PREFACE

Molecular dynamics (MD) is a computer simulation of physical movements of atoms and molecules. The atoms and molecules are allowed to interact for a period of time, giving a view of the motion of the atoms. This book presents current research on the theory, kinetics and implementation of molecular dynamics. Topics discussed in this compilation include the molecular dynamics of proteins; molecular dynamics simulations on the extraction of fluid transport properties at the nanoscale; investigation of structural properties of drug-metabolizing enzymes using molecular dynamics simulation; double-pulse laser control of ultrafast optical Kerr effect in liquid; ZnO nano-structures for biosensing; and molecular dynamics simulations of liquid and ionic solvation of carbon tetrachloride.

Chapter 1 - Conformational changes of biomolecules have been proposed as a cause and effect of biological events. Particularly, the content of a specific conformation of a protein in an intracellular localized space has suggested signals addressed to execute specific tasks. Sampling of these structural options, that make of proteins informational molecules, finds in molecular dynamics (MD) a theoretical and computational tool to explain and hypothesize the functionality at atomistic level. Conceptually, consider the "final" folded structure as the most functional conformation, possibly finding some obstacle to study the pleiotropicity of proteins and its structural basis. In this order of ideas, the evidence provided by MD in relation to folding and unfolding, where thermodynamic states and kinetic properties characterize conformational changes, sheds light on the pathways towards functionality of a protein. In this chapter, force fields and atomistic inter-actions considered as relevant parts of a MD simulations are reviewed and a typical protocol of stability is explained. Finally, statistical mechanics as a theoretical frame to

explore the conformational space is discussed in the context of available computational methods devoted to discover functional domains in proteins.

Chapter 2 - Pharmacokinetic studies play an important role in drug design and development. Recently, many drug candidates have failed to be released into the market owing to pharmacokinetic problems. Thus, drug metabolism should be investigated in the early stages of drug design. Because a large number of drug candidates are screened in the early stages of drug design and development, fast and low-cost estimations of drug metabolism using computational approaches are useful. Structure-based drug design (SBDD), in which three-dimensional (3D) structures of proteins are used for molecular design, is a widely used computational approach. SBDD approaches can be used for drug target as well as for drug-metabolizing enzymes in drug design testing. For example, undesirable inhibition of drug metabolism can be identified and the effects of genetic polymorphism can be predicted for drug candidates using the SBDD approach for drug-metabolizing enzymes. Although 3D structures of proteins are indispensable to the SBDD approach, experimental structures of many drug-metabolizing enzymes are still unknown. Thus, computational procedures for prediction and refinement of the 3D structures of drug-metabolizing enzymes are important. In this chapter, structural refinements of UDP-glucuronyltransferase using molecular dynamics simulations are described. Because there are polymorphisms for this enzyme, its detailed structure is essential for SBDD. Thus, molecular dynamics simulations are expected to be useful for structural refinements of drug-metabolizing enzymes.

Chapter 3 - The optical control of the molecular motions in the neat liquids of carbon tetrachloride CCl_4 and chloroform $CHCl_3$ at room temperature through the non-resonant excitation was enhanced by means of the double-pulse pump-probe technique. When the separation time of the pump pulses and their relative intensity were varied, the amplification or the cancellation of the coherent vibrations of the molecules was achieved. The molecular responses were detected by the time-resolved optically heterodyne-detected optical-Kerr-effect (OKE) technique. It was shown that the time-resolved polarization selective spectroscopy of the molecular vibrational and rotational dynamics in liquid can be based on the double-pulse laser control.

Chapter 4 - ZnO nanostructure is a material that is central for many nanotechnology applications, such as chemical and biological sensors. A systematic molecular dynamics study for the behavior of water droplet and electrolyte solutions interacting with ZnO were done. The contact angle of a water droplet on ZnO polar slabs and nanorods/-tubes array changes significantly as a function of the ZnO-water interaction energy and nano

structure geometry. The water contact angle served as a criterion to tune the intermolecular interactions. To recover a hydrophilic surface, voltage range from 1 to 20 volt were applied along the z-axis of the system to simulate the electrowetting behavior case. ZnO nanotube was used to study the permeation of water for equilibrium and applied voltage cases, illustrating the influence of the surface topography and the intermolecular parameters and surface charges on permeation kinetics. The author also studied the ionic currents through ZnO nanotubes simulating the case as field effect transistor (FET) of NaCl, KCl, CaCl2, and MgCl2 electrolyte solution for different concentrations (0.1, 0.5, 1.0, 5.0, and 10.0M) and calculate the solution conductance of these ions by applying a voltage difference (1-20V) along the z-axis of the system. Its possible to achieved, by these molecular dynamics simulations, the characteristic behaviors of ZnO nanostructure-electrolyte solution interactions and how it is suitable to use as ion selective sensor for intracellular micro environment.

Chapter 5 - A flexible body and nine-site fluctuating charge model to describe the intramolecular and intermolecular interactions for carbon tetrachloride is constructed based on the combination of atom-bond electro negativity equalization method and molecular mechanics (ABEEM/MM). The potential parameters are refined to accurately describe the structures and binding energies of $(CCl_4)_2$ and $Na^+(CCl_4)_n$ (n=1-4) clusters, then carried out liquid CCl_4 and Na^+solvationin liquid CCl_4 simulations to examine the potential parameters. The computed density of liquid CCl_4 is in excellent agreement with experimental value. The structures of liquid CCl_4 and Na^+ in liquid CCl_4 can be analyzed by examining the radial distribution functions and angular distribution functions. It is found that the liquid CCl_4 forms an interlocking structure and that a local orientation correlation is observed between neighboring CCl_4 molecules. In the study of Na^+ solvation in liquid CCl_4, It is possible to observe a well-defined solvation shell around Na^+ with five coordinated CCl_4 molecules. It is also found that Na^+ induces a strong local orientation order in liquid CCl_4. Moreover, the calculated diffusion constant of CCl_4 is in reasonable agreement with the experimental result. This work demonstrates that the new potential model is good enough to reproduce properties of liquid $CCl_4$and Na^+ in bulk liquid CCl_4.