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Title: How computer simulations help us understand recognition of ligands in proteins, vibrational Stark effect and infrared spectroscopy.

Date: Tuesday, February 13
Time: 2:00 EST
Location: Clark Hall 110

Abstract:

Protein structure-function relationship is one of the cornerstones of modern biology, and holds the key to decipher many problems in physiology and medicine. For example, the primary function of myoglobin (Mb) is to transport oxygen in organisms. Carbon monoxide is a poison of Mb, and the oxygenated form of Mb prevents nitric oxide from inhibiting cytochrome c oxidase, making Mb a protector of cellular respiration. Experiments have demonstrated that the structures of myoglobin enable the protein to function and to distinguish among oxygen, carbon monoxide and nitric oxide. To understand protein structure-function relationships and spectroscopy at the molecular level, computer simulations are often helpful and sometimes necessary. However, current simulation methods are often time- and labor-intensive, or they perform poorly in computing spectroscopic properties and protein-ligand binding energies.

To counter these difficulties, we have constructed a new model for computer simulations based on classical molecular electrostatics that includes, crucially, a proper treatment of polarization of atoms. When applied to myoglobin interacting with a ligand, our model successfully predicts the ligand-heme binding and bending energies, captures the vibrational Stark effect of ligands and discriminates the myoglobin binding affinities among carbon monoxide, nitric oxide and oxygen. Our model explains these properties and the preferential binding of one atom of the ligand to heme in intuitive electrostatic terms. Our approach demonstrates the power of computer simulations in understanding biology, and can be readily extended to investigate other problems of medical importance such as drug-receptor binding, amyloid formation and the effects of point mutations in cancer-related proteins, where electrostatics may play a significant role.