Toward Systems-Level Visualizations of Molecular Networks on Large-Scale, High-Resolution Displays

Jillian Aurisano* University of Illinois at Chicago
James A. Radosevich† University of Illinois at Chicago
Jason Leigh‡ University of Illinois at Chicago

ABSTRACT

The scale and complexity of high-throughput experimental techniques call for novel approaches to biological network visualization. Large, high resolution displays present the opportunity to communicate information in a way that cannot be matched on small, low-resolution displays and therefore, new approaches to biological network visualization ought to take advantage of these platforms. We have developed a prototype for tiled-display walls that integrates and visualizes over a thousand human molecular pathways from the Pathway Commons database in one view. This prototype will serve as a platform for the future development of novel approaches to visualizing the interconnected nature of biological pathways.

Index Terms: Information Interfaces and Presentation [H.5.m]: Miscellaneous—

1 INTRODUCTION

Life scientists have spent decades determining how small sets of interacting gene products produce cellular and molecular phenomena. The result is an increasingly well characterized understanding of how small sets of genes behave and interact in specific circumstances. As the volume of defined molecular relationships increased, and the need to better understand these relationships grew, the biological data visualization responded by producing a multitude of approaches to biological network visualization, from static, human-generated pathway diagrams to software suites that generate diagrams on-the-fly [7, 2].

With the proliferation of high-throughput experimental techniques such as gene expression microarrays, biological researchers have been able to query the state of entire systems, measuring changes in the transcriptome of a population of cells at one moment in time with relative ease. By performing multiple gene-chip expression studies, biological researchers are able to capture how gene-expression varies across conditions, genetic backgrounds and time-points. The scale and complexity of these data sets render inadequate many of the approaches to biological network visualization that suited the state of the field prior to the advent of systems-level interrogation of the transcriptome. Isolated and discrete pathway diagrams may help biologists understand the small-picture, but do not adequately capture the big-picture perspective required to understand systems-level data sets. Gene expression result sets can be overlaid atop discrete pathway diagrams in a multitude of software programs, but without systems-level visualization approaches, the biologist is left without an understanding of how a particular pathway, or a particular set of genes, fit within the entire system that produces systems-level transcriptional response. Without the ability to move fluidly between discrete pathway views and a systems-level view, a biologist will likely struggle to bridge the gap between his or her understanding of a local molecular phenomena, such as the activation of a signal-transduction pathway, and responses that are unmistakably system-wide [5].

While systems-level visualizations of protein-protein binding interactions have been attempted in organisms with smaller genomes, such as yeast, these approaches can lead to visualizations that resemble balls-of-string and are difficult to understand. These approaches represent a significant advance in network visualization, but further work is needed to make these systems-level views more comprehensible [3].

Further, current visualization approaches have not had the opportunity to explore the potential advantages of advances in visualization and display technologies. Large, high resolution displays present the opportunity to communicate information in a way that cannot be matched on small, low-resolution displays. Since these advances present an opportunity to show complex data in a new ways, the visualization of systems-level molecular dynamics stand to be advanced if created for these novel platforms [4].

2 PROPOSAL

We propose to create novel visualization approaches for large-scale, high-resolution displays that will provide a platform for exploring systems-level views of biological networks. In this effort, we aim to visually link together presently isolated molecular pathways and integrate these pathways with protein interaction data sets to create a flexible and interactive framework for exploring complex molecular systems, downstream consequences of molecular perturbations and gene-expression microarray data sets.

To this end, we have developed a prototype for large, high resolution display walls that integrates and visualizes over a thousand human molecular pathways from the Pathway Commons database in one view [1]. Human protein interaction data and molecular pathway data is processed in a multi-step data processing pipeline. Genes within each pathway are first laid-out in two-dimensional space using a force-directed graph layout algorithm. Then, a pathway-similarity metric is computed between all pathways. In this instance, the metric consists of the number of genes in common between two pathways. Then, treating each pathway as a node in a graph, with edges between pathways weighted by the computed pathway-similarity metric, a force-directed graph layout algorithm is applied to place pathways in three-dimensional space. Finally, pathways are visualized as plane in three dimensional space containing gene-products represented as spheres within the plane, an approach which builds upon the 2.5 dimensional multi-network visualization approach of Streit, et al. [6].

This prototype allows the user to move smoothly from a small set of molecular networks to a global view that presents over a thousand networks, taking advantage of the large screen space available on a tiled-display wall. By locating the networks in physical space, the prototype allows the user to create a mental map of networks, where proximal networks contain many genes in common relative to distal networks. The result is a view that resembles clusters of galaxies in a vast stretch of space, which serves as a compelling visual metaphor for the vast, yet inter-related nature of biological networks.

Future work will focus on developing this visual scheme into

*e-mail: jauris2@uic.edu
†e-mail:jrados@uic.edu
‡e-mail:spiff@uic.edu

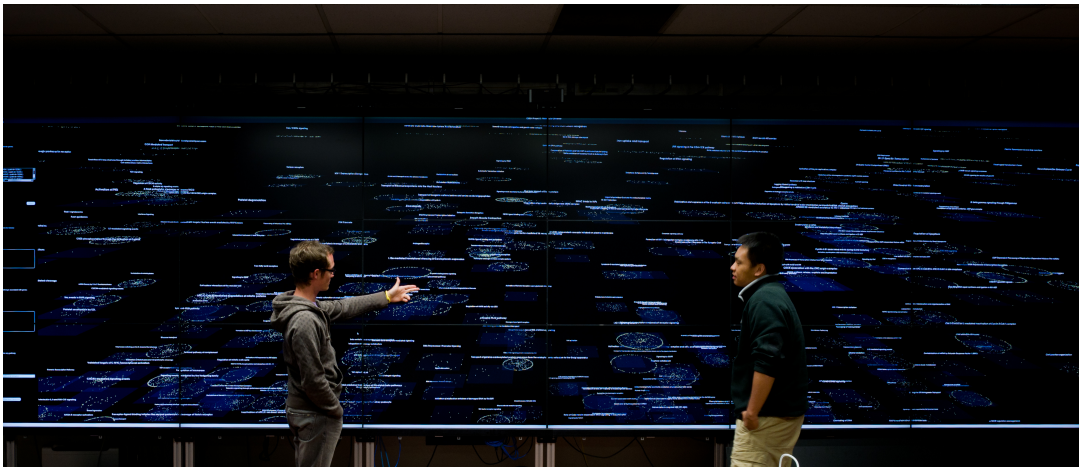

Figure 1: Visualization of over 1000 human biological pathways for large, high-resolution display walls.

Figure 2: A platform for the future development of novel approaches to visualizing the interconnected nature of biological pathways

a platform for exploring systems-level data sets and the systemic downstream consequences of local genetic and molecular perturbations. We believe this work will ultimately provide a powerful platform for exploring gene activity in a systems-level context.

REFERENCES

[1] E. G. Cerami, B. E. Gross, E. Demir, I. Rodchenkov, O. Babur, and N. e. a. Anwar. Pathway commons, a web resource for biological pathway data. *Nucleic acids research*, 39, 2011.

[2] N. Gehlenborg, S. I. ODonoghue, N. S. Baliga, A. Goesmann, M. Hibbs, H. Kitano, O. Kohlbacher, H. Neuweger, D. Schneider, R. Tenebaum, and A.-C. Gavin. Visualization of omics data for systems biology. *Nature methods*, 7(3):S56–68, 2010.

[3] E. Ho, R. Webber, and M. R. Wilkins. Interactive three-dimensional visualization and contextual analysis of protein interaction networks research articles. *Journal of Proteome Research*, 7(1):104–112, 2008.

[4] J. Jeong, B. Leigh, A. Johnson, L. Renambot, M. Brown, R. Jagodic, S. Nam, and H. Hur. Ultrascale collaborative visualization using a display-rich global cyberinfrastructure. *IEEE Computer Graphics and Applications*, 30(3):71–83, 2010.

[5] P. Saraiya, C. North, and K. Duca. Visualizing biological pathways: requirements analysis, systems evaluation and research agenda. *Information Visualization*, 4(3):191–205, 2005.

[6] M. Streit, M. Kalkusch, K. Kashofer, and D. Schmalstieg. Navigation and exploration of interconnected pathways. In *In Proc. of Eurographics Symposium on Visualization*, volume 27, 2008.

[7] M. Suderman and M. Hallett. Tools for visually exploring biological networks. *Bioinformatics (Oxford, England)*, 23(20):2651–2659, 2007.