Center for Computational Sciences, University of Tsukuba
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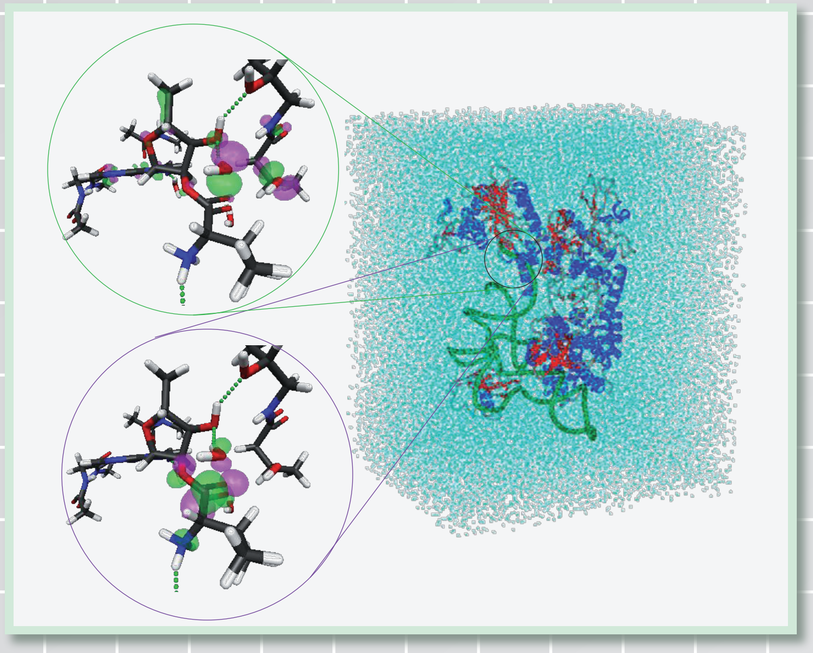
Biological Sciences on PACS-CS/T2K

Quantum Mechanics/Molecular Mechanics (QM/MM) hybrid calculations



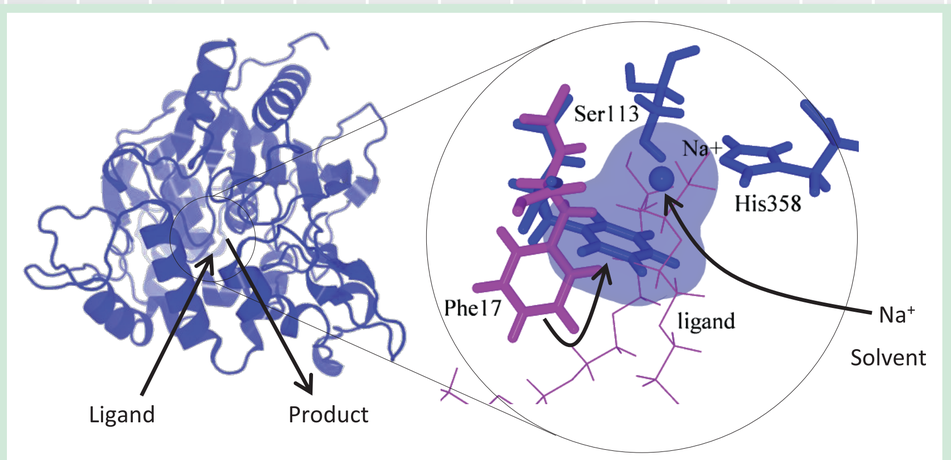
Quantum mechanical (QM) calculation is an important tool for investigations of functional mechanisms of biological macromolecules. However, the system size QM calculations can treat is usually up to a few hundred atoms, whereas those of most biological systems are 1,000 ~ 1,000,000. To overcome these difficulties, quantum mechanics / molecular mechanics (QM/MM) calculation has been used as an efficient method, in which the system is divided into QM and MM regions; the active sites to be investigated are assigned as the QM regions, which are described quantum mechanically, and the other regions of the macromolecular systems are assigned as the MM regions, which are described molecular mechanically. In this study, we have developed an interface program to connect conventional but highly-parallelized QM and MM calculation engines running on massively-parallel supercomputers with more than thousands of CPUs.

Actually, we have evaluated the accuracy and performance of the present system on our supercomputers, the PACS-CS system and the T2K Tsukuba. A calculated system using the developed program is a protein•RNA complex which play a crucial roles in biosynthesis of protein. First, we computationally constructed the model structure of the system which could not be obtained experimentally. Then, we have revealed the mechanism of the enzymatic reaction for ensuring fidelity of the protein synthesis, on the basis of the dynamical changes on electronic structures of the system.

A novel algorithm for evaluation of metal–π interactions in biological systems

The interaction between a cation and an aromatic ring, i.e., the cation–π interaction, is one of the strongest noncovalent forces, and is widely observed in biological macromolecules. Metal cations such as Na^+ and K^+ can also participate in the cation–π interactions, and are known to yield significant stabilization energy.

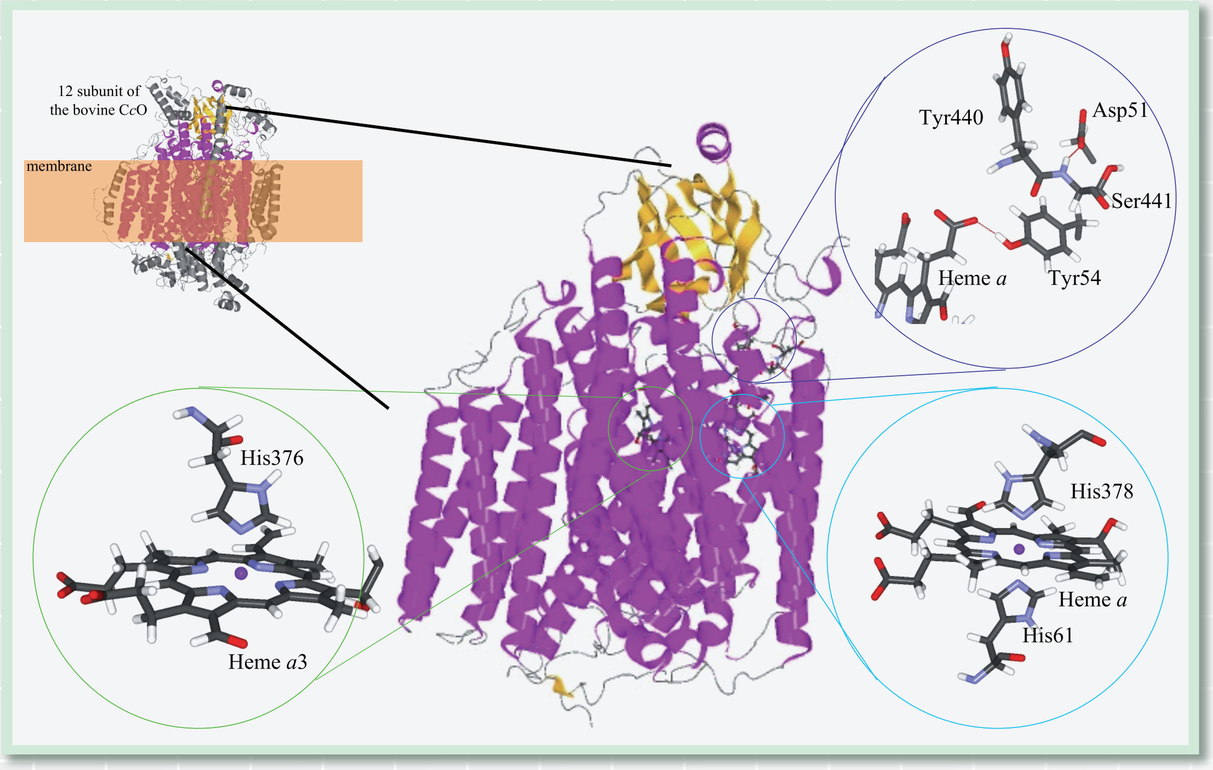
Molecular dynamics (MD) simulation is an important tool for investigations of dynamical properties and functional mechanisms of biomacromolecules. However, there is a serious error in the current force fields; they cannot correctly estimate the metal–π interaction energy. Although QM calculations provide reliable estimation, their huge computational costs prohibit long-time MD simulations. Accordingly, we developed a novel scheme to calculate the interaction energy with an accuracy comparable to that of advanced *ab initio*, and with computational costs comparable to those of force field calculations (the computational time of our algorithm is significantly reduced compared to conventional QM calculations by 10^4 fold).



Method	Standard energy function	Our scheme	Method proposed by Tsuzuki, et al.	CCSD(T)
Time (sec)	3.26	3.44	1.46×10^4	3.95×10^7

In this study, we have applied our algorithm to investigate functional roles of the Na^+–π interaction present in a protein, lipase, which depredates lipid molecules. We revealed that the Na^+–π interaction establishes a remarkably stable core structure, thus contributing to large functional structural changes. Currently, our scheme is the only way to perform long-time MD simulations with reasonable costs.

An application of our calculation system running on massively parallel supercomputers



Exploiting our QM/MM interface program, which connects highly-parallelized QM (GAMESS) and MM (AMBER) calculation engines (see above) on our supercomputers in CCS (PACS-CS and T2K Tsukuba), we investigated a functional mechanisms of a large membrane protein, cytochrome c oxidase (CcO) derived from bovine. In CcO, heme a and heme a_3 are included, being crucial in the catalytic reaction (i.e., the reduction of two oxygen molecules into a water molecule and the creation of the gradient of proton). A peptide group of Tyr440-Ser441 has been suggested that it pumps a proton to Asp51 along the H-pathway.

This system includes 20,966 atoms, and three different QM regions are set as 105, 90, and 50 QM atoms for heme a, heme a_3, and the structure close to Tyr440-Ser441, respectively.