TVNViewer: An interactive visualization tool for exploring networks that change over time or space

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ABSTRACT
Summary: The relationship between genes and proteins is a dynamic relationship that changes across time and differs in different cells. The study of these differences can reveal various insights into biological processes and disease progression, especially with the aid of proper tools for network visualization. Toward this purpose, we have developed TVNViewer, a novel visualization tool, which is specifically designed to aid in the exploration and analysis of dynamic networks.

Availability: TVNViewer is freely available with documentation and tutorials on the web at http://sailing.cs.cmu.edu/tvnviewer.

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1 INTRODUCTION

Biological relationships, such as those between proteins, between transcription factors and DNA binding sites, and between cells, differ across different tissues and change over time. Recent studies have shown that changes in network architecture from the cell cycle and in response to diverse stimuli are quite significant (Luscombe et al., 2004). Despite the dynamic nature of these interactions, the general scientific paradigm has often been to consider these relationships as static entities. However, many recent studies have advanced the field through insight from network dynamics across time or tissue in a variety of species including: human blood leukocyte response (Calvano et al., 2005), rice regulatory hierarchies of gene expression (Jiao et al., 2004), temporal interaction in Caenorhabditis elegans (Dupuy et al., 2007) and correlated changes in gene expression between mouse tissues (Keller et al., 2008). The study of network dynamics has the potential to produce crucial discoveries in gene regulation, cell cycle, and cancer progression.

Representing biological relationships visually through networks is considered the best way to demonstrate the interplay between different genes or proteins. Network representations of such data range from the small and simple networks to large, complex networks that represent thousands of genes. The potential for network visualization to aid in our fundamental understanding of biological relationships has resulted in an explosion of software platforms and visualization toolkits (Pavlopoulos et al., 2008; Suderman and Hallett, 2007). These software applications include popular tools such as Cytoscape (Shannon et al., 2003), Osprey (Breitkreutz et al., 2003), VisANT (Hu et al., 2009), Graphle (Huttenhower et al., 2009) and many more. While some tools are specific to biology, others such as Medusa (Hooper and Bork, 2005) are general purpose and can be customized to other domains.

TVNViewer is built for the visualization of small to moderate datasets of up to 500 nodes for gene–gene interactions, or if genes are grouped into a descriptor category (such as a GO category annotation). TVNViewer can handle up to 5000 nodes classified into 50 networks in text or xml format; detailed instructions on how to prepare files are available through TVNViewer’s import wizard. TVNViewer supports three visualization paradigms: a gene–gene interaction paradigm, a two-tiered gene–gene interaction paradigm and a descriptor paradigm where nodes are grouped according to a descriptor category. Each visualization paradigm provides a slightly different way to explore the network; examples of each paradigm are available by running the examples on the TVNViewer web site. TVNViewer can be used through a temporary session to upload data, or users also have the option to create a free user account on the server in order to save data for future access.

2 TVNVIEWER OVERVIEW

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3 TVNVIEWER VISUALIZATION TOOLS

There are many different views and controls available to users through TVNViewer, all of which are documented online.
Additionally, we have provided online video tutorials. Here, we outline a few of the views and analysis tools available.

One way that users can use TVNViewer to see the dynamic rewiring of their networks is directly through the circle view. The circle view automatically clusters nodes according to connectivity, reducing the number of cross-circle connections to enhance the visualization’s interpretability. Nodes are colored according to this clustering to give a natural representation of subgraphs that may exist. From this initial time point, users can scroll through the different graphs in the series, quickly moving through the networks to observe the rewiring taking place. The user has complete control over the node size, edge thickness, font size, presence of the node labels and the number of edges displayed in the graph. These can be adjusted according to the user’s visualization preference. TVNViewer provides users with a direct link to download a .pdf or .png file of any view directly to their desktop, enabling the production of figures such as Figure 1.

In addition to the circle view, the user can also explore the series of networks in a force-directed layout view. Again, the user can scroll through each time point in the series to observe the dynamics happening in their network series. The force-directed layout can also be stopped at any time and the nodes can be moved around in a user preference manner. The user can allow the network to update while scrolling through the time-series to see how the network structure is affected by the rewiring, or they can fix the location of the nodes and view only how the edges between nodes change.

In addition to exploring the network visualization directly, we provide two sets of analysis tools. These tools emphasize how the overall degree of different nodes changes over time. The other set of analysis tools includes two different views (a linear plot and a stacked plot) that users can use to explore how the degree of certain nodes or descriptors changes over time. Such a view may be useful to identify certain genes that may act as a transcription factor at some stages of development, but which fall back to other roles during other times. Additionally, users can use the web site to explore the dynamics of the network and also to analyze how the degree of different nodes in the network changes over time. Examples and further documentation are available from the TVNViewer web site: http://sailing.cs.cmu.edu/tvviewer.

4 IMPLEMENTATION NOTES

The TVNViewer web site is implemented using Adobe ActionScript, Apache and MySQL; TVNViewer runs on all major browsers with the Adobe Flash plug-in. TVNViewer’s ActionScript code is built off of the Flare library, an open-source web visualization project (bare.prefuse.org). Thus, TVNViewer takes advantage of a recent, powerful visualization library with real-time animation and dynamically updated views.

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