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Associative memory model of protein intrinsic disorder

Katsuyoshi Matsushita[1,2] and Macoto Kikuchi[1,3,4]
[1]Cybermedia Center, Osaka University
[2]Institute for Protein Research, Osaka University
[3]Graduate School of Science, Osaka University
[4]Graduate School of Frontier Biosciences, Osaka University

The specific protein structure characterizes protein function [1]. The folding into the structure had been considered to be necessary for the protein function in living cell. However intrinsically disordered proteins that are wholly or partially unfolded in physiological conditions have been shown to have various roles in the last decade [2]. Understanding the intrinsic disorder is expected to lead us to novel concepts of protein physics. Recently, a full atomic simulation clarified that an intrinsically disordered state consists of a characteristic structural ensemble including a specific functional structure [3]. The effects of the structure ensemble on the thermodynamic property of the intrinsically disordered state are unclear.

We consider an associative memory model which memorizes structures in the structural ensemble in order to gain insights into the effects. Previously we employed an Ising-like model and examined the thermodynamically feature of the intrinsically disordered state. The model reproduces the structural feature observed in the full atomic simulation [4]. In this case, a misfolded structure without function plays an important role: the misfolded state suppresses the folding into a specific functional structure and thereby introduces an intermediate state between a perfectly unfolded state and a misfolded state as an intrinsically disordered state. In this work, we show that the previous result is reproduced in the associative memory model with the two memorized structures, namely a specific functional structure and a misfolded structure. Furthermore we show that the associative memory model with four memorized structures (one of them is a specific functional structure and three of them are misfolded structures) exhibits thermodynamic properties qualitatively similar to that of the two-state model.

From this result, which does not depend on the number of misfolded states, we conjectured that the thermodynamic property does not seriously depend on most of the structures in the structural ensemble in the intrinsically disordered state. Namely the thermodynamics property is determined only from single or a few misfolded structures. Therefore, specifying the important misfolded structures based on machine learning from experimental data or full atomic simulation data may promote our deeper understanding of the intrinsically disordered state.

References

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