

4z Molecular Modeling of Peptides Crossing the Cell Membranes

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I have worked on developing efficient molecular computational techniques for studying various engineering problems. I developed novel Monte Carlo techniques to study adsorption of flexible molecules from liquid phase into the channels of zeolites [1,2,3]. Using a novel non-equilibrium molecular dynamics [4] technique I studied the transport of binary mixtures through channels of zeolites. During the last year I used a “growing string method” [5] to map out the reaction pathways for methane activation in sulfuric acid [6]. The growing string method explores the potential energy surface (quantum-mechanical) and finds the minimum energy pathway connecting the reactants and products. In addition we developed a path integral Monte Carlo method to calculate the single-molecule quantum-mechanical partition-function accurately.

I plan to use my expertise in molecular modeling and chemical kinetics to study how small molecules (such as a 20 amino acid peptide) cross the cell membranes. There are many examples in the field of drug discovery and disease prevention where understanding of such crossing events is important. A) Action of anti-microbial peptides on the cell membrane of bacteria B) Incorporation of amyloid beta-peptides into cell membranes with respect to Alzheimer's disease C) Incorporation GTPase-ras peptide into a bilayer with respect to cell signaling D) Crossing of cell membranes by therapeutic si-RNA. A few computational studies in the past have looked at some of these problems using regular Monte Carlo and Molecular Dynamics. However such studies can not cover all the time scales associated with such crossing events. Path based methods such as “growing string method” or “transition path sampling”[7] are suited for studying such events. I plan to use coarse grained models of the systems in conjunction with path based methods to study the mechanism of the crossings. Preliminary results of the crossing events modeling and highlights from my past research will be presented at the poster.

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