Abstract

Interactions between pairs of proteins are responsible for a diverse array of biochemical processes, including the proper functioning of the immune system. Antibodies are protective proteins that bind to viral proteins, called antigens, and mediate the body's response and defense against pathogenic macromolecules. The determination of the amino acid residues on antigens that facilitate this binding, referred to as the epitope, is critically important in the processes of vaccine design and monoclonal antibody development. Experimental methods, such as NMR and X-ray crystallography, which are used to identify interfacial residues have severe limitations and are inefficient. However, computational methods have been developed to predict the sites of protein-protein interactions and present efficient and effective alternatives to complement experimental methods.

Recently, we have submitted a manuscript to *BMC Bioinformatics* describing the development of the computational model, ISPIP, which uses machine learning to combine a variety of predictive features to determine interfacial residues on query proteins. ISPIP outperforms the state-of-the-art computational methods currently available. We intend to test the performance of ISPIP in predicting the interfacial residues on a diverse test set of antigens in which these residues have been experimentally determined. Additionally, antigens are known to have multiple epitopes, so there may be several potential sites of antibody-antigen interactions. Therefore, we intend to explore the implementation of clustering algorithms to divide the predicted interfacial residues into distinct potential epitopes. The performance of ISPIP will be compared with other computational models and assessed using four statistical measures which will elucidate the sensitivity and specificity of the predictions. We expect that ISPIP, coupled with the clustering algorithm, will successfully identify known epitope regions and reveal additional potential epitopes to be experimentally investigated.