【Grant-in-Aid for Scientific Research (S)】

Broad Section E

Title of Project : Clarification of Ubiquitous Proton Function in Photoreceptive Proteins by Quantum Molecular Dynamics Simulations

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【Purpose and Background of the Research】

Biological molecules possess the sophisticated mechanisms for achieving functions as a result of the long-time evolution. At the atomic level, protons ubiquitously exist in biological systems in various forms, and show heterogeneous dynamical behavior coupling with the electron-state changes and structural changes in the surrounding environment. The resulting proton transfers play a vital role in the mechanisms for achieving functions on life phenomena. Therefore, in order to elucidate the mechanisms for achieving functions in biological systems at the atomic level, it is important to correctly understand the dynamical behavior of ubiquitous protons.

In experimental studies, various structures of biological molecules have been determined from x-ray crystallography and cryo-electron microscopy. However, the positions and dynamical processes of protons have not been observed due to the limit of the temporal and spatial resolution. In theoretical studies, although chemical reactions have been analyzed with quantum molecular dynamics (QMD), the tractable number of atoms is limited to at most one thousand due to the high computational cost. Thus, elucidating the dynamical behavior of ubiquitous protons is significantly difficult.

In the present study, the microscopic mechanisms of life phenomena will be clarified using our original large-scale QMD.

【Research Methods】

Our original QMD, divide-and-conquer-type density-functional tight-binding molecular dynamics (DC-DFTB-MD), is further improved in combination with GPU accelerator. Extension of this method for excited states is also performed.

As an application to photoreceptive proteins, ubiquitous proton transfers in bacteriorhodopsin (BR), which has the function of light-driven proton pump, are analyzed. From DC-DFTB-MD of BR with lipid bilayer and water (Figure 1), multiple proton transfers on the photocycle are fully observed, and the microscopic origin of the unidirectional and active proton transport in BR resulting in light-energy conversion is elucidated.

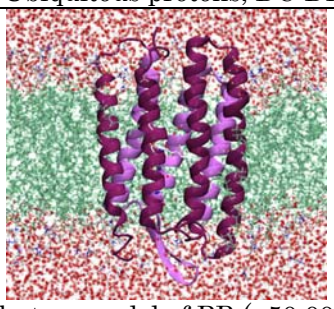

Figure 1. All-atom model of BR (~50,000 atoms).

In addition to BR, ion-transporting microbial rhodopsins and ATP synthase are targets of the present study. The microscopic mechanisms of various biological functions in these systems are clarified from the viewpoint of ubiquitous protons.

【Expected Research Achievements and Scientific Significance】

Theoretical basis of revealing the dynamical behavior of ubiquitous protons in arbitrary biological systems is constructed. Moreover, it is expected that we can gain microscopic insights into the essence of life phenomena involving chemical reactions and develop the biological materials with high efficiency.

【Publications Relevant to the Project】

・"Three pillars for achieving quantum mechanical molecular dynamics simulations of huge systems: Divide-and-conquer, density functional tight-binding, and massively parallel computation" H. Nishizawa, Y. Nishimura, M. Kobayashi, S. Irle, and H. Nakai, *J. Comput. Chem.*, **37**, 1983 (2016).
・"Rigorous pKa Estimation of Amine Species Using Density-Functional Tight-Binding-Based Metadynamics Simulations" A. W. Sakti, Y. Nishimura, and H. Nakai, *J. Chem. Theory Comput.*, **14**, 351 (2018).

【Term of Project】 FY2018-2022
【Budget Allocation】 151,100 Thousand Yen
【Homepage Address and Other Contact Information】

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