3P019 分子動力学法を用いた高圧下における c-Myb R2 ドメインのキャビティ圧縮と構造変化および揺らぎとの関係**A relationships among compression of the cavity of c-MybR2, conformational changes and fluctuation under high-pressure using MD simulation****Takuya Sogabe**¹, Hisashi Yoshida¹, Kazuyuki Akasaka² (¹*Graduate school of Biology-Oriented Science and Technology, Kinki University*, ²*Department of Computational Systems Biology, Faculty of Biology-Oriented Science and Technology, Kinki University*)

c-Myb protein is a transcription factor connected with proliferation and differentiation of hematopoietic cells. In this study, wild-type (WT) c-Myb with a cavity and a mutant-type (V103L) with a vanishingly small cavity were studied by molecular dynamics simulation at 1 and 3k bar for 200 ns in order to establish the relationship among the cavity, the compression, and conformational changes. We calculated the root mean square deviation (RMSD), the protein volume (probe size 1.1Å), cavity volume, and a difference map (DM) of c-Myb under pressure at 1 and 3k bar from the trajectories. From these results, we conclude that there must be a relationship between the cavity and characteristic conformational changes.

3P020 ヒスタミン H₁ 受容体の分子内情報伝達機構に関する理論的研究**Computational study on the intramolecular signaling mechanism of histamine receptor****Yuko Ishii**, Takakazu Ishikura, Takahisa Yamato (*Grad. Sch. Sci., Nagoya Univ.*)

The histamine H₁ receptor (H₁R), a member of GPCR, plays a key role in allergic and inflammatory reactions. In this work, the characteristic pattern of the inter-residue interactions of the wild-type H₁R was represented as an energy exchange network (EEN) using the current calculation for protein (CURP) program^[1,2]. The allosteric mechanism of H₁R was then investigated by comparing the EEN of H₁R with those of rhodopsin and β2 adrenergic receptor.

[1] T. Ishikura, T. Hatano and T. Yamato, *CPL* 539, 144-150, (2012).[2] T. Ishikura and T. Yamato, *CPL* 432, 533-537, (2006).**3P021 KcsA カリウムチャネルの開構造への構造変化前における分子揺らぎの増大****The Enhancement of Structural Fluctuations Prior to The Opening Conformational Changes of The KcsA Potassium Channel****Hirofumi Shimizu**, Masayuki Iwamoto, Yumiko Oota, Shigetoshi Oiki (*Univ.Fukui.Fac.Med.Sci*)

We have refined the Diffracted X-ray Tracking (DXT) method to reveal the conformational changes of the KcsA channels upon gating. To trace the gating conformational change in the single molecule level, the solution pH was jumped from neutral to acidic by using the caged proton, and the opening of the activation gate was examined. The structural fluctuation was enhanced immediately after the pH jump, and the twisting conformational change was initiated after a delay. This enhanced fluctuation was also observed at equilibrium acidic conditions. These findings will lead us to unveil the mechanism of gating.

3P022 Coarse-grained Generalized Born and surface area models and its application to protein docking**Le Chang**¹, Wenfei Li², Naoto Hori¹, Shoji Takada¹ (¹*Grad. Sch. Sci., Kyoto Univ.*, ²*Dept. Phys., Nanjing Univ.*)

The electrostatic and hydrophobic interactions are two major driving force of protein-protein docking. We developed the coarse-grained (CG) Generalized Born (GB) and surface area (SA) models in CaféMol software to achieve better accuracies in protein interactions. This work is divided into three parts. First, the fitting of CG GBSA parameters to all-atom GBSA energies. Second, optimizing the GBSA scaling factors by matching to all-atom GBSA forces. Finally, we test the optimized parameters in CG simulations.

3P023 Factor Xa に対する薬剤候補分子の結合自由エネルギー:3D-RISM 計算**Predicting binding free energy of drug candidates to Factor Xa : 3D-RISM study****Sayaka Kohara**¹, Masatake Sugita², Masanari Matsuoka¹, Takeshi Kikuchi¹, Fumio Hirata¹ (¹*Dept. Bioinf., Col. Life Sci., Ritsumeikan Univ.*, ²*Res. Org. Sci. Tech., Ritsumeikan Univ.*)

It is of essential significance to evaluate the binding free energy for searching a candidate of active drug in the in silico pharmaceutical design. To estimate the binding free energy, it is important to evaluate not only the interaction energy between protein and drug candidates but also the desolvation free energy. But, it is not an easy task for the MD simulation because of the difficulty in sampling of water configuration, especially, at the active site. The “3D-RISM theory” has been successful in evaluating the solvation thermodynamics of complicated solutes. In this study, we calculate the binding free energy between Factor Xa and the ligands using 3D-RISM theory, and compare the theoretical results for the relative binding free energy with experimental values.

3P024 多剤排出トランスポーター AcrB の構造回転機構に対する物理描像**Physical Picture for Mechanism of Conformational Rotation of Multidrug Transporter AcrB****Hirokazu Mishima**¹, **Hiraku Oshima**², Satoshi Yasuda², Masahiro Kinoshita² (¹*Grad. Sch. Energ. Sci., Kyoto Univ.*, ²*Inst. Adv. Energ., Kyoto Univ.*)

The multidrug transporter AcrB, which exports a variety of drugs in Gram-negative bacteria, comprises three protomers with different conformations. The conformations change in a cyclic way by the proton-motive force, leading to an apparent, conformational rotation of AcrB which induces the drug exportation. Here we investigate the packing structure of AcrB in terms of the entropic effect originating from the translational displacement of water molecules or hydrocarbon groups constituting nonpolar chains of lipid molecules. We find that the packing in AcrB is highly asymmetric. We construct a physical picture for the mechanism of conformational rotation elucidating how each protomer achieves such a drastic conformational change using only a small free energy.