**A Comprehensive Molecular-Based Study of the Stability of Clathrate Hydrates**

Abstract: Clathrate hydrates are crystalline structures that consist of water molecules forming cages via a hydrogen-bonding network enclosing small guest molecules. Such structures normally form at a conditions of high pressure and low temperature. Clathrate hydrates have always been a problem in the gas and oil industry because their formation can block pipelines and processing equipment. Prevention of such flow-line blockages and motivates an increase level of study of fundamental mechanisms for gas hydrate formation and decomposition. Computational, molecularly-based modeling methods play an ever-growing role in helping us to understand the molecular processes and properties that contribute to clathrate hydrate formation and stability. There are many variable to consider, including hydrate crystal structure, the chemical species, concentration, and distribution of the solute, conditions of temperature and pressure, nuclear quantum effects, and the impact of co-solutes. Any understand of hydrate nucleation and growth must begin with an understanding of their thermodynamic stability, to ensure that the molecular model is one that corresponds to the known thermodynamic behavior of clathrate hydrates. This requires examination of the free energy of formation. We start this examination by considering defect-free lattice, i.e. pure water or cages each with one single identical solute molecule. We employ lattice dynamics to calculate the free energy at very low temperature. Then, the harmonically targeted temperature perturbation method, which is an efficient technique for evaluating the free energy as a function of temperature, will be used to calculate free energy up to temperatures of interest. With the knowledge of free energy we can identify the stable crystalline form and locate the conditions where phase transitions occur.

Key words: Clathrate hydrate, free energy, stability, phase equilibrium