3P055 Improved Multi-Replica Metadynamics for Free Energy CalculationsRaimondas Galvelis¹, Yuji Sugita^{1,2} (¹RIKEN TMSL, ²RIKEN AICS)

Metadynamics (MTD) is an enhanced sampling algorithm applicable for the computational studies of biosystems with high energy barriers and slow modes of motion. It based on a history-dependent bias potential in a collective variable (CV) space. In particular, we are focused on multi-replica approaches such as the bias-exchange MTD (BE-MTD), where the CV space is divided into lower dimensionality subspaces for efficiency and scalability. We demonstrate that BE-MTD can be improved (shorter simulation times are required for the same accuracy) by replacing Metropolis-Hastings algorithm with advanced replica exchange schemes. Benchmarks on alanine polypeptides and a small protein are shown.

**3P058 バクテリア細胞質中の生体高分子ダイナミクスと相互作用：全原子分子動力学による研究
Dynamics and Interactions of Macromolecules in the Bacterial Cytoplasm: All-atom Molecular Dynamics Study**Isseki Yu¹, Tadashi Ando², Takaharu Mori¹, Jaewoon Jung³, Ryuhei Harada³, Yuji Sugita^{1,2,3}, Michael Feig⁴ (¹RIKEN, ²RIKEN QBIC, ³RIKEN AICS, ⁴Michigan State Univ.)

Discovering the molecular-level dynamics and interactions of macromolecules in realistic cellular environment is one of the major challenges for biophysical scientists. For this purpose, we constructed all-atom model of cytoplasm in the Mycoplasma Genetium, the smallest known bacteria. The size of the system is 100 nm x 100 nm x 100 nm, which is greatly exceeds that of typical molecular dynamics (MD) simulations, covering about 10% of the volume of an entire bacterium cell. Using the atomic trajectories generated by highly parallelized MD program GENESIS on K computer, translational and rotational diffusion of macromolecules are analyzed. The influence of crowding environment and protein-protein interactions on the dynamics of individual macromolecules are discussed.

3P056 タンパク質の高速折り畳みダイナミクスの一分子追跡を目指したライン共焦点顕微鏡の開発**Development of the line confocal system for the single molecule tracking of fast folding dynamics of proteins**Hiroyuki Oikawa¹, Kiyoto Kamagata¹, Munehito Arai², Atsuhito Fukasawa^{3,4}, Hiroaki Yokota⁴, Toru Ide⁵, Satoshi Takahashi¹ (¹IMRAM, Tohoku Univ., ²Grad. Sch. Arts. Sci., Univ. Tokyo, ³Hamamatsu Photonics, ⁴GPI, ⁵Grad. Sch. Nat. Sci. and Tech., Okayama Univ)

Single-molecule measurements are expected to reveal the detailed process of protein folding. By using the line confocal system, we could trace the single-molecule time evolution of FRET efficiency from the B domain of protein A (BdpA) with the time resolution of ~100 μ s. The time series from the BdpA suggest conformational heterogeneity in the unfolded state. In the case for our existing system, however, there is a trade-off between the time resolution and the observation time for single-molecule tracking. To obtain the better time resolution, we built a new system based on hybrid photo detectors. We could obtain time series with the time resolution of ~10 μ s and the observation time of ~10 ms. We will discuss the time series obtained by the improved system.

**3P059 回転および並進運動から観たタンパク質間相互作用
Protein-protein interaction revealed by the rotational and translational motion**Akane Kato¹, Etsuko Nishimoto² (¹Institute of Biophysics, Faculty of Agriculture, Graduate School of Kyushu University, ²Molecular Bioscience, Bioscience and Biotechnology, Kyushu University)

Precise description for weak protein-protein interaction has not been established. In the present studies, we extracted the experimental parameters concerning with the interaction from the diffusion of protein. The fluorescence anisotropy and correlation were employed for the interaction between lysozymes. The interaction parameter, k_{rot} estimated from the rotational diffusion, showed that the attractive interaction would be induced by monovalent cations. Since k_{rot} could discriminate the effect of cations, it is concluded that k_{rot} is an appropriate parameter for the weak protein interaction. The other parameter, k_{trans} was more effective for weaker interaction. Based on the results of k_{rot} and k_{trans} , protein-protein interaction induced by cations is discussed.

**3P057 アミノ酸置換による蛋白質の熱安定性変化の理論的予測
Theoretical Prediction of Thermal-Stability Changes upon Mutations of a Protein**Shota Murakami¹, Hiraku Oshima², Tomohiko Hayashi², Masahiro Kinoshita² (¹Grad. Sch. Energ. Sci., Kyoto Univ., ²Inst. Adv. Energ., Kyoto Univ.)

We have recently proposed a measure of the thermal stability of a protein, Σ : the water-entropy gain upon folding at 298 K normalized by the number of residues. It is calculated using a molecular model for water. In the present study, we apply Σ to the prediction of thermal-stability changes upon mutations of a protein. The structure of the mutant is assumed to be unknown. We find that the performance becomes considerably higher when an enthalpic component is incorporated in the measure: The resultant measure is denoted by Σ_{New} . Let ΔX be “ X of the mutant” minus “ X of the wild type”. We plot ΔT_m (T_m is the denaturation temperature) against $\Delta \Sigma_{\text{New}}$ for significantly many proteins and find that the two quantities exhibit fairly high correlation.

**3P060 蛋白質のドメイン間相互作用に及ぼすホフマイスター効果
Hofmeister effect on the domain-domain interaction of protein**Tomohiro Aoyama¹, Etsuko Nishimoto² (¹Institute of Biophysics, Faculty of Agriculture, Graduate School of Kyushu University, ²Molecular Bioscience, Bioscience and Biotechnology, Kyushu university)

Hofmeister effect is generally known as the cation or anion effect on the protein solubility and stability. Because of concerning with various biological phenomena, vigorous theoretical and experimental approaches have been examined. But the details are remained unclear. In the present investigation, monovalent cation effects on the domain-domain interaction of GFP-GST fusion protein. Using FRET between GFP chromophore and Cy3 conjugated with the terminal residue of GST, the change in the FRET distance were evaluated to be LiCl>NH₄Cl>NaCl>KCl>CsCl. This result suggests the domain-domain interaction would respond to the usual Hofmeister series. But it should be also interesting to note that LiCl and NH₄Cl shrunk FRET distance while other cations prolonged.