Extended Concept of Solvation toward Unified Analysis of Molecular Binding in Weakly Ordered Systems

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A key function of such weakly ordered systems as lipid membrane, micelle, and protein is their ability of acting as a host and binding other molecules. In the present work, a diverse class of binding is treated in unified manner as the solvation in an extended sense. The basic idea is view a solution system with host structure (membrane, micelle or protein) as a mixed solvent. The host is described not as solute species, but as part of the mixed solvent system, and the guest molecule is the only species regarded as the solute. A unified treatment is then implemented as the solvation in a mixed-solvent system, which often involves nano- or mesoscale inhomogeneity.

The key quantity governing the binding ability is the standard change of free energy. Within the (extended) notion of solvation, the quantity of interest is the solvation free energy, the reversible work to introduce the solute-solvent interaction. The free energy is notorious, however, for its heavy computational demand. A fast and accurate computation of free energy is a major challenge of theoretical/computational chemistry at present. We approach the free-energy computation by combing the molecular simulation with a statistical-mechanical theory of solutions.

Since the notion of solvation is not only extended to abovementioned nano-organized systems, but is also strongly desired to handle such emerging systems as ionic liquid, supercritical fluid, and quantum-classical coupled system, the theory of solutions needs to be (re-)formulated to treat these frontline subjects. To meet this necessity, we present a new type of solution theory called the method of energy representation. In this method, the solute-solvent distribution is expressed over the one-dimensional coordinate of solute-solvent pair interaction energy, and the energy distribution functions in the solution and reference solvent systems constitute an approximate but accurate functional for the solvation free energy. The method achieves a high computational efficiency compared to the standard free-energy perturbation method, while no deterioration is observed in terms of the agreement with experiment.

Two types of application are discussed. One is the molecular binding into lipid membrane and micelle. The distribution of hydrophobic solutes is investigated in DMPC bilayer and SDS micelle. Water is shown to delocalize the spatial distribution of hydrophobic solutes within DMPC membrane. The interaction of transmembrane protein with lipid membrane is also examined and the driving force of binding is discussed.

The other is the cosolvent effect on protein stability in aqueous system. Water and the cosolvent such as urea are viewed as mixed solvent, and all-atom analysis of protein solvation is conducted. The “direct” and “indirect” effect of cosolvent is examined by decomposing the solvation free energy into the water and cosolvent contributions.