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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1. Introduction

Since the mid-1990's, molecular dynamics and molecular modeling are the most powerful approaches of computer analysis. As a result, they have gained significant value in physics, biochemistry, chemistry, and other branches of natural sciences. The exceptional characteristics of these methods, such as accuracy, efficiency, direct comparison with experiment, and year-by-year increasing computing power, have made them high-demanded tools in science and technology. Today, the application of molecular modeling methods has reached the point from which it is able to provide a real view of the processes and mechanisms occurring in physical, chemical, and especially biological systems (DNA, proteins, and similar structures).

The goal of the present work is to study the molecular modeling and computer design of chemical nanostructures, systems, and compounds.

In order to achieve this goal, the following objectives were pursued:

1. The basic equations, potentials, and simulation techniques
2. The simulation of liquid model (Lenard-Jones potential)
3. The use of selected general-purpose code for the simulation of ionic, polymeric, and biochemical molecular systems
4. The theory of the basics of hybrid MD approach (classical quantum-chemistry potentials simulation methods)
5. MD test modeling.

2. Overview

2.1. The basic equations, potentials, and simulation techniques

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

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

Any molecule is characterized by the presence of a bond stretching between two atoms, an angle bending of three atoms, and a fixed torsion of four atoms. In addition to chemical bonds, there is the participation of unbound van der Waals interactions (non-bonding interactions), and if the atoms also have a charge, also electrostatic forces, and potentials (Coulomb interactions). Then the potential energy:

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

The test substance is often subjected to one or another heat treatment or external pressure, therefore, modeling should also be carried out under conditions as close as possible to the experiment. Various algorithms for introducing a barostat or thermostat take this part in molecular modeling. There are two most common types of thermostats: Berendsen and Nose-Hoover. The Berendsen thermostat is used for molecular modeling of large molecules; this does not work for systems with a small number of atoms. The Nose-Hoover thermostat does not have this disadvantage. The Nose-Hoover thermostat conserves the energy of the system but does not retain the total momentum of the system; and the Berendsen thermostat stores the total momentum, but not the energy.

Calculation of potential and forces from the point of computer consuming time is: (1) Intramolecular interactions, chemical bonds (1-2 Å), (2) Nonbonding (Van-der-Waals) forces, intermolecular interactions (short-ranged; 7-8 Å), (3) Coulomb electrostatics forces and potentials (long-ranged).

The correct calculation of the N^2 = N*N interactions is the central problem of the MD-modeling. Evaluation of the entire spectrum of N*N interactions for systems of a large set of particles (chemical or biological molecules) can take years even for one structure. Therefore, in some cases, the Coulomb forces and potentials can be calculated, simplifying the problem by introducing "cutoff ".

2.2. The simulation of liquid model (Lenard-Jones potential)

The Lennard-Jones potential is an intermolecular pair potential. Among the intermolecular potentials, the Lennard-Jones potential is the potential that has been studied most extensively and most thoroughly. It is considered an archetype model for simple yet realistic intermolecular interactions.

The commonly used expression for the Lennard-Jones potential is:

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

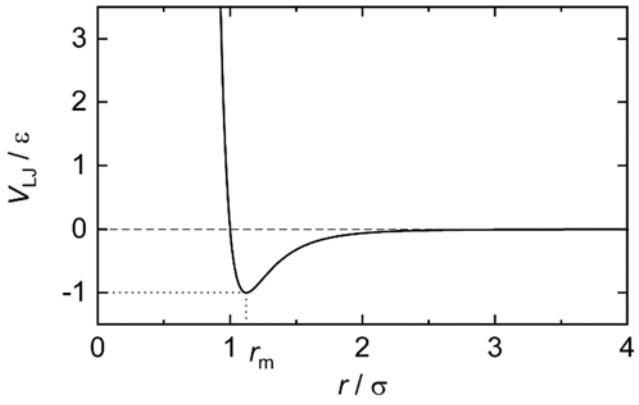

Fig.1. Graph of the Lennard-Jones potential function: Intermolecular potential energy as a function of the distance of a pair of particles.

The **radial distribution function (RFD)**, in a system of particles, describes how density varies as a function of distance from a reference particle.

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

RDF measures how atoms organize themselves around others; it is proportional to the probability of finding 2 atoms separated by distance. Also,

RDF has a central role in molecular modeling; it can be obtained from experiments to determine the structure of substances (X-ray diffraction analysis and neutron diffraction).

Order parameter is widely used for distinguishing of the equilibrium states:

$$\gamma_x = \frac{1}{N}\sum \cos(4\pi x_i/a)$$
$$\gamma_y = \frac{1}{N}\sum \cos(4\pi y_i/a)$$
$$\gamma_z = \frac{1}{N}\sum \cos(4\pi z_i/a)$$
$$\gamma = \frac{1}{3}[\![\gamma_x + \gamma_y + \gamma_z]\!]$$

Boltzmann distribution is used for the monitoring of the equilibrium:

$$H_x(t) = \int_{-\infty}^{+\infty} f(v_x)\, lnf(v_x)\, dv_x$$

2.3. The use of selected general-purpose code for the simulation of ionic, polymeric, and biochemical molecular systems

The DL_POLY computer code, which is used to investigate a range of chemical and biochemical systems, was developed at Daresbury Laboratories, England, by a molecular modeling group led by Bill Smith.

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). In accordance with the CONFIG file, it is necessary to compile a FIELD, which contains information about the structure of atoms and molecules, their masses and charges, parameters, and types of interaction potentials. CONFIG and FIELD must be consistent in structure. The CONTROL file contains data on the

simulation parameters (temperature, pressure, step of integration of the equations of motion and calculation time, thermodynamic parameters, and simulation methods, etc.), each line indicates a method or algorithm for MD modeling.

DL_POLY code can be used to study the dynamic and structural properties of various molecular systems - atomic and ionic structures, polymer chains and biological macromolecules.

2.4. The theory of the basics of hybrid MD approach (classical quantum-chemistry potentials simulation methods)

Quantum chemical methods of molecular dynamics (ab initio quantum chemistry) are based on the Schrödinger equation.

The main goal of the hybrid approach in MD simulation is to use more accurate quantum-chemical approximations to find approximations and the possibility of separating variables, which makes it possible to simplify the calculation scheme without involving experimental data.

Hybrid methods of classical and quantum-chemical MD is a neat approach in computer molecular modeling that is widely used in the study of a wide variety of systems. MD/qMD combinations are particularly useful in investigating the properties of the extended chemical or biological molecules.

The Tersoff potential is a three-body potential functional which explicitly includes an angular contribution of the force. The potential is widely used at present in various applications for silicon, carbon, germanium, etc. It is written in the following form:

$$U_{ij} = f_C(r_{ij})[f_R(r_{ij}) - \gamma_{ij} f_A(r_{ij})]$$

As a result, the Tersoff potential is used for hybrid modeling of covalent bonds in carbon nanotubes.

2.5. MD test modeling of future target

For future research, I had chosen to perform MD modeling of the system of carbon nanotube - nanoparticles - nucleotide chain. According to recent studies, metallic nanoparticles can interact with the nucleotide chain, therefore aiming at targeted cancer therapy.

The potential goal of modern research is the understanding the DNA interaction mechanism with metallic nanoparticles embedded by the CNT environment.

The simulation of this kind of molecular structure has been carried with gold nanoparticles. In my future work, I am targeting to simulate a similar molecular ensemble with silver nanoparticles in order to compare results with the existing ones.

3. Conclusions

The molecular modeling and computer design of chemical nanostructures, systems, and compounds have been studied. During the course, the following tasks were investigated: 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, the theory of the basics of hybrid MD approach (classical quantum-chemistry potentials simulation methods), MD test modeling.

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References

1. Kh. Kholmurodov MD-Simulation in Chemical Research: From Atomic Fragments to Molecular Compound // Dubna, Russia, 2011.
2. Musa Ozboyaci, Daria B. Kokh, Stefano Corni, Rebecca C. Wade, Modeling and simulation of protein – surface interactions: achievements and challenges // Quarterly Reviews of Biophysics (2016), 49, e4, page 1 of 45.
3. Khusenov M.A, Dushanov E.B, Kholmurodov Kh.T, Zaki M.M, Sweilam N.H., On Correlation Effect of the Van-der-Waals and Intramolecular Forces for the Nucleotide Chain - Metallic Nanoparticles – Carbon Nanotube Binding // The Open Biochemistry Journal, 2016, 10, 1-17.
4. M. A. Khusenov, E. B. Dushanov and Kh. T. Kholmurodov, Molecular Dynamics Simulations of the Nucleotides and Metallic Nanoparticles Interaction on a Carbon Nanotube Matrix // Materials Transactions, Vol. 56, No. 9 (2015), pp. 1390 to 1393.