

HIP Scientific Paper Example

Molecular Dynamics of Peptides on Graphitic Surfaces

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Abstract

The research project, Molecular Dynamics of Peptides on Graphitic Surfaces, was conducted at Wright Patterson Air Force Base in Dayton, OH under the guidance of Dr. Rajiv Berry. The goal of the project was to determine the binding nature of peptides with graphitic surfaces. Using the molecular dynamics software LAMMPS (Large-scale Atomic/Molecular Massively Parallel Simulator), the binding enthalpies of peptides with graphitic surface were computed. Binding enthalpies were computed for the triglycine (GGG) peptide with various graphitic surfaces. The average binding enthalpies obtained for interactions with armchair-edged nanoribbons (-11 kcal/mol) and hole-containing graphene sheets (-10 kcal/mol) were relatively larger than those of zigzag-edged nanoribbons (-6 kcal/mol) and pure graphene sheets (-6 kcal/mol). The calculated results indicate that the GGG peptide has a greater attraction to graphitic surfaces relative to the GFG peptide (F=phenylalanine).

Project Objectives

Graphene is a two-dimensional sheet of sp^2 hybridized carbon atoms packed into a honeycomb lattice (Figure 1). Its single-atom thickness and aromaticity give rise to many potential applications. Adsorption of a molecule on the surface of graphene may induce a change in the surface's properties as well as a change in the energy of the system. For this reason, graphene is being widely researched for use in ultra-sensitive sensors. One promising study¹ demonstrated that a graphene chemical sensor could detect trinitrotoluene (TNT) at the parts-per-billion range while other studies² have indicated successful detection of biological molecules at picomolar concentrations. This research project aims to efficiently compute the binding enthalpies of peptides with graphitic surfaces to better understand the interactions as a function of amino acid sequence. After understanding how small peptides interact with a surface, the knowledge can be applied to predict the behavior of larger proteins on the surface³. For this project, the tripeptide glycine-glycine-glycine (GGG) was examined. Then, the central amino acid was modified to a phenylalanine (F). The research project intends to continue modifying the central amino acid to study how different side chains interact with graphitic surfaces. To compute the binding enthalpy of the system, one must subtract the energy of the system when the peptide is infinitely far away from the surface from the energy of the system when the peptide is near the surface. This process can be made more efficient when the two large calculations are broken down into four smaller calculations (Figure 3). The TEAM AMBER force field used in this research

project accounts for the potential energy of the system using the equations given in Table 1. For the systems studied, the change in kinetic energy is approximately zero when comparing the system in which the peptide is close to the surface to the system in which the peptide is far away from the surface since the thermostat maintains a fixed temperature ($T = 298.15$ K) throughout all simulations. Thus, the total binding enthalpy of the system is a result of the change in potential energies. The bond energy term, E_{bond} , describes the change in energy that occurs when covalent bonds stretch or contract. Similarly, the E_{angle} term accounts for the change in energy as a result of a change in the bond angle. The dihedral energy term, E_{dihed} , represents a change in potential energy caused by the twisting about the bonds. The E_{impr} term expresses the out-of-plane dihedral changes. Together, the E_{bond} , E_{angle} , E_{dihed} , and E_{impr} terms compose the covalent contribution of the potential energy. Interactions between the molecules are accounted for by the van der Waals term, E_{vdwl} and the electrostatic interactions, E_{elec} . Electrostatic interactions can be described as the sum of the coulombic and long-range interactions between molecules. The E_{vdwl} and E_{elec} compose the nonbond contribution of the potential energy. The TEAM AMBER force field used in these studies does not include a polarizability term. Although graphene is a nonpolar structure, its metallic nature allows it to become polarized. Upon comparing computed binding enthalpy to those computed by a force field that includes polarizability, the accuracy of the TEAM AMBER force field's representation of the peptide-surface interaction can be evaluated. Quantum mechanical calculations⁴ can also be employed to examine the effect of polarizability.

In this project, four graphitic surfaces were examined: a pure graphene sheet, an armchair-edged nanoribbon, a zigzag-edged nanoribbon, and a graphene sheet containing a hole in the center (Figure 4). The surface with the hole contains both armchair and zigzag edges. In addition to amino acid sequence, this project seeks to discover how surface structure affects peptide interactions.

Materials and Methods

2.1 Software and Computer Applications

This research project was performed using Materials Studio, Discover, and Direct Force Field. Materials Studio from Accelrys was used to construct each system. The minimizations of each system were executed using Discover software, also from Accelrys. Direct Force Field, from Aeon Technologies, Inc., was used to assign TEAM AMBER force field parameters to each system. All simulations were performed on the AFRL supercomputer, raptor, using LAMMPS molecular dynamics software from Sandia Labs.

2.2 Preparation of Molecules

To prepare the surface-peptide systems, it was first necessary to develop the four surfaces being studied. GRA is a pure graphene measuring approximately 40×40 Å. Due to the use of periodic boundary conditions in the simulations, the sheet is extended infinitely in the x-y plane. ARM is an armchair-edged nanoribbon and ZIG is a zigzag-edged nanoribbon. Both ARM and ZIG measure approximately 20 Å wide and extend infinitely in the y and x direction, respectively. HOL is a graphene sheet with a hole cut out from the center. It measures approximately 40×40 Å with a 20×20 Å hole. The edges of the hole exhibit both armchair and

zigzag orientations. Next, a peptide solution system was constructed containing 2,500 water molecules and one peptide. The aqueous solution was at a neutral pH; consequently, the peptide was zwitterionic. Using Materials Studio, the peptide solution system was layered on top of the different surfaces. A total of five independent systems were created for each different surface-peptide combination. Following the efficient computation method illustrated in Figure 3, it was important to construct a water box, containing 2,500 molecules, and a surface-water system, containing 2,500 water molecules and a surface. Then, each system was minimized with Discover. After the system was minimized, the force field parameters were assigned. TEAM AMBER is not an available force field in the Materials Studio graphical user interface, so it was necessary to use Direct Force Field, a GUI capable of assigning the TEAM force field.

2.3 Submitting Files for Simulation

Direct Force Field is also capable of exporting the systems as a LAMMPS input file with a corresponding data file. Each input file must then be modified to compute each desired quantity. For each simulation, the kinetic energy, potential energy breakdowns, pressure, dimensions of the system, and the volume were tabulated every 100 steps (0.1 ps). The interaction of each individual amino acid of the peptide with the surface was also computed. Finally, the surface-solvent and solvent-peptide interactions were computed to ensure the systems were equilibrated with respect to these quantities. It was important to fix the x dimension of the ARM systems to prevent the neighboring ribbons from moving towards each other. The lattice was allowed to change dimensions in the y and z directions to maintain a constant total pressure of one atmosphere. Similarly, the y dimension of the ZIG systems were fixed, while the x and z dimensions remained free. The GRA and HOL systems were left free to change dimensions in all three dimensions to maintain a total pressure of one atmosphere. After the input file was modified, it was transferred to the supercomputer raptor with the corresponding data file. Each simulation took approximately 60 hours to run 20 million steps on 64 processors to produce a trajectory file and a table file. Twenty million steps corresponded to 20 ns of simulation.

2.4 Interpret Files from Simulations

The table files produced by LAMMPS contained the desired quantities (kinetic energy, potential energy breakdown, etc) for the duration of the simulations. The [table](#) files were imported to OriginPro. The first four nanoseconds were removed from calculations; during this time, the system was still approaching equilibrium and, therefore, is not an accurate description of the interaction energies. Then, the average quantities were calculated for the remaining 16 ns. The averaged results were then used to calculate the binding enthalpy by following the efficient computation method illustrated.

Data & Results

3.1 Surface Interactions of Water Molecules

Each LAMMPS simulation showed that the water molecules avoided the graphitic surfaces and did not come into contact with them (Figure 5).

3.2 Surface Interactions of Glycine-Glycine-Glycine

After five runs of the GGG peptide on the four surfaces, it was found that the GGG peptide was attracted to the armchair-edged nanoribbon, with a binding enthalpy of -11.2 ± 1.0 kcal/mol. A negative value of the binding enthalpy represents an attraction between the surface and the peptide. The binding enthalpy was largely a result of the van der Waals and electrostatic contributions. Similarly, the HOL surface had a binding enthalpy of -10.4 ± 0.5 kcal/mol. This interaction was predominantly due to the van der Waals and electrostatic contributions and was likely a result of the peptide interacting with the armchair edges of the hole. GRA and ZIG showed significantly less interaction with binding enthalpies computed to be -6.0 ± 3.5 and -6.5 ± 2.7 kcal/mol, respectively. See Table for [energy breakdowns](#).

3.3 Surface Interactions of Glycine-Phenylalanine-Glycine

After five runs, the binding enthalpy of GFG with the pure graphene sheet was found to be -2.4 ± 3.0 kcal/mol. This suggests minimal interaction between the graphene surface and the GFG peptide. GFG showed a slightly larger attraction to the ARM and HOL surfaces with binding enthalpies computed to be -3.1 ± 1.2 and -3.2 ± 0.3 kcal/mol. The zigzag-edged nanoribbon had a moderate interaction with the peptide; the computed binding enthalpy was -4.4 ± 0.8 kcal/mol and largely a result of van der Waals and electrostatic contributions. See Table for energy breakdowns.

Summary

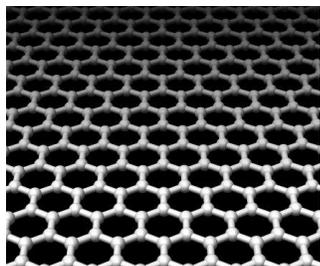
The interactions of graphitic surfaces were evaluated for two peptides, GGG and GFG. Twenty nanoseconds were simulated per system and after the first four nanoseconds were discarded as an equilibration period, the average energies were calculated. This calculation was repeated five times for each system. Then, the energies were averaged over the five independent runs. It was found that the GGG peptide consistently demonstrated a stronger interaction relative to the armchair-edged nanoribbon and the hole-containing surface. For both cases, the binding enthalpy was negative, indicating that the peptide was attracted to the graphitic surfaces. Although the GFG peptide showed minimal interaction with the pure graphene sheet, it showed a slight interaction with the other graphitic surfaces. Overall, it was concluded that the GGG peptide is more attracted to the graphitic surfaces than GFG. Future plans of this research project include evaluating the TEAM AMBER force field by comparing these results to those produced by a force field that includes polarizability. These force fields are relatively new and are able to compute energies of simple models containing water and hydrocarbons; however, REAX-FF may prove to be promising in modeling aqueous systems containing a peptide. Further, this project intends to continue studying the interactions of different tripeptide structures and those of larger peptides with graphitic surfaces.

Impact of Summer Research Experience

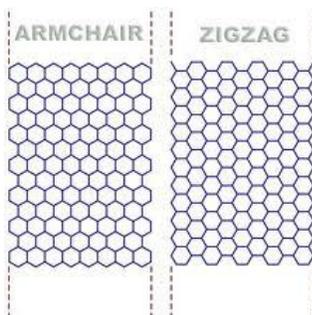
The JEOM internship program was an incredibly educational and rewarding experience for me. When I first began this internship in June, I did not know anything about modeling chemistry on the computer, I had never seen UNIX, and I had never heard of any of the software we use. Now, at the end of the summer, I feel very comfortable preparing simulations and submitting jobs to the supercomputers; I am also beginning to learn to analyze the results. I could not have learned everything so quickly without the help of the brilliant researchers here at

Wright Patterson Air Force Base. I greatly appreciate Yen Ngo, who introduced me to this field and helped me learn UNIX faster than I expected. I am also very grateful to Dr. Rajiv Berry, my outstanding mentor who deepened my understanding on atomic interactions and high performance computing. One of my favorite things that I learned in my ten weeks here was Materials Studio. When I took chemistry classes, all of the laboratory experiments were performed in beakers and test tubes. Modeling atom systems with the Materials Studio graphical user interface was really interesting because I could actually see the individual molecules and predict how they might interact. After running the first simulation, I was a little overwhelmed with the vast table of numbers produced, but when Dr. Berry explained how to begin analyzing the output, I could see that the numbers were telling a story, illustrating how the molecules behave. I feel very lucky that I was chosen for this opportunity to conduct research. I found it to be a very eye-opening experience, especially because it was in a field in which there was much I could learn. This summer internship has made me realize how much I enjoy researching. Although there were hours (or even days) that I was stuck on a problem, I greatly enjoy the challenge of solving something new. I was on the fence about going to graduate school, but now I know I want to attend. I hope to continue working in research after I obtain my Master's degree. This internship has taught me a great deal about how to be a researcher and has already opened the door to new opportunities.

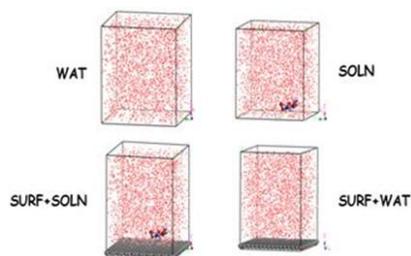
Figures, Graphs, & Tables



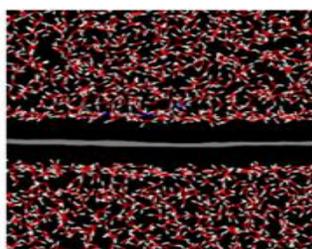
Structure of graphene.



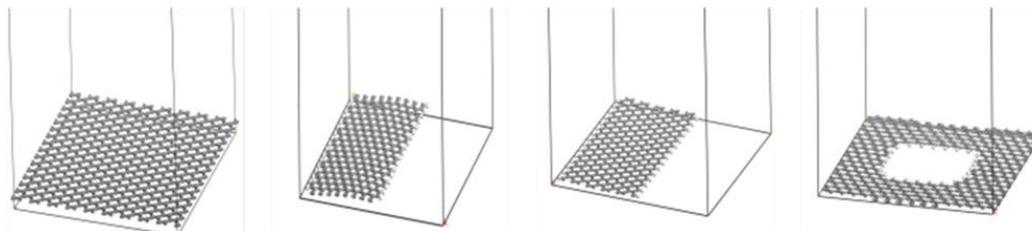
Armchair vs. zigzag



Calculation of binding



Water (Red Oxygens) tend to avoid contact with graphitic surfaces (grey)



Four types of graphitic surface. (L-R) GRA, ARM, ZIG, HOL.

Total Energy	Kinetic Energy (KE) + Potential Energy (PE)
PE	$E_{\text{bond}} + E_{\text{angle}} + E_{\text{dihed}} + E_{\text{impr}} + E_{\text{vdwl}} + E_{\text{elec}}$
E_{bond}	$\sum \frac{1}{2} k_b (l-l_0)^2$ bonds
E_{angle}	$\sum \frac{1}{2} k_a (\theta - \theta_0)^2$ angles
E_{dihed}	$\sum \frac{1}{2} V_n [1 + \cos(\eta\omega - \gamma)]$ torsions
E_{impr}	$K [1 + d \cos(\eta\phi)]$

GFG	Total Energy	KE	PE	E_{bond}	E_{angle}	E_{dihed}	E_{impr}	E_{vdwl}	E_{elec}
GRA	-2.4 ± 3.0	0.1 ± 0.1	-2.4 ± 3.0	-0.7 ± 0.9	-0.2 ± 0.3	-0.2 ± 0.5	0.0 ± 0.0	-3.6 ± 2.0	2.2 ± 6.0
ARM	-3.1 ± 1.2	-0.1 ± 0.1	-3.0 ± 1.2	0.1 ± 0.4	0.8 ± 0.7	0.7 ± 0.6	0.0 ± 0.0	-1.3 ± 1.2	-3.4 ± 1.8
ZIG	-4.4 ± 0.8	0.1 ± 0.1	-4.3 ± 0.8	-0.5 ± 0.3	0.1 ± 0.1	0.9 ± 0.2	0.0 ± 0.0	-2.3 ± 0.7	-2.5 ± 1.7
HOL	-3.6 ± 0.3	0.1 ± 0.1	-3.3 ± 0.4	-0.3 ± 0.2	0.8 ± 0.7	1.0 ± 0.5	0.0 ± 0.0	-1.7 ± 0.4	-3.0 ± 1.1

References

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