reality. The dielectric constant is expected to vary depending on the local electrostatic environments and the structural constraints imposed on the system. In this study, we calculated the local dielectric environments of protein-water systems by employing the theoretical framework proposed by Guest et al. (PCCP, 2011) where the dipole-dipole correlations are properly taken into account. We used long molecular dynamics simulation trajectories of the three systems (solvated myosin, solvated actin, and F_0 in the solvated lipid bilayer systems) to evaluate the dipole-dipole correlations. From the local dielectric constant map, we found that the regions around the flexible loops tend to exhibit a large dielectric constant. The regions with a large dielectric constant are supposed to respond well to the approaching charges of the binding partner and stabilize the electrostatic self-energy of the charges. Similarly, we will discuss the ion translocation path in F_0 portion of ATP synthase in terms of the local dielectric constant map. We also point out a technical problem that calculated dielectric constants sometimes become too large or even negative, and discuss a possible solution to this problem.

1PT170 シグナル伝達に関する PDZ ドメインの分子動力学データに対する時系列解析

The time series analysis of molecular dynamics data about PDZ domain in synapse

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The functions of a protein are supposed to have relation to its structures. We study the relationship between its functions and movement from data of molecular dynamics(MD) simulation. We analyse the protein called the PDZ domain. For human being, we can find them in a synapse of the nervous system. In particular, these proteins exist mainly in postsynaptic cells as domains of receptors. They play an important role in signaling in the nervous systems[1]. We chose one of the PDZ, and its PDB code is 1BE9. It is the third domain of PSD-95, where PSD-95 is a receptor which is in the center of the postsynaptic cell. For the signaling, the clustering of domain is essential, and is caused by interaction with other proteins. Here, we pay our attention to the mechanism of signaling. It is shown that it has a path within the domain and signals are transduced along this path[2]. We study its motion with wavelet transform and canonical correlation analysis. First, by wavelet transform, we can find the time-dependent spectra and find which parts of the secondary structure move with large amplitude. Second, in order to find whether we can see the flow of thermal energy along this path at room temperature, we compare the correlations between amino acids by canonical correlations analysis.

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1PT171 粗視化シミュレーションによる 3 ドメインタンパク質 suf1 のコ・トランスレーショナルフォールディングの研究

Co-translation folding of a three-domain protein suf1 studied by coarse-grained molecular simulations

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Proteins are synthesized linearly from N-terminus in ribosome and gradually extruded from it. The native interactions of extruded polypeptide chain may be initiated before the protein synthesis is completed. Protein folding which proceeds during the synthesis is termed co-translational folding. Because total conformation space of a polypeptide chain under translation is smaller than that of the full-length polypeptide chain of the protein, co-translational folding could be facilitated kinetically. In addition, the rate of translation is not uniform, but is affected by tRNAs abundance. Recently, it was found that the correct folding of suf1, a three-domain protein, is maintained by the particular use of rare codons. When the rare codons were replaced with codons by synonymous mutations, successful folding yield substantially decreased. However, the detailed mechanism of this phenomenon is unclear. To understand the mechanism, we developed a coarse-grained (CG) model and simulated suf1 co-translational folding as well as post-translational folding as a control. The CG model is a mixture of Go like atomic interaction based CG (AICG) model and generic hydrophobic interactions which makes correct folding and misfolding possible. Via comprehensive simulations, we address the difference between co- and post-translational folding.

1PT172 粗視化シミュレーションによるサテライトタバコモザイクウイルスの安定性とダイナミクス

Stability and dynamics of satellite tobacco mosaic viruses studied by coarse-grained simulations

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Satellite tobacco mosaic virus (STMV) is one of the smallest (about 170 angstrom diameter) and icosahedral virus ($T = 1$). The virus consists of 60 copies of single proteins to make a icosahedral capsid and a 1058-base RNA genome. The existence and importance of the viral genome for its stability have been acknowledged. Recently, STMV was analyzed by an all-atom MD simulation. The research indicated that their RNA is important to stable their capsid structure. All-atom simulation is, however, limited of the system size and the time scale. To overcome them, we used coarse-grained simulation (CafeMol developed by Our lab) to simulate STMV virus for longer time than all-atom MD could do. In this simulation, each amino acid is represented as a CG bead and interactions are modeled with structure-based potential. We first carried out simulation of STMV without their RNA in various environments to investigate the STMV particle stability and dynamics. For example at low ion strength or high temperature, how the virus is deformed has been studied. We discuss importance of the RNA genome for the stability of this virus.

1PT173 エピレギュリン抗体の分子動力学シミュレーション

Molecular dynamics simulation of epiregulin and its antibody

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We present a molecular dynamics study of protein target for cancer, epiregulin and its antibody. Epiregulin is a member of the epidermal growth factor family and stimulates EGFR-driven cancer cell growth such as pancreatic cancer. To investigate the structural stability and thermodynamic property of the epiregulin-antibody complex, we have performed 1- μ s molecular dynamics simulations and free energy calculations. In this meeting, we discuss the results of the simulations and compare with experimental results.

1PT174 Molecular Dynamics Simulation of Protein Using Robot Dynamics Algorithm

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In the simulation study of biophysical phenomena, the gap between the time scale of the simulation and that of the target process is a major bottleneck of Cartesian Molecular Dynamics (CMD). High frequency motions in proteins prohibit CMD from enlarging the simulation time step beyond 1.0-2.0 fs. To overcome this limitation, we adopted a strategy to consider the torsion angles as the only degrees of freedom (DOF) which enables us to employ a method developed originally in robotics, namely Articulated-Body Algorithm (ABA), which can solve the equations of motion of internal coordinates with the small computational cost that linearly depends on the number of DOF. The program of Molecular Dynamics in Torsion Angle space (TAMD) is equipped with an extended version of ABA, so-called Freed-end ABA developed by the authors. The program can treat the AMBER and ECEPP force field and with NVE and NVT ensembles. To evaluate our program, we compared the spectra of 20 distinct dipeptides calculated by TAMD to the results of the normal mode analysis in torsion angle space. From good agreements in this comparison, we confirmed that the program can give reasonable results. We also searched the maximum time step length to give reasonable energy conservation based on the simulations of three proteins, villin head piece subdomain, BPTI and ubiquitin. We concluded that time step 4.0 fs can be employed with the original force field, and 6.0 fs can be employed if we scale the torsion energy terms of the terminal chemical groups.

1PT175 4 量体型サルコシン酸化酵素の酵素-基質複合体の分子動力学解析 Analysis of enzyme-substrate complex of heterotetrameric sarcosine oxidase by molecular dynamic simulation

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