1P006 3 α ヒドロキシステロイド脱水素の分子動力学計算：基質結合ループの構造変化
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Molecular dynamics simulation of 3 α -hydroxysteroid dehydrogenase with NADH: Structural changes in the substrate-binding loop
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Bacterial 3 α -hydroxysteroid dehydrogenase (3 α HSD) is a member of the short-chain dehydrogenase/reductase (SDR) family. We performed an X-ray analysis on the enzyme from *Pseudomonas* sp. B-0831 (Ps3 α HSD) which has been known to form a dimer in solution as its complex with NADH. The resulting crystal structure showed that Ps3 α HSD exists as a structural heterodimer composed of apo- and holo-subunits. A distinct structural difference between them was found in the substrate-binding loop region, where the structure in the apo-subunit is disordered while that in the holo-subunit consists of two α -helices. To understand the structural difference of the substrate-binding loop region, we carried out a 100-ns molecular dynamics (MD) simulation of the heterodimer composed of apo- and holo-subunits at 300 K. The coordinates for the disordered region in the apo-subunit was modeled by referring to the corresponding part of the holo-subunit. During the simulation, the structure of the holo-subunit was kept unchanged due to NADH interaction with the substrate-binding loop. On the other hand, the substrate-binding loop in the apo-subunit became open because of the absence of NADH interaction, and largely fluctuated. It appeared that the open form of the substrate-binding loop in the apo-subunit is suitable for initiation of NADH binding. And the subsequent NADH binding may induce the conformational change of the substrate-binding loop to make the substrate-binding pocket.

1P008 グルタミン側鎖に関わる β シート間振動カップリングの理論的解析
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Theoretical analysis of the inter-beta-sheet vibrational coupling involving glutamine side chains
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In a recent study on the crystal structure of the amyloid-like fibrils consisting of the GNNQQNY peptide chains, it has been clarified that two beta-sheets face each other with the glutamine and asparagine side chains of one sheet interdigitating with those of the other sheet [1]. In this structure, the amide groups of the glutamine side chains of one sheet are closely located with the main-chain peptide groups of the other sheet. This gives rise to the possibility that the vibrational modes of the two groups are strongly coupled. In the present study, this possibility is examined theoretically by using the ab initio MO and DFT methods. The result of the calculations shows that the amide I mode of the Gln4 side chain of a beta-strand in one sheet are strongly coupled with that of the third peptide group of a beta-strand in the other sheet. There are also some strong main chain-side chain vibrational couplings of the amide I modes within a sheet. The signs and the magnitudes of those couplings are approximately represented by the transition dipole coupling mechanism [2], indicating that those couplings arise from the through-space interactions between the amide and peptide groups. This result may increase the applicability of the IR spectroscopy in studying the atomic-level structures of amyloid-like fibrils. [1] R. Nelson et al., Nature 435, 773 (2005). [2] H. Torii and M. Tasumi, J. Chem. Phys. 96, 3379 (1992).

1P007 タンパク質ユビキチンのNMR緩和と分子シミュレーション
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NMR Relaxation and Molecular Simulation of Ubiquitin
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We performed molecular dynamics (MD) simulation of ubiquitin in water to assess both the overall tumbling motion and the internal dynamics in solution. The calculated relaxation times and order parameters, defined as the rotational correlation functions of bond vectors, were compared with those obtained from NMR model-free approach. NMR order parameters, as is well known, agree with those from MD simulations. However, the relaxation times of internal dynamics of each residue and the global tumbling of overall protein show significant difference between MD simulation and model-free approach. Ubiquitin molecule simulated with commonly used water model, TIP3P, rotated faster than expected from model-free approach. We observed that this discrepancy can be improved by using distinct water models. We will report that how overall rotational relaxation times of protein depend on water models, analysis of back-calculated relaxation times using the model-free approach, and the relaxation mechanism of internal dynamics.

1P009 ミオシン分子モータードメインにおけるリガンド依存性的アロステリック構造変化に関する分子動力学計算
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Molecular Dynamics Study on Ligand Induced Allosteric Transition in Myosin Motor Domain
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A myosin molecule shows multiple crystal structures depending on the bound nucleotides. This leads to the lever-arm-swing hypothesis in which structural changes around the nucleotide binding pocket due to ligand binding induces allosteric transitions in the converter domain including lever arm as well as in the actin binding domain. However, because of the limitation in present experimental techniques, intermolecular allostery still remains unclear.

In this study, the effects of ligands binding to myosin are investigated by conducting all-atom molecular dynamics simulations in explicit water. We simulated different ligand binding states of myosin II: ADP-bound, ATP-bound, ADP+Pi-bound, and nucleotide free states. Furthermore, a divalent cation in the nucleotide binding pocket is known to be important in the allosteric mechanism: e.g., Mg²⁺ is shown to be necessary in the allosteric regulation in myosin V. To study the effect of the cation, we also investigate ligand binding states with or without Mg²⁺.

We find distinct structural states of myosin motor domain depending on the bound ligand, particularly the actin binding cleft seems to be affected by Mg²⁺ through the interaction between the cation and a negatively charged residue in the strut loop. This result suggests that Mg²⁺ is essential in mediating the allostery between the nucleotide binding pocket and the actin binding domain, eventually regulating the actin-myosin binding affinity. We will also discuss the allosteric transition in the converter domain.