Comparison of temperature dependent stability of a synthetic beta-hairpin through atomic simulation

-Manaal Tabassum Shaad, Huzaifa Kamran Khawaja, Angel Rodriguez,

Acknowledgements: Dr. Joshua Hanson, Patricia Posada
Luis Alcazar, Rene Rubio

ABSTRACT

We simulated a protein beta structure's stability to calculate the free energy of a synthetic beta-hairpin's(simple protein) unfolding transition. We simulated it at different temperatures to better understand the importance of entropy in the folding and unfolding process. We were able to visualize this process of the protein through VMD(Visual Molecular Dynamics) and NAMD (Nanoscale Molecular Dynamics), programs that display biological molecules in 3D.

INTRODUCTION

The purpose of this project is to see the different ways in which temperature changes and affects a synthetic beta-hairpin. Our goal for this project as a whole is to use proficient knowledge of programming and physical science(chemistry, biology, physics) to determine and visualize specific circumstances in which a beta-hairpin is affected by three different temperatures. The examples that we're going to show are the different ways in which the beta-hairpin is affected at 280K, 300K, and 320K. How are the three different temperatures going to affect the protein? Are the differences going to be significant? What other forces are at work and contributing to the changes in the beta-hairpin?

As the temperature increases, we expect to see more protein conformations(higher separation) but will ultimately be too high in energy to see other stable conformations.

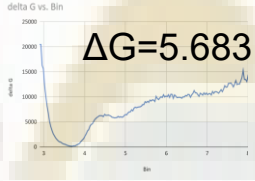
METHODS

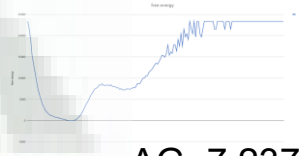
Using the VMD, biomolecule visualization software, we visualized our molecule in various ways.We were able to highlight specific peptide side-chains to see how their interactions could play a role. In order to simulate the peptide, we had to convert the standard protein file type into a structure file that our simulation software, NAMD(Nanoscale Molecular Dynamics), could recognize.

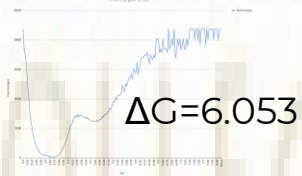
Protein structures typically leave out water because of how their structures are determined. But in order to simulate real world scenarios, we solvated (add water) the protein to model physiological conditions. After loading our structure into NAMD, we set up a thermostat for our desired temperature. Lastly, we set up a boundary condition that kept the center of mass of our protein in place. After the simulation was completed, we got our Trajectory simulation, which meant computing the flight path and other parameters, such as orientation and angular rates of the munition from the start to the end of its motion. We studied this peptide by looking at the distances between the two ends of our "U-shaped" protein. This is how we characterized its shape. With our trajectory files, we calculated all the distances between the terminal peptide residues.

STATISTICS

Beta-hairpin is affected at 280K, 300K, and 320K, respectively. By simulating three dimensional molecules at three different temperatures. We observed the conformational patterns and associated free energies of the synthetic protein 1UAO using Molecular Dynamics. The synthetic proteins (partially unfolded, upper left; fully folded, bottom left) are shown with the two end side-chains show explicitly. The x-axis represent distance between the ends of the peptide and y-axis, Gibbs free energies, ΔG units are KJ/mol.







RESULTS

Entropy is favored at higher temperatures. A folded protein typically has more enthalpy (bond energy) from all the hydrogen bonds and van der Waals forces. As the protein unfolds, the water molecules hydrogen bonds with the two exposed side chains, decreasing the water's entropy and, in turn, the overall entropy. At higher temperatures, we now know that the protein is more favored in the folded state because it maximizes the water's entropy

Conclusion

Goals- Our goal for this project was to utilize knowledge of programming and physical sciences to determine and visualize specific circumstances and extrapolate data in which a beta hairpin is affected by three different temperatures

Limitations-The simulation, which was on the nanosecond scale, which limited our overall sampling, we could have sampled at a different simulation timescale-- micro or millisecond process, 10^3 or 10^6

Further research we could process the simulation for more time to have a microsecond or millisecond of data more temperatures could have been selected for the aforementioned simulation, such as within the range of 200 Kelvin to 450 Kelvin we could have simulated the said protein at resolutions of 285,290, 295 etc The residues could have been further manipulated