Pressure Denaturation of Proteins in Water: Revisiting a Heteropolymer Collapse Model

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Introduction

Understanding the environmental factors that cause proteins to unfold from their native conformations to form biologically-inactive or denatured states represents one of the most important challenges in the biological and pharmaceutical sciences. Although it has been known for some time that proteins can be denatured by heating or cooling at high or low pressure, only semi-empirical thermodynamic approaches have been developed for predicting the range of protein stability in the pressure-temperature plane [1]. An analytical molecular-level theory that can give insights into the state-dependent driving forces for unfolding would be an extremely useful complement to recent experiments (see, e.g. [2]), information theory approaches [3], and computer simulations [4].

Discussion

In this talk, we revisit a simple mean-field theory for heteropolymer collapse that was introduced by Dill and co-workers [5] to explore how the balance of hydrophobic and conformational forces determines the thermal stability of proteins at ambient pressure. We generalize their approach to study pressure effects by introducing a simple statistical mechanical treatment for the hydration thermodynamics of amino acid side chains. In particular, we calculate the strength of the elementary interactions of amino acids with solvent using a molecular thermodynamic theory for the pressure- and temperature-dependent interfacial tension between liquid water and a solid hydrophobic surface. The revised theory predicts how the region of protein stability in the pressure-temperature plane depends on the size and hydrophobic content of the molecule, and it provides new insights into the possible mechanisms for pressure denaturation.

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