ABSTRACT
Summary: NAViGaTOR is a powerful graphing application for the 2D and 3D visualization of biological networks. NAViGaTOR includes a rich suite of visual mark-up tools for manual and automated annotation, fast and scalable layout algorithms and OpenGL hardware acceleration to facilitate the visualization of large graphs. Publication-quality images can be rendered through SVG graphics export. NAViGaTOR supports community-developed data formats (PSI-XML, BioPax and GML), is platform-independent and is extensible through a plug-in architecture.
Availability: NAViGaTOR is freely available to the research community from http://ophid.utoronto.ca/navigator/. Installers and documentation are provided for 32- and 64-bit Windows, Mac, Linux and Unix.
Contact: juris@ai.utoronto.ca
Supplementary information: Supplementary data are available at Bioinformatics online.

1 INTRODUCTION
The availability of protein–protein interaction (PPI) data is increasing rapidly through literature-derived databases (Bader et al., 2003; Breitkreutz et al., 2002; Hermjakob et al., 2004a; Peri et al., 2004; Xenarios et al., 2000; Zanen et al., 2002), high-throughput detection methods (Barrios-Rodiles et al., 2005; Rual et al., 2005) and computational predictions (Brown and Jurisica, 2005; Persico et al., 2005). These data, collectively referred to as the interactome, are critical to our understanding of both normal cellular processes and disease mechanisms. Visualizing the interactome, along with integrating orthogonal data types, may aid in the understanding of cell function, help elucidate hidden relationships within the data and help prioritize functional studies.

Several biological graph visualization tools are currently available, implementing a diverse range of approaches and algorithms (Breitkreutz et al., 2003; Chin et al., 2008; Hu et al., 2004; Ju and Han, 2003; Macpherson et al., 2009; Paananen and Wong, 2009). Cytoscape (Shannon et al., 2003), in particular, has been widely adopted by the biological community for its ease of use and extensibility through open source plug-in development.

2 SOFTWARE
2.1 Implementation
NAViGaTOR has been implemented in Java (v1.6), providing platform-independence, and uses JOGL (https://jogl.dev.java.net/) to enable OpenGL hardware-accelerated graphics rendering. At present, the core code-base is closed-source to ensure stability, but future enhancements will extend the plug-in API to an OSGi-compliant framework (http://www.osgi.org/Main/HomePage) that enables community-driven extensibility.

2.2 Features
NAViGaTOR enables interactive visualization and analysis of complex graphs that are typical in systems biology studies. Graphs can be loaded from PSI-MI XML, BioPax, GML and tab-delimited text files, or through online databases such as E2D (http://ophid.utoronto.ca/e2d) and cPATH (http://cbio.mskcc.org/cpath/). Both

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Fig. 1. Screen capture of the NA ViGaTOR user interface. Labels indicate the various tools and descriptive regions of the interface. A graph is shown in the ‘Graph Panel’, with edges adjusted automatically by ‘Edge Filters’. Filters can be used to automatically control visual attributes of both nodes and edges.

2D and 3D network views are fully interactive, allowing the user to manually manipulate the graph, or to use automated layouts such as circular, linear or concentric circular on subsets of nodes or entire graphs. A spreadsheet view supports selecting and deselecting nodes, edges and paths based on any attributes. Nodes and edges can be grouped into subsets, which can be collapsed or expanded to simplify views, or manipulated through set operations. Network analysis tools provide information about node and edge connectivity, shortest paths, identify hubs, cliques and articulation points and summarize network statistics. NA ViGaTOR can also use a multi-threaded implementation to efficiently generate random networks for enrichment analyses. Fully annotated graphs can be exported to six different graphics formats, including PDF and SVG. In summary, NA ViGaTOR provides a network analysis platform that is rich in the features essential to many biological applications, and yet is extensible through a plug-in interface to include additional features when required. See Figure 1 and the Supplementary Materials for examples of the NA ViGaTOR interface and rendered networks.

2.3 Advances
NA ViGaTOR’s ability to handle larger datasets is facilitated through optimized layout algorithms, hardware-based graphics acceleration and a reduced memory footprint relative to other software. NA ViGaTOR performs an initial layout using Graph Drawing with Intelligent Placement (GRIP; Gajer and Kobourov, 2002), which performs network layout in near linear time, and then continuously updates the layout of the graph using a multi-threaded grid-variant (Fruchterman and Reingold, 1991) of a force-directed layout algorithm. When benchmarked against the force-directed algorithms in Cytoscape and VisANT, NA ViGaTOR consistently provided graphs rendered in significantly shorter time (Fig. 2; Supplementary Fig. 3.3). Only the yFiles Organic plug-in for Cytoscape rendered in similar time to NA ViGaTOR, although the resulting graph was poorly optimized (compare Supplementary Fig. 3.5C to Supplementary Fig. 3.4C).

OpenGL enables NA ViGaTOR to take advantage of hardware-based acceleration to render larger graphs in both 2D and 3D. Additionally, the data structures within NA ViGaTOR were designed to maintain a small memory footprint in order to provide greater scalability for large datasets. When compared against Cytoscape and VisANT, NA ViGaTOR had a memory footprint approximately half that of Cytoscape, although a 12–38% larger footprint than VisANT (Supplementary Fig. 5.1).

The NA ViGaTOR user interface includes unique tools to help simplify the ‘hairball’, which is a common challenge in many PPI...
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**Conflict of Interest**: none declared

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