A Simple Coarse-Grained Model for Studying the Behavior of Proteins in Solution

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Introduction

Protein-protein interactions, the thermodynamic and kinetic stability of protein molecules, and the global phase behavior of protein solutions are subjects of great scientific and technological interest [1, 2]. For example, the condensation of proteins into aggregates has been implicated as an important factor in several diseases including Alzheimer's, Mad Cow's, and Down's syndrome [3, 4]. Moreover, since protein aggregation inhibits biological activity, it remains a formidable obstacle to increasing the shelf life of therapeutic proteins [5]. Although experimental tools can provide useful information about the collective behavior of proteins in solution, a basic molecular-level picture is still lacking. Computer simulations of model proteins [6] can serve as an insightful complement to the available experimental data; however, studying large-scale aggregation events with molecularly-detailed protein models and solvent is still computationally prohibitive.

Discussion

We have developed a very simple coarse-grained model for predicting state-dependent protein-protein interactions in solution based a heteropolymer collapse (HPC) theory for protein folding [7]. It allows us to analyze the behavior of protein solutions by both Reactive Canonical Monte Carlo (RCMC) simulations [8] and statistical mechanical theories of the liquid state. In this talk, we will use the model to explore how the properties of individual proteins (e.g., size and sequence) and the global environment (e.g., temperature and protein or solute concentration) affect protein stability and phase behavior. We will also analyze how the behavior of concentrated protein solutions derives from a balance of crowding effects (excluded volume), the intrinsic free energy of folding, and conformational aspects of the native state.

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