Structural Diversity of Amyloid Proteins in Intermediate States

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The aggregation of abnormally folded amyloid proteins is associated with a number of neurodegenerative disorders, such as type II diabetes, Alzheimers disease and Parkinsons disease. Due to the long period and diverse potential routes, the exact mechanism by which amyloid proteins aggregate and destroy tissue cells remains poorly understood. To develop an effective aggregation model, it is of critical importance indicating the conformations of multiple intermediate states along the amyloid self-assembled pathway.

In this work, we advance a new method, which is an interdisciplinary combination of mathematical, physical and biological tools. Our approach is based on energy function that derives from the universality, renormalization group and local gauge symmetry, and can cover very long time span for protein folding. The multi-soliton configuration which describes the structure of target protein is accurately constructed by the global minima of energy function. The unfolding and refolding kinetics is simulated by subjecting the multi-soliton to a series of heating and cooling processes. The statistical distribution of obtained conformations shows that heating-and-cooling procedure yields a variety of structural clusters which have different spatial shapes. These results clearly suggest that the intermediate states of amyloid proteins are structurally diverse.

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