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RESEARCH ARTICLE

Molecular Dynamics Simulations to Study the Role of Temperature on Carbon Nanotube and Protein Interactions

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Abstract

Background/Objectives: Almost all chemical reactions within our bodies are catalysed by proteins. The calcium signalling inside the eukaryotic cell structure is significantly influenced by the calcium modulated protein (3CLN). On the other hand, carbon nanotubes are an excellent choice for the aim of targeted drug delivery. Therefore, it is crucial to research how these two elements interact. **Methods:** In this work, we perform extensive molecular dynamics (MD) simulations of 100 ns each to study the interaction of 3CLN protein with a carbon nanotube (CNT) at 320 K, 420 K, 520 K, 590 K, and 660 K temperature ranges. The conformational changes in the calmodulin protein are studied with MD simulations at different temperature ranges using open-source software, VMD and NAMD. **Findings:** A significant dependence of the temperature is observed on the overall conformation change of the protein around the carbon nanotube. The quantitative comparison of the simulation data with complete studies shows the different aspects of the folding process. It can also give detailed structural results for the experimental observations as well as physical results for theoretical concepts without actual experimentation. **Novelty:** The protein is seen to form a stable corona structure around the CNT at a temperature of 520 K, as previously reported by the other researchers. While this stability is lost at higher temperatures. This interaction study can be used to investigate the impact of environmental factors on the dynamics of a particular protein in conjunction with a nanomaterial. It will open up new avenues for future research.

Keywords: Carbon Nanotube; Calmodulin Protein; Eukaryotic Cell; NanoMolecular Dynamics (NAMD); Simulation; Visual Molecular Dynamics (VMD)

1 Introduction

Biophysics plays a crucial role in the medical science as it will aid in the treatment with much better ways[1–4]. A carbon nanotube (CNT) resembles a cylindrical structure with a nanoscale diameter and appears like a rolled graphene sheet[5–8]. The interaction between a carbon nanotube and 3CLN (Calmodulin) protein was examined[9,10] computationally with the aid of open-source software VMD and NAMD. This interaction will be helpful in the targeted drug delivery applications. The need for this interaction will give a pathway for further research also as it will help to study the role of environmental conditions on a specified protein. It will play an important role in the drugs delivery as CNT is a very small structure of nano scale diameter which makes it possible for the drug to easily pass through the blood stream.

To better understand the use of carbon nanotubes in drug delivery systems, it is crucial to understand how they interact with proteins like 3CLN. Different types of amino acid chains make up the proteins. All eukaryotic cells include some of the proteins in their cytoplasm. The supply of amino acids can effectively control the production of muscle proteins[11]. These large, intricate molecules known as proteins play numerous important and vital jobs in our bodies. Proteins are large and complex molecules that play different kinds of significant and critical roles inside our body. Proteins do most of the work inside the cells and are needed for various functions, structures, and regulations of body tissues and organs in a proper way.

Proteins[12,13] perform different kinds of functions like an antibody, an enzyme, a messenger, growth hormones, structural components, transporter, storage, etc. For a specific type of drug delivery through the CNT, its interaction[14] with the protein needs to be studied under different environmental conditions like pH, temperature, and ionic concentration etc. Earlier reported work is done on the interaction of CNT and proteins but the effect of various environmental conditions[15] are not explored in detail. The protein interaction with a CNT is earlier reported by Nicholas et al. using the mass the spectrometry data[16]. The absorption of protein on the CNT is observed to be governed by the corona structure formation but the different temperature ranges are not explored[17]. Water remediation is also studied using the protein CNT corona structure formation by Carlos et al.[18]. Cryogenic transmission techniques are used to show that the corona thickness is a function of nanotube diameter.

The physical movement of atoms and molecules in various kinds of systems is extensively studied using molecular dynamics (MD) simulations. Prior until now, MD simulations were conducted to investigate the impact of the geometric shape of the roughnesses on the fluid flow via a nanochannel[19]. To explore the liquid-vapor for multi-phase flows, pseudopotential lattice Boltzmann modelling has been used in the past[20]. The impact of various boundary wall temperatures in the range of 84 K to 133 K on the flow properties of Argon fluid flow is further investigated using molecular dynamics simulations[21]. An earlier work of this kind using equilibrium and non-equilibrium MD simulations of DNA structure with exact atomic configurations was published[22].

With the help of in-depth molecular dynamics simulations, which provide a thorough atomistic explanation in a comparatively shorter amount of time, we concentrate on the interactions between the 3CLN protein and carbon nanotubes at various temperature ranges in the current work. In the current work, in-depth MD simulations are carried out to explore the 3CLN protein's interaction with the CNT at various temperature ranges. This is the first type of in-depth computational investigation that we are aware of. The development of a corona structure confirms the suitability of the protein-CNT complex for use in drug delivery purposes.

2 Methodology

2.1 Visual molecular dynamics (VMD)

VMD is a software with a capability of showing the molecular shapes in different ways. VMD is designed for showing and studying of molecular assemblies, particularly in biopolymers such as proteins and nucleic acids etc[23]. VMD can simultaneously display any number of structures using a wide variety of rendering styles and colouring methods. VMD is developed as a tool to observe and analyze the results of molecular dynamics simulations as well. It includes tools for observing volumetric and sequence of data, also for arbitrary graphics objects. Figure 1 shows the structures of a CNT and CNT interacting with protein created with the help of VMD program. VMD can supports computers running MacOS X, Unix, or Windows, and is distributed free of cost, and including source codes.

2.2 Nanoscale Molecular Dynamics (NAMD)

NAMD is a parallel Molecular Dynamics code which helps in describing the classical molecular dynamics force field, equations of motion, and integration methods along with the efficient electrostatic evaluation algorithms. It also employs the different temperature and pressure controls. NAMD is used to run efficiently on parallel machines for simulating large scale molecular

systems. NAMD helps as an interactive simulation tool with the Visual Molecular Dynamics (VMD) molecular software[24]. NAMD has ORCA and MOPAC (utilized in chemistry also), also act as a processes interface to many other quantum packages. Together with VMD and QwikMD,NAMD's interface helps to access to hybrid QM/MM simulations in a unit, descriptive, customizable, and easy-to-handle and easy to use.

NAMD is also available as a free tool for non-commercial use by single person or academic institutions, also for corporation's in-house uses. The main advantage of using NAMD over other methods used by earlier workers for this kind of a study is the repeatability over different environmental conditions in an easier way. NAMD along with VMD can be applied for a variety of problems related to the field of nano-biotechnology. The interaction of a protein with another protein or with a nano material/device can be studied using NAMD at different environmental conditions such as temperature, pH and ionic concentration.

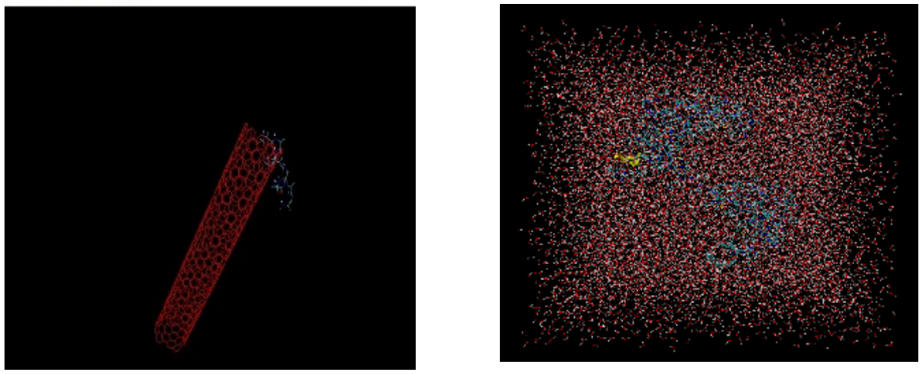


Fig 1. (a) Structure of 3CLN protein with Carbon nanotube (b) Structure of 3CLN Protein with CNT in a water box

3 Results and Discussion

In this work we have performed five sets of simulations at 320 K, 420 K, 520 K, 590 K, and 660 K temperature ranges to study the interaction of CNT with 3CLN protein. The present work is an extension of our earlier work in which we had studied this interaction at few temperature ranges[25]. Kinetic energy and temperature are found to be stable at 320 K, 420 K, and 520 K as shown in Figure 2. The root means square deviation (RMSD) is as shown in Figure 3 for 320 K. At this temperature RMSD is found to be variable and not stable from 0 to 100 ns as observed in Figure 3. A stable dynamic behaviour is observed between the CNT and the protein at 320 K as seen in Figure 4. As clearly observed from the snapshot in Figure 4, CNT remains close to the protein during the whole duration from 0-100 ns.

At higher temperatures such as 420 K and 520 K, a dynamic interaction is observed between the protein and carbon nanotube. At 420 K, RMSD is found to be nearly stable from 20 ns to 100 ns with slight variation as shown in Figure 5. At this temperature the protein is observed to come in the proximity of the carbon nanotube around 60 ns. Around 85 ns the protein nearly wraps around the CNT as shown in Figure 6. At 520 K, RMSD is found to show slight variation from 20 ns to 80 ns in an increasing manner with slight variation and from 80 ns to 90 ns in deceasing manner after that it shows stability as shown in Figure 7. At this temperature the protein is observed to come in the wrapping proximity of the carbon nanotube at around 65 ns. Around 85 ns the protein is wrapped around the CNT as shown in Figure 8 forming a corona structure as reported by the earlier workers[17]. This structure is observed to remain stable till the end of the simulation and is important from the point of view of application of the CNT in the targeted drug delivery.

At 590 K, RMSD is found to be nearly stable from 5 ns to 90 ns and from 90 ns to 100 ns in an increasing manner with slight stability as shown in Figure 9. At this temperature the protein is observed not to come nearly of the carbon nanotube from starts to 100 ns as shown in Figure 10, means no interaction is happening at this temperature. At 660 K, RMSD is found to be showing nearly stable variation from 10 ns to 80 ns and from 80 ns to 100 ns it is decreasing with slight stability. At this temperature the protein is observed not to come close to the carbon nanotube throughout the simulation which means that no interaction occurs at this temperature between the CNT and the protein. This interaction is important from the point of view of applications in drug delivery.

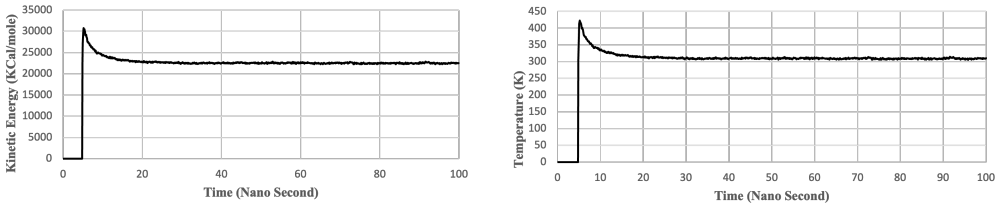


Fig 2. (a) Kinetic energy as a function of time at 320 K. (b) Temperature as a function of time at 520 K

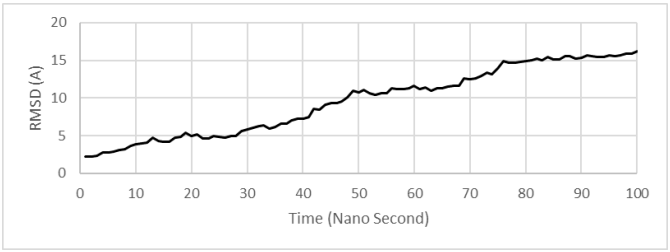
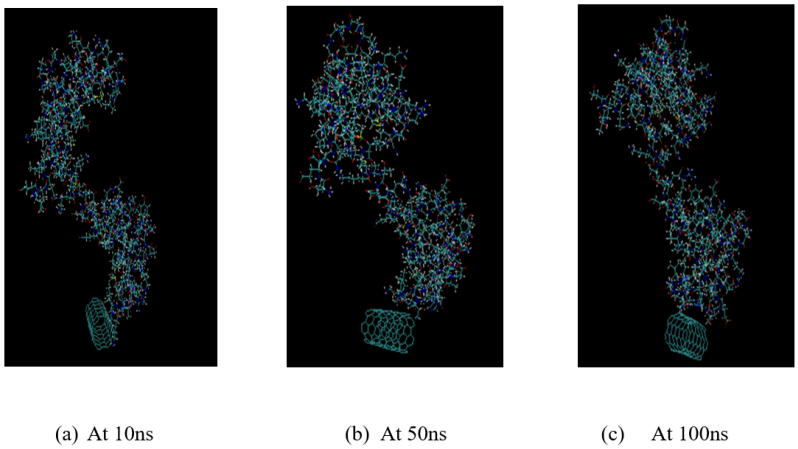


Fig 3. Root Mean Square Deviation(RMSD) as a function of Time at 320 K



(a) At 10ns (b) At 50ns (c) At 100ns

Fig 4. (a) Snapshots at time 10 ns (b) at time 50 ns(c) at time 100 ns showing a stable interaction between the CNT and protein at 320 K

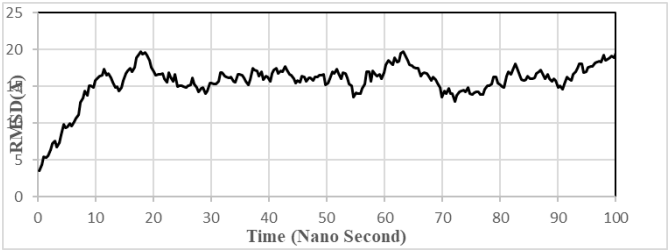
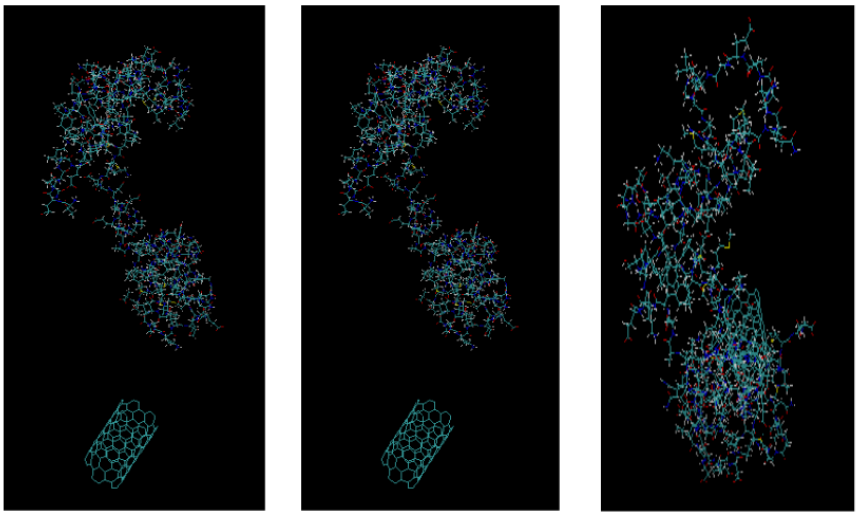


Fig 5. Root Mean SquareDeviation (RMSD) as a function of Time at 420 K



(a) At 20 ns (b) At 60 ns (c) At 85 ns

Fig 6. (a) Snapshots at 20ns (b)at 60ns (c) at 85ns time showing a dynamic interaction between the CNT and protein at 420 K

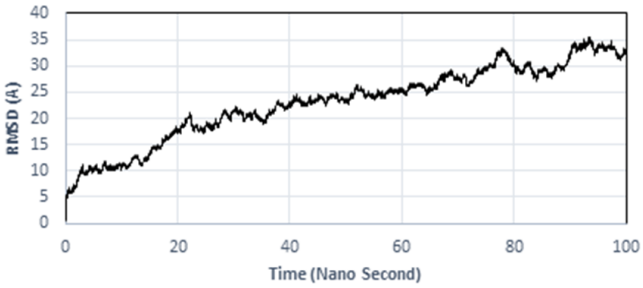
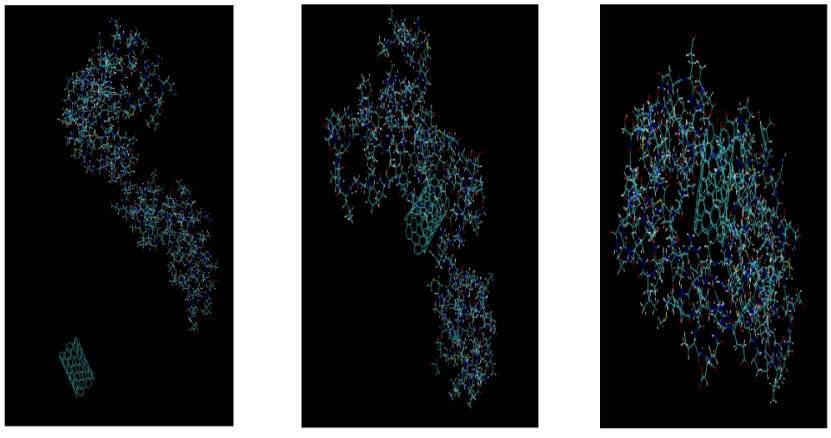


Fig 7. Root Mean Square Deviation(RMSD) as a function of Time at 520 K



(a) At 8ns (b) At 65ns (c) At 85ns

Fig 8. (a) Snapshots at 8ns (b) at65ns (c) at 85ns time showing a dynamic interaction between the CNT and proteinat 520 K

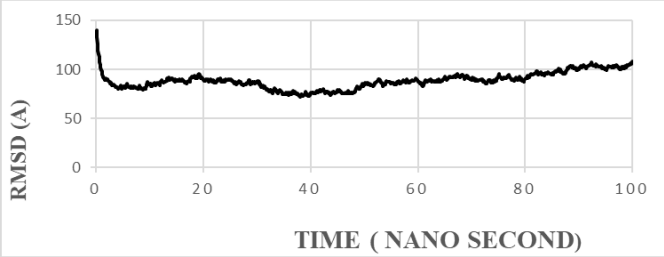
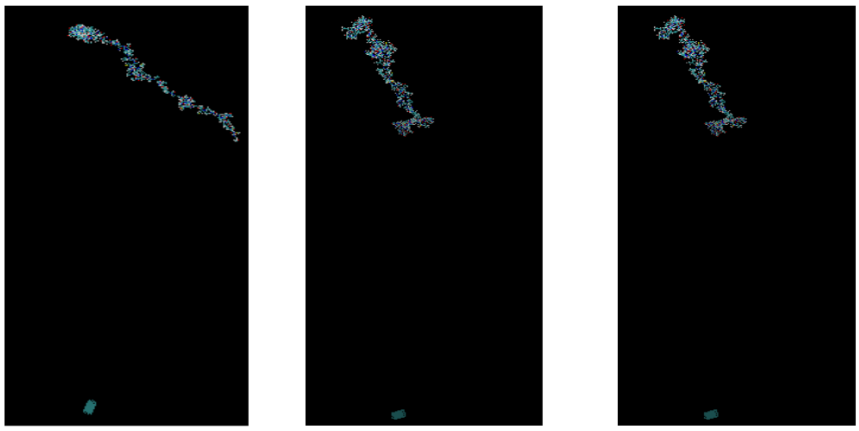


Fig 9. Root Mean Square Deviation(RMSD) as a function of Time at 590 K



(a) At 10 ns (b) At 50 ns (c) At 95ns

Fig 10. (a) Snapshots at 10ns (b) at 50ns (c) at 95nstime showing no interaction of CNT and 3CLN protein simulation at 590 K

4 Conclusion

The interaction of the 3CLN protein with carbon nanotubes is investigated using 100 ns molecular dynamics simulations with the aid of the NAMD and VMD software at various temperatures, including 320 K, 420 K, 520 K, 590 K, and 660 K. According to our earlier investigation, a close relationship between the temperature and the overall dynamics of the protein and carbon nanotube is seen. The structures are discovered to be displaying a steady dynamic at 320 K. At higher temperatures, such as 420 K and 520 K, a dynamic interaction between the protein and carbon nanotube is seen, and towards the end of the simulation, the protein is seen to wrap around the CNT structure to form a stable protein corona structure. Above 590 K, denaturation of the protein is seen at higher temperatures. As a result, 320 K to 420 K is shown to be an appropriate temperature range where the 3CLN protein exhibits close interaction with the carbon nanotube. The uses of such systems for the purposes of tailored medicine delivery will benefit from this interaction.

Acknowledgement

This is to acknowledge that the preliminary part of this work is published in which we studied the protein carbon nanotube interaction at a few temperature ranges. The present work is an extensive study covering more temperature ranges.

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