concentration (~15 % for MY; 5 % for HM), which is similar to that of lysozyme [1], where the osmotic pressure induces change of hydration shell. Both proteins show cross-beta transition by the elevation of temperature. The presence of PVP descends the transition temperature of the whole structure, suggesting the destabilization of the native structures. The cross-beta transition was also influenced by PVP addition. The detailed results and discussion will be given.

[Reference]

I. M. Hirai, K. Takeuchi, et al., *Thermochimica Acta* 532 (2012) 15.

2PT130 Motion Tree 法で解析された SERCA の大規模な構造変化

Large-scale conformational changes of SERCA analyzed by Motion Tree method

Chigusa Kobayashi¹, Ryotaro Koike², Motonori Ota², Yuji Sugita^{1,3,4} (¹RIKEN, ASI, Theoretical molecular science, ²Graduation school for information science, Nagoya University, ³RIKEN, AICS, ⁴RIKEN, QBiC)

Sarcoplasmic reticulum Ca²⁺-ATPase (SERCA) is structurally and functionally the best studied member of P-type ATPases. To uptake Ca²⁺ from the cytoplasm to sarcoplasmic reticulum lumen against a large concentration gradient, SERCA undertakes rearrangements of the transmembrane helices coupled with large-scale cytoplasmic domain movements. Although atomic structures of SERCA in different physiological states have been determined by X-ray crystallography, the differences between two crystal structures are significantly large, leaving the molecular mechanisms underlying the structural transitions elusive. In this study, we develop an approach to analyze such large-scale conformational changes of SERCA or other proteins, based on the motion tree algorithm originally developed by Koike et al. (manuscript in preparation). Using the method, we characterize structural transition pathways computed by Climber, a morphing software, and 100ns molecular dynamics (MD) trajectories starting from E2 and E2.Pi states. We conclude that the method is useful to observe intermediate structures for describing large-scale conformational transitions in more detail.

2PT131 H-ras GTP 複合体と H-ras GDP 複体の分子動力学シミュレーションにおける水分子の解析

Analysis of water molecules in molecular dynamics simulations of H-ras GTP and GDP complexes

Takeshi Miyakawa¹, Ryota Morikawa¹, Masako Takasu¹, Kimikazu Sugimori², Kazutomo Kawaguchi³, Hiroaki Saito³, Hidemi Nagao³ (¹Sch. Life Sci., Tokyo Univ. Pharm. and Life Sci., ²Dept. Phys. Therapy, Faculty Health Sci., Kinjo Univ., ³Inst. Sci. and Eng., Kanazawa Univ.)

We study the structures of H-ras GTP complex and H-ras GDP complex in solution by molecular dynamics (MD) simulations in order to understand the hydrolysis of the GTP to GDP in the H-ras complex, which play a key role in overcoming human cancer. We have derived the potentials and the atomic charges around Mg²⁺ in H-ras GTP complex and H-ras GDP complex by quantum chemical calculations using hybrid B3LYP functional with 6-31G** basis set. We performed MD simulations using potential parameters of AMBER03 and our parameters around Mg²⁺. And we analyzed the properties of water molecules around GTP and GDP in each complex. Our analysis shows that the diffusion of water molecules around GTP and GDP is nearly equal to the diffusion of ordinary water molecules. The distance of the closest water molecule from one of P or O atoms in GTP or GDP depends on the species of this atom in GTP or GDP. The probabilities that the water closest to one of P or O atoms in guanine nucleotide is the same water closest to another P or O atom in guanine nucleotide have large value for bonded P-O pairs. We also found that the probabilities in GTP are higher than the probabilities in GDP. This implies that these high probabilities in GTP make the water molecule come to the appropriate position to activate GTP hydrolysis in H-ras-GTP complex.

2PT132 T4 ゲノムパッケージングモーターの分子ダイナミクス

Molecular Dynamics of T4 Genome Packaging Motor

Kazuhiro Takemura¹, Akio Kitao^{1,2} (¹IMCB, Univ. of Tokyo, ²JST,CREST)

Almost all bacteriophages have a process of packaging genome into vacant procapsids. The packaging of DNA is powered by ATP hydrolysis and the packaging motor. T4 genome packaging motor consists of gp20, gp17, and gp16. The cryo-EM reconstruction study reported that gp17 forms pentamer and that the X-ray crystal structure of monomeric gp17 could not be fitted into cryo-EM image which is expected to be related to its function. Molecular dynamics

simulations were performed to model the atomic structure of pentameric gp17 and to investigate the mechanism of the DNA packaging. Gp17 is composed of N-terminal (1-360) and C-terminal (361-610) domains. A domain motion was detected as the first mode of the principal component analysis for the gp17 monomer in solution which contributes 50 percent of its molecular fluctuation. The observed domain motion might be related to its function and the structural difference between the cryo-EM image and the X-ray crystal structure. To model the gp17 structure close to the EM image from the X-ray crystal structure, we used the recently developed sampling method, PArallel Cascade Sampling MD (PACS-MD, R. Harada and A. Kitao in preparation) in which the snapshots close to the target structure are selected and velocities are redistributed. Using PACS-MD, we successfully obtained the structure of monomeric gp17 which is close to the structure of EM image. Starting from the obtained structure of monomeric gp17, we are currently modeling the atomic structure of pentameric gp17 using PACS MD.

2PT133 タンパク質へのリガンド結合過程の粗視化シミュレーション：タンパク質の立体構造変化の影響の解析

Coarse-grained MD simulations of ligand binding to proteins: Effect of the conformational changes of the proteins

Tatsuki Negami¹, Tohru Terada², Kentaro Shimizu^{1,2} (¹Department of Biotechnology, Graduate School of Agricultural and Life Sciences, The University of Tokyo, ²Agricultural Bioinformatics Research Unit, Graduate School of Agricultural and Life Sciences, The University of Tokyo)

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 the docked structure. The process of ligand binding remains to be clarified. We have demonstrated that coarse grained simulations with the MARTINI force field can reproduce the processes of ligand binding to proteins. However, this method is not directly applicable to proteins that change their conformations upon binding to ligands because elastic network is used to conserve protein structures in the simulation with the MARTINI force field. Since conformational changes of proteins often occur upon ligand binding, it is necessary to extend the method to enable the conformational change of a protein in the coarse grained simulation. Here, we combined a double-well network model with the MARTINI force field for this purpose. First, we constructed Elnedyn elastic network potentials for the ligand-free and ligand-bound structures, and then connected them smoothly to make a double-well potential. We observed frequent conformational transitions between the two states during coarse grained simulations with the double-well potential for several proteins. Furthermore, we performed a few-microsecond simulation randomly arranging ligand molecules around these proteins. We found that the ligands correctly bound to the ligand-binding sites. We will discuss the coupling between the conformational change and the ligand binding affinity.

2PT134 分子動力学シミュレーションによるリジン 48 結合型ジユビキチンのコンパクト構造の解析

Molecular dynamics simulation study of Lys48-linked diubiquitin in compact conformation

Sotaro Fuchigami¹, Mitsunori Ikeguchi¹, Akinori Kidera^{1,2} (¹Grad. Sch. of Nanobioscience, Yokohama City Univ., ²CSR, RIKEN)

Protein ubiquitination is a post-translational modification involved in regulation of diverse cellular processes, including protein degradation, cell signaling, DNA damage response and transport processes. Ubiquitin can be conjugated not only to a target protein but also to another ubiquitin via one of its seven lysine residues, resulting in formation of polyubiquitin chains with diverse types of linkages. The most examined is Lys48-linked polyubiquitin chain, which acts as a tag for protein degradation by 26S proteasome. Several studies have shown that Lys48-linked diubiquitin is in the compact conformation, in which the hydrophobic patches of both ubiquitins interact with each other. It is considered that the Lys48-linked diubiquitin changes its conformation to interact with its receptors, whereas its mechanism is not well understood. In the present study, we performed molecular dynamics simulation of the Lys48-linked diubiquitin in the compact conformation and investigated its conformation stability. More than one microsecond simulations revealed that the compact conformation was fairly stable even though interaction between the hydrophobic patches was partially disrupted by local conformational changes of ubiquitins. We attributed the high stability of the diubiquitin to main-chain hydrogen bonds between ubiquitins and confirmed this by mutant simulations.