JOINT INSTITUTE FOR NUCLEAR RESEARCH
Frank Laboratory of Neutron Physics

FINAL REPORT ON THE INTEREST PROGRAMME

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

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Participation period:
October 30 – December 10, Wave 9

Dubna, 2023

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ABSTRACT

Molecular dynamics (MD) simulations are a powerful tool for analyzing the physical movement of atoms and molecules and their interactions.

Throughout the INTEREST program, we discussed the following subjects:

1. the basic equations, potentials and simulation techniques;

2. the computer code description for 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.

The result of the program was this overview report and the invaluable knowledge acquired during the lectures.

INTRODUCTION

Molecular dynamics (MD) is a powerful tool used in various scientific disciplines to simulate the behavior of molecules over time. MD simulations are crucial in understanding how molecules behave and what properties they exhibit.

The simulations generated through MD provide a detailed view of molecular systems, offering valuable information that might be challenging or impossible to obtain through experimental methods alone. It employs Newton's equations of motion to model the interactions between atoms and molecules, allowing scientists to understand and predict how these particles move, interact, change conformation, and respond to external conditions [1].

This approach has significantly contributed to advancements in various scientific fields:

- in biology, MD simulations can elucidate the behavior of proteins, DNA, and other biomolecules, providing insights into their structure-function relationships, folding mechanisms, and interactions with drugs or other molecules;
- in chemistry, these simulations help in studying reactions, exploring the behavior of chemicals, and understanding the properties of materials at the atomic and molecular levels;
- in materials science, MD aids in understanding the mechanical, thermal, and electrical properties of materials, paving the way for designing new materials with specific desired characteristics.

Goals and tasks of the project

1. Studying the fundamental principles of MD simulations, including Newtonian mechanics, force fields, and numerical integration methods.
2. Enquiring various simulation techniques used in MD.
3. Considering the application of MD simulations in diverse scientific domains, highlighting its significance in understanding biological processes, chemical reactions, and material properties.

These goals aim to provide a comprehensive understanding of MD simulations, enabling to apply this knowledge in various research fields and fostering a solid foundation for further exploration.

1. THEORETICAL BACKGROUND

1.1 The basic equations, potentials and simulation techniques

In molecular dynamics simulations, atoms are represented as spheres that interact with each other by virtue of a potential energy function, usually called the force field (FF). The coordinates of molecular entities and their velocities concerning simulation time are determined by solving Newton's equations of motion (Figure 1), which incorporate the mass of each atom (m_i), spatial coordinates (r_i), time (t), forces acting on individual atoms (F_i), and the potential energy U(r) derived from the FF [2].

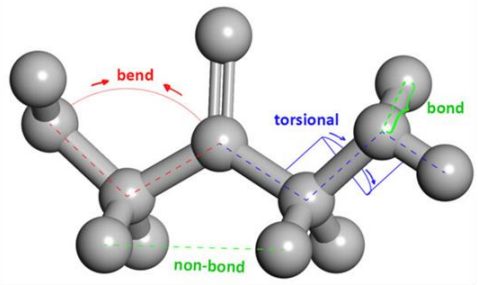
$$m_i \frac{d^2 r_i}{dt^2} = F_i = -\nabla U(r)$$

Figure 1. Newton's equations of motion

This approach is based on two fundamental assumptions. Firstly, it assumes that the motion of electrons can be adequately represented by the dynamics of corresponding nuclei, following the Born-Oppenheimer approximation. Secondly, it posits that atomic nuclei, being considerably heavier than electrons, can be modeled as point particles adhering to classical mechanics, which is a valid approximation in scenarios where quantum effects are negligible [3].

The majority of FF used in chemistry are empirical in nature, constructed through a summation of various forces. These FF primarily encompass bonded forces related to chemical bonds, bond angles, and bond dihedrals. Despite the fact that MD simulations, by their design, don’t explicitly consider electrons, they serve as a valuable tool for systems largely governed by non-covalent interactions like electrostatic forces and Van der Waals interactions. The potential energy of a chemical molecule therefore consists of a large sum from several contributions from pairwise atom-atom interactions (Figure 2).

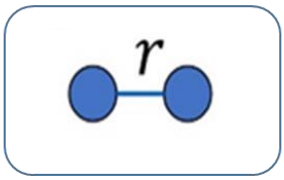
$$U(r) = \underbrace{U_b + U_\theta + U_\varphi}_{\textit{Bonded interactions}} + \underbrace{U_{LJ} + U_{el}}_{\textit{Non-Bonded interactions}}$$



Bonded interactions

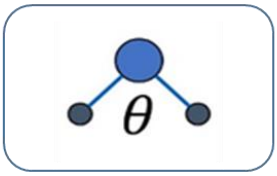
Valence length potential,

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



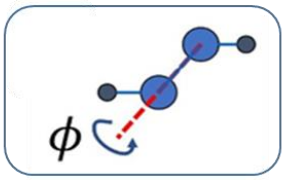
Valence angle potential,

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

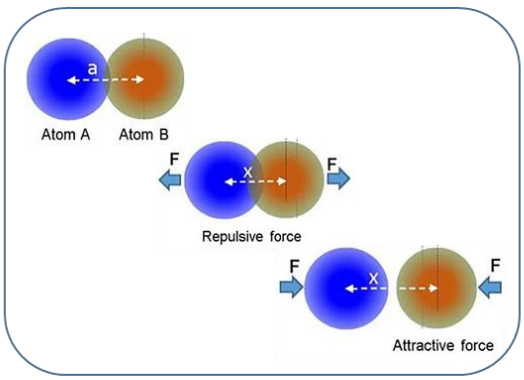


Torsion dihedral potential,

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



Non-Bonded interactions



Van der Waals Interaction Potential:

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

Electrostatics potential,

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

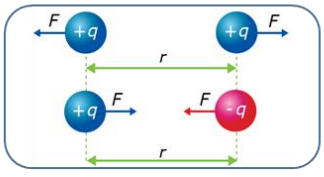


Figure 2. Bond lengths, bond angles, dihedral angles and non-bonded interactions contribute to the potential energy function

Upon defining FF resembling the empirical potentials governing atom-atom interactions, the MD method computes classical motion trajectories for macromolecular atoms, incorporating the representation of the macromolecule's internal thermal mobility within subnanosecond time intervals under a specified FF. To achieve this, it becomes imperative to generate initial velocities for all particles at the onset of the simulation, facilitating the subsequent numerical solution of equations of motion. This entails the iterative calculation, at each simulation step, of forces acting on particles, subsequently determining new particle coordinates and velocities (Figure 3). Molecular trajectories upon post-processing yield structural insights, alongside energetic information.

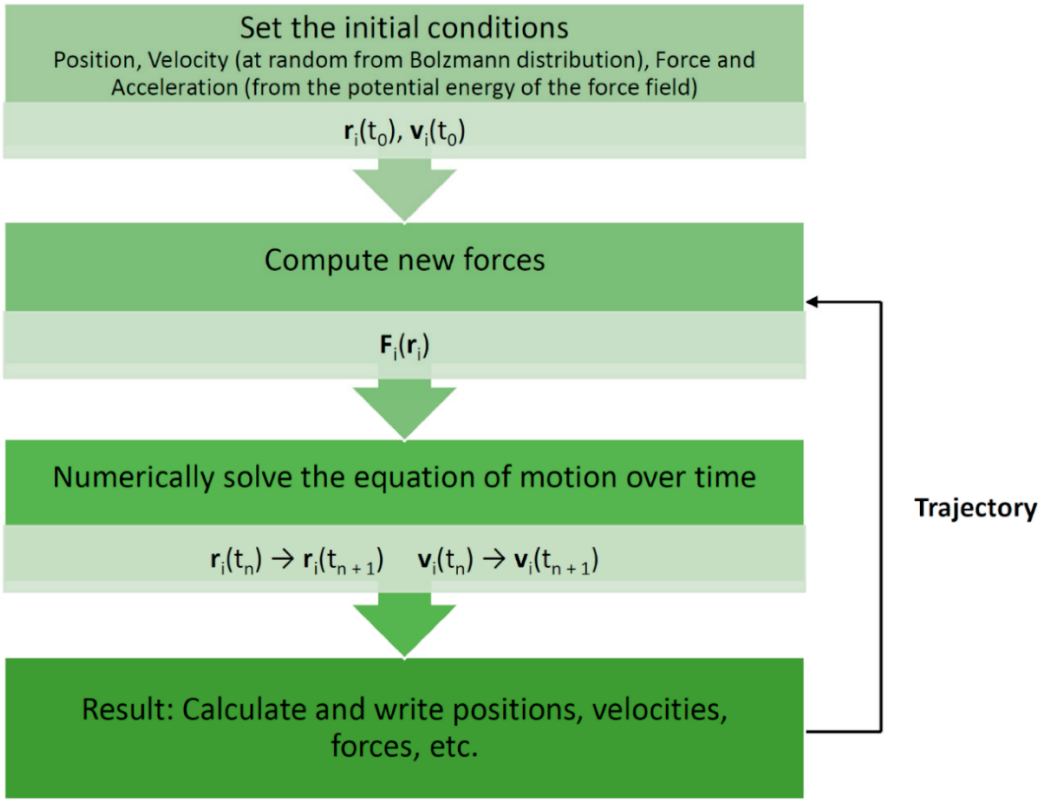


Figure 3. Basic molecular dynamics simulation algorithm [4]

1.2 The Lennard-Jones potential

The Lennard-Jones (LJ) potential is widely used for modeling physical and biochemical systems, including solids, gases, and liquids. This potential is an integral part of all well-known MD simulation packages. It is particularly successful in studying the properties of liquids and liquid-like compounds, accurately reproducing numerous characteristics and physical parameters such as melting temperature, surface tension, heat capacity, and critical points of phase transitions [2].

The LJ potential, also known as the 12-6 potential, has the following form as presented in Figure 4.

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

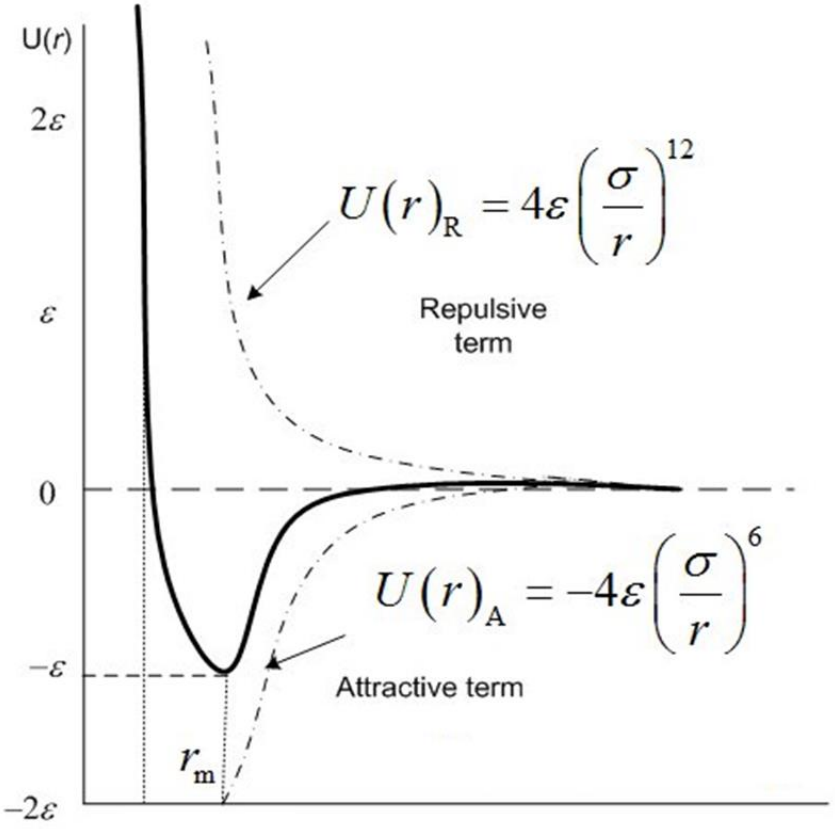
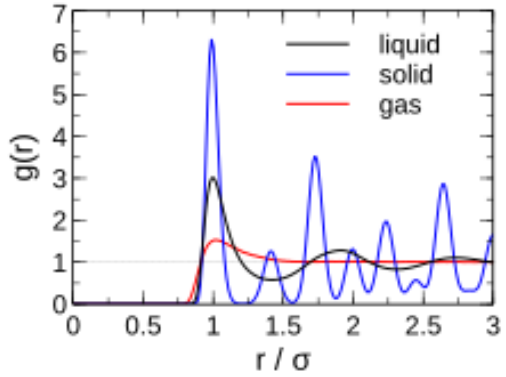
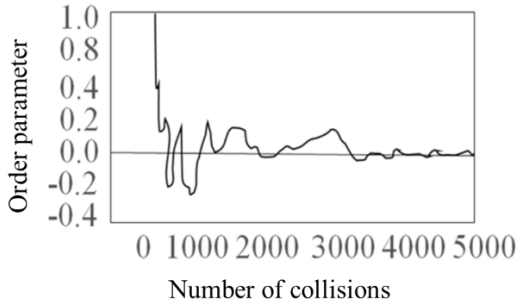
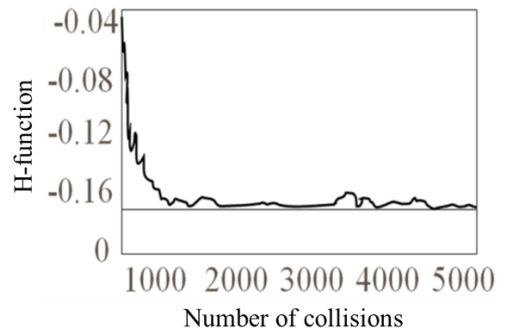


Figure 4. Equation and graph of the Lennard-Jones potential

The primary objective of MD simulations is to gradually steer a system, typically composed of a vast ensemble of particles, towards thermodynamically equilibrated states. For instance, starting the study of a molecular system from a crystalline state and employing the aforementioned modeling techniques, we gradually and deliberately heat and thermally equilibrate the system on a computer, thereby bringing it to an equilibrium state (liquid). The collection of statistics, which involves analyzing physical or chemical laws, essentially begins after achieving a state that corresponds to stable equilibrium particle distributions.

Essential to delineate three critical functions within the context of MD simulations: the radial distribution function (RDF), the order parameter, the Boltzmann distribution. Brief information about each parameter is presented in the Table 1 [2].

Table 1. Description of main functions of MD simulations

Radial distribution function (RDF)		
The radial distribution function specifically quantifies the likelihood of locating a particle's center at a particular position, a radial distance r away from the center of a reference sphere. In MD simulations, the RDF serves as a crucial tool for monitoring the equilibrium status of systems	$\rho g(r) = \frac{1}{N} < \sum_{i}^{N} \sum_{j \neq i}^{N} \delta[r - r_{ij}] >$	
Order parameter		
The order parameter is a highly valuable quantity that characterizes the thermal displacements of atoms within the lattice nodes in MD modeling. The behavior of the order parameter function is utilized to identify the attainment of equilibrium states within a system.	$\gamma_x = \frac{1}{N} \sum \cos(\frac{4\pi x_i}{a})$ $\gamma_y = \frac{1}{N} \sum \cos(\frac{4\pi y_i}{a})$ $\gamma_z = \frac{1}{N} \sum \cos(\frac{4\pi z_i}{a})$ $\gamma = \frac{1}{3}[\gamma_x + \gamma_y + \gamma_z]$	
Boltzmann distribution		
The Boltzmann distribution or H function is also widely used to identify equilibrium states.	$H_x(t) = \int_{-\infty}^{+\infty} f(v_x) ln f(v_x) dv_x$	

1.3 Simulation software

There is a wide selection of software that can be used for MD simulation. Now widely used software are DL_POLY, Groningen Machine for Chemical Simulations (GROMACS), AMBER, CHARMM and Nanoscale Molecular Dynamics (NAMD).

During the project, we discussed in detail two programs for MD simulations: DL_POLY [5] and AMBER [6]. A comparative analysis of these two programs is presented in Table 2.

Table 2. Comparison of various simulation software

Name	*DL_POLY*	*AMBER*
Research Direction	Simple atomic systems, unpolarisable and polarisable point ions and molecules, polymers, proteins, macromolecules, metals and metal alloys, ets.	Mostly biological systems (proteins, macromolecules, DNA), few chemical systems
Advantage	Verified accuracy and reliability, high computational efficiency	Convenient modeling of new macromolecules and models
Disadvantage	Low parallel processing efficiency	Low computational efficiency and slow speed

Flowchart schemes illustrating the input and output files of DL_POLY and AMBER are depicted in Figures 5 and 6, respectively.

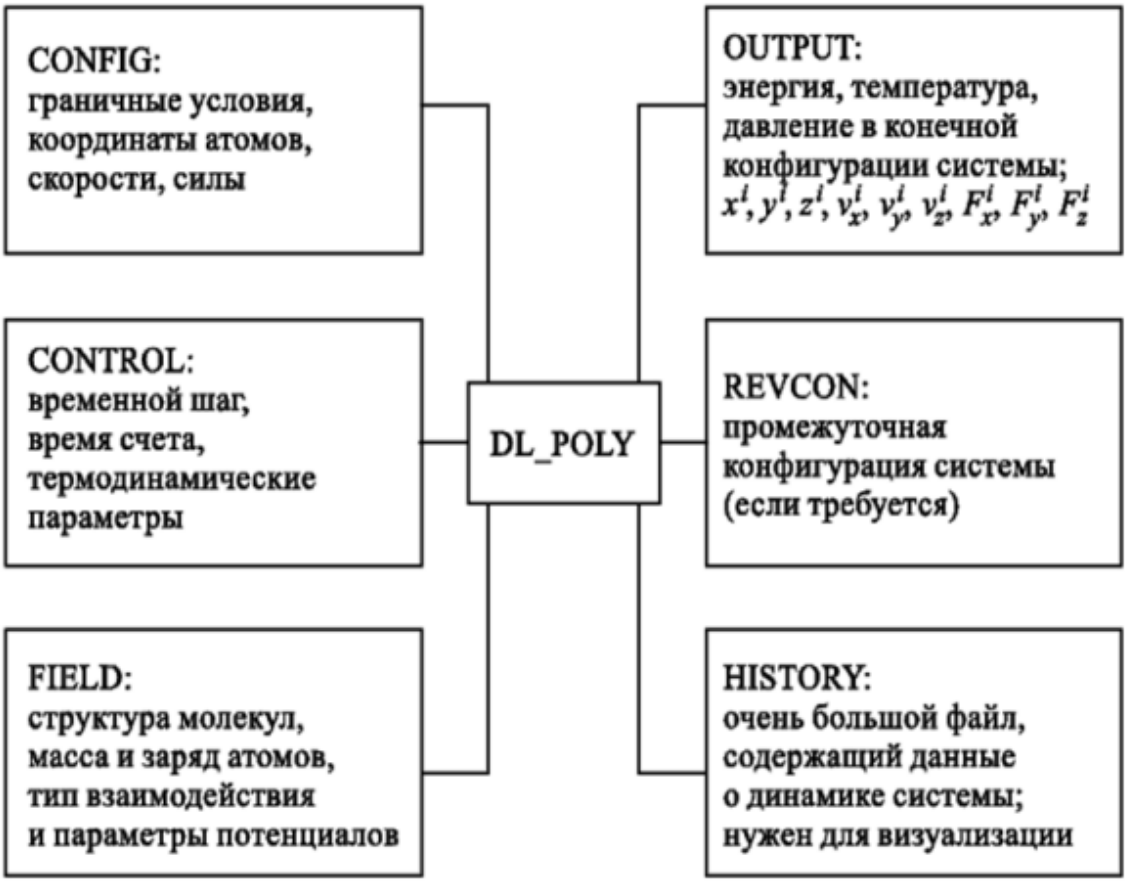


Figure 5. A flowchart scheme of the input and output files of DL_POLY [2]

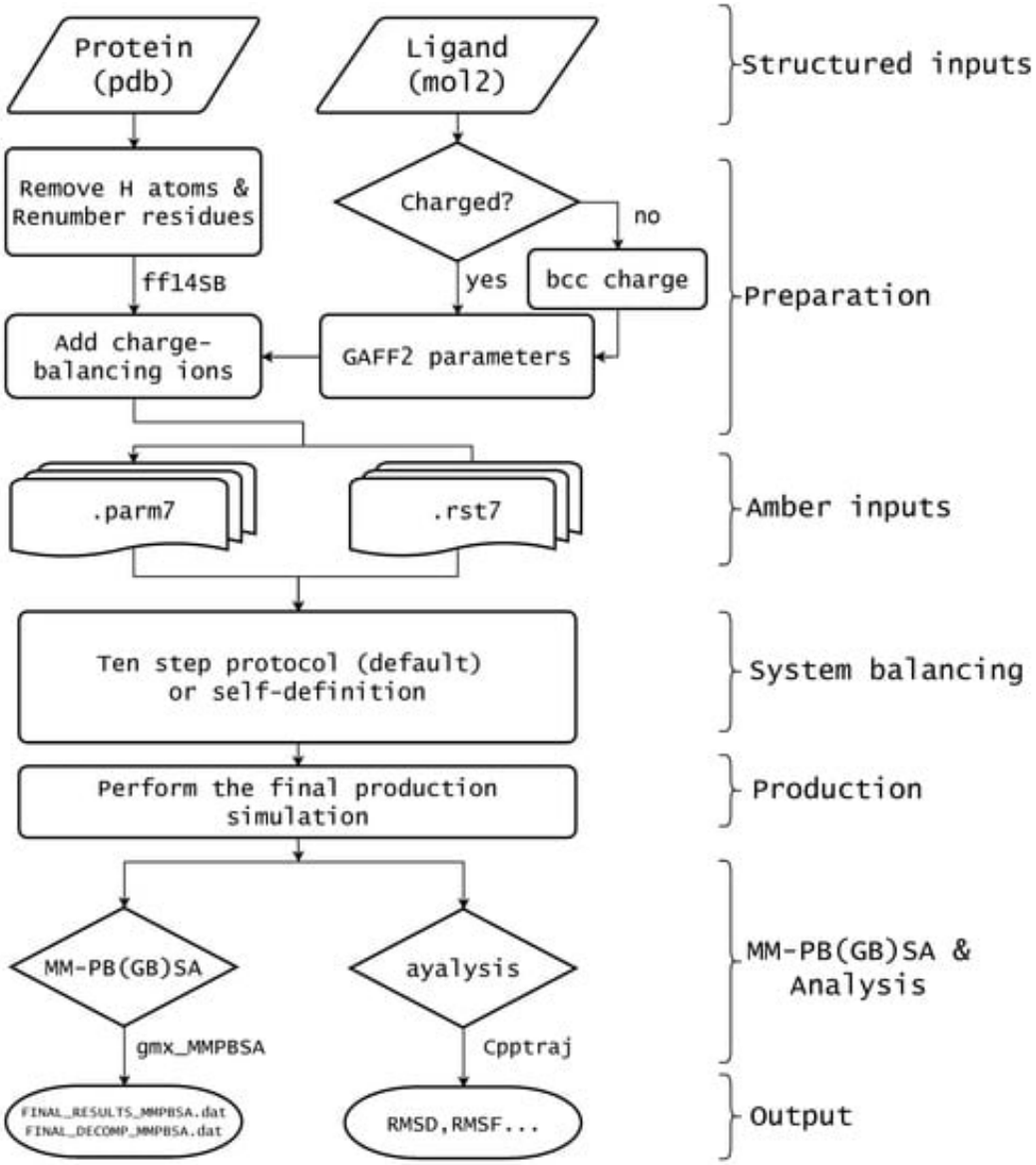


Figure 6. A flowchart scheme of the input and output files of AMBER [7]

2. FUTURE GOALS

I am a first-year PhD student at the International Sakharov Environmental Institute of Belarusian State University and a junior researcher at the Institute for Nuclear Problems of Belarusian State University. My research focuses on exploring the production methods of boron-nitride quantum dots (BNQDs) and investigating their wide-ranging applications.

BNQDs are zero-dimensional nanomaterials with a graphene-like structure forming six-membered rings comprising of boron and nitrogen atoms. They have unique photophysical properties and exhibit potential applications in visualizing biological processes or tumor biology in vivo, facilitating diagnosis and staging of tumors, aiding in therapy planning, and offering targeted treatment for specific types of tumors.

MD simulation can be useful in exploring the size, shape, surface chemistry, electronic band structure, and optical properties of BNQDs. In addition, this technique will be helpful in investigating the effects of surface functionalization, doping, or modifications on the properties and behavior of nanomaterials. Also, it can be used to simulate interactions with different functional groups or substrates to explore possibilities for tuning their electronic and chemical properties. Understanding the structure-property relationships is crucial for tailoring these quantum dots for applications in electronics, photonics, and optoelectronics.

Moreover, exploring the mechanisms underlying the permeation of BNQD through cell membranes is key for the practical application of such nanomaterials in medicine. The permeation process of nanomaterials through different lipid membranes can be evaluated using MD simulations [8].

I possess a high level of proficiency in laboratory practical techniques. I am confident that the knowledge I gain from this project in MD modeling will significantly enhance my scientific capabilities in this research topic.

CONCLUSIONS

MD simulations play a pivotal role in elucidating the behavior and properties of molecular systems. Employing computational algorithms grounded in classical mechanics, these simulations bridge the gap between microscopic details and macroscopic observations. By leveraging techniques such as the integration of Newton's equations of motion, molecular dynamics enables the exploration of molecular interactions, structural changes, and dynamic behaviors within diverse systems, encompassing biochemical, chemical, and material sciences. This project provides a concise overview of the principles underlying MD simulations, emphasizing their instrumental role in studying the intricacies of molecular systems, understanding their thermodynamic properties, and guiding future research and applications across various scientific domains.

To sum up, MD simulations are a powerful tool for understanding how tiny particles behave. They help us see how molecules interact and change over time. These simulations are essential in chemistry, biology, and making new materials and medicines. By improving our computer methods, we keep learning more and using this knowledge to make new discoveries and better technology.

ACKNOWLEDGEMENTS

I am grateful to the INTEREST program for granting us an excellent opportunity to broaden our knowledge and gain experience through collaboration with esteemed researchers. I am also appreciative of my supervisor, Professor Kholmirzo Kholmurodov, for allowing me the privilege of joining this project and for providing invaluable guidance and support. His teaching approach and provision of necessary educational materials have been instrumental in maximizing the benefits I derived from this project.

REFERENCES

[1] Hollingsworth S. A., Dror R.O. Molecular Dynamics Simulation for All // Neuron. – 2018. – Vol. 99(6). – P. 1129–1143. doi: 10.1016/j.neuron.2018.08.011.

[2] Kholmurodov K. MD-simulation in chemical research: from atomic fragments to molecular compound (materials provided by the supervisor).

[3] Padhi A. K., Janežič M., Zhang K. Chapter 26 - Molecular dynamics simulations: Principles, methods, and applications in protein conformational dynamics / Editor(s): Tripathi T. and Dubey V. K. // Advances in Protein Molecular and Structural Biology Methods, Academic Press. – 2022. – P. 439–454. doi: 10.1016/B978-0-323-90264-9.00026-X.

[4] Salo-Ahen O. M., et al. Molecular Dynamics Simulations in Drug Discovery and Pharmaceutical Development // Processes. – 2021. – Vol. 9. – P. 71. doi: 10.3390/pr9010071.

[5] Smith W., Todorov I. T. A short description of DL_POLY // Molecular Simulation. – 2006. – Vol. 32. – P. 935–943. doi:10.1080/08927020600939830.

[6] Case D. A., et al. The Amber biomolecular simulation programs // J Comput Chem. – 2005. – Vol. 26. – P. 1668–1688.

[7] Zhang Z.-W., Lu W.-C. AmberMDrun: A Scripting Tool for Running Amber MD in an Easy Way // Biomolecules. – 2023. – Vol. 13. – P. 635. doi: 10.3390/biom13040635.

[8] Zhang P., et al. Molecular dynamics simulation of transport mechanism of graphene quantum dots through different cell membranes // Membranes. – 2022. – Vol. 12. – P. 753. doi: 10.3390/ membranes12080753.