

Fault Tolerance in Protein Interaction Networks: Stable Bipartite Subgraphs and Redundant Pathways

As increasing amounts of high-throughput data for the yeast interactome becomes available, more system-wide properties are uncovered. One interesting question concerns the fault tolerance of protein interaction networks: whether there exist alternative pathways that can perform some required function if a gene essential to the main mechanism is defective, absent or suppressed. One signature pattern for redundant pathways is the BPM (between-pathway model) motif, first suggested by Kelley and Ideker. Past methods proposed to search for BPM motifs have had several important limitations. First, they have been driven heuristically by local greedy searches, which can lead to the inclusion of extra genes that may not belong in the motif; second, they have been validated solely by functional coherence of the putative pathways using GO enrichment, making it difficult to evaluate putative BPMs in the absence of already known biological annotation. We show how a simple "folk" theorem in graph theory (probably due to Erdos) can help us identify possible BPMs in such a way that not only do we get better coherence of biological function, but we also have a direct way to validate our results based directly on the structure of the network.

We uncover some interesting biological examples of previously unknown putative redundant pathways in such areas as vesicle-mediated transport and DNA repair.

We then show how a separate source of high-throughput data, based on microarrays, can be used to further independently validate putative BPMs.