

## Section 5: Networks

The two readings introduce the landscape of research around networks and graph theory. The first, Barabasi and Olvai, is a review paper introducing essential concepts and the state of the field. The second, Cooper and Shendure, is an analysis of the protein-protein interaction network in yeast, providing insights on the nature of different protein “hubs”. Both papers demonstrate the utility of network theory in evaluating new data made available through high-throughput protein sequencing and analysis.

Barabasi and Olvai cover the various uses of networks in biological applications. First, they discuss the foundations of such theories, including degree distributions, scale-free networks, mean free path, modularity, and clustering coefficients. Then, they describe how biological networks tend to distribute themselves. There are more high-connectivity hubs than would be expected from a random network, resulting in a power law degree distribution. Moreover, they cross-apply understanding from social and internet network analysis to demonstrate the “ultra-small world effect,” where almost all protein pairs are connected with very few links, as well as the robustness of networks. They also describe how biological networks tend to have hierarchical natures, with different modules arising from temporal features (cell cycle) and spatial features (organelles), as well as other features. The authors then argue that network biology, while a nascent field, will be crucial for integrating cellular interactions at a bigger picture.

Ekman et al. study the protein-protein interaction network in fission yeast. They derive their datasets from two sources: the database of interacting proteins, and the filtered yeast interactome. They find in their analysis that interactions are not fully explained by binding to similar proteins. Multi-domain proteins and long proteins are enriched in high-connectivity hubs. Moreover, the authors distinguish between party hubs and date hubs, where the latter contain more long and disordered regions, indicating that they are more functionally useful in dynamic interactions. Moreover, party hubs exhibit a greater degree of associativity, where they interact with each other in highly clustered functional modules. Lastly, the authors demonstrate that hubs tend to be older protein domains, which fits into the additive theory described by Barabasi and Olvai.

- Ekman D, Light S, Björklund AK, Elofsson A. (2006) What properties characterize the hub proteins of the protein-protein interaction network of *Saccharomyces cerevisiae*? *Genome Biol.* 2006;7(6):R45.
- Barabási, AL, Oltvai, ZN (2004). Network biology: understanding the cell's functional organization. *Nat. Rev. Genet.*, 5, 2:101-13.