Chapter V
Discovering Protein–Protein Interaction Sites from Sequence and Structure

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ABSTRACT

This chapter gives a comprehensive introduction of the sequence/structural features that are characteristic of protein-protein interaction sites and reviews state-of-the-art methodologies for protein-protein binding site prediction. Protein-protein interaction residues are largely responsible for mediating physical binding processes such as inhibitory effects through enzyme-inhibitor interaction, initiating immune response by an antibody-antigen interaction, and regulation of cell signaling proteins. Currently, various methods are available for predicting protein-protein interaction sites, which allow a residue-level understanding of the physical protein binding phenomena presented by the global construction protein-protein interaction networks. The overview of the discussed protein-protein binding site prediction strategies and detailed comparison of their weaknesses and strengths is aimed towards assisting protein researchers in gaining more insight to protein-protein interaction networks.

INTRODUCTION

In the recent years, the biology community has been fascinated by snapshots of complex inner workings of cellular activities from various different angles enabled by the advancement of high throughput experiments. The construction of proteome-wide protein-protein interaction maps provided us for the first time a vivid visualization

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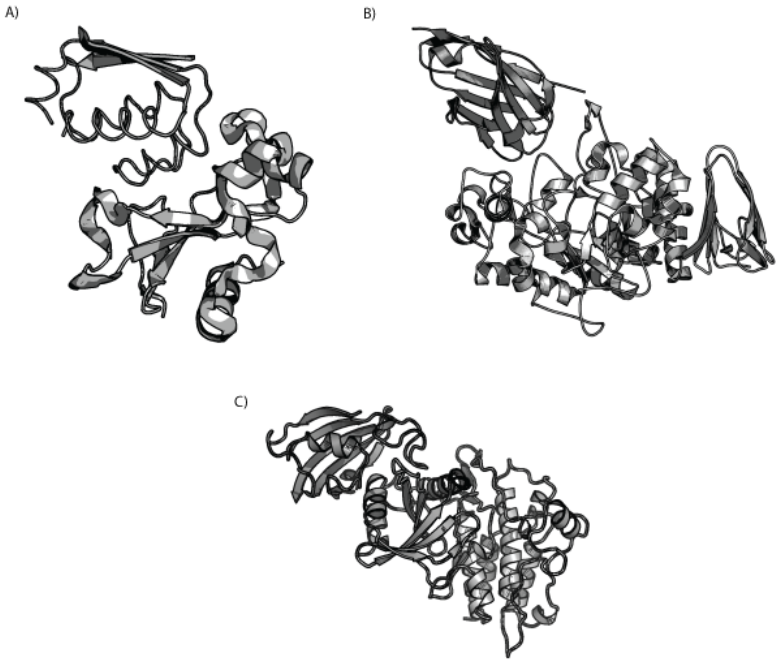
of networks of physical protein binding which maintain cellular events involving cell signaling, gene regulation, and metabolism (Giot *et al.* 2003;Uetz *et al.* 2000;Ito *et al.* 2001). On the other hand, genome sequencing projects and structural genomics projects continue to accumulate sequence and structure information of individual proteins. Therefore, the urgent need in the post-genomic era is to capitalize these two types of enormous amount of data to provide useful and practical information to the biology community. Effectively, protein-protein interaction sites plays a crucial role in proteomics; a greater understanding of protein-protein interaction sites ultimately bridges the gap between abstract information of protein-protein interaction (PPI) network and physical entity of protein structures, substantiating protein-protein interaction data as a critical platform for advanced molecular recognition research and experimental design. For example, knowing (or predicting) binding residues in a PPI site enables designing point mutation experiments to verify the role of the residues in the PPI network. In this chapter, we review current computational methods for predicting PPI sites from sequence and structure and extend discussion to the future direction of this field.

Physical aspects of protein-protein interactions are well studied in the context of protein-protein docking prediction. In the protein-protein docking area, at a molecular basis, these physical protein-protein binding events are commonly classified into three major groups in the context of their function: (1) enzyme-inhibitor complexes, (2) antibody-antigen interactions, and (3) other types of interactions (Hwang *et al.* 2008;Mintseris *et al.* 2005;Chen *et al.* 2003). This classification has been proved quite useful to atomic-level analysis employed for protein-protein binding site prediction and protein-protein docking. A genome-scale PPI network would include interactions of proteins of much broader range of functions, but here we mention these three classes to illustrate variation of the nature of protein-protein interaction.

Figure 1. Examples of the different groups of protein-protein interactions: (A) PDBID: 1BRS, a Barnase-barstar complex (B) PDBID: 1KXQ, an alpha-amylase to antibody interaction, and (C) PDBID: 1B6C, an example of the other types of interactions such as those transient that involve kinase to isomerase binding.



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