

# 3DProIN: Protein-Protein Interaction Networks and Structure Visualization

Hui Li<sup>1</sup>, Chunmei Liu<sup>1\*</sup>

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## Abstract

3DProIN is a computational tool to visualize protein-protein interaction networks in both two dimensional (2D) and three dimensional (3D) view. It models protein-protein interactions in a graph and explores the biologically relevant features of the tertiary structures of each protein in the network. Properties such as color, shape and name of each node (protein) of the network can be edited in either 2D or 3D views. 3DProIN is implemented using 3D Java and C programming languages. The internet crawl technique is also used to parse dynamically grasped protein interactions from protein data bank (PDB). It is a java applet component that is embedded in the web page and it can be used on different platforms including Linux, Mac and Window using web browsers such as Firefox, Internet Explorer, Chrome and Safari. It also was converted into a mac app and submitted to the App store as a free app. Mac users can also download the app from our website. 3DProIN is available for academic research at <http://bicompute.appspot.com>

*Keywords:* Protein-protein interaction; Tertiary structures; Graph visualization; Protein-protein interaction network

## 1. Introduction

Knowledge of protein-protein interactions is critical for a complete understanding of the cellular function and biological process on the molecular level. The graphical visualization of protein-protein interactions is intuitive and easier for biologists to investigate the mechanisms of the interactions between proteins, genes and metabolites. The protein-protein interaction network inferred from a large scale proteomics data provides a direct way to disclose the complicated interactions between proteins. In the last decades, many protein-protein interaction visualization tools have been developed. For example, Medusa(Hooper and Bork, 2005) optimizes protein-protein interaction data taken from STRING or protein-chemical and chemical-chemical interactions taken from STITCH. It is a 2D visualization tool for small networks with up to a few

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\*Corresponding e-mail: [chunmei@scs.howard.edu](mailto:chunmei@scs.howard.edu)

1 Department of Systems and Computer Science, Howard University, Washington, DC 20059, USA

hundred nodes and edges (Hooper and Bork, 2005); Cytoscape (Shannon, et al., 2003) incorporates statistical analysis of the networks and makes them easy to cluster or detects highly interconnected regions which provide 2D representations; BioLayout Express3D (Theocharidis, et al., 2009) offers a different analytical approach to microarray data analysis in Java 1.5 and uses the JOGL system for OpenGL rendering; ProViz (Iragne, et al., 2005) visualizes protein-protein interaction networks in both 2D and pseudo-3D mode; PATIKA (Demir, et al., 2002) provides 2D representations of single or directed graphs. It supports the input of .xml format. Ondex provides 2D directed, undirected and weighted networks and combines heterogeneous data into one network. Ondex is good at text mining and sequence and data integration analysis (Kohler, et al., 2006). These tools have illustrated the complex biological interactions as graphical networks but still miss to visualize the 2D protein structure information together with the 3D structure information and do not handle input files of .XML format. In this paper, we present a software named 3DProIN which provides a user friendly interactive interface which visualizes protein-protein interactions in both 2D and 3D views on the basis of one clicking or dragging and displaying. 3DProIN is compatible with protein data bank (PDB) datasets. We use the large graph layout (LGL) algorithm which is used to dynamically visualize large networks on the order of hundreds of thousands of vertices and millions of edges proposed by Adai et al (Adai, et al., 2004) to visualize the protein-protein interaction networks. 3DProIN can be used to integrate and visualize the structure of protein-protein interaction networks in the view of either 2D or 3D. It also allows users to edit the networks according to their professional knowledge. The main features of 3DProIN include: 1) Provide visualized view of protein-protein interactions in both 2D and 3D; 2) By one click on a node in either 2D or 3D mode, the 3D structure information of the proteins shows up simultaneously; 3) Accept multiple input formats such as .txt, .xml, and .pdb; and 4) Both 2D and 3D images can be exported into .jpg, .bmp and .png formats.

## 2. Implementation of 3DProIN

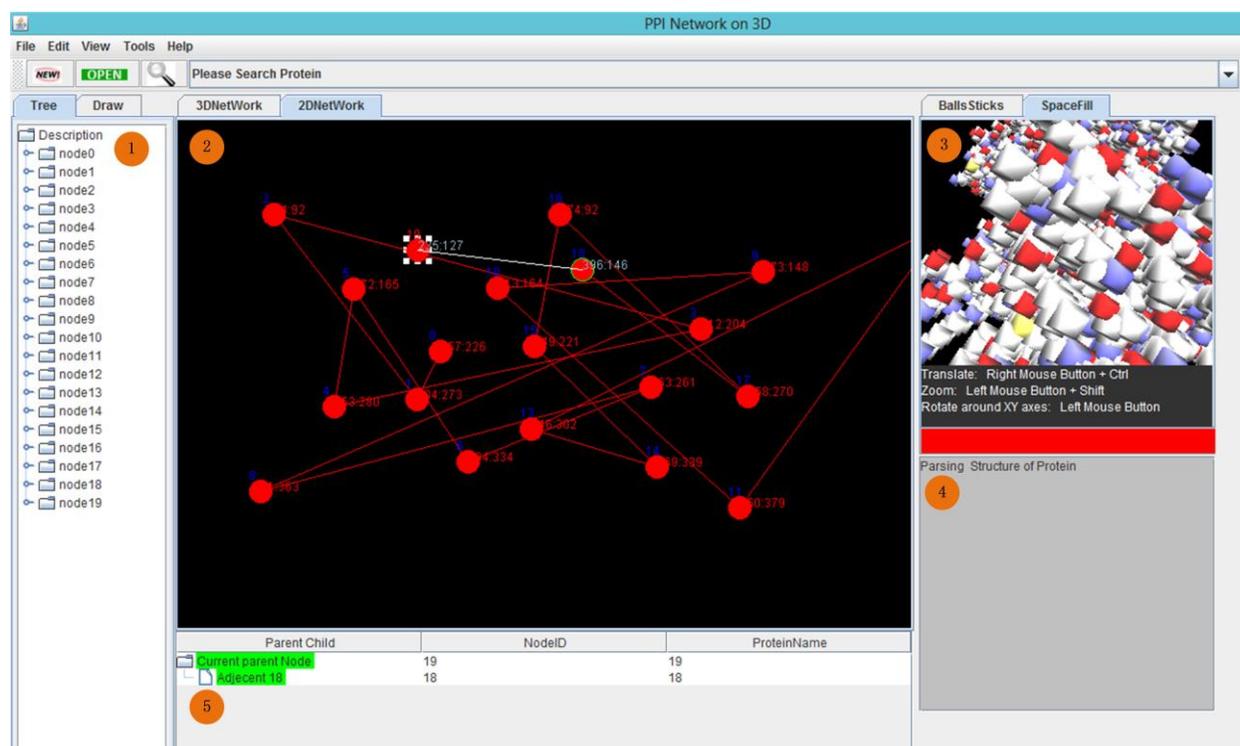
In the protein-protein interaction network inferred from diverse protein-protein interaction databases, proteins are represented as nodes and the interactions between the proteins are edges. The most challenging problem of the graphical visualization of large scale networks is to add 3D protein information that allows users to visualize the interested biological relations in the dataset, and to transform between 2D structures and 3D structures efficiently. 3DProIN borrows the merits of existing protein-protein interaction network visualization tools. It also provides online PDB data transforming and parsing functions.

3DProIN aims to integrate knowledge from public databases to predict the interactions between proteins. In particular, it can analyze the structures of complex networks and the 3D structures of a protein by parsing the data from PDB rest xml service. The 3D protein structure information including the coordination of each atom and angle between interacted protein pairs is listed in the summarized table. In addition, common used editable tools including magnifier, render, eraser and zoom is provided to allow users to change the layout and shape of the graph. Shifting between 2D and 3D is used for checking protein-protein interaction partners in a flexible way. The import and export files of .xml format are available.

3DProIN allows users to input and query a specific protein structure with its PDB ID, or input a list of pairwise interacted proteins. The queried protein and its interactions are displayed in both 2D

and 3D panels. In either panel, the users can freely drag and adjust the position of the node and change the render color, font and name of the node. In the 3D panel, users can zoom in or out and rotate the network by pressing the left button of the mouse. Scrolling the middle wheel of the mouse and then dragging the mouse, the graph zooms in or out proportionally. By selecting any node in the graph, the 3D structures of the corresponding protein will be displayed graphically in the top right panel. In the right panel, the interacted domain and the complexity information of this protein are shown. The source names, IDs and structure information are displayed in the right-bottom table simultaneously. Users can correct, add and comment the structure of the interested protein. The modification or comments are saved locally in a default file.

**User interface:** The snapshot of the 2D user interface is shown in **Fig. 1**. Users can add a new node or an edge to the network in the 2D view by clicking the edit menu. Every change is mapped to the 3D view accordingly. There are 5 functional areas: (1) the left panel shows the management tree to list all the nodes in the network; (2) the top middle panel shows the protein-protein interactions in 2D view. The red node represents the selected protein and its interacting proteins, which are highlighted in different colors; (3) the top right panel shows the structures of the proteins selected in the middle panel; (4) the bottom right panel shows the detailed information of the queried protein; (5) The bottom panel shows the statistic information of the nodes in the network.



**Fig. 1.** The protein-protein interactions in 2D view

While **Fig. 1** depicts the protein-protein interactions in 2D view, **Fig. 2** shows the snapshot of the protein-protein interactions in 3D view. Panels (1) and (2) are the same as those in **Fig. 1**; (3) the top right panel shows the molecule information of the queried protein. The bottom white text is the

short description of the functions; (4) the bottom right panel shows protein structure information including the number of the chains and the name and ID of the protein; (5) the bottom panel is the same as the bottom panel in Fig. 1.

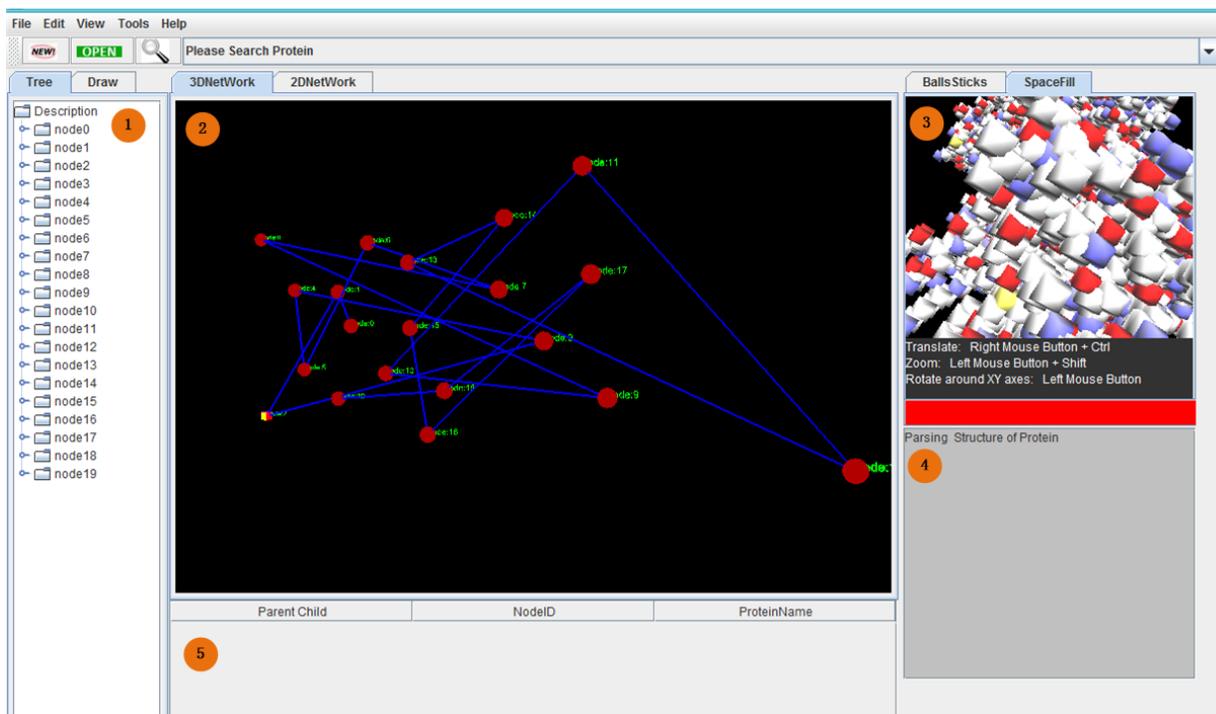


Fig.2. The protein-protein interactions in 3D view

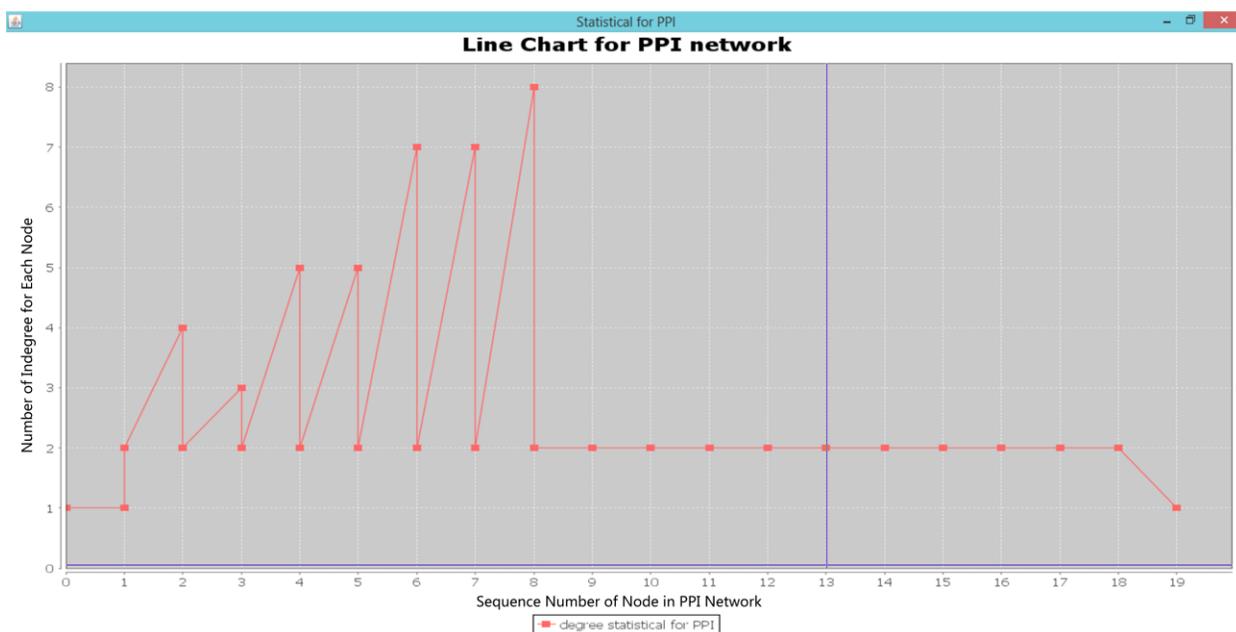


Fig.3. The snapshot of the statistical function provided by 3DProIN

3DProIN provides a graphical statistical summary function to show the properties of the network. Figure 3 depicts the number of indegree for each node. For example, the maximum of nodes 8 has 8 incoming connections.

### 3. Conclusion

We use Java3D technique to implement the standard GUI operations such as 3D zoom in and out, rotation, mouse operation and scaling. The nodes and edges in 3DProIN are editable which allow users to rename, remove, add, and change the colors and shapes of the nodes. By clicking the node in the graph, the detailed information of the selected protein will display in the right bottom table and blink with a highlighted color; if clicking the edge, the interaction information of the two proteins will be high-lighted in the table. Users can customize the 2D or 3D interfaces by selecting the editing function. Any updated information of the network will be saved. 3DProIN also allows users to export the images either in the 2D or 3D view.

We use Java 3D component to implement the node text, color and shape change in the 3D mode. The application of 3DProIN not only help biologists to discover novel protein interact partners efficiently but also annotate protein interaction networks. The software is web based tool and the corresponded App of Mac submitted to Apple store as a free app.

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### References

- A dai, A.T., Date, S.V., Wieland, S. and Marcotte, E.M. (2004) LGL: creating a map of protein function with an algorithm for visualizing very large biological networks, *J Mol Biol*, 340, 179-190.  
<http://dx.doi.org/10.1016/j.jmb.2004.04.047>
- Demir, E., Babur, O., Dogrusoz, U., Gursoy, A., Nisanci, G., Cetin-Atalay, R. and Ozturk, M. (2002) PATIKA: an integrated visual environment for collaborative construction and analysis of cellular pathways, *Bioinformatics*, 18, 996-1003.  
<http://dx.doi.org/10.1093/bioinformatics/18.7.996>
- Hooper, S.D. and Bork, P. (2005) Medusa: a simple tool for interaction graph analysis, *Bioinformatics*, 21, 4432-4433.  
<http://dx.doi.org/10.1093/bioinformatics/bti696>
- Iragne, F., Nikolski, M., Mathieu, B., Auber, D. and Sherman, D. (2005) ProViz: protein interaction visualization and exploration, *Bioinformatics*, 21, 272-274.  
<http://dx.doi.org/10.1093/bioinformatics/bth494>
- Kohler, J., Baumbach, J., Taubert, J., Specht, M., Skusa, A., Ruegg, A., Rawlings, C., Verrier, P. and Philippi, S. (2006) Graph-based analysis and visualization of experimental results with ONDEX, *Bioinformatics*, 22, 1383-1390.  
<http://dx.doi.org/10.1093/bioinformatics/btl081>
- Shannon, P., Markiel, A., Ozier, O., Baliga, N.S., Wang, J.T., Ramage, D., Amin, N., Schwikowski, B. and Ideker, T. (2003) Cytoscape: a software environment for integrated models of biomolecular interaction networks, *Genome Res*, 13, 2498-2504.  
<http://dx.doi.org/10.1101/gr.1239303>

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Theocharidis, A., van Dongen, S., Enright, A.J. and Freeman, T.C. (2009) Network visualization and analysis of gene expression data using BioLayout Express(3D), *Nat Protoc*, 4, 1535-1550.  
<http://dx.doi.org/10.1038/nprot.2009.177>