

Title: Using Simulations to explore the folding properties of the 2CI2 Protein

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As practical experiments become more expensive and time consuming, coupled with the fact that direct measurement of transition states and intermediates in physical experiments are prohibitably difficult. Therefore, research in this field would normally be a largely philosophical discussion. A new methodology that has risen to study these difficult structures is the use of simulations as a means to understand experimental research more fully. Learning how to perform simulations and to compliment experiments is an important and unique skill. Our simulation study used a Linux-based Ubuntu Virtual Machine and used Gromacs and VMD software to explore three-dimensional folding of both 1AKI (Lysozyme) and 2CI2 (Chymotrypsin inhibitor 2) proteins. The simulations provided the means to study proteins as they truly are, the amalgamation of many microstates. This kind of analysis would be impractical to do with traditional experimental methods. Within the research we also explored how the kinetic energy can alter Q (the fraction of folded state contact pairs found in the crystal structure). Next, we learned how to identify a folding state as folded, unfolded or transition state based on their Q values. Working with the terminal and using Dr. Finke's Training Tasks that showed example UNIX command line techniques and steps, I was able to set up simulations for both proteins, use VMD software to create 3D models, and to create graphs of simulation output. These techniques and programs were then combined to help explore the effects of "knock out" or "deletion" mutations on 2CI2 protein, and how removal of attractive forces impacts the delta G of different folding states to a different degree. These differences were directly compared with experiments of actual folding structures of the 2CI2 protein and showed a similar fit, especially with a linear regression that removed the negative experimental phi-values and allowed the simulation (which cannot process negative phi-values) to be similar enough fit to be used in simulating the 2CI2 mutations. This kind of comparison of many mutant proteins would be too time consuming and difficult to perform by only using experiments. The new technologies offered with simulation, and the skills to apply them, are a powerful tool in the scientist's arsenal.