Unfolding Behavior of Proteins in the Presence of a Pulling Force

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Recent experiments [1] based on atomic force microscopy have demonstrated that proteins unfold when two residues are mechanically pulled apart. This unfolding process is different from the unfolding process under the raise of temperature or the addition of a chemical denaturant. Experiments [2] have also shown that the pulling forces required to initiate unfolding vary considerably depending on the location within the protein of the applied forces. In this study, a method based on the Gaussian network model (GNM) is developed to study the unfolding pathways in different force locations. GNM is a schematic model that is topology based and is independent of sequence specificity. In this work the protein unfolding process is mimicked through the breaking of native contacts one by one. First, force induced deformations were calculated. Next, interaction bonds of residue pairs that were found to have inter-residue distance greater than a cutoff distance are made to break. The force deformations of the new network are recalculated, and the cycle continues until all bonds break. Using this approach, the unfolding process of three proteins CI2, Gankyron and Green Fluorescent proteins are simulated for different applied force locations. We found that some of the unfolding sequences revealed by this method are almost identical to thermally induced unfolding as obtained by Monte Carlo simulations [3]. However, certain force locations lead to quite different unfolding pathways. We also found that although the protein is being pulled along a fixed direction, it unfolds in one or more cooperative steps that are reminiscent of a first order phase transition and similar to the force induced helix–coil transition in DNA [4].

References:

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