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)

Supervisor:

Prof. Dr. Kholmirzo Kholmurodov

Student:

Sofija Stanimirović, Faculty of Physical Chemistry, University of Belgrade, Serbia

Participation period:

March 03 – April 20, Wave 12

Dubna, 2025

Contents

Abstract

The use of molecular dynamics (MD) simulation in the investigation of biomimetic chromatography systems is examined in this report. MD offers in-depth understanding of atomic-level interactions and dynamic behavior by resolving Newton's equations of motion for molecular systems. The report highlights simulation techniques, talks about popular MD software, and shows how these tools can be used to model molecular interactions and retention mechanisms in biomimetic settings. This study highlights how MD simulations can contribute to the logical design of analytical systems and enhance our comprehension of molecular behavior in biologically inspired chromatographic processes through both theoretical and practical engagement.

1. Introduction

In current scientific research, molecular dynamics (MD) simulation has become a potent computational technique that makes it possible to thoroughly examine matter at the atomic and molecular scale. MD simulations offer a time-resolved description of atom and molecular behavior by solving Newton's equations of motion for systems of interacting particles. This enables the investigation of complex systems' structural, thermodynamic, and kinetic characteristics. This method is based on well-defined force fields that characterize the potential energy landscape governing atomic interactions and is rooted in classical mechanics. Because of this, MD simulations provide a solid, physics-based framework for examining phenomena that are frequently unavailable through pure theoretical or experimental methods.

The ability of molecular dynamics to close the gap between macroscopic observations and microscopic interactions is what makes it valuable. MD simulations can capture fast atomic motions by using very small time steps, usually on the order of a few femtoseconds. Depending on the computational resources available, the cumulative simulation time can reach nanoseconds, microseconds, or even longer. Important biological and physicochemical processes, including protein folding, conformational transitions, ligand-receptor binding, membrane dynamics, solvation effects, and ion transport, can be observed in real time by researchers thanks to this temporal resolution.

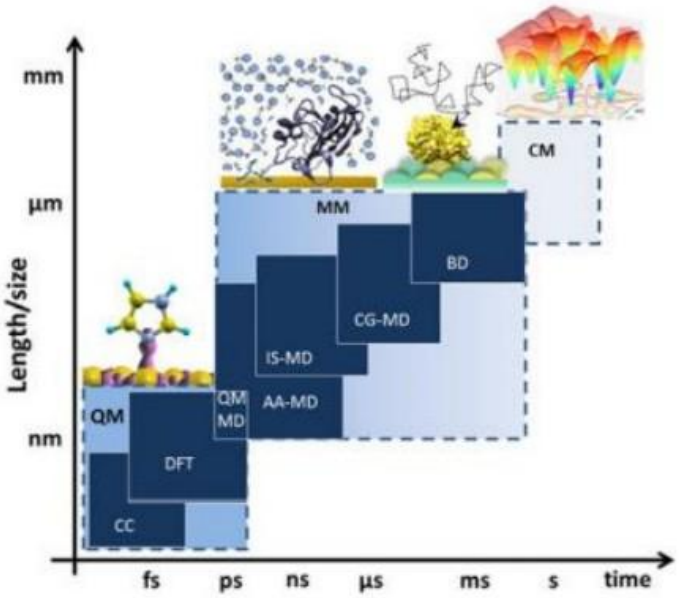

Figure 1. Typical time and length scales of different simulation techniques

The use of computer simulations in the biological and physical sciences has grown dramatically in the last few decades. Together with theory and experiment, they are now seen as a third essential pillar of scientific discovery rather than just auxiliary instruments. Individual mechanisms in complex systems can be isolated and studied thanks to the controlled environment provided by computational simulations, which allow for the systematic manipulation of particular variables. Additionally, the use of molecular dynamics has become more accessible across a wide range of fields, including structural biology, chemical physics, materials science, and

pharmaceutical sciences, thanks to the development of advanced software packages and the growing availability of high-performance computing infrastructure.

MD simulations are now essential for comprehending the dynamic behavior of biomolecules in the fields of computational chemistry and biophysics. They make it possible to characterize binding affinities, investigate reaction pathways at the molecular level, and clarify conformational changes in proteins. When studying systems with limited experimental resolution or when it is difficult to observe dynamic processes directly, these simulations are especially helpful. MD simulations provide predictive insight and direct additional experimental research by forecasting how a molecular system will react to perturbations like mutations, ligand interactions, pH changes, or temperature changes.

In the context of this project, molecular dynamics simulation was employed to explore the potential of MD methodologies in biomimetic chromatography and related fields. Through hands-on engagement with simulation software and theoretical instruction, the project aimed to demonstrate how MD techniques can be utilized to study complex molecular interactions relevant to analytical chemistry and drug discovery. The investigation involved the use of established MD packages such as DL_POLY and AMBER, with a focus on understanding how simulation outputs can be used to model and predict molecular behavior within artificial chromatographic systems that mimic biological environments.

2. The basic equations

2.1. Equations of motion and potential

Molecular dynamics (MD) simulations rely on Newton's equations of motion to describe the evolution of atomic and molecular systems over time. Newton's second law is expressed as:

$$F_i = m_i a_i$$

where F_i is the force acting on an atom , m_i is its mass, a_i and is its acceleration. The forces arise from interatomic interactions and are computed using molecular mechanics (MM) force fields such as FF94 or FF99SB. The force F_i is derived from the potential energy function V as:

$$F_i = -\nabla_i V$$

Numerical integration of Newton's equations generates atomic trajectories, providing insights into molecular motion, energy distribution, and system dynamics. The governing differential equation is:

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

where r_i represents atomic coordinates. This equation is solved iteratively to predict atomic movements while conserving momentum and energy.

Newton's third law also applies, ensuring conservation of linear momentum:

$$F_1 = -F_2$$

These principles allow MD simulations to reveal dynamic molecular behaviors crucial for chromatography studies.

2.2. Potential energy

The potential energy function is essential for figuring out how a system will behave at the atomic level in molecular dynamics (MD) simulations. By taking into account various kinds of interactions within the molecular system, the force field employed in these simulations approximates the total potential energy. The AMBER force field, which simulates potential energy as a function of bonded and non-bonded interactions, is one of the most widely used force fields. Bonded interactions and non-bonded interactions are the two primary components that make up the total potential energy in molecular systems. Van der Waals forces and electrostatic (Coulomb) interactions are examples of non-bonded interactions, whereas bond stretching, bond-angle bending, and torsional (dihedral) interactions are examples of bonded interactions. Both intramolecular (covalent) and intermolecular forces are reliably represented in the force field calculations thanks to this decomposition.

The deviation of two bonded atoms from their equilibrium bond length is referred to as bond stretching. A harmonic potential, in which the energy rises quadratically with the departure from the equilibrium bond length, is used to model this interaction in the majority of force fields. Extreme stretching or bond breaking, which may call for more complicated potential functions, are where this harmonic approximation falls short. It performs well for small deviations. The following formula represents the bond stretching potential energy:

$$V_{bond} = \sum_{i,j} K_b \left(r_{ij} - r_{ij}^{eq}\right)^2$$

where K_b is the bond force constant, r_{ij} is the bond length between atokms i and j, and r_{ij}^{eq} is the equilibrium bond length.

In the same manner, variations from the ideal bond angle between three covalently bonded atoms are explained by angle bending. A harmonic function, in which the energy rises as the angle deviates from the equilibrium value, is frequently used to depict it. This bending interaction's energy can be written as follows:

$$V_{angle} = \sum_{i,j,k} K_\theta \left(\theta_{ijk} - \theta_{ijk}^{eq}\right)^2$$

where K_θ is the force constant for angle bending, θ_{ijk} is the bond angle between atoms i, j, and k, and θ_{ijk}^{eq} is the equilibrium bond angle.

The energy involved in one part of a molecule rotating relative to another about a bond is known as torsional (dihedral) interaction. A periodic potential, which characterizes the numerous minima present in the torsional potential energy surface, is commonly used to model this kind of interaction. Torsional interactions' energy contribution can be expressed as follows:

$$V_{tors} = \sum_{i,j,k,l} V_n \left(1 + \cos\left(n\varphi_{ijkl} - \varphi_{ijkl}^{eq}\right)\right)^2$$

where V_n is the barrier height for the torsional potential, n is the number of minima (which dictates the periodicity), φ_{ijkl} is the torsion angle between atoms i, j, k, and l, and φ_{ijkl}^{eq} is the equilibrium torsion angle.

When simulating interactions between atoms or groups of atoms that are not directly bonded to one another but are in close proximity, non-bonded interactions are crucial. Van der Waals (Lennard-Jones) and electrostatic (Coulomb) interactions are the two most important non-bonded interactions.

Electrostatic interactions arise from the attraction or repulsion between charged particles and are modeled using Coulomb’s law:

$$V_{Coul} = \sum_{i,j} \frac{q_i q_j}{4\pi\epsilon_o r_{ij}}$$

where q_i and q_j are the partial charges of atoms i and j, r_{ij} is the distance between the two atoms, and ϵ_o is the permittivity of free space.

The total potential V_{Total} energy for a molecular system can be expressed as the sum of these bonded and non-bonded interactions:

$$V_{Total} = V_{bonded} + V_{non-bonded}$$

where the bonded interactions are the sum of bond stretching, angle bending, and torsional terms:

$$V_{bonded} = V_{bond} + V_{angle} + V_{tors}$$

And the non-bonded interactions are given by:

$$V_{non-bonded} = V_{VdW} + V_{Coul}$$

These equations allow for the modeling of molecular systems, ranging from simple molecules to more complex biomolecules like proteins and nucleic acids.

2.3. Lennard-Jones potential

A key idea in molecular dynamics (MD) simulations, the Lennard-Jones (LJ) potential is used extensively in a variety of disciplines, including chemistry, physics, biology, and mechanics, to simulate interactions between molecular species. For simple molecules and atomic interactions in particular, it offers a useful method of reflecting the fundamental physics of intermolecular forces. Although the conventional LJ potential is widely used, it should be noted that it is based on a century-old method and contains a somewhat arbitrary repulsion exponent, the r^{-12} term, which has been criticized in recent years.

A pairwise interaction potential with both repulsive and attractive components is commonly referred to as the LJ potential. The short-range repulsion that happens when two molecules' electron clouds overlap is represented by the repulsive term. Because the electrons are no longer protecting the positively charged nuclei, a force pushes the molecules apart, causing this repulsion. This repulsive term is represented as an exponential function in certain representations:

$$U_{rep} = Aexp(-BR)$$

where A and B are constants specific to the interacting species and must be determined experimentally. However, a more general approach uses a term that decays as r^{-12}, leading to the well-known Lennard-Jones potential:

$$U_{LJ}(r) = \frac{C_{12}}{r^{12}} - \frac{C_6}{r^6}$$

Here, C_{12} and C_6 are constants that also need to be determined from experimental data for the particular molecular species. The attractive part of the potential is modeled with the r^{-6} term,

which represents the van der Waals forces, such as London dispersion forces, while the repulsive part is modeled by the r^{-12} term.

For practical use, the Lennard-Jones potential is often written in a more convenient form:

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

In this equation, σ is the distance at which the potential is zero, and ϵ is the well depth, which is equivalent to the minimum energy of interaction. The strength and range of the intermolecular forces are revealed by the two parameters, ϵ and σ, which are unique to each interacting species. These parameters are frequently calculated for a broad range of atoms and molecules and can be determined experimentally or through quantum mechanical computations.

A key component of the study of liquid systems, the LJ potential offered a good approximation of the interatomic forces in the early studies of the properties of liquid argon. For computational efficiency, the LJ potential in MD simulations is usually shifted upwards and truncated at the potential's minimum position, particularly in systems where excluded volume effects, rather than the attractive forces, are the main focus. For applications where the emphasis is on molecular packing rather than intermolecular bonding, this modification, known as the Weeks-Chandler-Andersen (WCA) potential, retains the repulsive aspect of the LJ potential while eliminating the attractive portion.

In some systems, particularly those involving charged species, the LJ potential is supplemented by Coulombic interactions. The Coulombic potential accounts for the long-range electrostatic forces between charged particles and is given by:

$$V_{Coulomb}(r) = \frac{Q_1 Q_2}{4\pi\epsilon_0 r}$$

where Q_1 and Q_2 are the charges on the interacting particles, ϵ_0 is the permittivity of free space, and r is the distance between the particles. The inclusion of Coulombic interactions is crucial in simulations of systems involving polyelectrolytes, biomolecules, or ionic liquids, where electrostatic forces play a dominant role.

3. Temperatures and pressure control

Controlling the temperature and pressure in molecular dynamics (MD) simulations is essential for faithfully simulating actual experimental conditions. Specialized algorithms called thermostats and barostats are used to maintain constant temperature and pressure in simulations because many physical and chemical processes take place at these levels.

In order to create a statistical ensemble at a regulated temperature, thermostats alter the Newtonian equations of motion. Thermostats make sure that the temperature fluctuates around a desired average rather than fixing it rigidly because in MD, temperature is directly correlated with the average kinetic energy of particles ($\langle K \rangle \propto T$). For this, a number of algorithms have been created:

- The Berendsen Thermostat relaxes the system toward the desired temperature over a characteristic time by coupling it to an external heat bath and applying a weak scaling factor to the particle velocities. Although it doesn't create a proper canonical (NVT) ensemble, it works especially well with macromolecules like proteins.
- Nose-Hoover Thermostat: This algorithm allows the system to equilibrate while saving energy by adding an extra artificial degree of freedom that simulates the effect of a heat bath. The Nose-Hoover thermostat is better suited for small systems where energy conservation is crucial because it produces a proper canonical ensemble, in contrast to the Berendsen thermostat.
- The Langevin thermostat simulates the stochastic interactions between the system and an implicit heat reservoir by adding a friction coefficient and random forces to the equations of motion. In biomolecular simulations, where solvent effects must be approximated, it is especially helpful.

Each of these thermostats has its advantages and limitations, with the choice depending on the nature of the system under study and the desired level of ensemble accuracy.

In addition to temperature, pressure control is essential for simulating systems under realistic environmental conditions. The pressure in a classical many-body system is computed using the Clausius virial theorem:

$$P = \frac{2}{3V}(K - \Xi)$$

where K is the kinetic energy, and Ξ is the virial term, which depends on the interatomic forces and distances. By modifying Ξ, barostats adjust the system's volume or particle momenta to maintain a target pressure. Some widely used barostat algorithms include:

- Like its thermostat equivalent, the Berndsen Barostat uses a weak coupling technique to gradually change the system's volume in order to raise the pressure to the required level. Although it does not generate a proper isothermal-isobaric (NPT) ensemble, it is computationally efficient.
- Parrinello-Rahman Barostat: This technique treats the simulation box as a dynamic variable that varies in response to pressure changes, extending the concept of the Nose-Hoover

thermostat to pressure control. It is especially helpful for materials under mechanical stress and anisotropic systems.

The choice of thermostat and barostat depends on the simulation goals. For equilibration, weak coupling methods like Berendsen are often preferred due to their efficiency. However, for rigorous statistical sampling, Nose-Hoover and Parrinello-Rahman methods provide more accurate ensemble distributions.

By integrating thermostats and barostats, MD simulations can accurately reproduce experimental conditions, making them powerful tools for studying molecular behavior under controlled thermodynamic states.

4. Boundary conditions

Since they dictate how atoms and molecules interact at the edges of a finite simulation box, boundary conditions are essential to molecular dynamics (MD) simulations. Because MD simulations only simulate a small number of particles in a small area, improper boundary effect management can result in large artifacts that distort the results from actual bulk-phase behavior. Periodic Boundary Conditions (PBCs), which enable the simulation to approximate an effectively infinite system, are frequently used to address this problem.

Atoms at the edges of a simulation that is contained within a finite box encounter forces that differ from those at the center. This occurs as a result of an artificial imbalance in intermolecular interactions caused by the absence of neighboring atoms on one or more sides. Furthermore, an atom would normally be lost from the system if it moved outside the simulation box, causing density fluctuations and upsetting equilibrium characteristics. It is challenging to derive useful macroscopic properties from MD simulations because of these effects.

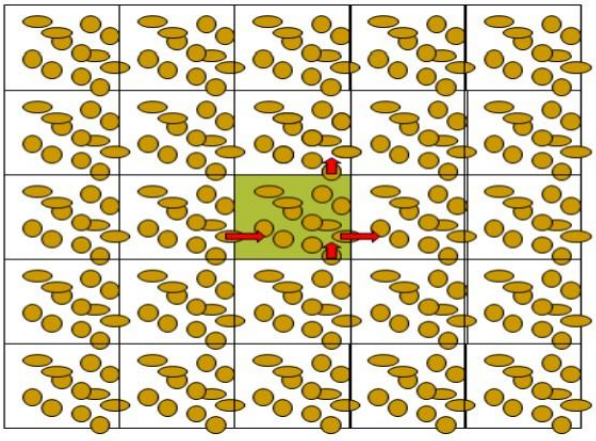

Figure 2. Periodic boundary conditions in MD modeling

PBCs address these problems by creating an infinite tiling of the system by replicating the main simulation cell in all three dimensions. In the adjacent virtual boxes, every atom in the simulation box has an identical counterpart. This keeps the number of particles in the main simulation cell constant by ensuring that when an atom leaves one side of the box, an identical

image enters from the other side. The system can act as though it were a part of a much larger material because all atoms experience a uniform environment, which lessens finite-size effects.

One of the main benefits of PBCs is that they enable interaction between atoms in the simulation cell and their periodic images in nearby cells, in addition to other atoms inside the box. In contrast to a finite, isolated system, this guarantees that intermolecular forces stay constant across boundaries, more closely resembling bulk properties found in the real world.

Although PBCs successfully remove boundary effects, they also present a computational difficulty because, in theory, each atom in the replicated simulation space has an infinite number of interaction partners because the system is periodically replicated. It would be computationally impossible to calculate each of these interactions directly. This problem is solved by introducing a cutoff radius (R_c) beyond which intermolecular forces are disregarded.

Van der Waals forces are described by Lennard-Jones (L-J) interactions, where the potential rapidly diminishes with distance. This permits a useful truncation at a specified cutoff distance, usually between 7 and 8 Å, after which the interaction is deemed insignificant. But when the potential is abruptly cut off at R_c, two issues arise: the potential function becomes discontinuous, resulting in unphysical forces at the cutoff distance, and energy conservation is violated because interactions beyond the cutoff are abruptly eliminated rather than fading out gradually. Potential shifting and smoothing functions are used to lessen these problems. While smoothing functions alter the force calculation to avoid abrupt energy jumps, potential shifting makes sure that the potential energy smoothly approaches zero at R_c. The accuracy and stability of MD simulations are preserved in part by these adjustments.

Electrostatic interactions, like Coulombic forces between charged particles, decay with distance substantially more slowly than Van der Waals forces. In biological and polymer simulations, where long-range charge interactions are essential for establishing molecular structure and behavior, merely applying a cutoff truncation to these interactions can result in substantial errors.

Ewald summation is used to precisely calculate long-range electrostatic interactions under PBCs. By dividing the electrostatic potential into real-space and reciprocal-space components, this technique makes it possible to compute long-range interactions quickly. The following represents the total Coulombic energy:

- A short-range real-space sum, which is computed directly within a certain cutoff distance.
- A long-range reciprocal-space sum, which is computed in Fourier space to account for interactions beyond the cutoff.
- A self-interaction correction term, which ensures that each charge does not interact with its own periodic images in the replicated cells.

A key component of MD simulations, boundary conditions have a direct impact on the precision and realism of the outcomes. Periodic Boundary Conditions (PBCs) are frequently used to effectively simulate bulk-phase materials and remove surface effects. Nevertheless, managing intermolecular interactions in PBCs calls for careful thought. Long-range electrostatic forces

require more complex methods, such as Ewald summation, to ensure accurate modeling, whereas cutoff truncation works well for short-range Lennard-Jones interactions. MD simulations can produce dependable and physically significant results for a variety of physics, chemistry, and biological applications by carefully implementing boundary conditions and interaction handling techniques.

5. Software and methods

To simulate how atoms and molecules behave under specific physical conditions, molecular dynamics (MD) simulations use specialized computer software. Many simulation packages have been created over time, each intended to handle a distinct facet of MD modeling, ranging from materials science applications to biomolecular simulations.

AMBER, DL_POLY, NAMD, GROMACS, LAMMPS, and CHARMM are a few popular MD software programs. The approaches, computational efficiency, and optimization for particular molecular systems of these programs vary. Although each piece of software has unique benefits, they all aim to solve the Newtonian equations of motion for a particular molecular system and reveal information about its kinetic and thermodynamic characteristics.

For the purposes of this program, we mainly concentrated on DL_POLY and AMBER, two popular tools for classical molecular dynamics simulations with proven frameworks for managing a variety of molecular systems.

- W. Smith and associates created the general-purpose MD simulation program DL_POLY at Daresbury Laboratory. It is especially useful for simulating a wide variety of molecular systems, such as complex biochemical macromolecules, polymers, ionic compounds, and simple atomic structures. Because of its great scalability, DL_POLY can run in parallel on clusters of high-performance computers.
- The suite of applications known as AMBER (Assisted Model Building with Energy Refinement) was created mainly for biomolecular simulations. AMBER, which was first created in the late 1970s, contains a collection of force fields that are frequently used in molecular modeling. It is a well-liked option for researching proteins, nucleic acids, and small organic molecules because of its capabilities, which include energy minimization, molecular dynamics simulations, and free energy calculations.

The particular needs of a study, such as system size, required accuracy, and computational resources, determine which MD simulation program is best. DL_POLY offers a flexible platform for researching a variety of molecular systems, whereas AMBER is best suited for biomolecular simulations. Researchers can improve chemistry, materials science, and biophysics by employing these tools to obtain important insights into atomic-level molecular behavior.

6. Application of MD simulation in biomimetic chromatography research

A thorough, atomistic perspective of the interactions taking place in biomimetic chromatography is offered by molecular dynamics (MD) simulations. In order to optimize chromatographic conditions, MD helps clarify retention mechanisms, solvent effects, and analyte-stationary phase interactions by simulating molecular motion over time.

Using hydrophilic interaction liquid chromatography (HILIC), affinity chromatography, or other specialized stationary phases, biomimetic chromatography frequently replicates biological interactions. Researchers can identify non-covalent interactions that contribute to retention, such as hydrogen bonding, van der Waals forces, and electrostatic interactions, as well as investigate how changes to the stationary phase impact separation performance, with the aid of MD simulations. For instance, MD can show how changing the acetonitrile (AcN) content affects solute partitioning and retention in non-aqueous HILIC systems.

Chromatographic separations depend heavily on the composition of the solvent, particularly in biomimetic systems where interactions are influenced by buffer solutions, organic solvents, or water. By examining solvent-analyte interactions, MD simulations enable researchers to optimize mobile phase compositions, observe how changes in solvent polarity impact molecular binding, and explore the solvation shell surrounding analytes and stationary phase ligands. For example, designing a peptidebased ligand for the purification of human serum albumin (HSA) can be done using molecular docking and molecular dynamics (MD) simulation (Aghaee, 2014).

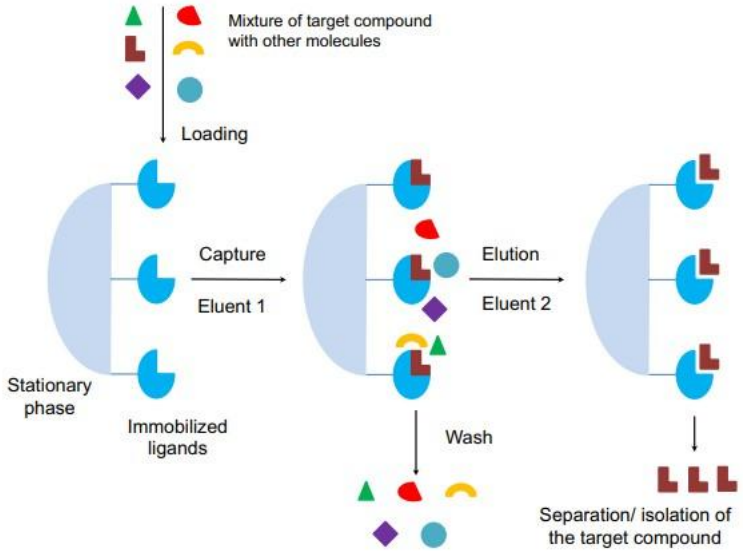

Figure 3. Flowchart of the afnity chromatography process

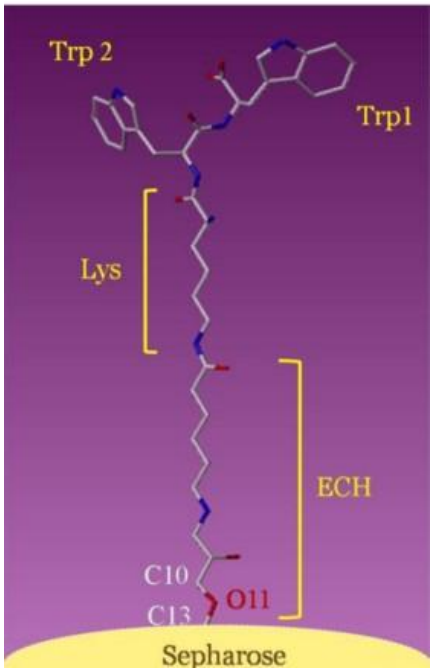

Figure 4. Hypothesized structure if solid phase

MD simulations aid in the prediction of chromatographic selectivity by modeling the interaction energies between analytes and biomimetic stationary phases. While enhanced sampling techniques like metadynamics enable researchers to investigate uncommon binding events that affect retention, computational techniques like Free Energy Perturbation (FEP) and Molecular Mechanics/Poisson-Boltzmann Surface Area (MM-PBSA) aid in quantifying binding free energies. By fine-tuning ligand-stationary phase interactions, molecular docking followed by MD refinement enhances predictions. These techniques aid in the logical design of biomimetic phases by correlating retention factors with molecular characteristics.

Machine learning and statistical modeling techniques can be used to integrate MD results with experimental data in order to validate chromatographic models. Principal Component Analysis (PCA) assists in classifying analytes according to their molecular interactions in simulations, while Genetic Algorithm-Multiple Linear Regression (GA-MLR) and Genetic Algorithm-Support Vector Machine (GA-SVM) employ descriptors derived from MD to forecast retention behavior. Predictive models that can direct the choice of mobile and stationary phases for the best chromatographic performance can be developed thanks to this integration.

Coarse-grained MD is used to simulate large biomolecules in affinity chromatography; AI-driven MD simulations are used to predict optimal chromatographic conditions based on large-scale MD datasets; and Quantum Mechanics/Molecular Mechanics (QM/MM) hybrid simulations are used to describe electronic effects in chromatographic interactions more precisely. By using these cutting-edge methods, MD simulations will keep improving chromatographic methods, increasing the effectiveness and precision of biomimetic separations.

Acknowledgment

I would like to express my sincere gratitude to my project supervisor, Prof. Dr. Kholmirzo Kholmurodov, for his invaluable guidance, and dedicated mentorship throughout this project. His insightful lectures, thorough explanations, and patient teaching style made the complex topic of molecular dynamics simulation both approachable and inspiring.

My heartfelt thanks also go to the INTEREST Programme Team for organizing such an enriching online scientific initiative. Their dedication to making high-level research accessible across borders has not only broadened my academic experience but also strengthened my ability to work in a remote scientific setting.

Refrences

1. Kholmurudov K. *MD Simulation in Chemical Research:From Atomic Fragments to Molecular Compounds*.

2. Hinchliffe A. *Molecular Modelling for Beginners*. Wiley; 2003.

3. Rapaport DC. *The Art of Molecular Dynamics Simulation*. 2nd ed. Cambridge University Press; 2004.

4. Computational soft matter: from synthetic polymers to proteins. 2: Lecture notes. In: NIC series. NIC; 2004.

5. Fang YM, Lin DQ, Yao SJ. Review on biomimetic affinity chromatography with short peptide ligands and its application to protein purification. *J Chromatogr A*. 2018;1571:1-15. doi:10.1016/j.chroma.2018.07.082

6. Wang RZ, Lin DQ, Chu WN, Zhang QL, Yao SJ. New tetrapeptide ligands designed for antibody purification with biomimetic chromatography: Molecular simulation and experimental validation. *Biochem Eng J*. 2016;114:191-201. doi:10.1016/j.bej.2016.06.030

7. Aghaee E, Ghasemi JB, Manouchehri F, Balalaie S. Combined docking, molecular dynamics simulations and spectroscopic studies for the rational design of a dipeptide ligand for affinity chromatography separation of human serum albumin. *J Mol Model*. 2014;20(10):2446. doi:10.1007/s00894-014-2446-7

8. Tsopelas F, Stergiopoulos C, Danias P, Tsantili-Kakoulidou A. Biomimetic separations in chemistry and life sciences. *Microchim Acta*. 2025;192(3):133. doi:10.1007/s00604-025-06980-x