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DYNAMICS OF BIOLOGICAL NETWORKS: SESSION INTRODUCTION

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Biological network analysis has become a central component of computational and systems biology. Because such analysis provides a unifying language to describe relations within complex systems, it has played an increasingly important role in understanding physiological function. Significant efforts have focused on analyzing and inferring the topology and structure of cellular networks and on relating them to cellular function and organization. However, much of this work has taken a static view of cellular networks, despite the knowledge that biological networks can change with time, context, and conditions. We introduce this session on The Dynamics of Biological Networks to encourage and support the development of computational methods that elucidate the dynamic interactome.

Biological networks encompass many types of variation. Temporal variation can be inferred via experimentally determined large-scale (static) cellular networks, along with other high-throughput experimental data sets that provide snapshots of biological systems at different times and conditions. These data are often integrated with static interaction data (e.g. protein-protein, domain-domain, or regulatory interactions), time- or environment-dependent expression data, protein localization data, or other contextual information. Temporal variation also operates at the evolutionary scale and can be inferred via comparison of biological networks across species. An evolutionary perspective on network dynamics can help shed light on molecular function and

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behavior as well as on the phylogenetic relationships between species. Contextual variation overlaps heavily with temporal variation, but focuses more specifically on characterizing *reactive* variation and the conditions that cause it. Studying context may also encompass examining sequence or genetic variation within a population of contemporaries and exploring how that variation affects network topology and function.

Uncovering the dynamic nature of cellular networks has clear relevance to human health, as defects in signaling and regulatory pathways are associated with many serious diseases, such as cancer. Correlating changes in genotype with changes in disease phenotype and studying these changes in the context of protein-protein interaction networks, signaling networks and transcriptional networks has begun to provide new understating of mechanism of complex diseases as well as help uncover markers for disease recognition and classification.

As in the previous year, this year's session on Dynamics of Biological Networks brings together scientists working on various aspects of the dynamic nature of biological networks. The session includes an invited talk, six contributed papers, and a panel discussion. The invited talk, by Edward Marcotte, relates gene networks to disease and evolutionary dynamics. Specifically, he will discuss new methods for linking genes to traits that reveal surprising disease models and that are intimately connected to evolutionarily conserved gene networks.

The papers selected for presentation address a broad spectrum of problems related to network dynamics. Several papers explore context specificity. In particular, Fang, *et al.,* directly link gene expression data with context or medical conditions. They present an algorithm that finds sets of genes that are highly co-expressed in many samples from a given context (such as cells grown in a nutrient-deficient condition), but that are *not* co-expressed in most samples in a different context (such as cells grown in normal media). Their approach defines gene sets likely to form context-specific pathways.

Many approaches to finding functional modules in biological networks rely on graph-partitioning algorithms that optimize a single objective function. In contrast, the paper by Navlakha, *et al.* looks at ensembles of optimal and near-optimal partitions to determine node centrality in modules and module variability. The variation observed between the different partitions may shed light on context-specific variations in the composition of functional modules.

Chowdhury and Koyutürk also focus on finding functional modules or subnetworks of protein-protein interaction networks that are coordinately dysregulated in disease. Their work builds on the idea that a group of genes that are individually only marginally dysregulated with respect to the phenotype might provide a clearer signal when considered together.

Building and evaluating dynamic network models is another theme of the session. Context specificity is also an underpinning of the work of Morcos *et al.,* who use a combination of methods to predict protein and domain interactions and apply belief propagation to provide support for a theoretical model of mobility for *M. xanthus*.

Venkatraman *et al.* introduce a mathematical model of activation of Plasmin and urokinase-type plasminogen proteases regulating the extracellular environment. The computational simulation of

the dynamics of their model predicts that the system exhibits bistable behavior, a prediction that is then validated experimentally.

A final theme of the session focuses on studying dynamics at an evolutionary time scale. Chindelevitch, *et al.,* present a new algorithm for global alignment of protein-protein interaction networks. The edge-swapping technique that they use to search the space of possible alignments is not only efficient in practice, but also helps to generate hypotheses about the evolutionary dynamics of the protein interaction networks between the described species.

In addition to the oral presentations, one paper has been selected for presentation in the proceedings. In this work, Przulj *et al.* describe a new model for the evolution of protein-protein interaction networks, and compare a number of different evolutionary dynamic models on a range of data sets.

Though the topics are varied, all of the work presented in this session shares the common goal of relating system dynamics to our understanding and modeling of biological networks. We hope that this session stimulates further research into characterizing and interpreting the dynamic interactome.

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