Analysis of specific interactions between transcriptional regulatory protein and DNA: molecular simulations combined with MD and *ab initio* FMO methods

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1. Introduction

Transcription mechanism of gene information from DNA to mRNA is controlled by transcriptional regulatory proteins such as a lactose repressor (LacR) and their ligand molecules. Biochemical experiments elucidated that ligand-binding to LacR drastically changes the mechanism. However, the effect of the ligand-binding has not been clarified at an electronic level. In our previous study [1], molecular simulations combined with classical molecular dynamics (MD) and *ab initio* fragment molecular orbital (FMO) methods were performed to elucidate the specific interactions between LacR, DNA and ligand. We here considered the complex with LacR dimer, DNA and ligand and investigated the effect of dimerization on the specific interactions.

2. Details of molecular simulations

The initial structure of the complex with LacR dimer, DNA and anti-inducer ONPF was obtained from PDB (PDB ID: 1EFA). From this structure, the initial structures of the LacR-DNA complex without ligand and the LacR-DNA complex with inducer IPTG were constructed. Solvating water molecules were added around the structures, and the solvated structures were optimized by using MM program Gromacs (ver.4.5.3). AMBER99SB-ILDN and TIP3P force fields were used for protein and water molecules, respectively, while GAFF force fields based on RESP charges obtained by *ab initio* MO calculations were adapted for ligand molecules. 10 ns MD simulations at 300 K were performed under periodic boundary conditions. For some structures obtained by MD simulations, specific interactions between LacR dimmer, DNA and ligand were investigated by using the FMO method.

3. Results and discussion

The structure of LacR-DNA-ONPF complex optimized by Gromacs is shown in Fig. 1. Two ONPF ligands bind to LacR dimer, and the DNA-binding domains of the both LacRs bind specifically to DNA. The results for the other complexes will be shown at the symposium.

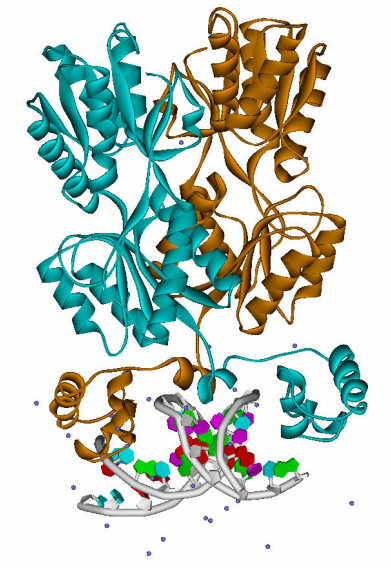

Fig. 1

[1] T. Ohyama et al., J. Comp. Chem., 2011, 32, 1661-1670.

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