

FUNCTIONAL TOPOLOGY IN A NETWORK OF PROTEIN INTERACTIONS - N. PRŽULJ, D.A. WIGLE AND I. JURISICA. BIOINFORMATICS VOL. 20 NO. 3, PAGES 340 – 348.

ABSTRACT

This paper offers a systematic analysis of a *Protein-Protein Interaction (PPI)* network based on graph theory. The idea is to uncover network properties and construct computational models for predicting properties of lethal mutations and proteins participating in genetic interactions, functional groups, protein complexes and signaling pathways. Mathematically, a PPI network is represented as a graph, with nodes representing proteins, and edges representing protein-interactions. Following this, important graph properties were found using several in-built routines in the *Leda software library*. These include: average, SD and skew for *degrees* (number of edges containing the node), *articulation points* (whose removal causes graph disconnectedness), *hubs* (highly connected nodes on the graph's MST) and *shortest paths* between nodes and *clusters* (highly connected sub graphs).

Upon analysis of the above graph properties, the authors made the following conclusions: *Lethal mutations* – those which potentially lead to the death of an organism – occur with a higher frequency in proteins that are *hubs* and *articulation points*. *Viable mutations* – those which are favorable – tend to occur with higher frequency in proteins that are siblings. Distinct classes of proteins have different properties. For instance, translation proteins have highest average *degree* whereas transport and sensing proteins have lowest average *degree*. It was also noticed that over 70% of the top 10 most frequent proteins are *inviolate* and *structure* proteins rather than *signaling* proteins. To determine signaling pathways in protein networks, *MAPK (Mitogen-Activated Protein Kinase)* pathways were used. On a related note, articulation points on these linear pathways are more likely to be lethal mutations or likely to participate in genetic interactions.

In sum, the results of the above analysis are potentially powerful, as they not only provide better knowledge about existing protein networks, but also provide insightful information about predicting and annotating uncharacterized proteins. These predictions could then be used to propose better hypotheses about cellular structure.

DISCUSSION

Three papers were discussed in class related to Protein Interaction Networks. The first paper talks about constructing genome-wide interaction networks for several organisms, based on the concept of *Interologs*. The results of these networks are then stored in a database for further use. The second paper talks about *scale-free networks*. It introduces the concept of “*hubs*”, small yet significant proportions of proteins, to study cellular properties like robustness. The hubs are classified into *party hubs* and *date hubs*, depending on the method, time and location of interactions. The third paper highlights the fact that most network studies look only at small subsets of networks are not always scale-free. It provides reasoning for the fact that properties for a subset of protein interactions cannot be extrapolated to the entire network always.

The current paper is more general in nature. It talks about finding important properties of proteins using graph analysis. While the other papers talk either about constructing interaction networks and study methodologies, this paper leverages mathematical computation models and graph theory to analyze protein interaction networks and deduce structure-function relationships.