

**HYDROPHOBIC HYDRATION AND INTERACTIONS IN
EXTENDED THERMODYNAMIC SPACE: LENGTHSCALES,
ATTRACTIONS AND ADDITIVE EFFECTS**

By

Manoj V. Athawale

An Abstract of a Thesis Submitted to the Graduate

Faculty of Rensselaer Polytechnic Institute

in Partial Fulfillment of the

Requirements for the Degree of

DOCTOR OF PHILOSOPHY

Major Subject: Chemical Engineering

The original of the complete thesis is on file
in the Rensselaer Polytechnic Institute Library

Examining Committee:

Prof. Shekhar Garde, Thesis Adviser

Prof. Wilfredo Colón, Member

Prof. Jonathan S. Dordick, Member

Prof. Angel E. García, Member

Prof. Ravindra S. Kane, Member

Rensselaer Polytechnic Institute
Troy, New York

June 2007

(For Graduation August 2007)

ABSTRACT

Numerous experimental and theoretical investigations over the past few decades have shown that the pertinent structure and function of biomolecules and larger assemblies rely upon the thermodynamic and structural properties of water and water-mediated interactions. Therefore, understanding and modeling of such biophysical processes at a fundamental level would necessitate the study of various water-mediated interactions including hydrophobic and electrostatic, that drive these processes. Of all the water-mediated interactions, hydrophobic interactions have assumed special significance given the critical role of solvent water in aqueous self-assembly. The primary goal of this research is to obtain a fundamental understanding of hydrophobic hydration and interactions at the molecular as well as nanoscale level. Specifically, the dependence of hydrophobic phenomena on the extended thermodynamic parameter space including size, charge and various environmental perturbants is explored.

At the fundamental level, there are hierarchically complex models to characterize hydrophobic phenomena in biological self-assembly. For example, studying simple models such as the ‘hydrocarbon transfer’ model, hydrophobic interactions between pair of solutes in water, and also many body interactions, provides useful insights into protein unfolding thermodynamics. However, several recent studies have highlighted an interesting lengthscale dependence of these rudimentary model processes. We present a systematic analysis of the lengthscale dependence of hydrophobic hydration and interactions at the level of a single solute as well as a complex many body model hydrophobic polymer. Specifically, we present results on the effects of varying solute-water interactions on the solvation of small and large single hydrophobic solutes. We also develop predictive theoretical models to capture this dependence of hydrophobic hydration on lengthscales and solute-water attractions.

These parametric dependences of hydrophobic hydration are also expected to have important consequences on the structural and thermodynamic aspects of the association of two hydrophobic solutes in solution. We present an extensive study on the lengthscale dependence of hydrophobic interactions between model hydrophobic solutes, and the ef-

fects of varying solute-water attractive interactions on those is also explored. At the next highest level of complexity, a detailed simulations study of manybody hydrophobic phenomena and its dependence on solute lengthscales is presented. The folding-unfolding of model hydrophobic polymers in water is studied with varying polymer lengthscales and polymer-water attractive interactions. At all different levels of interaction, detailed structural and thermodynamic characterization was used to address the drying or dewetting phenomenon associated with lengthscale dependent hydrophobicity.

Further, although solvent water is the dominant component of solution environment for various biophysical phenomena, numerous other molecules such as salts and osmolytes that constitute the solution as well, are expected to have a direct or indirect consequence on the stability and function of various biomolecules. We have carefully studied the thermodynamic and structural aspects of the effects of different additives including salts and osmolytes on hydrophobic phenomena at small and large lengthscales. Our work for the first time highlights the origin of biocompatibility of osmolyte molecules at high intracellular concentrations, and an unique lengthscale dependence of additive effects on hydrophobic interactions.