Title: Analysis of Protein Networks

Protein-protein interaction (PPI) networks may be studied through the lens of both 3-dimensional protein structures as well as the large-scale genome variation data being generated as part of next-generation sequencing initiatives. In terms of protein structural data, I will describe how mapping the structures of protein complexes onto PPI networks enables the classification of hubs into two distinct types: multi- and singlish-interface. These two categories exhibit very distinct properties, especially in terms of the well-known preferential attachment model of network growth. Secondly, I will discuss how the integration of alternative conformations with PPI networks further highlights interesting disparities, with the permanent multi-interface hubs tending to exhibit a greater degree of conformational plasticity relative to singlish-interface hubs. In addition, I will briefly discuss how alternative conformations are being culled from the PDB to study the significance of sequence variation in the context of allosteric behavior. I will then discuss the some of the insights gained by integrating variation data with these networks (especially when using population-scale sequencing data from the 1000 Genomes Project). Several well-known results are recapitulated using this data: greater network centralityis associated with a greater degree of negative selection, and the proclivity of the network tends to be under positive selection. Finally, I will show how this type of data further illuminates aspects of the intricacies of protein structures and motions.

Integration of protein motions with molecular networks reveals different mechanisms for permanent and transient interactions.
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Integrative annotation of variants from 1092 humans: application to cancer genomics.
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