PRISM: A Web Server for Prediction and Visualization of Protein-Protein Interactions

Abstract

PRISM is a web server for the querying, visualization and analysis of the protein interfaces and putative protein-protein interactions derived from known protein structures in PDB. Putative interactions between proteins are predicted with an efficient algorithm using structural and evolutionary similarities. The algorithm seeks possible binary interactions between proteins (targets) through similar known interfaces (templates). Template dataset is the structurally and evolutionarily representative subset of biological interfaces in PDB. Starting with all available ~50,000 interfaces as of February 2006, 8205 distinct interface clusters are generated with their representative interfaces. After elimination of the antigen-antibody complexes, peptides, ligands, synthetic proteins, membrane proteins and interfaces having less than 3 hotspots – evolutionarily conserved residues on the interfaces – at each partner chain and consideration only biologically relevant interfaces, 1738 template interfaces are obtained. Target dataset is the sequentially non-redundant subset of all structures available in PDB which have less than 50 % homology. Target dataset contains 16415 structures, of which 4952 are complex structures, 11463 are monomeric structures. Surfaces of the target proteins are extracted by invoking NACCESS. If relative surface accessibility of a residue is greater than 5%, it is considered as surface residue. The prediction algorithm based on that if two proteins contain similar regions to complementary partner of a template interface, it is proposed that these two proteins interact through these similar complementary regions. After the template interfaces are split into its complementary partner chains, these partners are structurally aligned with the surfaces of the target proteins. To measure the similarity, a scoring function is used, which contains two parts; i) evolutionary similarity score and ii) structural similarity score. Evolutionary similarity includes hotspot match ratio; structural similarity part includes RMSD and residue match ratio between target protein and one partner of template interface. Prediction algorithm results in 58817 potential interactions for a score threshold of 0.85.

For a biological evidence, we used the p53 (tumor suppressor protein) interaction network generated by Kohn *et al*., in 1999. In this network, there are 94 interactions between 55 PDB structures. We verified 84 of these 94 interactions by PRISM with a score threshold of 0.5. These verified interactions support the consistency of our prediction algorithm.

Using PRISM web server, one can browse and query template, target datasets and the predicted interactions. Another feature of PRISM is the visualization of Protein Interaction Network derived from the predicted binary. This tool is based on a multi-modal network

representation, incorporating the relationships between entities such as interfaces, proteins, domains, and functional annotations. This model together with its automatic layout feature results in identifying biologically important network modules. The server is available at http://prism.ccbb.ku.edu.tr