3-2016

Human Insulin Adsorption to monolayer graphene. A molecular dynamics study.

Richard Overstreet
Clemson University

Brian Dominy
Clemson University

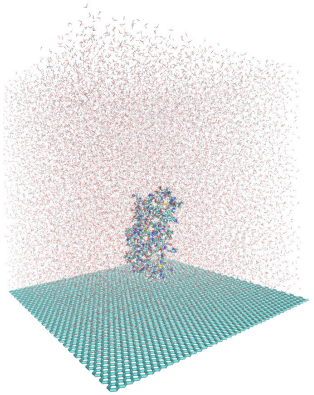
Human Insulin Adsorption to monolayer graphene. A molecular dynamics study.

Richard Overstreet, Brian Dominy. Clemson University.

Molecular dynamics simulations were conducted using the CHARMM22 potential and TIP3P solvent to model human insulin adsorption to graphene. TIP3P explicit solvent was used to capture the hydrophobic effect, the mechanism responsible for the adsorption of proteins to hydrophobic surfaces. This water model was originally parameterized for the CHARMM22 potential and amino acid residues thus it was required to develop Lennard-Jones graphene carbon parameters to reproduce the empirical water graphite contact angle of 86 degrees. Adsorption was modeled with three different orientations about the graphene monolayer. Insulin shows varying degrees of adsorption surface area and correlated binding affinity due to limiting solvent exposure to the surface between the different orientations.

Motivation:

- Simulate how different orientations of the protein affect the binding of human insulin to graphene.
- Correlate the surface area of adsorption and solvent accessible surface area (SASA) to the binding affinity of the protein.

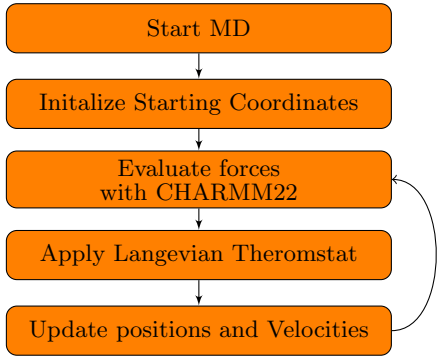


System Introduction:

- Graphene
  - One atom thick layer of sp2 hybridized carbons, with unique electronic and physical properties.
  - The conductivity of graphene is dependent on the charge carrier concentration and carrier mobility which changes at the single electron level, while maintaining a high signal to noise ratio
  - Enables the detection of single molecules at RT such as NH_3, CO, and NO_2 at concentration of 1 ppb.
- Human Insulin
  - Protein is 51 amino acids long containing two chains linked by a disulfide bonds at sites A/B 7 and A/B 20.
  - Secreted from the pancreas into the hepatic portal vein and liver to maintain glucose homeostasis in the body.
  - Highly conserved across many species.

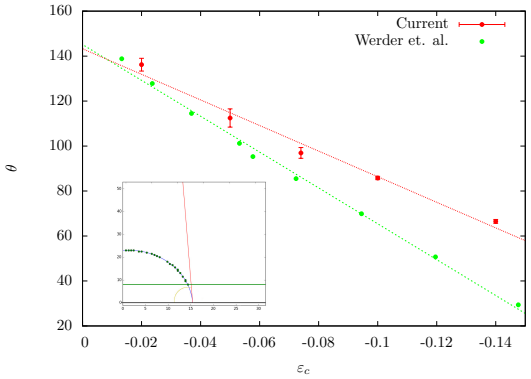
Methods:

- Molecular Dynamics with the CHARMM22 potential TIP3P explicit water and Langevian thermostat.

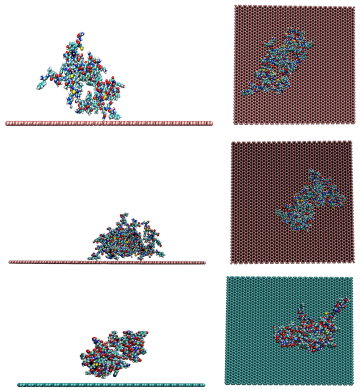


Results:

- Calibration of CHARMM22 Non-bonding Parameters for graphene carbon.



- Protein configurations post Adsorption.



Conclusion:

MD simulations were conducted on human insulin and a graphene monolayer to model adsorption events with different orientations about the monolayer. Parameterizing the CHARMM22 potential showed that the TIP3P water model is less sensitive to perturbations in the ε_c parameter for the Lennard-Jones potential. This difference can be attributed to the smaller hydrogen oxygen bond angle in TIP3P water compared to SPC/E 104.52^o and 109.47^o respectively. Preliminary results show that SASA is not correlated to the binding affinity of the protein. Binding affinities of the protein to graphene for systems **I-III** were -2.1802e5, -2.1267e5, and -2.1167e5 kcal/mol, respectively.

References

[1] W. Bocian, J. Sitkowski, E. Bednarek, A. Tarnowska, R. Kaw*cki, and L. Kozerski. Structure of human insulin monomer in water/acetonitrile solution. *Journal of Biomolecular NMR*, 40(1):55–64, 2008.

[2] M. Federwisch. Insulin and related proteins - structure to function and pharmacology.

[3] T. Wei, M. A. Carignano, and I. Szleifer. Lysozyme adsorption on polyethylene surfaces: Why are long simulations needed? *Langmuir*, 27(19):12074–12081, 2011. PMID: 21846132.

[4] T. Werder, J. H. Walther, R. L. Jaffe, T. Halicioglu, and P. Koumoutsakos. On the water−carbon interaction for use in molecular dynamics simulations of graphite and carbon nanotubes. *The Journal of Physical Chemistry B*, 107(6):1345–1352, 2003.