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蛋白質の構造変化ダイナミクス ― 1分子統計力学の視点からの考察

○伊藤 一仁¹, 笹井 理生¹

¹名大院・工学・計算理工

Protein Conformational Dynamics from a Viewpoint of Single-molecule Statistical Physics

Kazuhito Itoh and Sasai Masaki, (Dept of Computational Science & Engineering, Graduate School of Engineering, Nagoya Univ)

Recent single-molecule experiments revealed the anomalous correlation in distance fluctuation in proteins, which provided evidence for the broad distribution of timescales and the memory effect in protein conformational dynamics[1]. In the present study, we examine these dynamical features from a viewpoint of single-molecule statistical physics by emphasizing the multi-degree-of-freedom nature of single protein. In single-protein systems, large infrequent thermal fluctuations have critical effects on dynamical properties even in equilibrium. Using a statistical physical model, we show that large thermal conformational changes in a local region of a protein crucially affect the slow global collective motions. The global collective motions enhance the correlation in fluctuation between two sites and extend the relaxation time even when those two sites are far apart from the local region where the thermal conformational changes are induced. Repeat of such large thermal conformational changes around the relatively unstable region may lead to the broad distribution of timescales and the memory effect in protein conformational dynamics. We also discuss conformational dynamics in protein functioning in terms of interplay between the collective motions and the large thermal conformational changes.[1] H. Yang et al., Science 302, 262 (2003)

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タンパク質アロステリーの格子モデル

○斉藤 稔^{1,2}, 菊池 誠^{1,2,3}

¹阪大サイバー、²阪大院理、³阪大院生命機能

Lattice model for allosteric protein

Nen Saito (1,2) and Macoto Kikuchi(1,2,3)(1: Cybermedia center, Osaka Univ 2: Dept Phys , Osaka Univ 3: Graduate School of Bio Science, Osaka Univ)

Recently, some groups suggest large structural fluctuations occur at a functionally important region of a protein. We expect that also on allosteric proteins ligand binding induce some change in structural fluctuation at a distant region. In this study, we construct a lattice model for an allosteric protein. We discuss mechanism of allostery qualitatively based on a free-energy landscape obtained by Monte Carlo simulations.

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アデニル酸キナーゼにおけるアロステリックコミュニケーションのカメレオン Go モデルによる研究

○山下 貴弘¹, 笹井 理生^{1,2}, 寺田 智樹¹

¹名大院・工・計算理工、²CREST-JST

A chameleon Go model study of the allosteric communication in adenylate kinase

Takahiro Yamashita(1), Masaki Sasai(1,2) and Tomoki P. Terada(1) (1: Dept. of Computational Science and Engineering, Grad. Sch. of Engineering, Nagoya Univ; 2: CREST-JST)

Allosteric transitions are global conformational changes between two (or more) definite structures, which are induced by local events such as ligand binding. As they occurs on a millisecond timescale, the nature of the allosteric transitions are expected to be determined by global topological features and therefore may well be described by coarse-grained models.

Recently, candidates for such models have been proposed by several authors. Although they succeeded to produce a transition between two definite structures, they fall into one of two categories: (a) local interactions always stabilize two possible local structures, or (b) every local part in a protein simultaneously switches between two possible local structures. Thus they failed to describe how local structural preference propagates throughout the global structure, which is central to the allosteric communication. Here we have performed a molecular dynamics simulation of allosteric transition of adenylate kinase with a "chameleon Go model". This model includes a chameleon-like switching of local interactions which can stabilize one of two local structures according to the local structural environment. By monitoring the closeness of local structures to those in each of two structures and modulating the local interactions accordingly, two-state transition of global structure are reproduced by this model. Furthermore, we can determine key residues for the allosteric transition by analyzing how the structural transition gradually propagates throughout the global structure.

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de novo モデリングにおける非経験的フラグメント構造予測法に向けて - ネイティブフラグメントの物理化学的特性 -

○山浦 雅弘¹, 千見寺 浄慈¹

¹名大院・工・計算理工

Non-empirical fragment prediction for free modeling - Toward understanding physico-chemical property of fragments of native structures -

Masahiro Yamaura (1) and George Chikenji (1). (1: Dept. of Computational Science and Engineering, Graduate School of Engineering, Nagoya University)

Currently, the most successful *de novo* protein structure prediction method is the fragment assembly (FA) method. The FA method consists of two parts: First, fragment candidates for all possible short segments of the chain are extracted from PDB by profile-profile comparison. Second, protein tertiary structures are generated by assembling fragment structures. Although FA method is the most powerful tool, there are much room for improvement. For example, recent results from new fold (or free modeling) category of CASP experiments suggest that accurate fragment structure prediction is the most important part, but empirical fragment prediction methods such as profile-based one often fail to prepare correct (near native) fragment structures. Thus, non-empirical fragment prediction method is needed for improvement of *de novo* structure prediction. For the purpose, we are developing the non-empirical fragment prediction protocol. Our methodology is as following: First, we made a non-redundant (NR) fragment library by performing hierarchical clustering using RMSD measure to all short segments extracted from PDB. This NR fragment library can be considered as representative of all possible conformations of short peptides. Second, target fragment sequences are threaded onto these NR fragment library. In this threading part, we use physics-based energy function as a score function. In this presentation, we will give detail description of our methodology and results of native (or near native) structure discrimination test.