and docked into the crystal structure of catalytic domain. Then, a spherical box of water molecules was placed around the subsites. Molecular dynamics simulations in explicit water were carried out at 300 K, and stable structures were chosen from the trajectories by using the cluster analysis. The key residues for the oligosaccharide recognition based on the subsite theory were identified. In the bound oligosaccharide, the glucose unit on the non-reducing end was more fluctuated than that on the reducing end. Taken together with the experimental results of binding thermodynamics, the energetic contribution on the respective subsites could be elucidated.

1PT131 α ヘリックス・ β ストランドレプリカ交換分子動力学シミュレーション法の開発と応用

Development and application of the helix-strand replica-exchange molecular dynamics method

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Biomolecules such as proteins have complicated free energy surfaces with many local minima. Conventional molecular dynamics (MD) and Monte Carlo (MC) simulations tend to get trapped in these local-minimum states. One of the powerful techniques to avoid this difficulty is the replica-exchange method. We propose helix-strand replica-exchange molecular dynamics method. We apply this method to a design peptide and show the results.

1PT132 PDB データベースによるアミノ酸ごとに最適化した主鎖二面角力場 Development of a force field of backbone dihedral angles for each amino acid using Protein Data Bank

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A force field is widely used in the field of molecular simulations for biomolecular systems and is determined by an atomic model based on classical mechanics. Many commonly used force fields for protein systems such as AMBER, CHARMM, GROMACS, OPLS, and ECEPP have amino-acid-independent force-field parameters of main-chain torsion-energy terms. Here, we propose a new type of amino-acid-dependent torsion-energy terms in the force fields. As an example, we applied this approach to AMBER ff03 force field and determined new amino-acid-dependent parameters for ϕ and ϕ' angles for each amino acid by using our optimization method, which is based on the minimization of some score functions by something in the force-field parameter space, where the score functions are derived for the protein coordinate data in the Protein Data Bank (PDB) [1-3]. In order to test the validity of the new force-field parameters, we then performed folding simulations of α -helical and β -hairpin peptides, using the optimized force field. The results showed that the new force-field parameters gave structures more consistent with the experimental implications than the original AMBER ff03 force field.

[1] Y. Sakae and Y. Okamoto, *Chem. Phys. Lett.* 382, 626-636 (2003).

[2] Y. Sakae and Y. Okamoto, *J. Theo. Comput. Chem.* 3, 339 (2004).

[3] Y. Sakae and Y. Okamoto, *J. Theo. Comput. Chem.* 3, 359 (2004).

1PT133 コフィラクチンフィラメントの分子動力学モデルの構築 Molecular dynamics model of cofilactin filament

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Cofilin is an actin regulatory protein which disassembles and severs actin filaments. The binding affinity of cofilin to actin filament is regulated via biochemical pathways. In addition, it has been pointed out that tension in actin filament prevents cofilin from binding to the filament. Because cofilin binding put a twist on the helix of the actin filament that might be incompatible filament conformation caused by the tension, we suppose that structural change of actin filament is related to the mechanism on tension-induced inhibition of cofilin binding. In order to obtain better understanding the mechanism at molecular level, we need to investigate energetic and structural effects on binding domains of actin and cofilin caused by the conformational change of the filament.

To achieve the research mentioned above, in this study, we construct molecular dynamics (MD) model of cofilin-decorated actin (cofilactin) filament. First, we placed cofilins in the vicinity of their binding domains on actin along the filament based on the PDB data of actin-cofilin complex. Second, MD simulation for 20ns was conducted to obtain an equilibrium structure of cofilactin filament. Because this equilibrium structure has included thermally-

induced various twist angles, a cofilin-bound actin trimer with a moderate angle has been extracted from the equilibrium structure as a sample of cofilactin complex. In this way, we succeeded to construct MD models of cofilactin complexes with distinct twist angles.

1PT134 ロボット機構の運動学に基づくタンパク質の内部運動解析 Internal Motion Analysis of Proteins based on Robot Kinematics

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From the perspective of robot kinematics, we investigated a method for predicting the internal motions of proteins using data from PDB. The protein model used in this method is simple; it comprises main chains and linear springs between the alpha carbons. The main chains are considered to be robot manipulators that control the positions of the alpha carbons or the distances between them, where the dihedral angles on the main chains correspond to the joint angles of robot manipulators. We apply forces in static equilibrium to the model and evaluate the deformation caused by them. The deformation magnitude differs depending on the direction of the force, despite the magnitude of applied forces being the same. It can be concluded that deformations of a large magnitude occur easily. Here, forces are applied in two different manners. One is the application of forces at the alpha carbons in the residues interacting with other molecules and the other is the application of forces at the centroids of the atomic groups (e.g., secondary structures, domains, and subunits). The formulation of basic equations for this method is similar to that for kinematic analysis of robot manipulators. We applied this method to data from PDB of some proteins (e.g., calmodulin, lactoferrin, and aspartate transcarbamoylase). Despite being a simple model, the results are almost consistent with the actual internal motions.

1PT135 コンピュータシミュレーションによる 4-helix bundle タンパク質を基にしたタンパク質分子間相互作用面の設計

Simulation study for designing protein-protein interaction interfaces based on a four-helix bundle protein

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Some proteins have the ability to self-assemble and form fibers. The purposes of our study are: i) designing binding interfaces on two proteins which specifically interact to each other; ii) inducing self-assembly through the intermolecular interaction between the two proteins; and iii) forming co-polymers. A four-helix bundle structure is chosen as a model for designing the binding interface. Using the four-helix bundle as the scaffold, we designed the binding interfaces on the target protein YciF involving charged and hydrophobic amino acid residues. To evaluate the designed binding interfaces, we performed molecular dynamics (MD) simulation of the variants of YciF proteins with the designed binding interface using GROMACS [1]. For the initial state, two protein molecules with the designed interface were placed with appropriate distance, and their binding interfaces faced each other. After 5ns simulation, we calculated the distance between centroid of binding interface of the molecules, and visualized the structures using Pymol [2]. The details will be presented at the conference.

[1] Berendsen, et al. *Comput. Phys. Commun.* 91 (1995) 43. [2] <http://www.pymol.org>

1PT136 透明で柔軟性を持った実用性の高いタンパク質分子模型 A Soft and Transparent Handleable Protein Model

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The field of molecular and structural biology currently relies on computer-generated graphical representations of three-dimensional (3D) structures to conceptualize biomolecules. As the size and complexity of the molecular structure increases, model generation and peer discussions become more difficult. It is even more problematic when discussing protein-protein interactions wherein large surface area contact is considered. This report demonstrates the viability of a new handleable protein molecular model with a soft and transparent silicone body similar to the molecule's surface. A full-color printed main chain structure embedded in the silicone body enables users to simultaneously feel the molecular surface, view through the main chain structure, and manually simulate molecular docking. The interactive, hands-on