nitrogen-containing cellular constituents such as plant. Although this multi-electron reaction is a novel type of biological catalysis for the reaction specificity and regulation, the reaction mechanism is not fully understood yet because of the complicated reaction process. In this study, the mixed quantum mechanical/classical mechanical (QM/MM) method was applied to investigate the reaction mechanism of aNiR. We discuss the reaction efficiency of Nii3, one of the aNiR, based on the calculated intermediate states and the reaction energy profile.

3PT223 RNase H の RNA 加水分解反応機構の理論的研究

Computational study of the phosphodiester hydrolysis of RNA by RNase H

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The phosphate diester hydrolysis is an important reaction in biology. The ribonuclease H (RNase H) catalyzes the nonspecific hydrolysis of RNA in RNA/DNA hybrids, yielding a 3'-hydroxyl and a 5'-phosphate at the hydrolysis site. This enzyme is found that the Mg^{2+} ion is essential for the enzymatic reaction and that aspartate and glutamate are coordinated the Mg^{2+} ion in the active site. This catalytic mechanism is ubiquitous among nucleic acid processing enzymes and ribozymes. In particular, RNases H has emerged as important therapeutic targets because RNase H activity is absolutely required for proliferation of HIV and other retroviruses. Although the X-ray crystallographic structures of RNase H are determined, there are controversies about the catalytic mechanism of RNase H, the number of Mg^{2+} ions, the proton transfer pathway, and the protonation states of the active site residues. In the present study, we have explored the hydrolysis of the phosphate diester group of RNA by RNase H, using density functional theory to elucidate how many Mg^{2+} ions are required for the catalysis of RNase H. Our computation demonstrates that both one- and two-metal models show the step-wise hydrolysis pathway and lower the activation barriers, compared to the non-enzymatic hydrolysis of phosphate diester. However, the activation barrier of the two-metal model is smaller than that of the one-metal model by about 10 kcal mol⁻¹.

3PT224 First principles molecular simulation with a generalized-ensemble algorithm for studying chemical reactions of biomolecular systems

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It is important to study chemical reactions by molecular simulations because we have to treat a chemical reaction to understand an interesting chemical system such as biomolecular systems including enzymes. We can perform a first principles molecular simulation to understand these systems. However the time scale of a first principles molecular simulation is limited because its computational cost is much higher than a simulation with some force fields.

In order to overcome such a difficulty, we need to use generalized-ensemble algorithms, which enhance conformation sampling in molecular simulations. In this study, we used a simulated tempering method, Simulated Tempering Umbrella Sampling (STUS). Molecular simulations with this method can enhance a chemical reaction in reaction coordinate space. As a result, we can obtain the free energy of the chemical reaction accurately.

We performed first principles molecular dynamics simulations with the simulated tempering method for the system of malonaldehyde in water. The reaction coordinate fluctuated in large conformational space. As a result, we were able to calculate the potential of mean force of the reaction coordinate accurately. We found that molecular simulations with STUS also allow us to understand chemical reactions of biomolecular systems.

3PT225 大規模量子化学計算(FMO 法)による HIV-1 糖鎖認識抗体 2G12 と糖鎖間の相互作用解析

Interaction Analysis of HIV-1 Antibody 2G12 and Glycans by Large-Scale Quantum Chemical Calculations based on FMO method

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Human antibody 2G12 is capable of recognizing the high-mannose glycans on the HIV-1 surface glycoprotein, gp120. Doores et al. found that Fab-2G12 is bound to D-fructose stronger than the original ligand, D-mannose. Details of the neutral carbohydrate-antibody interaction remain unclear. To elucidate the differences in the ligand-binding, we carried out ab initio fragment molecular

orbital (FMO) calculations at MP2/6-31G(d) level for Fab-2G12 with D-mannose/D-fructose complexes using their crystal structures (PDB ID: 1OP3, 3OAY). The interaction energy between Fab-2G12 and D-fructose was smaller than that between Fab-2G12 and D-mannose excluding the effects of water, which was not consistent with the experimental result. We further investigated the interaction involving water molecules observed in the crystal structures and found notable pair interaction energies among D-fructose, waters, and several amino acid residues. In addition, we constructed a model glycan ligand without a side chain group of the D-fructose and studied its interaction with the antibody to evaluate the effect of the substituent of the ligand on the interaction. The obtained results indicated a significant role of C2-OH group of D-fructose in the ligand-antibody interaction.

3PT226 FTIR 法による光合成酸素発生マンガンクラスター近傍の水素結合ネットワークの構造解析

FTIR analysis of the hydrogen bonding network around the O₂-evolving Mn₄CaO₅ cluster

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Photosynthetic O₂ evolution is performed at the Mn₄CaO₅ cluster in photosystem II (PSII) through five intermediates called S states (S₀-S₄). Recent X-ray structure of PSII showed that two water molecules are bound to the Ca²⁺ and form a hydrogen-bond network between the Mn₄CaO₅ cluster and Y_Z. To clarify the roles of the water molecules and the hydrogen-bond network around the Ca²⁺, we have investigated the effect of the replacement of Ca²⁺ with Ba²⁺ on these structures using Fourier transform infrared (FTIR) difference spectroscopy. S₂/S₁ FTIR difference spectra of moderately hydrated films of NaCl-washed PSII membranes of spinach were recorded at 283 K in the presence of either Ca²⁺ or Ba²⁺. The weakly hydrogen-bonded OH bands of water at 3617/3587 cm⁻¹ observed in Ca²⁺-PSII were absent in Ba²⁺-PSII. A broad feature at 2900-2600 cm⁻¹, which arises from strong hydrogen bonds with high proton polarizability, also disappeared in Ba²⁺-PSII. These results strongly suggest that the above bands of water OH and strong hydrogen bonds originate from the water molecules bound to Ca²⁺ and the surrounding hydrogen bond network, respectively, and the replacement of Ca²⁺ with Ba²⁺ with a larger ion radius changed or destructed these structures. The data support the idea that either of the water molecules attached to the Ca²⁺ functions as a substrate and that the hydrogen-bond network from the Ca²⁺ to Y_Z plays an important role in proton transfer in the S₂→S₃ transition, which is blocked by Ba²⁺ substitution.

3PT227 QM/Langevin-MD と振動モード解析を用いた光合成初期過程における光化学系 II の理論的研究

A study of QM/Langevin-MD simulation and vibrational analysis for photosystem II in early process of photosynthesis

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In the early process of photosynthesis in photosystem II (PSII) protein, the oxidation reaction, evolving one oxygen molecule by oxidizing two water molecules, occurs in oxygen-evolving complex (OEC) forming oxo-bridged cluster consisting of four manganese and one calcium ions (Mn₄O₅Ca). This reaction goes through the five oxidation states denoted S_n (n=0-4), called Kok cycle. Here we have performed a QM/Langevin-MD simulation and FTIR spectrum calculation for OEC and residues surrounding it. The structure of PSII solved by X-ray crystallography at 1.9 Å was used in this study (PDB entry 3ARC). The structure was optimized using QM/MM calculations. And by changing Mn oxidation numbers at the same as S₂ state ones, the structure satisfying four Mn oxidation numbers in the S₂ state was predicted using QM/MM calculation from the structure of S₁ state. For these optimized structures, QM/Langevin-MD and vibrational frequency were performed in many variation of four Mn oxidation numbers. From the experimental evidences, one Mn ion in the cluster is oxidized during going through S₁ to S₂ states, and meanwhile the spectra of Ala344 and Glu354 show the clear peak shift in IR spectra. We have observed the same peak shift in our vibrational frequency calculation. And the trajectory of QM/Langevin-MD simulation reveals the most stable Mn oxidation numbers of S₁ state in the thermal fluctuation. In addition, based on the trajectory of the S₁ state, we will discuss about four Mn oxidation numbers in the S₂ state.