Computational Simulation Of Electromagnetic Effect On Magnetic Alginate Nanosphere: Molecular Dynamics Approach

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ABSTRACT
Alginate-based nanoparticles are a promising substrate for a number of applications owing to their biocompatibility, biodegradability, and ability to encapsulate a broad range of chemicals. A number of studies were used to understand the simulation findings of magnetic alginate-based nanoparticles, which we refer to as alginosomes. The MD simulation was applied in the NVT ensemble for a set period of time to collect trajectory data for analysis, which comprised total and potential energy parameters, RDF, and RMSD, all of which were computed using the DERIDING forcefield. The LAMMPS software tool was used to simulate an external electromagnetic field and calculate atomic behavior, Nano stability, and the disintegration process. The simulation findings showed that the total energy of the magnetic alginosome converged to -7479 kcal/mol . At the same time, the zeta potential of the Nano system reached -0.45 mV in response to an external electromagnetic field during an exothermic process. In addition, the size and form of magnetic nanoparticles in MD simulation may have a considerable impact on the RDF of a magnetic alginate-based nanosphere. Finally, the discovery of magnetic alginate-based nanoparticles has revealed their behavior. It may be used to drive the design process for improving their performance in a number of biological applications. It can provide useful insights into the behavior of magnetic nanoparticles under a range of situations, as well as aid in the optimization of nano-system techniques.

Keywords: alginosome, Molecular Dynamics, LAMMPS.

INTRODUCTION

In recent years, there has been significant interest in alginate's potential as a medicinal material. Alginate, a naturally occurring polysaccharide extracted from brown seaweed, has garnered considerable attention in the field of biomedical engineering due to its remarkable properties. Its biocompatibility, biodegradability, and ability to form hydrogels make alginate an ideal candidate for various applications, particularly in drug delivery systems. Alginate-based hydrogels can effectively encapsulate therapeutic agents, providing controlled release and enhancing the stability of drugs in physiological environments. The combination of alginate and magnetic nanoparticles creates a powerful platform for advancing drug delivery and nanomedicine. This composite system not only facilitates targeted delivery of therapeutic agents but also enables controlled release mechanisms that can be tailored to meet specific therapeutic needs. For instance, in cancer treatment, alginate-coated MNPs can deliver chemotherapeutic drugs directly to tumor sites while simultaneously generating localized heat through magnetic hyperthermia, thereby improving treatment outcomes. In recent years, magnetic alginate nanoparticles (MANPs) have attracted substantial scientific attention due to their potential applications in MRI contrast agents, hyperthermia treatment, and medication administration. MANPs are a compelling choice for targeted medication administration and imaging applications due to their unique magnetic properties. [1-4].
MANPs are designed and optimized for numerous biological applications through MD simulations, which offer a comprehensive understanding of their atomic behavior. MANPs can be produced by integrating magnetic nanoparticles with alginate nanoparticles. The magnetic properties of MANPs are determined by the type and dimensions of the magnetic nanoparticles employed, as well as their dispersion within the alginate matrix. The physical and chemical properties of alginate, such as its swelling behavior, mechanical strength, and degradation rate, may be influenced by the integration of magnetic nanoparticles. The incorporation of MD simulations to investigate the impact of

electromagnetic fields on magnetic alginate marks a notable progression in material science and nanotechnology. Magnetic alginate, a composite created by embedding magnetic nanoparticles within alginate matrices, possesses distinctive characteristics that render it advantageous for various applications. The electromagnetic fields can induce various physical and chemical changes in magnetic alginate, affecting its structural integrity, mechanical properties, and functional capabilities. Studies have shown that exposure to electromagnetic radiation can lead to alterations in the conformation of alginate chains, influencing their interaction with embedded magnetic nanoparticles. This interaction is critical in applications where controlled drug release or targeted delivery is required. The molecular simulation of electromagnetic effects on magnetic alginate is a promising area of research that holds significant potential for advancing various applications in medicine and environmental science. By utilizing MD techniques, researchers can gain a deeper understanding of the interactions at play, leading to the development of more effective drug delivery systems, enhanced environmental remediation strategies, and innovative tissue engineering solutions. As the field continues to evolve, integrating computational methods with experimental approaches will be essential for unlocking the full potential of magnetic alginate materials. In tissue engineering, magnetic alginate scaffolds can be engineered to react to external stimuli, thereby facilitating cell adhesion and proliferation. Evaluating the electromagnetic effects via MD simulations can guide the development of scaffolds that replicate the characteristics of the natural extracellular matrix, thereby improving cellular interactions and promoting tissue regeneration. MD simulation may offer information regarding the structure, dynamics, and thermodynamics of MANPs, as well as their interactions with other molecules or surfaces. Various computer approaches, such as MD simulations, Monte Carlo simulations, and finite element analysis, can be employed to simulate external fields at magnetic nanoparticles. Thermodynamic characteristics associated with alginate interactions and phase transitions can be determined through Monte Carlo simulations. By simulating a variety of variables (such as temperature and concentration), researchers can obtain free energy, enthalpy, and entropy changes. These changes are essential for comprehending the behavior of alginate in various formulations. The stability and release behavior of drug-laden materials can also be assessed using computational simulations. Researchers employed MD simulation to investigate the release of doxorubicin from MANPs at a variety of pH levels. Alginate hydrogels are extensively utilized in the field of tissue engineering, primarily because of their favorable biocompatibility. Evaluating the impact of electromagnetic fields can guide the development of alginate scaffolds that are responsive to external stimuli, thereby enhancing cellular proliferation and differentiation. MD simulation can be employed to assess the mechanical characteristics of alginate in different electromagnetic environments, ensuring that these scaffolds effectively replicate the properties of the natural extracellular matrix.

There is a scarcity of literature specifically examining molecular dynamics simulations that consider the effects of electromagnetic fields on magnetic alginate. Most current research emphasizes the properties of alginate and its interactions with magnetic nanoparticles, yet it fails to explore the molecular dynamics dimension in the context of electromagnetic effects. For example, a study from recently reviews the integration of magnetic nanoparticles within alginate hydrogels, which facilitates unique motion patterns when exposed to magnetic fields, but lacks in providing comprehensive insights into molecular dynamics [15-18] By simulating the behavior of magnetic alginate nanospheres under electromagnetic influence, researchers can gain insights into their structural stability, mechanical properties, and response to external stimuli. MD allows for exploring various parameters such as temperature, pressure, and electromagnetic field strength, providing a comprehensive understanding of the nanosphere's behavior. In this computational study, we will examine the intricacies of an MD simulation of alginate nanoparticles to gain insight into their atomic behavior. Magnetic alginate, which combines the biocompatibility of alginate with the magnetic properties of nanoparticles, offers unique advantages for various applications. The versatility of magnetic alginate in Nano systems is enhanced by its responsiveness to external stimuli through the utilization of MD simulation.

Computational Simulation Details

The LAMMPS (Large-scale Atomic/Molecular Massively Parallel Simulator) 2021 package, a software that is widely used for its high accuracy and efficiency in simulating diverse molecular systems, is the subject of this computational study. The MD simulation of magnetic alginate Nanosphere was carried out. The Following stages, atomic configuration setup: Fig.1 illustrates the process of employing alginate monomer (PubChem CID 91666318) to generate the alginate nanoparticle, which is subsequently modified using VMD and Avogadro to reduce its energetics. The iron oxide nanoparticles were placed in a simulated cage encircled by alginate nanoparticles using the Packmol software program. To prevent any artificial interactions, the box size is determined to ensure sufficient space between the periodic images of the nanoparticle and the nanoparticle. To alleviate steric conflicts and relax the structure, a conjugate gradient approach is implemented to decrease the system's energy. To construct the surface mesh, the OVITO tool generated surface manifolds that illustrate the three-dimensional morphology of atomistic objects through the alpha-shape approach.[19-20]

MD set up and force field parameters

Atomic interactions are characterized using the DERIDING force field, which includes bond stretching and bending forces, Van der Waals (VdW) forces, and Coulombic forces. The force field characteristics of alginate are derived from previous experimental research. The force field coefficients for each atom simulation were constructed using the NVT ensemble, allowing for periodic boundary conditions in three dimensions, as well as constant temperature and volume parameters. The temperature is maintained at 300 K by the Nose-Hoover thermostat. To ensure that the system achieves equilibrium, the simulations are performed for 10^7 fs. An external electromagnetic field can be simulated in LAMMPS by including a fix command in the input script. The electromagnetic wave's frequency and polarization, along with the electric field's intensity and direction, can be controlled using the fix efield command. A time-varying electromagnetic field was introduced to the simulation box to mimic the interaction between atoms and electromagnetic fields. We applied the fix efield command to utilize an electric field for all atoms in the simulation box, including an electric field of 0.1 V/Å in the x-direction and a force of 1 eV/Å in the z-direction. Furthermore, the equation "B equals 0.1*sin (0.05*time)" is specified as a variable command in the LAMMPS input file to simulate magnetic conditions passing through the simulation box [21–22]. OVITO can be used to analyze the simulation's output data. Calculating mean square displacement (MSD), radial distribution functions (RDF), and other relevant characteristics may be part of the investigation.

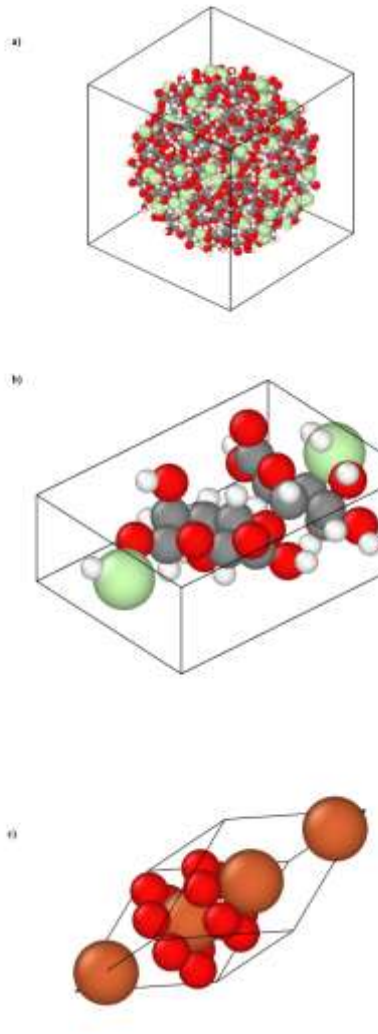


Figure .1 a) a perspective view of Fe2O3 Crystal b) a perspective view of Alginate Structure c) perspective view of Atomic Representation of Magnetic Alginate Nano sphere (alginosome) in current theoretical research.

Results and discussion

LAMMPS enables the observation of the impact of an external electromagnetic field on the breakdown of magnetic alginosomes by illustrating particle trajectories and fields with OVITO visualization capabilities.

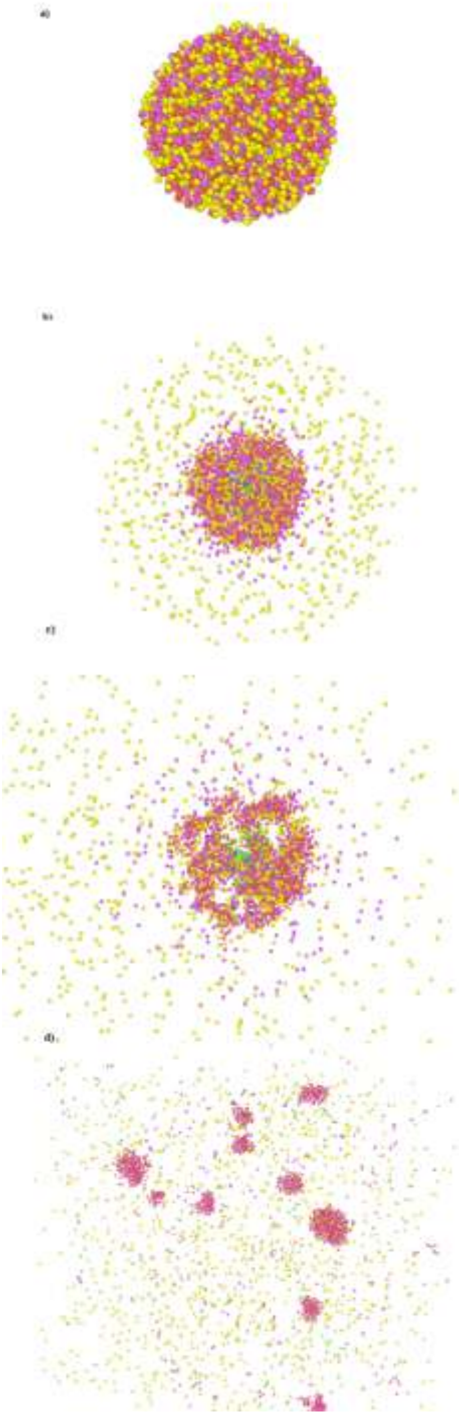


Figure 2. Atomistic evolution and Disassembly of magnetic Alginosome snapshots under external electromagnetic field from a) initial step to d) 10000000 fs at interval of simulation time

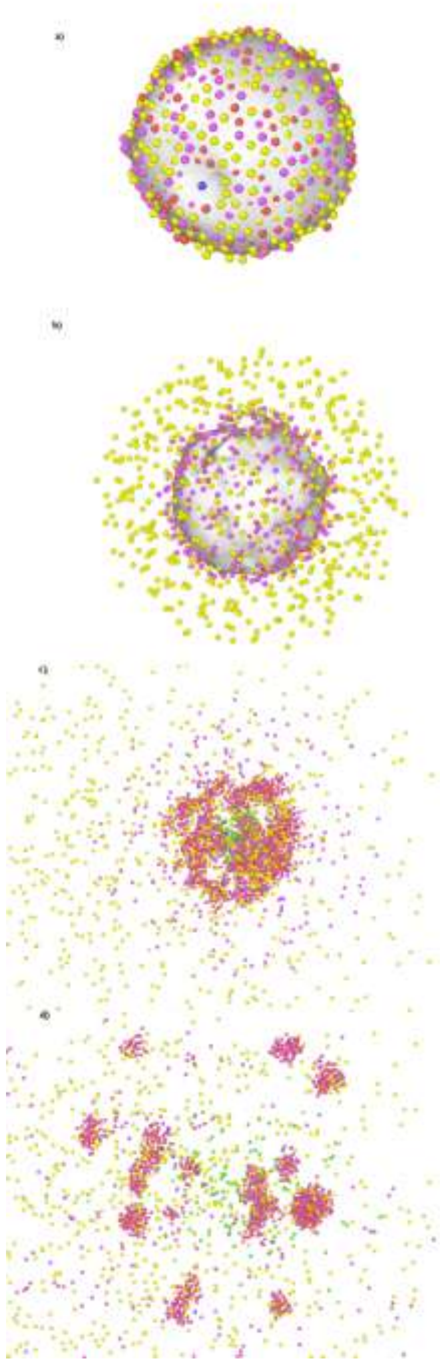
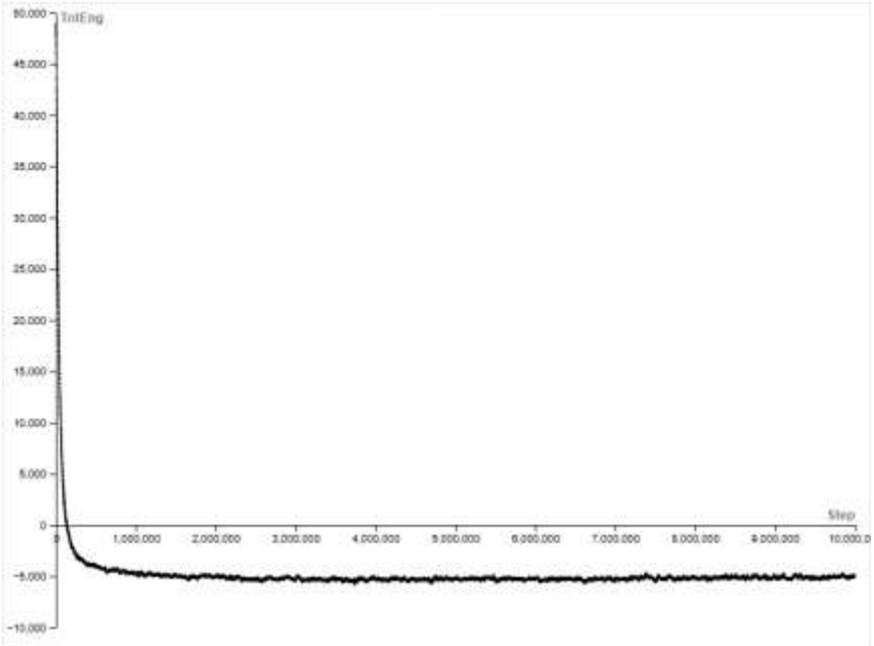


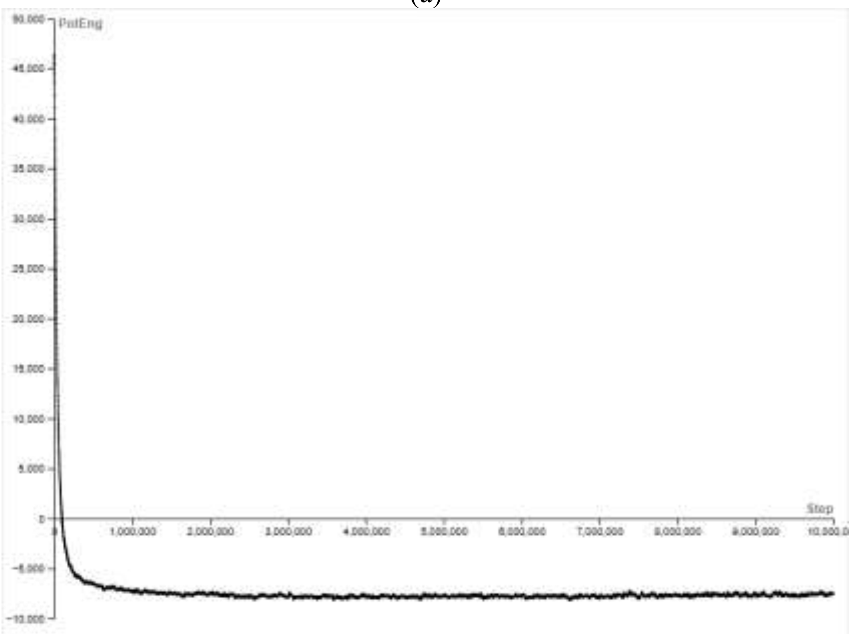
Figure 3. Surface mesh changes of the Disassembly process of magnetic Alginosome from a) initial step to d) 10000000 fs at simulation time interval. it represents the outer layer of the nanosphere, capturing the arrangement of atoms for understanding the deformation and dynamic behavior of Magnetic Alginosome under an external electromagnetic field

Fig. 3a-3d illustrate differences in surface mesh throughout the disassembly process. The surface mesh of a nanosphere is a crucial representation of its nanoscale geometric structure. It comprises a network of interconnected vertices, edges, and faces that form the three-dimensional geometry of the nanosphere. The mesh resolution and quality affect the accuracy of the nanosphere's surface attributes, including curvature, roughness, and imperfections. High-quality surface meshes are essential for nanosphere computer modeling and simulation, since they enable precise finite element analysis, fluid dynamics calculations, and other numerical methods [23-24].

As mention in Fig.4a, the total energy of a magnetic alginate-based nanosphere is determined by summing the kinetic and potential energies of all particles inside the system. Instability may arise if the system's total energy exceeds a certain threshold, resulting in the nanosphere's disintegration. Nevertheless, the nanosphere may collapse if the total energy is insufficient. Therefore, it is imperative to preserve an equilibrium between potential and kinetic energies to ensure the stability of the magnetic alginate-based nanosphere [25-27]. The disintegration process is exothermic, as evidenced by the negative change in the total energy of a system in Fig.4b The discharge of energy may facilitate the disintegration of the nanocarrier, rendering it thermodynamically advantageous. The potential energy function typically includes terms for bound interactions (such as bond stretching and angle bending), non-bonded interactions (such as electrostatics and van der Waals forces), and any external forces that apply an electromagnetic field to the Nano system.



(a)



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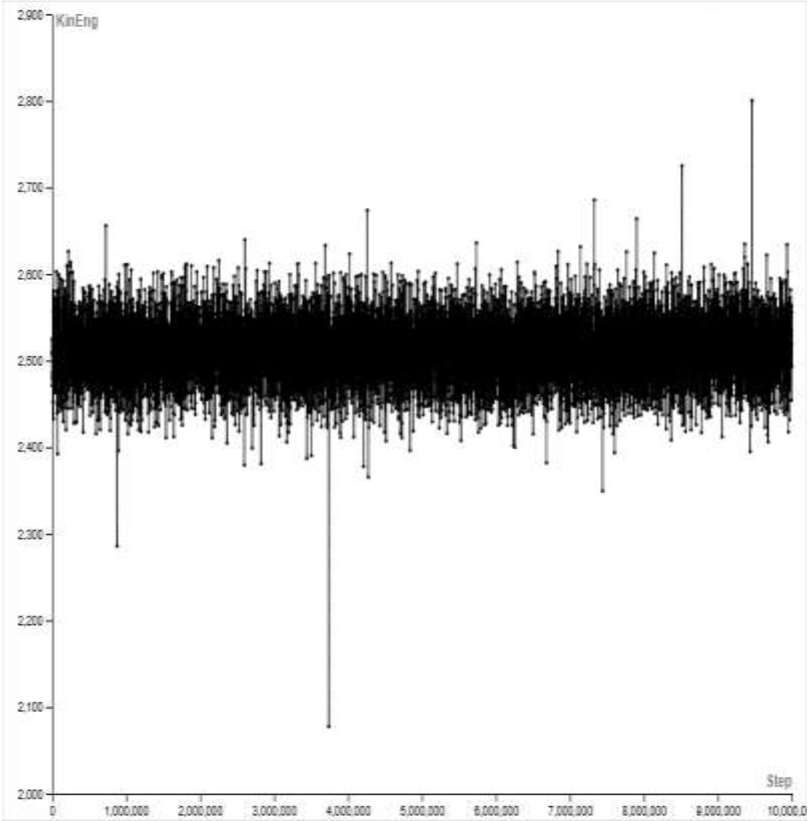
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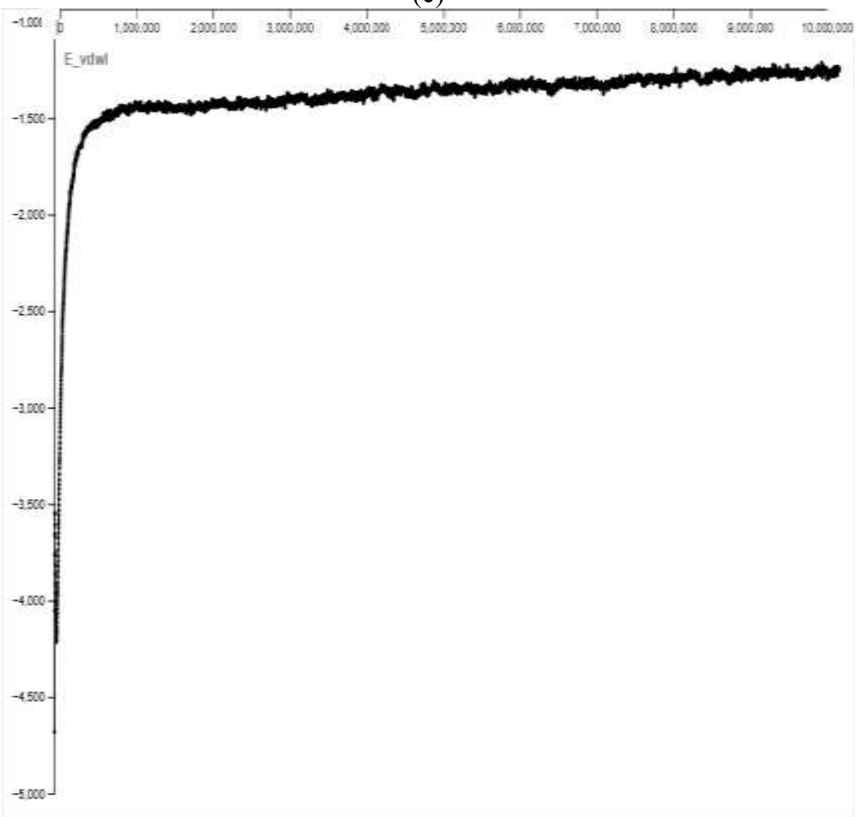
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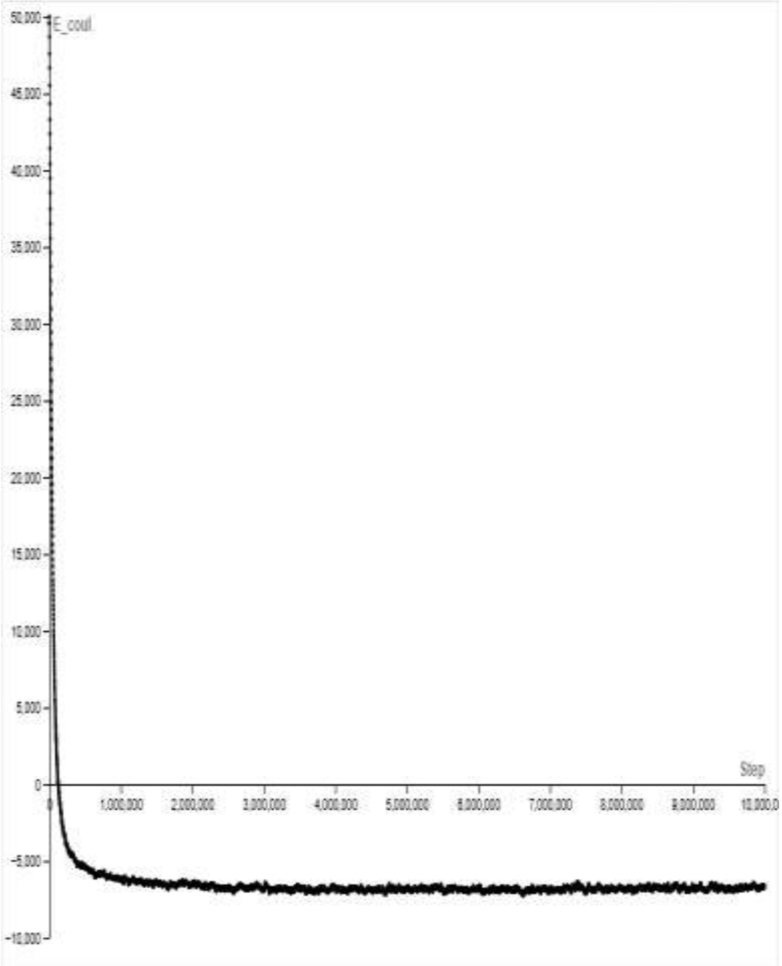

(e)

Figure 4. a) Total energy curve b) Potential Energy curve c) Kinetic Energy Curve d) Vander Waals energy e) Coulombic pairwise energy curve of alginosome after 10000000 fs MD simulation time which proved disassembling of Magnetic Alginosome under electromagnetic field

The misfit of the potential energy graph was reduced to -7479 kcal/mol and was preserved as Magnetic Nano alginate was progressively annihilated, as illustrated in Fig. (4a-4e). Nevertheless, the kinetic energy plot demonstrated a conserved pattern of approximately 2500 kcal/mol throughout the simulation. The van der Waals energy (VdW) is an intermolecular force that arises from the interaction of uncharged atoms or molecules. Van der Waals energy is a critical factor in determining the stability of magnetic alginate-based nanospheres. The van der Waals energy between the atoms or molecules in the system is equal when the alginosome is stable. If this equilibrium is disturbed by changes in temperature or pressure, the van der Waals energy may become either too feeble or too potent, resulting in system instability (Fig. 4d). Therefore, it is imperative to comprehend the VdW energy of the magnetic alginate-based nanosphere in MD to guarantee its stability and utility as a Nano system. By investigating the interactions between its molecules and atoms, researchers may acquire the knowledge necessary to optimize the stability and efficacy of the nanosphere in molecular dynamics simulations. The stability of nanoparticles may be substantially influenced by their molecular energy. The energy of the system is constantly fluctuating in MD simulations as molecules interact and move. In a molecular dynamics simulation, the amount of thermal energy released or absorbed as a nanosphere discharges its payload molecule is known as the enthalpy of nanoparticle release. A nanosphere's size and form may affect its enthalpy of release in a number of ways. Because of the greater surface area-to-volume ratio, smaller nanoparticles often have a higher release enthalpy than larger ones. This suggests that a greater percentage of the atoms or molecules in smaller nanoparticles are found near their surface, facilitating easier contact with the environment and releasing energy. The shape of the sphere may also affect its enthalpy of release. For example, the release enthalpy is greater for more spherical nanoparticles than for irregular or elongated ones. Because atoms and molecules are more evenly distributed throughout their structure, spherical nanoparticles can transmit energy during the discharge process more effectively. [28–29]

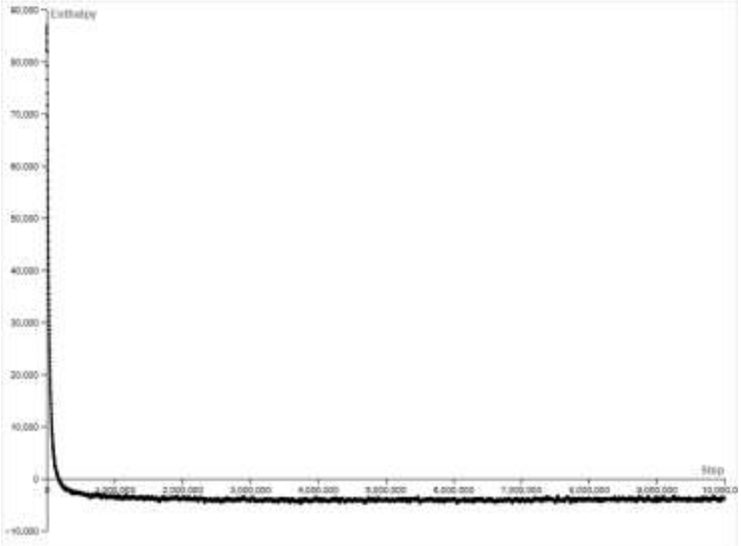

Figure 5. Enthalpy landscape of Alginosome disassembly` nanosphere reached -3736 kcal/mol after 10000000 fs after MD simulation process

Notably, as shown in Fig. 5, the enthalpy of disassembly for a particular nanosphere reached -3736 kcal/mol after 10000000 fs; the enthalpy (total heat content) of the disassembly process is lower than that of the constructed state. Designing stimuli-responsive nanostructures requires an understanding of disassembly thermodynamics, which suggests that the system releases heat as it moves into a lower energy state. Mean Squared Displacement (MSD) measures how much movement a particle or molecule undergoes over time. MSD is a crucial metric in the study of nanosphere dynamics for understanding the diffusion behavior of nanoparticles. By measuring their MSD, it is possible to determine the nanoparticles' velocity, distance traveled, and contact mode with their surroundings. This knowledge is essential for understanding how nanoparticles behave in biological systems and for creating efficient delivery devices. [30–31]

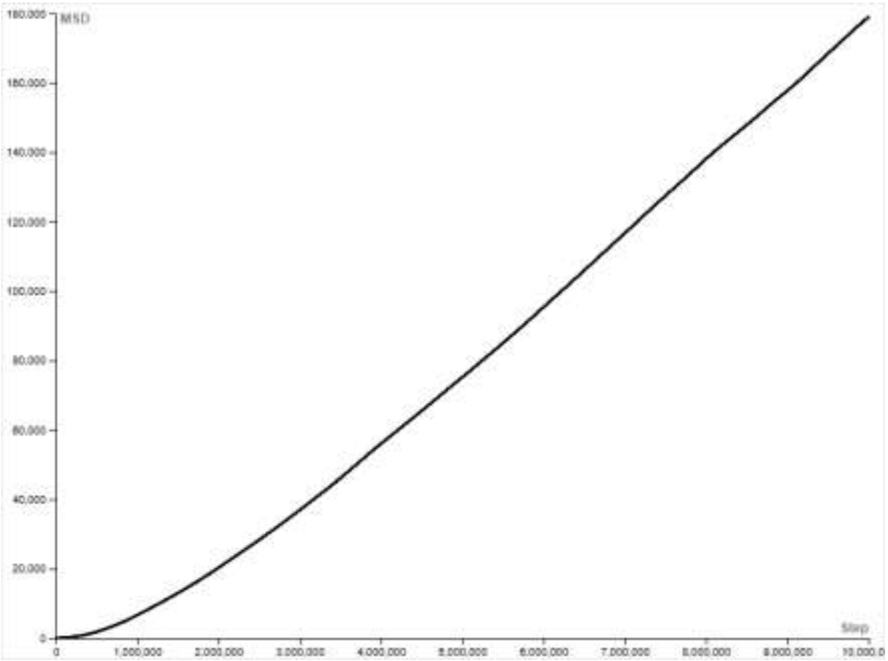

Figure 6. MSD curve of magnetic Alginosome in deformation process over simulation time

Fig.6 shows how the MSD parameter increased during the simulation process. Generally speaking, smaller nanoparticles have greater MSD values than bigger ones. Moreover, the form of the nanosphere may have an impact on its MSD. For example, due to variations in surface area and shape, the diffusion of a spherical nanosphere may differ from that of a cylindrical one. MSD is a crucial metric in the study of nanosphere dynamics to understand the diffusion behavior of nanoparticles. It is possible to determine the nanoparticles' velocity, distance traveled, and contact mode with their surroundings by measuring their MSD. Understanding the behavior of nanoparticles in biological systems and creating efficient medication delivery methods depend on this knowledge. Overall, MSD analysis is a powerful tool for studying nanoparticle dynamics and may provide important information about their behavior.

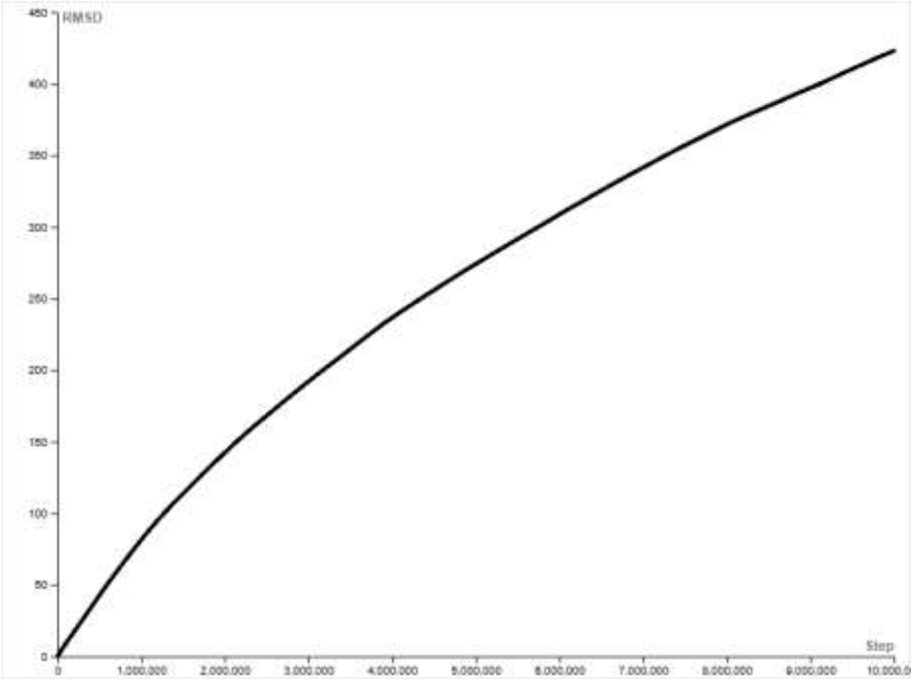

Figure 7. RMSD curve of disassembly process and structural breakdown of the alginosome after simulation time

Fig.7 shows a somewhat linear growing trend, with a rise of up to 400 Å during the simulation process. When the RMSD value is low, the structure is stable; when it is large, it is less stable and can have seen Major changes; consequently, the disassembly of the alginosome occurs due to the induction of an electromagnetic. The field has caused the structural breakdown of the alginosome. RMSD is a basic measure of the average distance between atoms of stacked molecular structures. Researchers may assess the stability of the nanosphere and ascertain how much the structure has altered over time by computing the RMSD value. [32–33] Fig.7 describes RMSD of magnetic Alginosome in the disassembly process

Fig.8 shows the magnetic alginosome's radius of gyration (Rg). The root-mean-square distance between the center of mass and every atom in the sphere is represented by this value. It may be used to compare different systems or confirm experimental findings, and it can provide important details about the size and shape of the system or molecule. The distance from the axis of rotation to the point at which the body's mass is most effectively concentrated.

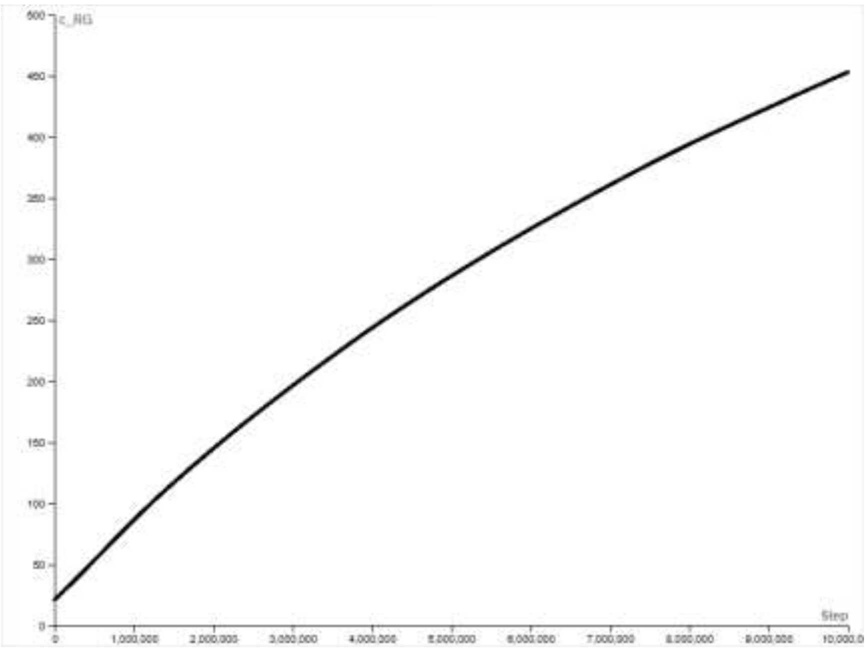

Figure 8. Rg of magnetic Alginosome in disassembly process describes deformation and magnetic

alginosome after simulation time
Additionally, a higher Rg value suggests that the molecules are distributed more dispersedly, which may lead to a delayed dissociation rate and a protracted circulation period in the body. In contrast, a reduced radius of gyration may indicate a more compact structure, which could lead to shortened circulation periods and faster release rates. Furthermore, the radius of gyration may affect the stability and structural integrity of the nanosphere. While a lower Rg can increase the probability of deformation and the potential loss of structural integrity, a higher Rg can increase the probability of instability [34]. The Radial Distribution Function (RDF) is a mathematical representation that illustrates the spatial distribution of particles around a center particle inside a system. The RDF provides insight into the spatial distribution of magnetic nanoparticles inside the alginate matrix during MD involving magnetic alginate-based nanoparticles. The radial distribution function (RDF) estimates the spatial distribution of particles around a center particle. The dimensions and morphology of magnetic nanoparticles may affect the radial distribution function of the nanosphere. I The magnetic moment of small magnetic nanoparticles often exceeds that of bigger nanoparticles. This may affect the RDF of the nanosphere by modifying the interactions among the particles and with the surroundings. Moreover, the radial distribution function of the nanosphere may be affected by the shape of the nanoparticles. For example, elongated particles may demonstrate different interactions with their neighbors compared to spherical particles. [35-36]

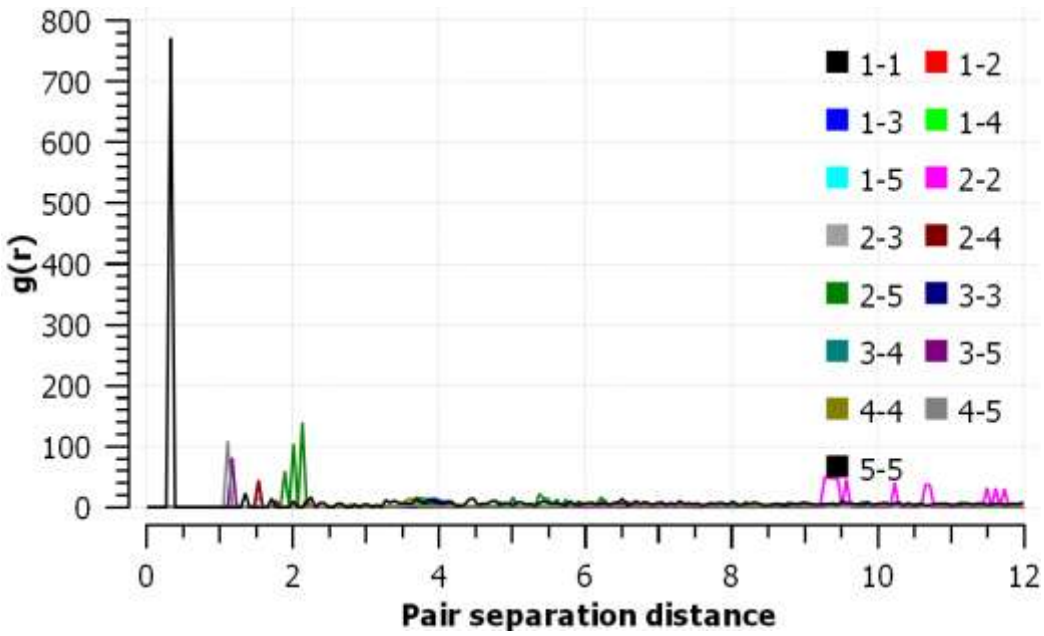

Figure 9. RDF of magnetic Alginosome at final MD stage represents the arrangement of neighbors and 1-1 as most probable site for neighboring particles for Magnetic alginosome

The extent of particle aggregation may be determined, and the stability of the nanosphere can be anticipated by analyzing the RDF of the nanosphere in different environments. This information may aid in the design and enhancement of the nanosphere's functioning for certain applications. Fig.9 illustrates the graph of the function g(r) plotted on the y-axis against the distance r on the x-axis. The little colored squares in the graph denote the pair number of atoms according to the LAMMPS DATA file. With g(r) as the Y axis signifying the probability of finding a particle at a certain distance from another particle, it provides information on the composition and interactions of particles in a system. Each peak in the RDF plot indicates a preferred distance where particles are more likely to be found. The most probable site for neighboring particles is the C-C pair (black line), the first peak in the RDF plot. This peak is crucial for understanding the local structure and interactions within the alginate Nanosphere, as it represents the arrangement of the closest neighbors for alginate nanoparticles (NPs). Further peaks, which represent additional coordination shells, demonstrate particle organization beyond the initial layer of neighbors. It is essential to comprehend the locations and heights of these peaks to comprehend the stability of the Nano alginate structure. The valleys between peaks also reveal regions where particles are less likely to be found, which may indicate a lack of nearby particles or regions of repulsion. The arrangement of iron atoms in the alginosome (1-4,2-4,3-4) demonstrates the state of iron oxide nanoparticles in the interior of the nanosphere. In summary, the particle distribution in the RDF plot, in addition to other metrics, demonstrates the geometric stability and integrity of the nano system. Various electromagnetic fields may be implemented in MD simulations that utilize LAMMPS. Magnetic fields, electric fields, and electromagnetic radiation are among the most frequently employed types. Simulating the behavior of a pharmaceutical molecule in an electromagnetic field may require a significant amount of processing power and time. Additionally, the simulation's precision is contingent upon the quality of the force field, which is not always reliable. It is essential to remember that not all medication delivery methods can use external electromagnetic fields. The success of this method is contingent upon the medication molecule, the target tissue's size, shape, and distinctive characteristics. The zeta potential, essentially the electrostatic charge on the surface of the nanoparticles, is a significant factor in determining the stability and behavior of the nanosphere in nano systems. The zeta potential of a nanosphere may have a substantial impact on its cellular absorption. Additionally, the zeta potential may affect the nanosphere's stability in biological fluids and its ability to conceal itself from the immune system. The zeta potential of a nanosphere must be meticulously adjusted to optimize its cellular absorption and overall effectiveness. Additionally, the zeta potential may affect the nanosphere's stability in biological fluids and its ability to conceal itself from the immune system. The zeta potential of a nanosphere must be meticulously adjusted to optimize its cellular absorption and overall effectiveness.[37]

Figure 10. zeta potential curve presents a stability of -0.45 mV during the disintegration of alginosome over simulation timeframe

The zeta potential variations of the system during the simulation phase are illustrated in Fig.10. Consequently, the zeta potential increases and attains a stability of -0.45 mV during the disintegration of alginosome. This MD simulation may provide an accurate approximation of the behavior of magnetic nanoparticles in the presence of external fields; however, its accuracy should be verified by comparing it to experimental data. This can be achieved by contrasting the simulation findings with experimental data and adjusting the parameters. Additionally, it is imperative to bear in mind that models may not entirely accurately represent magnetic nanoparticles. Consequently, a combination of experimental and simulation methodologies is frequently necessary to gain a comprehensive understanding of their behavior and characteristics. Conventional MD simulations have been employed to investigate the behavior of alginate-based nanoparticles. These investigations have examined the structure, behavior, and interactions of alginate-based nanoparticles with pharmaceuticals and biological systems. For example, MD simulations have been employed to investigate the influence of alginate content on the stability and structure of alginate-based nanoparticles.[38] Coarse-grained (CG) simulations are an additional type of molecular simulation that can be employed to investigate large systems over extended periods of time. Representing multiple elements reduces the computational cost of CG simulations by a single particle. CG simulations have investigated the self-assembly of alginate-based nanoparticles and their interactions with cell membranes. [39] The behavior of alginate-based nanoparticles in isolation and in their interactions with biological systems can be investigated using molecular simulations. For example, MD simulations have examined the interaction between alginate-based nanoparticles and mucus, which is a substantial impediment in numerous drug delivery applications. MD simulations have also been employed to investigate the assimilation of alginate-based nanoparticles by cells. While molecular simulation offers numerous advantages, it also has drawbacks when evaluating simulation results. One substantial disadvantage of conventional MD simulations is the accuracy of the force fields employed. Despite the fact that force fields are typically parameterized using experimental data or quantum mechanical calculations, they may not accurately depict all of the interactions that take place between atoms in a system. Another disadvantage of quantum mechanical simulations is their high computational cost, which limits their application in small systems. In conclusion, molecular simulation is a valuable method for investigating the atomic behavior of alginate nanoparticles in an electromagnetic field.

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Declarations
Conflicts of interest/Competing interests The author declares that they have no conflicts of interest.
Ethics approval N/A
Consent to participate N/A
Consent for publication N/A
Availability of data and materials: Data are available on request from the authors
Code availability: LAMMPS main input is available on request from the authors.
Authors' contributions Maziar Bahreini and Fereydoon Bondarian: Designed the analysis, performed the analysis, wrote the paper.

Conclusion
The electromagnetic impact of alginate-based nanoparticles was investigated in this study through molecular modeling in terms of computational parameters. Molecular modeling illuminates the disintegration behavior of alginate-based nanoparticles at the atomic and molecular levels. The findings indicated that electromagnetic fields can be employed to control magnetic alginosomes. In summary, the MD technique was employed to model the behavior of magnetic alginate nanospheres under the influence of electromagnetic fields. This computational approach facilitates a deeper understanding of the interactions among these particles at the molecular scale. Additional research is necessary to validate these models and convert their outcomes into practical applications. In conclusion, the Simulation results can guide experimental strategies by identifying optimal conditions (e.g., magnetic field strength) that enhance desired properties or behaviors of magnetic alginate nanospheres.

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