Protein Stability of a 21 Alanine Based Peptide

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Introduction

Protein folding is one of the most significant fields of study in science today. The ability to a priori fold a protein into its native 3-dimensional structure from primary sequence is extremely difficult. Progress has been made in the ab initio folding of short sequences; however, the folding of a medium to large sequence is not feasible. Experimental methods along with computational models one is able to generate insight into the complex energy landscape. A recent experimental technique using ultraviolet raman spectroscopy is able to measure the free energy landscape of a 21 amino acid sequence. In conjunction, a molecular dynamics simulation of this 21 amino acid sequence has been able to reproduce that free energy landscape. In addition to measuring the free energy of folding both the experiment and computational modeling work is able to look at the stability of folding as a function of salt concentration. Initial efforts in this area appear to follow know experimental evidence that some salts increase helix formation while others destabilize helix formation. This is known as the Hofmeister series. The reason(s) leading to salt stabilization or destabilization is not well understood.

Hypothesis

Our hypothesis is that the sulfate anion destabilizes alpha helix through the change in water activity.

Specific Aims

We will test our hypothesis in the following specific aims:

1. Calculate the free energy landscape for a 21 residue alanine based peptide in the presence of sulfate ions. In this aim we will perform a series of molecular dynamics simulations on a 21 residue alanine based peptide in explicit water and sulfate ions using AMBER9. The data collected from these simulations will be used to construct a free energy landscape as a function of the psi angle.
2. Calculate the activity of sulfate ion in water. A series of molecular dynamics simulations will be run to collect data in which the activity of sulfate in water will be determined. The calculated sulfate activity in water will be compare to experimental activity data.
3. Analyze the peptide in water simulation data to determine the reason(s) for alpha helix destabilization. The molecular dynamics simulation data will be analyzed to determine which of the following mechanisms are responsible for stabilization/destabilization
    a. Debye screening
    b. Ion-pair
    c. Electrostatics
    d. Water activity

References

1. E.K. Asciutto et al. "Experimental and Computational insight into the unfolding of a 21 residue alanine based peptide." (not yet published)
2. A.D. MacKerrell et al. "All-atom empirical potential for molecular modeling and dynamics studies of proteins." *Journal of Physical Chemistry.* 1998
3. D.A. Case et al. "The amber biomolecular simulation program." *Wiley InterScience.* 2005.
4. G.E. Marlow et al. "Salt effects in peptide solutions: theory and simulation." *Chemistry Review.* 1993.