MAGIC AND MYSTERIES OF MODERN MOLECULAR DYNAMICS SIMULATIONS

A Basic Introduction

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Abstract

Since the first molecular dynamics simulations of hard spheres by Alder and Wainwright in the fifties of the last century (Alder, B.J. and Wainwright, T.E. (1957) Phase transition for a hard sphere system, J. Chem. Phys. 27, 1208-1209), this method has evolved to a powerful and intensively used technique in the computer simulations of physical, chemical and biological systems. The present article is meant as a brief and easy starting point for the very beginner in this field. It gives an introduction to the basic principles of the method and sketches also some of the more elaborate extensions and recent methodological developments such as first-principles molecular dynamics simulations (Car-Parrinello simulations) and mixed quantum mechanical/molecular mechanical (QM/MM) approaches. A final outlook attempts to summarize the state-of-the-art of what is possible today including the main limitations that presently exist and some of the current strategies of how to overcome them.

1. Guidelines

Over the last decades, molecular dynamics (MD) simulations have become a mature, highly developed, and extensively used technique, with applications ranging from material science to molecular biology. A comprehensive review of all the recent methodological developments and practical applications would go far beyond the limited scope of this Chapter. However, a large number of excellent books [1-9] and reviews [10-13] are available on this and related topics such as Car-Parrinello simulations [14-25] and QM/MM approaches [26-29].

The present Chapter is mainly addressed to students who are complete newcomers to the field of MD simulations. It focuses on the underlying ideas with the aim of providing a first basis and a convenient starting point for those who would afterwards like to study different aspects and extensions in more detail. To this end, supplementary literature is mentioned throughout the text. The main objective of this short tour through the field of MD simulations is to convey some of the basic fascination of this simple
and powerful technique and to outline its current and future potential. At the same time, this article also gives a first glimpse on some of the more intricate, 'mysterious', aspects that are involved, such as e.g. on the art of developing reliable force fields.

2. Basic Principles

2.1. GOALS

We are looking for a theoretical tool that is able to provide us with a microscopic picture of complex chemical and/or biological systems. At the same time, this approach should also enable a study of the dynamic properties. In other words, we are trying to find a method that also allows us to generate the time evolution of a system directly on the computer. Data on the specific mobility of different parts of a protein, or information about the nature of different thermally accessible conformations are only few examples of what we expect from such a technique. In addition, it should be able to give us access to a wealth of other properties such as, for instance, the velocity with which a molecule diffuses through a given condensed phase environment or a prediction of possible phase transitions in solids.

Naturally, as we are dealing with molecular systems that are made out of atomic nuclei and electrons, a fully adequate theoretical description is only possible in the framework of quantum mechanics. More specifically, as we are especially interested in the dynamic properties of these systems, we have in principle to solve the many-particle, time-dependent Schrödinger equation for a mixed system of nuclei and electrons

\[
-\frac{i\hbar}{\partial t} \Psi(\vec{R}_1, \vec{R}_2, \ldots, \vec{R}_N, \vec{r}_1, \vec{r}_2, \ldots, \vec{r}_n, t) = H\Psi(\vec{R}_1, \vec{R}_2, \ldots, \vec{R}_N, \vec{r}_1, \vec{r}_2, \ldots, \vec{r}_n, t) \tag{1}
\]

where capital indices run over nuclear and small indices over electronic coordinates. The solution of the combined nuclear/electronic Schrödinger equation (Eq. (1)) is a formidable task and is currently simply impossible for the systems we are interested in, that comprise typically 10,000 - 100,000 atoms. We will thus have to introduce suitable approximations to Eq. (1) that will allow us to realize our goal of describing the dynamic evolution of these systems.

2.2. BASIC ASSUMPTIONS

For a first simplification of the problem, we will make use of the fact that the mass of the electron is at least three orders of magnitude smaller than that of any nucleus. We can therefore assume that the electrons move on a much faster time scale than the atomic nuclei, i.e. the electrons are so light that they follow adiabatically the motion of the nuclei and thus adapt instantaneously to changes in the nuclear coordinates. Due to this separation in characteristic time scales, we are allowed to consider the nuclear and the electronic problem separately and write the total wave function in the form of a product.