MPHYCC-5: Modelling and Simulation

Dr. K B Singh Lecture Notes PG II Semester

Unit 5: Molecular Dynamics

Molecular dynamics is a technique for computer simulation of complex systems, modelled at the atomic level. The equations of motion are solved numerically to follow the time evolution of the system, allowing the derivation of kinetic and thermodynamic properties of interest by means of 'computer experiments'. Biologically important macromolecules and their environments are routinely studied using molecular dynamics simulations.

There is a complex network of chemical entities that evolve dynamically creating life at the molecular level. For example, proteins and nucleic acids fold (adopting specific structure consistent with their function), ions are transported through membranes, enzymes trigger cascades of chemical reactions, etc. Because of the complexity of biological systems, computer methods have become increasingly important in the life sciences. With faster and more powerful computers larger and more complex systems may be explored using computer modelling or computer simulations. Molecular dynamics (MD) emerged as one of the first simulation methods from the pioneering applications to the dynamics of liquids by Alder and Wainwright and by Rahman in the late 1950s and early 1960s. Due to the revolutionary advances in computer technology and algorithmic improvements, MD has subsequently become a valuable tool in many areas of physics and chemistry. Since the 1970s MD has been used widely to study the structure and dynamics of macromolecules, such as proteins or nucleic acids. There are two main families of MD methods, which can be distinguished according to the model (and the resulting mathematical formalism) chosen to represent a physical system. In the 'classical' mechanics approach to MD simulations molecules are treated as classical objects, resembling very much the 'ball and stick' model. Atoms correspond to soft balls

and elastic sticks correspond to bonds. The laws of classical mechanics define the dynamics of the system. The ‘quantum’ or ‘first-principles’ MD simulations, which started in the 1980s with the seminal work of Car and Parinello, take explicitly into account the quantum nature of the chemical bond. The electron density function for the valence electrons that determine bonding in the system is computed using quantum equations, whereas the dynamics of ions (nuclei with their inner electrons) is followed classically. Quantum MD simulations represent an important improvement over the classical approach and they are used in providing information on a number of biological problems. However, they require more computational resources. At present only the classical MD is practical for simulations of biomolecular systems comprising many thousands of atoms over time scales of nanoseconds. In the remainder of this article the classical MD will simply be referred to as MD.

Experiment plays a central role in science. It is the wealth of experimental results that provides a basis for the understanding of the chemical machinery of life. Experimental techniques, such as X-ray diffraction or nuclear magnetic resonance (NMR), allow determination of the structure and elucidation of the function of large molecules of biological interest. Yet, experiment is possible only in conjunction with models and theories. Computer simulations have altered the interplay between experiment and theory. The essence of the simulation is the use of the computer to model a physical system. Calculations implied by a mathematical model are carried out by the machine and the results are interpreted in terms of physical properties. Since computer simulation deals with models it may be classified as a theoretical method. On the other hand, physical quantities can (in a sense) be measured on a computer, justifying the term ‘computer experiment’. The crucial advantage of simulations is the ability to expand the horizon of the complexity that separates ‘solvable’ from ‘unsolvable’. Basic physical theories applicable to biologically important

phenomena, such as quantum, classical and statistical mechanics, lead to equations that cannot be solved analytically (exactly), except for a few special cases. The quantum Schro¨dinger equation for any atom but hydrogen (or any molecule) or the classical Newton's equations of motion for a system of more than two point masses can be solved only approximately. This is what physicists call the many-body problem. It is intuitively clear that less accurate approximations become inevitable with growing complexity. We can compute a more accurate wave function for the hydrogen molecule than for large molecules such as porphyrins, which occur at the active centres of many important biomolecules. It is also much harder to include explicitly the electrons in the model of a protein, rather than representing the atoms as balls and the bonds as springs. The use of the computer makes less drastic approximations feasible. Thus, bridging experiment and theory by means of computer simulations makes possible testing and improving our models using a more realistic representation of nature. It may also bring new insights into mechanisms and processes that are not directly accessible through experiment. On the more practical side, computer experiments can be used to discover and design new molecules. Testing properties of a molecule using computer modelling is faster and less expensive than synthesizing and characterizing it in a real experiment. Drug design by computer is commonly used in the pharmaceutical industry.