The Effect of Dynamics on Protein-Ligand Interactions

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With recent advances in both, experiment and computer simulations, it has become possible to follow in detail how small molecules interact with proteins. This is of particular interest because small ligands can be used to probe the interior of proteins or interfaces between the protein and the solvent. In this presentation I will focus on two systems for which the dynamics of the ligand plays a different role.

One of the paradigm system for protein-ligand interaction is myoglobin interacting with small molecules such as O_2, CO, and NO. All three systems have been extensively studied both experimentally and theoretically. Detailed information is available for structural, spectroscopic and energetic aspects of the interaction between CO and Mb. With refined and carefully parametrized electrostatic models it has become possible to understand a variety of experimental observations.

The situation is quite different for insulin. Although insulin is a physiologically very important hormone, its active structure is not yet known. Recent experiments have suggested that insulin interacts quite favourably with glucose. Using computational docking studies and molecular dynamics simulations it was possible to show that the preferred interaction site of glucose corresponds to the one inferred from experiment. In addition, the binding site is not only found statically but also dynamically stable.