2P043  アロステリック機構の分子論的理解に向けたシグナルタンパク質 CheY の研究
Toward a molecular level understanding of allostery in the signaling protein CheY

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Allostery is one of the most important regulatory mechanisms of cellular processes, but the detailed dynamic events that underlie allosteric conformational transitions remain largely unknown. CheY is a response regulator protein that exhibits allosteric transitions upon phosphorylation, and recent NMR experiments suggested that it does not follow the conventional two-state switching mechanism. In this work, using μs-MD simulations and various recently developed analysis techniques, we have identified the structural coupling network responsible for allosteric communication. We will further discuss the μs-ms switching mechanism of the leading residues by characterizing the relevant free energy landscape and comparing the results to state-of-the-art NMR studies.

2P044  MARTINI 粗視化力場を用いたタンパク質-リガンド結合過程の比較シミュレーション
Comparative simulations of protein-ligand binding processes using the MARTINI coarse-grained force field

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Clarifying the mechanism of protein-ligand interactions is one of the most important research subjects in the field of biophysics. However, most of the research efforts have been devoted to predicting docked structures. The process of the ligand binding can be predicted to be clarified. Previously, we have shown that the ligand-binding processes can be reproduced in coarse-grained (CG) simulations with MARTINI. In this study, we classified protein-ligand complex structures in PDB into groups according to the physicochemical and geometric properties of the ligands and the ligand-binding pockets. Then, the CG simulations were performed for a representative protein-ligand pair from each group. We will discuss the effects of these properties on the ligand-binding processes.

2P045  粗視化モデルによるPPARγの基質依存的な活性変化の考察
Coarse-grained model study of ligand-dependent reaction activity of PPARγ

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PPARγ is a nuclear receptor of transcription factors controlling genes implicated in Antidiabetic effect and Bone metabolism. Recent experimental studies reported that PPARγ binds with some ligands and its activity is influenced by the ligand properties. However, the recent X-ray crystal structure analysis implies the structure of PPARγ is almost independent of ligand types. This fact indicates the ligand modifies not the structure but the dynamics of PPARγ, and such dynamics is important for its activity.

Then, we construct and analyze a coarse-grained model of PPARγ. By the normal mode analysis and the molecular dynamics simulation, we identify the ligand-dependent effective intra-molecular interaction network and its contribution to the molecular function.

2P046  構造変化を介した分子内情報伝達パターンの探索: 粗視化分子動力学計算による試み
Screening for Mechanical Communication in Proteins by Coarse-Grained Molecular Dynamics

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Molecular machines such as motors operate through their conformational changes. Some of them can respond to external stimuli (e.g. forces) and change their properties. As they are typically a huge molecule or complex with multiple subunits, communication inside the molecule or complex is essential for their concerted operation. To probe mechanical communication, we employed steered molecular dynamics simulations using coarse-grained elastic network models. We applied static forces in many randomly-chosen directions to each residue, to show transmission patterns of mechanical perturbations. As an application of this method to a variety of structural data, here we present screening for proteins with a certain mode of mechanical communication.

2P047  粗視化シミュレーションによるリン酸化酵素複合体(MEK1-ERK2)のドッキングダイナミクス
Docking dynamics of MAP kinase: MEK1-ERK2 complex system studied by coarse-grained simulation

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MAP kinases are central transducers of extracellular signals from hormones, growth factors, cytokines, and environmental stresses. Experimentally, the most studied mammalian MAP kinase pathway is the Raf/MEK/ERK pathway. However the molecular (detailed) mechanism for activation (phosphorylation) of ERK2 by MEK1 is still unknown, because the complex structure for MEK1-ERK2 system is not available. So, in this study, to investigate the stable complex structure of the MEK-ERK system and their docking dynamics which is required for their efficient signal transmission, we apply the atomistic interaction based coarse-grained (AICG) model in which the parameters of interaction are physico-chemically well tuned depend on amino-acid sequence (and secondary structures).

2P048  酵母MAPK経路における伝達制御機構の分子シミュレーション研究
Molecular simulation study on signaling control in yeast MAPK pathway

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Signal transmission is important and highly regulated in the cell. In yeast, pheromone response is transmitted through a MAPK pathway, a cascade of phosphorylation of signaling proteins; Ste11, Ste7, and Fus3. Ste7 is commonly used in another pathway and thus its activity and target are precisely controlled to prevent crosstalk. Experimental studies have suggested that a scaffold protein, Ste5, has crucial roles in that regulation. To reveal the entire mechanism at the molecular level, we performed a series of coarse-grained MD simulations. Particularly we focused dynamics of a long tail at the N-terminus of Ste7, which contains Fus3-binding motifs. Our simulations show how the phosphorylation state and/or the scaffold protein affect the accessibility of substrates.