Molecular Dynamics Simulations of Protein Crystals

Justin Kim[1], Eugene Klyshko[1], Lauren McGough[2], Rama Ranganathan[2] and Sarah Rauscher[1]

[1]Department of Chemistry, University of Toronto, ON, Email: kimjus11@mail.utoronto.ca
[2]University of Chicago, USA

Molecular dynamics (MD) is a computational method that can be used to simulate proteins with atomistic detail. When utilized appropriately, MD can deliver valuable insight into experimental results, while also providing future research guidance. While MD simulations are generally performed with proteins in solution, most of the protein structures deposited on the Protein Data Bank are, contrastingly, experimentally resolved using x-ray crystallography. Then, any comparisons made between simulations and crystallographic experiments are not an exact correspondence, due to the environmental differences between the two systems. Therefore, crystallographic MD simulation is required to appropriately assess the comparison.

This talk will present the current findings of our MD simulations of a protein crystal. Using multiple forcefields, we simulate the second PDZ domain of LNX2 in both crystal and solution environments. The protein crystal is composed of 3x3x3 unit cells, each with 4 copies of the LNX2 PDZ2 domain for a total of 108 proteins per simulation system. Due to the protein density and crystal contacts in the system, the simulation methodology for a typical protein-water system is not directly transferable. However, we demonstrate that by modifying these existing simulation protocols, simulations of protein crystals can be performed within existing MD frameworks. Furthermore, protein crystals provide an excellent test system with which to validate atomistic molecular dynamics simulations.