Abstract of Doctoral Thesis

Title：Prediction of the location and robustness of important regions for structural formation based on the amino acid sequence analysis

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A protein automatically folds into its unique native structure. The formation process is also called as a “folding process”, which is a crucial step for proteins to act as biopolymers. If a protein folds in a wrong way, it does not only become unable to function, but also affects badly on the surrounding environment and causes lethal diseases. Because most of the proteins fold into their native structure properly without misfolding, we can avoid such folding diseases. Thus, studying folding is very interesting. However, in many cases, there are no experimentally observable transient structures along the folding process because they are unstable. That makes hard to characterize the folding properties of a given amino acid sequence with experimental methods. Instead of the direct measurement, there are alternative ways to characterize the properties based on their native structures. Although, such folding property should be essentially coded in its amino acid sequence, the property should be extracted from the sequence in principle. In chapter 2, the commonality of folding units in the protein structural space is validated using Globin-like fold, based on the study that insists a protein can be decomposed into some stable partial structure units that are common in the protein structural space. In chapter 3, the relationship between nonfunctionally conserved residues and folding units is discussed for all-α, α+β, all-β class proteins. In chapter 4 and 5, the effects of amino acid substitutions on the folding units and the conservation of such units are discussed using TIM-barrel (α/β) or Ferredoxin-like fold (α+β) proteins. In chapter 6, based on the knowledge obtained in the previous chapters, a method to evaluate the robustness of folding units for a given amino acid sequences by means of artificial mutations is proposed. In chapter 7, the folding mechanisms of proteins with high sequence identities but different structures (3α or 4β+α) are discussed based on their amino acid sequence.