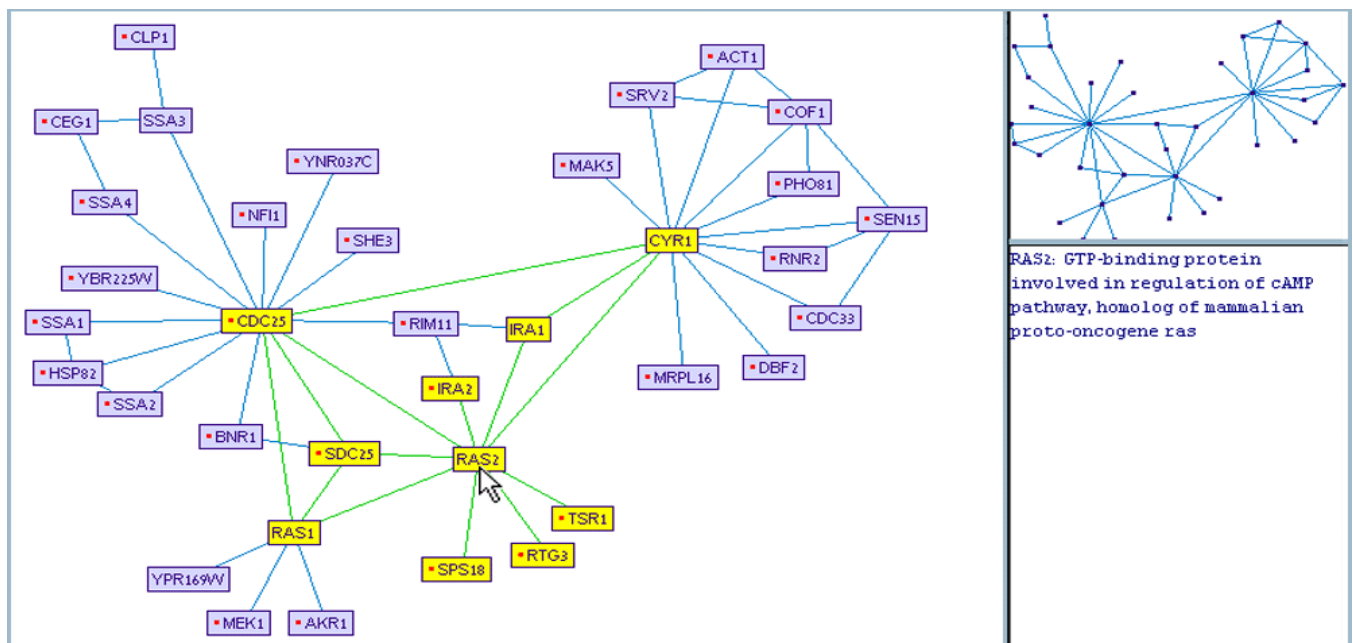

Figure 1. PIVOT main screen. Left: the main working window with the current graph of interactions. Top right: satellite window, with a full zoom-out of the graph. Bottom right: functional annotation of the focus protein, pointed at by the mouse cursor. Red dots indicate proteins with additional non-showing interactions. Boxes in yellow show the neighbors of the current focus protein, when the "Neighbors Marker" option is on.

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also linked to an Internet information page that can be opened on demand.

Auto Layout: The map's proteins are automatically arranged by PIVOT's layout mechanism, which groups interacting proteins together while placing others farther apart. The layout mechanism is dynamic and interactive: the graph layout is changed gradually so the user can easily follow it, and can intervene to manually fix the location of some proteins while the layout mechanism dynamically places the others.

Datasets: PIVOT allows the user to visually explore diverse datasets of interactions. The origins of interaction data are numerous - some are discovered in genome-wide experiments, others are identified in specific small-scale studies. Some interactions were only predicted using computational methods, while others were proven biologically more than once. An accompanying tool enables the user to create personal datasets by selecting from public databases the interactions she finds reliable and wishes to use, and combine them with her own observations.

Neighborhood View: PIVOT's "expand node" option allows the user to directly explore the interactions neighborhood of any map protein by indicating the maximal expansion distance around it. It retrieves the neighborhood from the database and updates the interactions map with it.

Neighbors Marker: Interactions are sometimes hard to follow in dense areas of the map. For those situations, PIVOT offers an optional visual aid - the "Neighbors Marker". When turned on, it highlights all proteins interacting directly with the map protein, which the user is pointing at (Figure 1).

Linking Distant Proteins: In many cases, several proteins seem to operate together although the biochemical mechanism of their interaction is unknown. Such cases occur, for example, when proteins are co-precipitated, or when several proteins are considered to be functionally linked as indicated by their common expression pattern or by comparative genomics techniques (Eisenberg *et al.*, 2000). To test the hypothesis that a protein is functionally linked to another protein or group of proteins, the user can ask PIVOT to search for a connection between them, using a bounded number of intermediates. The user can select any sub-graph and request PIVOT to connect the "new" protein to any protein in it, by the shortest path(s) (Figure 2). The "new" protein may already be present in the map, in which case PIVOT will search for connecting paths shorter than those currently displayed.

Homology Maps: Because many biological systems were conserved throughout evolution, researchers can deduce potential interactions between proteins in one species from known interactions between their homologs in other organisms. PIVOT allows the user to select a target species, and switch the view mode from "basic view" to "homologs view", which replaces all protein labels with the designation of their homologs in that species (when a homolog is not known, the original designation is displayed, surrounded by an ellipse). The displayed interactions are the same interactions described in the dataset, only displayed as hypothetical interactions in another species. Homologs are defined according to BLAST results available at SGD's website. The homologs list is stored in an input table which can be edited by users.
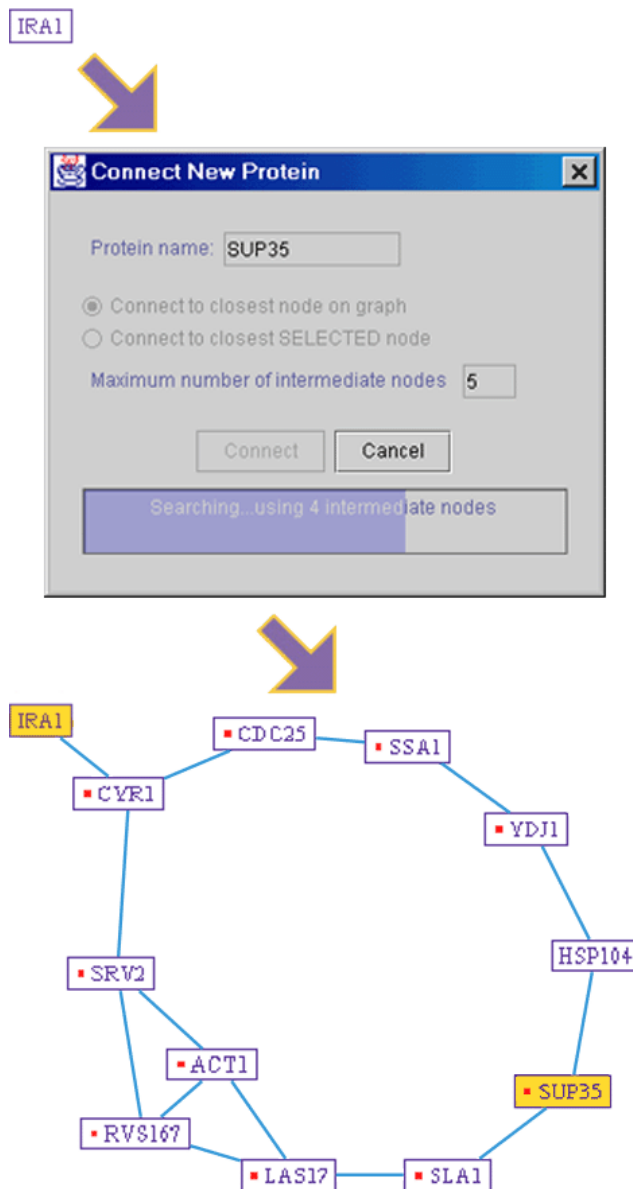

Figure 2. PIVOT's path finding utility. Given source and target proteins (IRA1 and SUP35 in this example), PIVOT searches for all shortest paths that connect them.

REFERENCES

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