3P019 The role of the flexible loop in Staphylococcal nuclease on its catalytic activity

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Deleting an internal loop of SNase substantially reduces its hydrolytic activity. In order to clarify the role of the loop, we performed crystal structure and 3D-RISM analysis on the $\Delta 44-49$ and WT. While their static structures are almost identical, but dynamical properties especially on loops were found to be different from each other. The crystal structures also showed that a water molecule involved in the catalytic reaction locates at the same position between WT and the mutant. The 3D-RISM analysis, however, revealed that the coordination of the water to the ligand is altered upon the deletion. From these results, the loops influence the dynamical properties, and in addition, the local reaction coordinate, which might be indispensable for catalytic reactions.

3P020 触媒アスパラギン酸の電荷改変による HIV-1 プロテアーゼの分子動力学シミュレーションへの影響 Molecular dynamics simulations of HIV-1 protease-inhibitor complex with modified charges for catalytic aspartate

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HIV-1 protease (PR) exists as a homo-dimer. Either of two catalytic aspartates (D25/D25') seems to be protonated in PR with its inhibitors (PIs). Therefore, for molecular dynamics (MD) simulations of PR-PI, distinct protonation states and charges are generally set between D25/D25'. However, since PR has structure with C2-symmetry, we hypothesized that symmetrical charges for D25/D25' can improve stability of structure of PR-PI like those in the crystal structures, during their MD simulations. Indeed, the hydrogen bond network around D25/D25' as seen in the crystal structures were stabilized during MD simulations with AMBER9 and with the modified charges, compared with the simulations by the default charges. The modification would be useful to develop novel PIs.

3P021 超音波によるアミロイド β オリゴマー破壊の非平衡分子動力学シミュレーション Non-equilibrium molecular dynamics simulation for disruption of an amyloid- β oligomer by hypersonic wave

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We performed non-equilibrium MD simulations of an amyloid- β oligomer in explicit water to study cavitation around the oligomer and the oligomer destruction by the bubbles. The simulation was started from the experimentally-known amyloid oligomer structure in the amyloid fibril. To express supersonic wave, sinusoidal pressure was applied between -100 MPa and 300 MPa. When the pressure was decreased to a negative value of -100 MPa from a room pressure, a bubble formation was observed around the C-terminal region, the amino acid residues of which were hydrophobic. Even after the bubble size increased, the secondary structures of the oligomer were maintained. When the pressure was increased to a positive value, the bubble shrank, and the oligomer was disrupted.

3P022 Structure and Interactions in Fibrillation of Human Calcitonin Hormone

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The human calcitonin (hCT) is a thyroid polypeptide hormone that has a 32 amino acid residues. The hCT peptide aggregates to form insoluble fibril toward the diseases of osteoporosis. In the fibril formation of hCT, the local conformation changes from an α -helix in a monomeric hCT to a β -sheet structure in a fibril. The β sheet conformation was determined as mixed antiparallel structure using by REDOR-NMR experiments. The role of the amino acid residues is unclear, therefore, we simulated to determine the interaction energies between amino acid residues for stability of fibril using molecular dynamics simulation.

3P023 結晶環境における弾性ネットワークモデルを用いた高分解能 X線構造における温度因子の再現 Thermal fluctuation in high-resolution crystal structures reproduced by normal modes based on an elastic-network model in the crystal

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We have developed a computer program that performs normal mode analysis (NMA) based on an elastic network model which includes intermolecular atom pairs between a target molecule and surrounding molecules in crystalline state. Taking advantage of the relatively small number of degrees of freedom required to describe a molecular structure in dihedral angle space, we aimed to develop the program applicable to a full-atom system of any molecule in the Protein Data Bank (PDB). Here, we illustrate the performance of the program with proteins, nucleic acids, and their complexes, and show that the atomic fluctuations calculated by NMA reproduce the temperature factor data of these molecules in high-resolution crystal structures in the PDB.

3P024 カブトガニ由来抗菌ペプチド Tachyplesin I とキチン結合能に関する研究 Analysis of chitin binding ability of an antimicrobial peptide tachyplesin I derived from horseshoe crab

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Tachyplesin I (TP I), an antimicrobial peptide found in hemocytes of horseshoe crab, has a broad antimicrobial activity against Gram-negative and Gram-positive bacteria and fungi. Although it has been already known that TP I can bind to chitin which is a component of cell wall of fungi, there are no structural information about the interaction between them. In order to clarify the key structural factor for chitin-binding of TP I, we investigated the binding of TP I for chitin. From the NMR studies, F4, R9, Y13 and R17 residues of TP I were suggested to be involved in binding to chitin. Then we performed chitin binding assay of TP I mutant whose F4, R9, Y13 and R17 were replaced with Ala. The results showed that these residues are essential for binding to chitin.