3G0936 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**Molecular dynamics simulations of the structures of H-ras GTP complex in solution and H-ras GDP complex in solutions****Takeshi Miyakawa¹**, Ryota Morikawa¹, Masako Takasu¹, Hiroaki Saito², Hidemi Nagao² (¹*Tokyo University of Pharmacy and Life Sciences*, ²*Kanazawa University*)

We study the structures of H-ras GTP complex and H-ras GDP complex in solution by Molecular dynamics simulations. We have derived the potentials and the atomic charges around Mg^{2+} in H-ras GTP complex and H-ras GDP complex by quantum chemical calculations. We will perform MD simulations and sample the structures of H-ras GTP complex and H-ras GDP complex in solution as NPT ensembles.

3G0948 天然構造のデータのみから構築されたタンパク質モデル構造の絶対的な質の評価法**An absolute quality evaluation method of protein model structures developed based only on the native structure data set****Matsuyuki Shirota¹**, Ishida Takashi², Kengo Kinoshita^{1,3} (¹*Grad. Sch. Info. Sci., Tohoku Univ.*, ²*Grad. Sch. Info. Sci. Eng., TITech*, ³*IDAC, Tohoku Univ.*)

In protein structure prediction, it is important that the model structure predicted from amino acid sequence can be assessed for its absolute quality, i.e. its structural similarity to the corresponding native structure. Statistical pair potentials extracted from the native protein structure data set are widely used in quality assessment, but they have not been represented as the absolute quality scores. On the other hand, existing absolute quality estimation methods, such as machine learning ones, require a data set of model structures of known quality for training, in addition to the native structures. In this study, we developed a method that can evaluate the absolute quality of a model structure using only a set of native structures, by way of normalizing statistical pair potentials. This normalization was based on a natural extension of the idea of the native and reference states, which are the necessary components of statistical potentials, applied to each of the model structures to be evaluated. We tested this method using the model structures of various proteins developed in CASP (Critical Assessment of Techniques for Protein Structure Prediction) contests. As results, our method showed comparable performance with current state-of-art machine learning-based methods in terms of correlation with the true absolute quality and in terms of discrimination of native structures. These results show that statistical potentials can evaluate the absolute quality if they make full use of statistical information in the native structures.

3G1012 分子動力学シミュレーションによる Rad51 リコンビナーゼの分子モデリング**Molecular modeling of Rad51 recombinase using molecular dynamics simulations****Yuichi Kokabu**, Mitsunori Ikeguchi (*Yokohama City Univ*)

The exchange of strands between two homologous DNA molecules, which is a central reaction in homologous recombination, is catalyzed by Rad51 recombinase in eukaryotes. In the reaction, a filament comprised of Rad51 and ssDNA searches a homologous DNA strand, and exchanges those strands. In the presence of ATP, Rad51 can form active filaments even without ssDNA. Electron microscope studies have shown that the pitch of the active filament is ~100 Å. However, in the crystal structure, the pitch of the filament is ~130 Å, which is distinctly different from the pitch observed by electron microscope. Further, no ATP is bound to the crystal structure of Rad51.

To elucidate the atomic structure of the Rad51 active filament, homology modeling was carried out using the crystal structure of an archaeal homolog, RadA, in which the pitch of the filament is ~100 Å, and ATP is bound in the interface between protomers. Then, we performed an all-atom molecular dynamics (MD) simulation with explicit water for the modeled dimer that is a minimum unit of the filament.

During the MD simulation for the modeled structure, the dimer structure retained the initial arrangement, and the adenyl ring of ATP tightly interacted with both protomers of the dimer. The stable salt bridge between Arg in the P-loop of one protomer and Glu of the other protomer was observed, which is a unique interaction in Rad51, not in RadA.

3G1024 ハブ蛋白質のリガンド依存構造変化：ユビキチンの場合**Ligand-dependent conformational changes of the promiscuous protein: A case for Ubiquitin****Bhaskar Dasgupta^{1,2}**, Akira Kinjo¹, Haruki Nakamura¹ (¹*Osaka University, IPR*, ²*JBIC*)

Protein-protein interactions play dominant roles in proper functioning of the cell. In the network of such interactions, the proteins that bind multiple partners (or ligands) are critically important. Recognition of different ligands by these so-called hub proteins (or receptors) should be controlled by collective motions of the receptor and ligand chains. To demonstrate the dynamic nature of protein-protein recognition by hub proteins in atomic level, we have performed all-atom normal mode analysis of 11 protein-protein complexes, where Ubiquitin receptor is binding to diverse ligands. Specificity of recognition was analyzed by observing change in the internal and external motion of the receptor due to binding different ligands. Our results indicate that coupling of the external motions of the ligands to the motions of the receptor may be crucial for the protein-protein recognition. Moreover, we observed higher flexibility of residues and atoms in the common overlapping region relative to the total multi-binding interface (that bind to all types of ligands). Curiously, we also observed some residues (and atoms) that show large mean square fluctuation are distant from the protein-protein interface.

3G1036 カメレオンモデルによる DHFR の構造転移の研究**Conformational transition of DHFR simulated with the chameleon model****Toru Kimura¹**, Tomoki Terada², Masaki Sasai² (¹*Dept. of Applied Physics, Grad. Sch. of Engineering, Nagoya Univ.*, ²*Dept. of Computational Science and Engineering, Grad. Sch. of Engineering, Nagoya Univ.*)

Most proteins undergo the conformational changes in their functioning. Single-molecule observations and NMR experiments have revealed the existence of the conformational transition within the preexisting equilibria, which is related to their functions. Furthermore, conformational transitions can correspond to the rate-limiting steps in the catalytic cycle, which is experimentally suggested in some proteins (and may be more general). A well-characterized protein dihydrofolate reductase (DHFR) is one of such proteins. Although their conformational change is relatively small, NMR relaxation dispersion analysis has suggested that three (out of five) steps in the catalytic cycle are accompanied by the two-state conformational transition with a free energy barrier. To obtain further insight into these transitions, we have performed coarse-grained molecular dynamics simulation using the chameleon model. In this model, the single energy minimum of local interaction is assumed to move between two limits defined by two crystal structures, depending on the local structure around the interaction sites. Calculated free energy landscape has indicated that the two basins are stabilized energetically whereas the free energy barrier between them is stabilized entropically, which is consistent with the loop motions expected from the visual comparison of two crystal structures. This suggests that the free energy barrier height is decreased at higher temperature, which can be tested experimentally.

3G1048 機能に関する選択圧による蛋白質の進化シミュレーション**Simulated evolution of protein by a selective pressure on function****Masahiro Yamamoto¹**, Takeshi N. Sasaki², Kengo Sawada¹, Shintaro Minami³, George Chikenji³, Tomoki P. Terada³, Masaki Sasai³ (¹*Dept. of Apply. Phy., Univ. of Nagoya*, ²*Dept. of Human Info., Fac. of Human Info., Aichi Shukutoku Univ.*, ³*Dept. of Comp. Sci. Eng., Univ. of Nagoya*)

[Background] Features which distinguish proteins from other polymers are their specific functions. To have some function, active site of each protein needs to take a definite structure upon functioning. A plausible scenario is that the primitive protein-like polymers which did not have any specific functions nor definite 3D structures have evolved to acquire some configuration at their active residues to interact with other molecules. We may be able to expect that the other features such as the globular shape of the whole structure and the local orders at the other sites have appeared as consequences of such evolution in functionality. [Purpose] To examine this hypothesis, we computationally simulated the process that random polypeptides evolve to have a function. [Method and Results] A DNA binding protein, the λ phage repressor, was chosen as a model protein. The original first amino acid sequence of the length