Monte Carlo Simulations of Supported Biomembranes and Protein Folding

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ABSTRACT

Cell membranes and proteins constitute central functional units in living organisms. This thesis deals with simulations of processes in proteins (folding) and so called supported lipid (bio)membranes. Proteins are present in every living organism, where they are responsible for a large variety of functions. Understanding protein structure and dynamics is of key importance for the development of medicine and biotechnology. The bulk of understanding of protein folding kinetics has been acquired via simplified protein models, where the lack of tiny details is compensated by the ability to simulate the complex protein folding process from the beginning to the end. In this study, the lattice approximation of proteins was used, where the protein chain is represented as an embedding on a lattice. We showed that by combining two conceptually different lattice models, new opportunities in protein folding simulations appear. We also investigated the relative role of the standard set of monomer moves in the folding process of general lattice proteins.

Cell membranes constitute another class of important biological "building blocks" and functional units, with outstanding functions in living organisms. A very promising platform for studying and using biomembranes is supported lipid bilayers (SLBs). Research on SLBs is accelerating and many future applications await, or are already ongoing, like biosensors, artificial photosynthesis, and drug screening devices. SLBs are commonly formed through vesicle adsorption on silica surfaces. Unravelling the basic principles governing the lipid deposition processes on such surfaces has only begun. Many variables, often co-operating ones, determine the final outcome of a lipid vesicle adsorption experiment. Recent experiments on SiO_2 revealed a temperature activated transition from intact vesicles on the surface to formation of a complete SLB. We constructed a kinetic model of this system, which quantitatively reproduced the experimental results, demonstrated explicitly the vesicle rupture channels involved, and identified the main cause of the temperature activated transition. Other recent experiments, involving AFM measurements on adsorbed vesicles, revealed setpoint and tip-shape dependent influences on the vesicles. We constructed a model of the vesicle-tip-substrate system, and managed to quantify AFM imaging artifacts at small setpoint forces, and that, at large setpoint forces, a sharp tip preferentially displaces a vesicle laterally while a blunt tip preferentially induces rupture of the vesicle. We also provided the details of the latter processes. A model was furthermore constructed to study the influence of lipid heterogeneity on the interaction between vesicles and surfaces.

Keywords: SLBs, vesicle adsorption and rupture, AFM-image artifacts, AFM manipulation, vesicle composition, protein folding, lattice models, Monte Carlo simulations