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Analysis of antibody-antigen interactions and prediction of their complex structures

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A deeper understanding of antibody-antigen interactions is essential for the design of antibody drugs. To design an antibody drug having a high affinity with the target antigen, it is desirable to obtain an antibody structure in complex with its target antigen. Because it is generally not easy to determine protein complex structures by experimental methods, such as X-ray crystallography and NMR, model structures of protein complexes predicted by bioinformatics techniques are considered to be important for drug discovery.

Previous studies have found canonical conformations of antibody proteins, in particular, Complementarity-Determining Regions, based on the analyses of their sequences and structures [1,2]. In terms of antibody-antigen interactions, an antigen binding site on an antibody, paratope, and an antibody binding site on an antigen, epitope, have been analyzed and several epitope prediction methods have been developed [3].

In this study, we performed a careful analysis of antibody-antigen interactions from multiple perspectives, and developed a method for predicting paratopes and epitopes separately, towards accurate prediction of antibody-antigen complexes suitable for drug design. We are now developing a method for predicting antibody-antigen complex structures, where a probable combination of the predicted paratope and epitope sites is selected based on a scoring function constructed from our new observations, combined with the knowledge of antibody-antigen interactions elucidated previously.

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