2P049 平衡条件下において形成される二つの天然変性蛋白質融合蛋白質のフォールディング中間状態**Folding intermediates formed by the fusion protein of two intrinsically disordered proteins under equilibrium condition**

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GTPase binding domain of WASP (GBD) assumes partially folded state in isolated form but readily folded into well-ordered structure by binding to either Rho GTPase, VCA domain or R33 of EspFU. However, the less much is known about this folding process.

Here, the equilibrium unfolding processes of a fusion protein of GBD C-terminally connected to R33 (GBD-R33) were analysed by circular dichroism and fluorescence spectroscopy under various conditions. GBD-R33 assumes stable native-like folded state at pH 7.0, whereas it unfolded into the intermediate state at acidic pH. The data suggested that this intermediate contains partially folded GBD and highly unfolded R33. Thus, GBD-R33 could be a useful model to analyse the mechanism of coupled folding and binding by GBD and R33.

2P050 天然タンパク質の分子サイズに関する統計解析**Statistical analysis on the molecular size of native proteins**Hidenobu Kawai¹, Daisuke Takahashi², Munehito Arai^{1,2,3} (¹Dept. Integ Sci. Univ. Tokyo, ²Dept. Life Sci., Univ. Tokyo, ³PRESTO,JST)

A radius of gyration, R_g , is an essential parameter that represents an outline of protein structure, especially a size of a protein molecule. It has been theoretically shown that an R_g of a polymer scales with the number of residues, N , according to the equation: $R_g = R_0 N^v$, where v is a scaling exponent. To comprehensively examine whether the scaling relationship holds for native proteins, we calculated R_g of 167,546 protein domains classified in SCOPe database. The results show that the scaling relationship holds to a large extent for native proteins. Moreover, there appears to be the lowest limit of R_g at each chain length. Structural and functional characteristics of the maximally compact native proteins will be presented at the meeting.

2P051 アクチンフィラメントの引張, ねじり, 曲げ挙動の定量評価: 粗視化分子動力学法による検討**Quantifying how actin filament is stretched, twisted and bent:****A coarse grained molecular dynamics simulation study**

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Actin filaments are double helix-shaped polymers that display conformational stretching, twisting and bending motions. Although modulation of these motions is crucial for regulatory actin-binding protein functions in many mechanical cellular activities, couplings between these dynamics, stretch-twist, twist-bend and bend-stretch couplings, have not been evaluated. In the present study, we quantitatively evaluate the stretching, twisting and bending dynamics of the filament by using coarse grained molecular dynamics simulations. We analyzed stretching, twisting and bending Brownian motions of the filament consisting of 56 actin subunits, then evaluated the coupling between these motions.

2P052 Calculation methods for configurational entropy from molecular dynamics simulations

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Configurational entropy is an important factor of free energies in biomolecular systems. Here, we evaluate seven calculation methods for configurational entropy from molecular dynamics (MD) simulation. The Clausius method is used to assess other methods, because the Clausius method is capable of accurately estimating entropy changes with temperature. The other methods are based on the quasi-harmonic approximation with Cartesian or internal coordinate system. For convergence of configurational entropy, replica exchange MD simulations were used to generate trajectories for small molecules. Our results indicate that the internal coordinate system is more suited to calculate configurational entropy.

2P053 ヒトカルシトニンのアミロイド様線維形成機構とその阻害効果の解析**Analysis of amyloid fibrillation mechanism and its inhibition effects of hCT**Hikari Watanabe(Itoh)¹, Ken Takeuchi¹, Javkhlantugs Namsrai¹, Kengo Daidoji¹, Izuru Kawamura¹, Kazuyoshi Ueda¹, Hiroshi Hirota², Tsutomu Nakayama³, Akira Naito¹ (¹Grad. Sch. Eng, Yokohama Natl. Univ., ²Wako Inst., Riken, ³Faculty of Applied Life Sci., Nippon Veterinary and Life Sci. Univ.)

Human calcitonin (hCT) is known to form amyloid fibril and has been studied as a model peptide to clarify the mechanism of amyloid fibril formation. TOCSY NMR experiments were performed on the fibrillations of hCT in the addition of Curcumin (Cur) at pH 7.4. It was noted that peaks of Phe16, 19 and His20 did not disappear in the spectrum, indicating that those residues may interact with Cur. By the turbidity measurements, rate constants, k_s of hCT were determined to be significantly slower than those of hCT in the presence of Cur. These results indicate that the core part of hCT is inhibited in the first step of a two-step autocatalytic reaction mechanism. Besides, the results of MD simulation support that Cur interacts with hCT at the sites around Phe16, 19 and His20.

**2P054 MSSES 法によるリガンド結合過程の全原子構造解析
Ligand binding process at atomistic resolution revealed by multiscale enhanced sampling**Kei Moritsugu¹, Tohru Terada², Akinori Kidera¹ (¹Grad. Sch. of Med. Life Sci., Yokohama City University, ²Grad. Sch. of Agri. and Life Sci., University of Tokyo)

Ligand binding to protein molecules plays a fundamental role for biological processes such as signal transduction. Since atom interaction and desolvation are involved, in this study, we aim at simulating the ligand binding process at atomistic resolution and including explicit solvent using multiscale enhanced sampling (MSSES).

MSSES allows an enhanced sampling of the all-atom structure in explicit solvent, by coupling with the accelerated dynamics of the coarse-grained model (CG). Here, this extension using multiple CGs has been applied to glutamine binding protein which has been studied as a simplest ligand-binding model. Free energy landscape calculated from the sampled conformations has revealed the coupling between ligand interaction and protein structural change.