JOINT INSTITUTE FOR NUCLEAR RESEARCH
Frank Laboratory of Neutron Physics

FINAL REPORT ON THE INTEREST PROGRAMME

MD-SIMULATION RESEARCH (FROM ATOMIC FRAGMENTS TO MOLECULAR COMPOUND)

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Participation period:
February 14 – March 25,
Wave 6

Belgrade, 2022

Abstract

In the report, I discuss the basic concepts of molecular dynamics that I have acquired during the course. MD-simulation was first developed in the early 1950s in the United States, and numerous methodologies and techniques have been developed since then. Molecular dynamics is a method of quantitatively solving motion equations. MD-simulation is a computational modeling tool based on Newton's law for evaluating the interaction between atoms and molecules. The following topics were covered during the course: basic equations, potentials, and simulation techniques, simulation of a liquid model (Lenard-Jones potential), use of selected general-purpose code for the simulation of ionic, polymeric, and biochemical molecular systems, theory of the basics of hybrid MD approach (classical quantum-chemistry potentials simulation methods), MD test modeling.

Introduction

Molecular dynamics and molecular modeling have been the most powerful approaches to computer analysis since the mid-1990s. As a result, they have become extremely valuable in physics, biochemistry, chemistry, and other fields. MD-simulation is a computational modeling tool based on Newton's law for evaluating the interaction between atoms and molecules. We can simulate and model a variety of surface interactions, including biomolecules with surfaces, minerals, polymers, nanoparticles, and carbon allotropes are examples of inorganic surfaces. [1,2] Molecular dynamics simulations are useful for investigating the physical foundation of biological macromolecule structure and function. The classical definition of Proteins' inflexibility has

given way to a dynamic structure. Internal motions and the resulting conformational changes are the focus of this concept. [3]

Quantum physics, DFT approaches, MD-simulations (All-atom (AA), Coarse grain (CG), Implicit solvent (IS), and Brownian dynamics (BD) are the different simulation techniques, as depicted in Figure 1. Biomolecules typically have tens of thousands of atoms in their structure, and MD modeling allows us to determine their interaction parameters even with tens of thousands of atoms.

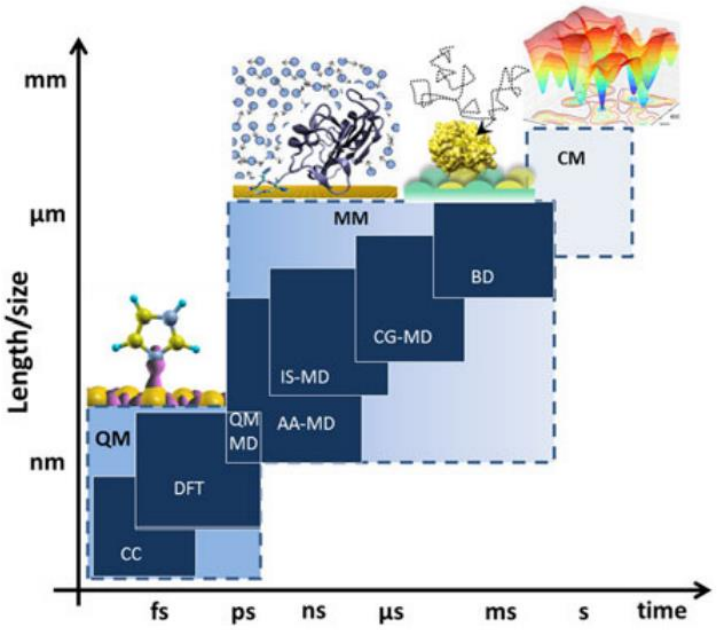

Fig 1. Typical time and length scales of different simulation techniques [1]

The basic equations, potentials and simulation techniques

Molecular dynamics is based on the equation of Newton's second law:

$$m_i \frac{d^2 r_i(t)}{dt^2} = F_i(r)$$

The finding of a molecule's geometrically optimal configuration entails determining the structure with the lowest free energy. Molecular force fields are used to compute a molecular structure's equilibrium free energy. A molecular force field is a mathematical function that describes the dependency of a molecule's potential energy on the coordinates of its atoms. In addition to chemical bonds, there are unbound Van der Waals interactions, as well as electrostatic forces and potentials (Coulomb interactions) if the atoms have a charge. After that, there is the potential energy:

$$U(r) = U_b + U_\theta + U_\varphi + U_\omega + U_{LJ} + U_{el} + U_{HB} + \cdots$$

Macromolecules are reduced to a set of atoms held together by simple harmonic forces, Coulombic interactions, and Van der Waals interactions when using such a force field model. The force field must be simple enough to be analyzed fast yet detailed enough to represent genuine structural properties for practical calculations.

A molecule is defined by the presence of a bond stretching between two atoms, a three-atom angle bending, and a four-atom fixed torsion, as depicted in Figure 2.

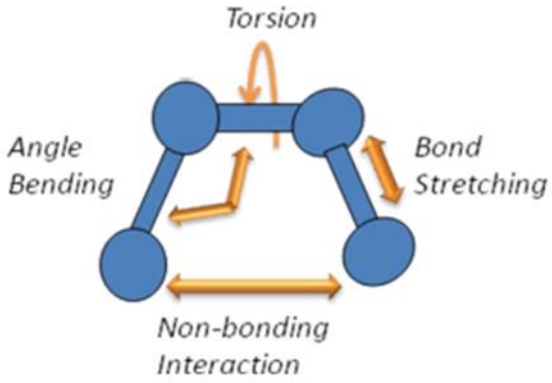

Fig 2. Different types of interactions [1]

The first term in the molecular force field describes covalent bond extension. A simple harmonic function that modulates the length of covalent bonds is frequently used to describe bond stretching.

$$U_b = \frac{1}{2}\sum_b K_b(r - b_0)^2$$

The bond angle distortion is described by the second force field term. The energy associated with bending an angle created by at least three atoms: A-B-C, when there is a chemical connection between A and B, and between B and C, is referred to as bond angle distortion.

$$U_\theta = \frac{1}{2}\sum_\theta K_\theta(\theta - \theta_0)^2$$

The distortion of dihedral angles from their preferred values is described by the third force field term. The dihedral term must be included in the force field

if a molecule has more than four atoms in a row, which is a given in macromolecules.

$$U_{\varphi} = \frac{1}{2}\sum_{\varphi} K_{\varphi}[\cos(n\varphi - \delta) + 1]$$

The electrostatic forces that arise between atoms with ionic charges are described by the fourth term. Salt bridges are interactions between positive and negative ions that play an important role in protein structure stabilization.

$$U_{el} = \sum_{i,j} \frac{q_i q_j}{r_{ij}}$$

Van der Waals forces are described by the force field's fifth term. An electric dipole moment is created as electrons travel around the atomic nucleus. This dipole polarizes nearby atoms, resulting in a short-range attractive force between the non-bonded atoms.

$$U_{LJ} = \sum_{i,j} \left(\frac{A}{r_{ij}^{12}} - \frac{B}{r_{ij}^{6}} \right)$$

Lenard-Jones potential

An intermolecular pair potential is the Lennard-Jones potential. The Lennard-Jones potential is the intermolecular potential that has been investigated the most extensively and carefully. Lennard-Jones potential describes Van der Waals nonbonding interaction between two atoms. Lennard-Jones potential expressed by following equation:

$$V(r) = 4\varepsilon\,[(\frac{\sigma}{r})^{12} - (\frac{\sigma}{r})^{6}]$$

Where V(r) is the Lennard-Jones potential, ε is the energy unit, r is the distance between two atoms centers, and σ is the average atomic density.

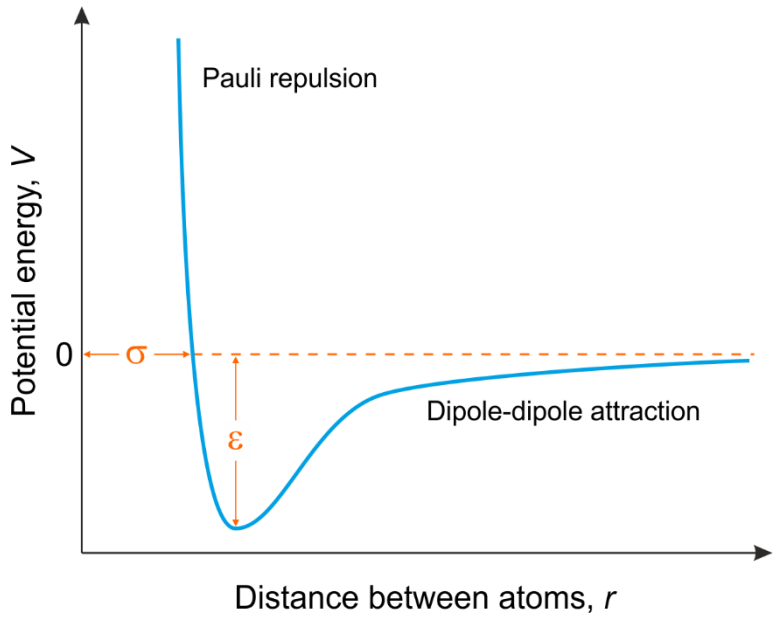

Fig 3. Graph of the Lennard Jones potential function

Radial Distribution Function

The Radial Distribution Function (RDF) is commonly applied in MD simulation to monitor system equilibrium states:

$$\rho g(r) = \frac{1}{N} < \sum_{i}^{N} \sum_{j \neq i}^{N} \delta[r - r_{ij}] >$$

Where N is the total number of atoms, ρ is the atomic density, r_{ij} is the distance between two atoms centers, and g is the 0 for distance less than one atomic diameter and 1 for larger distance.

Order parameter

The following function-parameter γ is used to distinguish between equilibrium states:

$$\gamma_x = \frac{1}{N} \sum \cos(\frac{4\pi x_i}{a})$$

$$\gamma_y = \frac{1}{N} \sum \cos(\frac{4\pi y_i}{a})$$

$$\gamma_z = \frac{1}{N} \sum \cos(\frac{4\pi z_i}{a})$$

$$\gamma = \frac{1}{3} [\gamma_x + \gamma_y + \gamma_z]$$

Boltzmann Distribution

Used for the monitoring of the equilibrium

$$H_x(t) = \int f(v_x) ln f(v_x) dv_x$$

MD Simulation Packages

MD can be performed with a variety of software packages, the following are some of the most prominent MD simulation programs: AMBER, CHARMM, DL_POLY, NAMD, GROMACS.

I.T. Todorov, W. Smith, A.M. Elena, and others developed DL POLY, a classical molecular dynamics (MD) simulation software at Daresbury Laboratory [4]. The advantage of the DL POLY software is that it can simulate a wide range of materials, including: simple atomic systems and mixtures, polarisable point ions and molecules, polymers with rigid bonds, macromolecules and biological systems, covalent systems and many others. There are three input (CONFIG, CONTROL, FIELD) and three output (OUTPUT, REVCON, HISTORY) files in the DL_POLY computer code. The initial molecular structure, CONFIG, contains 3-dimensional coordinates (x, y, z) of all atoms, sets the boundary conditions, as well as the initial values of the velocities (V_x, V_y, V_z) and interatomic forces (F_x, F_y, F_z).

FIELD contains information about the structure of atoms and molecules, their masses and charges, parameters, and types of interaction potentials.

CONTROL file contains data on the 7 simulation parameters (temperature, pressure, step of integration of the equations of motion and calculation time, thermodynamic parameters, and simulation methods, etc.)

Conclusions

To find the target conformer with the lowest energy configuration, molecular dynamics and molecular mechanics are frequently combined. The basic equations, potentials, and simulation techniques, the simulation of a liquid model (Lenard-Jones potential), the use of selected general-purpose code for the simulation of ionic, polymeric, and biochemical molecular systems, and the theory of the basics of hybrid MD were all covered during the course. A molecular modeling can, however, provide very important information to chemists and biologists involved in medical research if utilized with caution.

Future work

When I will finish my bachelor program on School of Electrical Engineering in Belgrade, I will work on looking for opportunity to get a Master degree in Biomedical engineering. This course help me to learn basic equation and programming skills for my future Master programe. I will try to do some research on this topic in Petnica Science Centar, to get more information about Molecular Dynamics.

Acknowledgements

First and foremost, I would like to thank my supervisor Prof. Kholmirzo Kholmurodov, for his support and general concern for my development as a young researcher. Prof. Kholmirzo Kholmurodov has been a supportive advisor who encourages me to think of new ideas. It has been a privilege for me to work under his supervision. Also, I would like to thank the Joint Institute for Nuclear Research, Dubna, Russia.

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