UNDERSTANDING STRUCTURE, FUNCTION AND EVOLUTION OF PROTEIN-PROTEIN INTERACTIONS BY COMPUTATIONAL MODELING AND ANALYSIS

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ABSTRACT

Currently, with the growth of experimental structural data on protein-protein interactions and larger protein complexes, the trend in computational biology and structural bioinformatics is towards applying such resources to model and analyze structures, functions, and evolutions of PPIs. Nevertheless, due to the rapid growth of the number of experimental structures, it becomes necessary to introduce bioinformatics methodologies, which rely on the advanced machine learning and information retrieval techniques, capable of handling complex and massive structural data.

The research in this dissertation introduces and develops several computational methodologies to understand PPI 3D structures. First, we introduced an alignment-free similarity measure to detect structural similar PPI interfaces. This approach is capable of finding similar PPI interfaces formed by non-related protein subunits. Second, applying our similarity measure for PPIs, we showed our ability to use feature based interface similarity to classify and retrieve similar interface structures efficiently. Third, we used a set of simple protein interface structural features to test the classification and scoring performances for docked protein complexes, by using supervised and semi-supervised learning. Fourth, we analyzed the conservation patterns of charged residues located in PPI interfaces on a sampled set of PPI data. Last, we processed a genome-wide analysis of alternative splicing (AS) effects on human PPIs.