Size Dependent Graphene Quantum Dot (GQD) Interactions with Protein Biomarkers

Ayoola Abimbola[1], Sabita Saldanha[2], Prabir Patra[1,3], Isaac Macwan[1]
[1]Department of Biomedical Engineering, University of Bridgeport
[2]Department of Biological Sciences, Alabama State University
[3]Department of Mechanical Engineering, University of Bridgeport

Abstract

Gamma-H2Ax protein is seen at the DNA damage sites and it is also incorporated randomly in to the histones throughout the DNA, which produce other necessary components for the DNA repair. It also contributes to the stable nucleosome formation when the histone molecules wrap the DNA. The histone complexes comprise of proteins called H2A ,H2B, H3 and H4. The H2A protein family further contains the highest number of variants, which are H2A1, H2A2, H2AX and H2AZ. This protein has a unique carboxyl tail which consist of a conserved reactive site of one serine residue at the position 139. H2Ax becomes phosphorylated at Serine 139, which is 4 residues from the C-terminus, in the presence of DNA damage. Gamma-H2Ax is further acetylated at Lys 5 and ubiquitinated on Lys 119. Graphene quantum dots (GQDs) have a size less than 10nm and they are about 1-10 of layers of graphene, which are used in the various biomedical applications. Some of their important properties include chemical stability and quantum confinement effect. *In this study we investigate the effects of the different sizes of GQDs as they interact with H2AX to form a molecular basis of isolating different protein biomarkers based on their molecular weight.*

Simulation Steps:

- The pdb file (3QSD) of Gamma-H2AX, which is 17 kDa protein was obtained from the pdb bank.
- Based on the size requirement, three different GQDs are modeled using 'Nanotube Builder' plugin in the VMD – GQD1 (2 x 3 nm), GQD2 (5 x 6 nm) and GQD3 (8 x 9 nm), each of them having two layers.
- CHARMM parameters are used for the force field.
- TIP3 water model with a neutralizing concentration of salt is used.
- 50 ns each all-atom simulations are carried out using NAMD and analyzed using VMD.
- The initial energy minimization was carried out for a time period of 2500 steps to stabilize the H2AX/GQD complex and it was equilibrated for 500,000 steps (1ns).
- Periodic boundary conditions are considered with a constant pressure of 1 atm and constant temperature of 300K.
- The preliminary data analysis involve **RMSD**, **hydrogen bonds and interaction energy**.

Results:

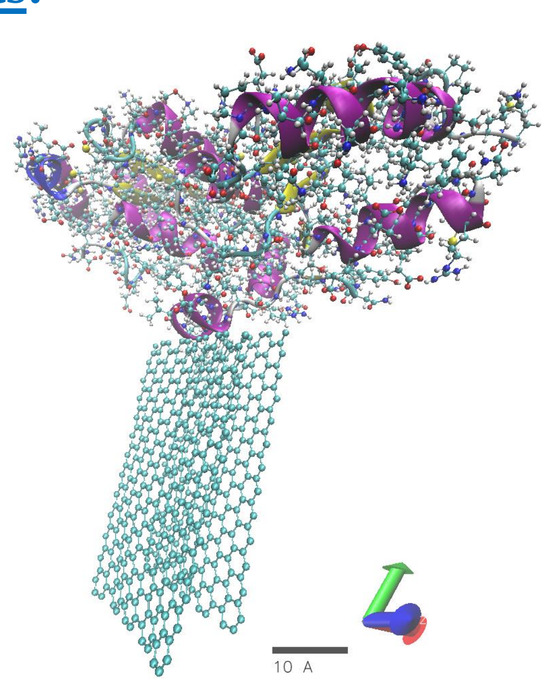

Figure1: Image of Gamma H2Ax and graphene quantum dot I in MD Simulation

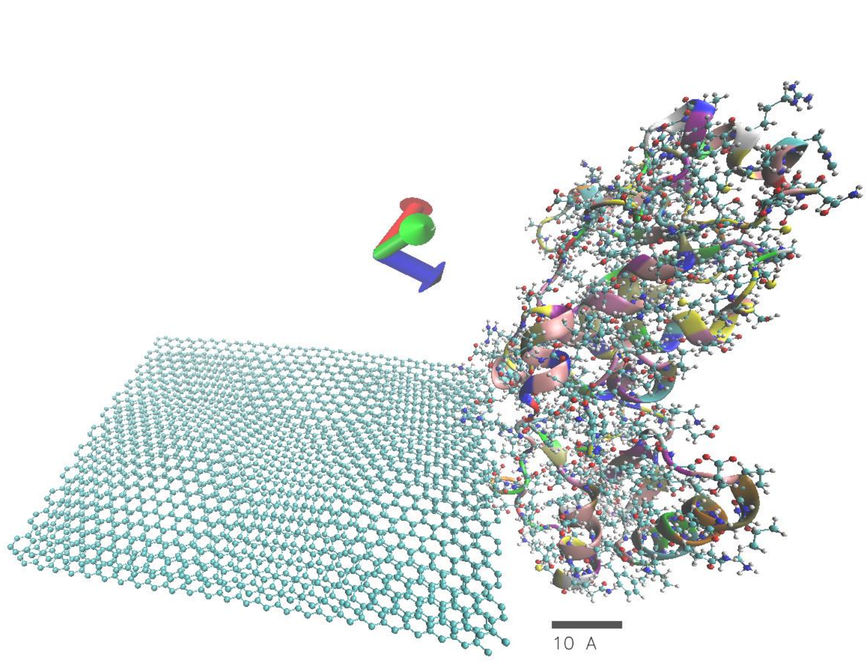

Figure 2: Image of Gamma H2A and graphene II in MD Simulation

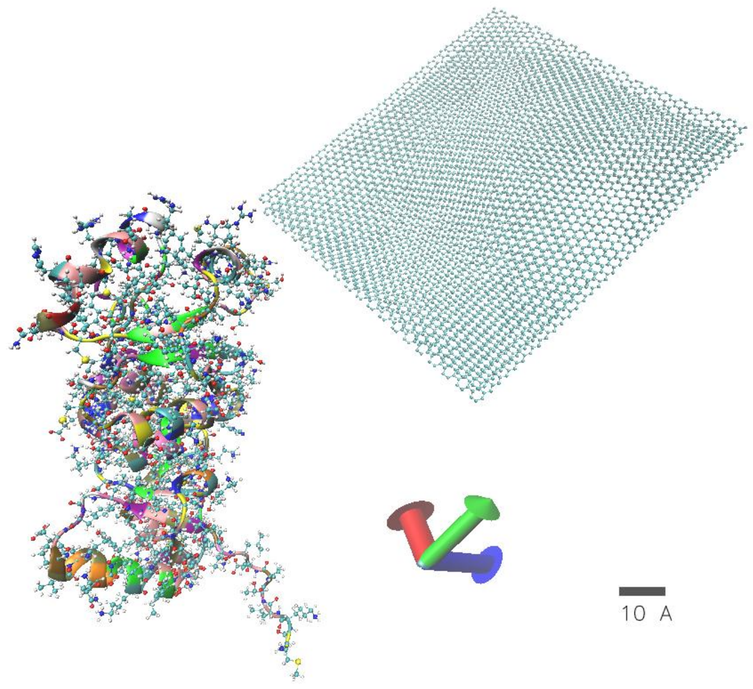

Figure 3: Image of Gamma H2Ax and graphene III in MD Simulation

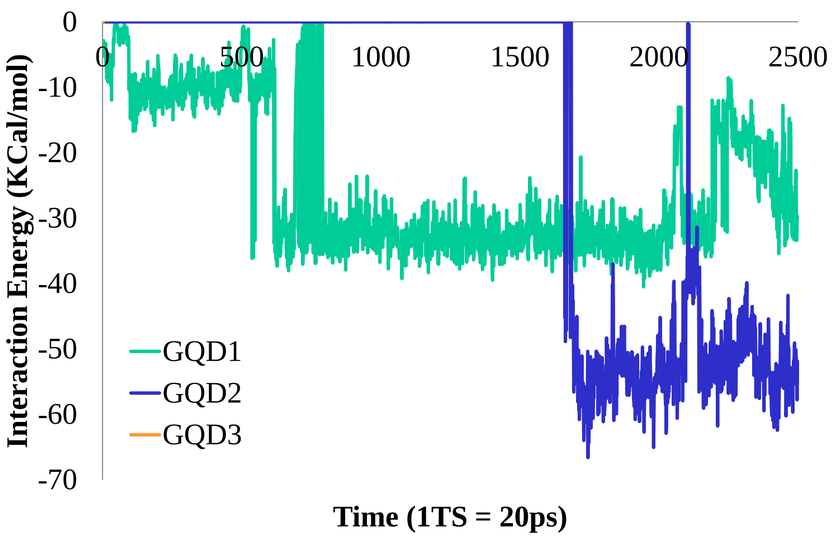

Figure 4: Analysis of non-binding energy between Gamma-H2AX and GQDs.

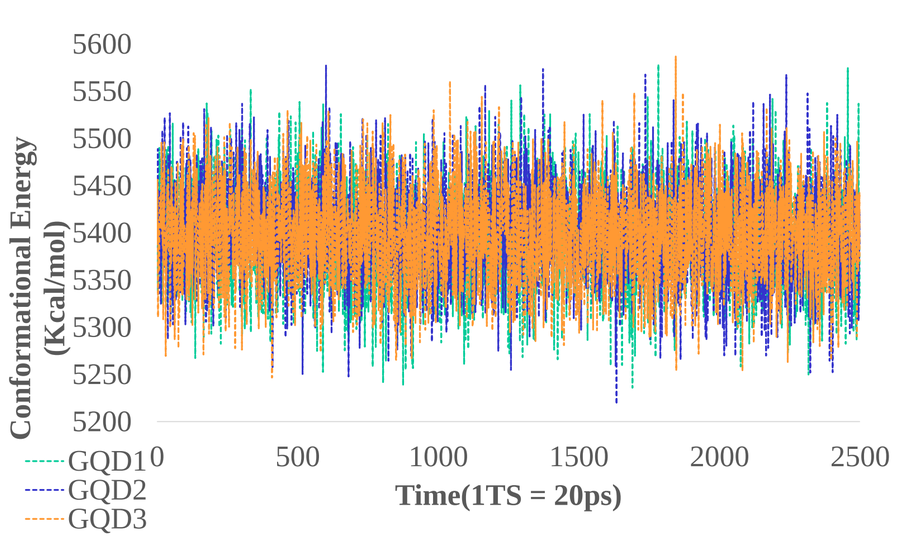

Figure 5: Analysis of the conformational energy in MD Simulation

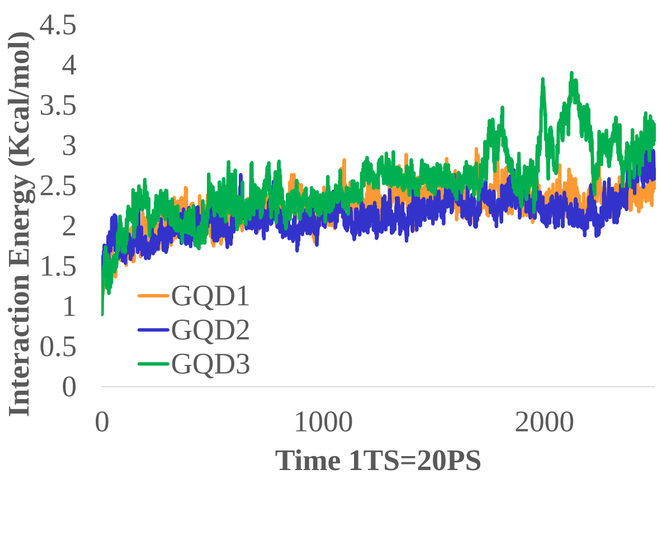

Figure 6: RMSD of Gamma H2Ax with three GQDs.

Preliminary Observations and Future Work:

- It was observed that as the sizes of GQDs increase, the protein moved further away from the graphene surface to avoid denaturation.
- There are no significant changes in the conformational energy of the protein in the presence of three different GQDs.
- GQD1 interacted for a longer time. However, GQD2 interacted with the highest non-binding energy.
- GQD3 did not show any interactions with Gamma-H2AX.
- Two other protein biomarkers viz. MDR-1 (141 kDa) and p53 (53 kDa) will be compared to study the mw-based interactions.

References:

1. Kuo, Linda J, & Yang, Li-Xi. (2008). γ-H2AX-a novel biomarker for DNA double-strand breaks. *In vivo*, *22*(3), 305-309.
2. Yan, Wei, Shao, Zhenhua, Li, Fudong, Niu, Liwen, Shi, Yunyu, Teng, Maikun, & Li, Xu. (2011). Structural basis of γH2AX recognition by human PTIP BRCT5-BRCT6 domains in the DNA damage response pathway. *FEBS letters*, *585*(24), 3874-3879.
3. Macwan I, Khan MDH, Aphale A, et al. Interactions between avidin and graphene for development of a biosensing platform. *Biosens Bioelectron*. 2017;89:326-333.