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The folding mechanisms prediction of IG-like beta sandwich proteins based on inter-residue average distance statistics methods

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Abstract

To understand the folding mechanism of a protein is one of the goals in bioinformatics study. Nowadays, it is enigmatic and difficult to extract the folding information from its amino acid sequence by using standard bioinformatics techniques or even experimental protocol which cost and time consuming. To overcome these problems, we aim to extract the initial folding unit for titin protein (Ig and fnIII domains) in the mean of inter-residue average distance statistics, average distance map (ADM) and contact frequency analysis (F-value). TI I27 and TNfn3 domains are represented for Ig-domain and fnIII-domain, respectively. Beta-strand two, three, five and six are significant for the initial folding processes of TI I27. On the other hands, the central strands of TNfn3 were predicted as a primary folding segment. Furthermore, known 3D structure and unknown 3D structure domains were investigated by structure or non-structure based multiple sequence alignment, respectively, to seek the conservation hydrophobic residue and predicted compact region through the evolution. Our results show well corresponded to experimental data, phi-value and protection factor of H-D exchange manner. It is confirming the significance of conserved hydrophobic residues near F-value peaks for structural stability by using hydrophobic packing. Again, our prediction methods could extract the folding mechanism by only its amino acid sequence.

Nonnative interactions cause energetic frustrations in protein folding and were found to dominate key events in folding intermediates. However, systematically characterizing energetic frustrations that are caused by nonnative intra-residue interactions at residual resolution is still lacking. Recently, we studied the folding of a set of homologous all-α proteins and found that nonnative-contact-based energetic frustrations are highly correlated to topology of the protein native-contact network. Here, we studied the folding of nine homologous immunoglobulin-like (Ig-like) β-sandwich proteins, and examined nonnative-contact-based energetic frustrations Gō-like model. Our calculations showed that nonnative-interaction-based energetic frustrations in β-sandwich proteins are much more complicated than those in all- α proteins, and they exhibit highly heterogeneous effects on the folding of secondary structures. Further, the nonnative interactions introduced distinct correlations in the folding of different folding-patches of β-sandwich proteins. Taken together, a strong interplay might exist between nonnative-interaction energetic frustrations and the protein native-contact networks, which ensures that β-sandwich domains adopt a common folding mechanism.

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