the McMD simulation in explicit water. Our target protein, motif-1 in human glutamyl-prolyl tRNA synthetase (PDB ID: 1fyj), consists of two helices. The structural ensemble obtained from the simulation showed that the N-terminal helix of the protein comparatively unstable than C-terminal one. In addition, we compared the NOE distances determined from an NMR experiment with those reproduced from the simulated structural to confirm the reproducibility of the simulation. Refer to our poster for more details.

1P-008 X線小角散乱法と分子動力学を用いたタンパク質の構造変化の解析

Analysis of protein structural change using Small-angle X-ray scattering and molecular dynamics simulation

Kenichi Kobiki (1), Yasunobu Sugimoto (1). (1: Div of Biophysical Engineering, Graduate School of Engineering Science, Osaka Univ.)

Small-angle X-ray scattering (SAXS) is a useful experimental technique to study the structure of biomolecules under physiological conditions in solution. It is suitable for investigation of large conformational changes of proteins occurred by ligand binding. The scattering intensities, however, are spherically averaged one-dimensional data and lacking phase information. To predict the three-dimensional structure from the one-dimensional pattern, we have to construct trial-and-error models based on some other methods. In this study, we construct the structural model of the global conformational changes of protein by combining SAXS and computational simulation method of molecular dynamics (MD) instead of trial-and-error modeling. The simulation is done to model the conformational change of protein from the SAXS data. The starting model is atomic coordinate data before the structural change. The MD simulation leads the model of the new structure which satisfies the scattering intensity of SAXS. In the simulation, we calculate the sum of squared differences between calculated and observed SAXS intensities, and include this value as a constraint energy function to the normal potential energy function. First, we used calmodulin for the modeling study. In this simulation, the structure of calcium-free calmodulin was determined from the calcium-binding calmodulin structure and the scattering data of calcium-free structure. Next, the actin-detached conformation of scallop myosin was determined from the rigor conformation of that.

1P-009 透過型電子顕微鏡を用いた三次元再構成法によって明らかにされた、TRPM2 陽イオンチャネルの膨れたベル形構造

Three-dimensional reconstruction of TRPM2 cation channel reveals a swollen, bell-shaped structure

Yusuke Maruyama (1), Toshihiko Ogura (1), Kazuhiro Mio (1), Shigeki Kiyonaka (2), Kenta Kato (2), Yasuo Mori (2) and Chikara Sato (1). (1: National Institute of Advanced Industrial Science and Technology (AIST); 2: Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University)

Transient receptor potential melastatin type 2 (TRPM2) is a calcium-permeable cation channel, which belongs to TRP superfamily with diverse sensory functions. TRPM2 channel is activated by various signals such as redox state and temperature change. TRPM2 molecule contains adenosine diphosphate ribose pyrophosphatase (ADPRase) domain within the sequence, and ADPR binding to this domain activates the channel function. In this study, we purified the tetrameric TRPM2 channel, analyzed it using negatively stained electron microscopy, and reconstructed the three-dimensional structure. TRPM2 has a bell-like shape of 18 nm in width and 25 nm in height. TRPM2 contains a large cytoplasmic domain, double-layered structure in which enables multiple-docking of the messenger molecules and thus integration of the signals. These structural features of the cytoplasmic domain are similar to another TRP channel, TRPC3. However, TRPM2 molecule protrudes a unique square prism at the end of cytoplasmic domain. Close to this protrusion, the ADPRase domain could be assigned by antibody which recognizes the fused tag near this domain. Therefore, the agonist-binding ADPRase domain is separately located from the ion gate in the transmembrane region.

1P-010 ATP加水分解におけるミオシンモータードメインの局所構造変化の相関

Correlations among change of local structures in myosin motor domain during ATP hydrolysis

Hiroshi Kagawa (1), Yoshinori Nagai (2), and Hiroshi Wako (3). (1: Physics Lab, Nippon Medical School; 2: Center for Information Science, Kokushikan Univ; 3: School of Social Sciences, Waseda Univ)

We have been studying to analyze protein structures using patch analysis for a folded string. Our previous work applied patch analysis to crystallized motifs of myosin motor domains binding different ATP analogs, and found varied structures around switch I, switch II, P-loop, and actin-binding site. The used data in the previous work were X-ray diffraction data of 1MMA, 1MMD, 1MMG, 1MMN, 1MND, and 1VOM in the PDB. In the recent study we have added the analyzed results of 1D0X, 1D0Y, 1D0Z, 1D1A, 1D1B, 1D1C, 1FMV, 1FMW, 1LVK, 1MNE, 1W9I, 1W9J, 1W9K, and 1W9L. Some of them are very similar to one of previously analyzed ones, but they give new information about structural change of myosin motor domain. Using those patch analysis data we give a speculation to solve a puzzle of an image for continuing structural change of the myosin motor domain during ATP hydrolysis and generating motive force to contract myosin and actin filaments. We also want to know how those structural changes cause what kind modification of molecular orbitals given by the quantum chemical calculations for locally selected small structures. These calculations also

contribute to make an image for the relationship between ATP hydrolysis and force generation by interaction between a myosin motor domain and an actin.

1P-011 天然構造を特徴づける蛋白質内水素結合パラメータ

Parameters related to intramolecular hydrogen bonds characterizing the protein native structure

Koji Oda (1), Yuichi Harano (2), Takashi Yoshidome (3), Yuji Sugita (4), Mitsunori Ikeguchi (5) and Masahiro Kinoshita (3). (1: Taisho Pharm.; 2: Global Edge Inst., Tokyo Inst. Tech.; 3: Inst. of Advanced Energy, Kyoto Univ; 4: RIKEN; 5: Supramolecular Biology, Yokohama city Univ.)

Prediction of the protein native structure presents important challenge for understanding its construction principle. Decoys, misfolded structures artificially made, are useful for the prediction tests. So far, we have successfully discriminated the native fold from the decoys in "Decoys'R'Us" datasets by considering the water entropy and the total dehydration penalty. Water tries to force the protein to take a compact structure maximizing the water entropy. Compared to the fully extended structure, in a more compact structure some hydrogen-bond donors and acceptors are buried in the interior after the break of hydrogen bonds with water molecules. There is no problem if the intramolecular hydrogen bonds are formed. However, it is not always formed, leading to the dehydration penalty. The native structure is optimized in terms of the water entropy and the total dehydration penalty.

In this study, we investigate the protein intramolecular hydrogen bonds. Donors and acceptors are categorized into several classes by examining whether they are buried in the interior or exposed to water, they make hydrogen bonding or not, they belong to the backbone or side chains, and so on. Hydrogen bonds are also categorized into the similar classes. We have found some features of the native structure which are not shared by the decoys. The features arise from the requirement that the water entropy be maximized and at the same time the total dehydration penalty be minimized.

1P-012 蛋白質サイズが統計ポテンシャルに与える影響

Effect of protein size on statistical potentials

Matsuyuki Shirota(1), Takashi Ishida(1), Kengo Kinoshita(1),(2) (1:Inst. Med. Sci., Univ. of Tokyo, 2:SORST, JST)

The size of a protein is an important factor for understanding the sequence-structure relationship. The increase in size decreases the surface regions relative to the volume of core regions, and it increases the fraction of buried residues. Statistical potentials are the ways to estimate the stability of protein structures from the structure database under the assumption of Boltzmann distribution. It has been pointed out that they can vary due to the difference of the database. We assumed that a potential derived from larger proteins would evaluate buried residues more favorably and that the potentials derived from large (or small) proteins would discriminate the native structure of large (or small) proteins. We created the single-body potential of Verify3D type, which takes into account the secondary structure and the burial and polar interaction of side chain of each residue. The potential derived from larger proteins tended to evaluate buried residues more favorably. They also preferred buried hydrophilic residues with polar interactions. The discrimination of native structure from decoys was improved by using potentials derived from proteins of similar sizes instead of the potential from all the proteins in the database. We also created distance dependent atomic two-body potentials with several reference states. In this case, the performance of potential was not improved by considering protein size. The factors concerning the performance of potentials are discussed.

1P-013 核酸分解酵素におけるループの揺らぎと機能の関係

The role of the flexible loop in staphylococcal nuclease on its catalytic activity

Shigehumi Tadokoro, Hironari Kamikubo, Shigeo Yamaguchi, Yoichi Yamazaki and Mikio Kataoka (Graduate School of Materials Science, Nara Institute of Science and Technology)

To reveal relationship between flexibility and function of protein, we are studying on staphylococcal nuclease (SNase) as a model protein. In the present study, we focus on the flexible Ω -loop of SNase (44-49). We prepared the Ω -loop mutants, the Ω -loop truncated mutant, $\Delta 44-49$, and the artificially designed Ω -loop mutant, $\Omega\Delta 46$. Thermal denaturation experiments of these mutants in the presence and the absence of the inhibitor, prAp, and Ca^{2+} showed that the mid-temperatures of the denaturation for these mutants increase in the presence of prAp and Ca^{2+} , suggesting that the inhibitor can bind to these mutants. The $\Delta 44-49$ and $\Omega\Delta 46$, however, lost their hydrolytic activity. In order to clarify the reason for the loss of the activity, we aimed the crystallographic studies on WT, $\Delta 44-49$ and $\Omega\Delta 46$ in the presence and the absence of ligands. The crystal structures of the inhibitor bound form of $\Delta 44-49$ and $\Omega\Delta 46$ showed that the orientation of Glu43, the component of catalytic site, of $\Omega\Delta 46$ is deviates from the appropriate alignment toward the phosphate group of the ligand shown in WT, suggesting that the mutation on the Ω -loop restricts the mobility of Glu43. The crystallographic analysis of the other states of the mutants will be also presented.

1P-014 グロビンフォールドヘリックスE-H単位の立体構造の普遍性

—残基間平均距離統計を用いた解析—

Generality of the 3D structure of the helix E-H unit in the globin fold -Analysis based on the interresidue average distance statistics-

Takeshi Kikuchi. (Dept Bioinformatics, Col Biosciences, Ritsumeikan Univ)

It is well-known that the globin fold consists of the A-H helices and its 3D