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Interaction Free energy landscape of water dimer using direct ab initio MO-MC

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<Introduction> Molecular recognition plays an important role in biological systems. However, the mechanism of the specific interaction is not well understood yet. Molecular recognition takes place in the finite temperature and many interaction configurations of almost the same interaction energies can contribute to the recognition. Thus, the interaction energy (ΔE) of one interaction configuration on the potential minima is inadequate to understand the specificity. We need to calculate interaction free energy (ΔA). So far we have calculated ΔA landscapes between DNA and amino acid side chain [1], and between DNA and a water molecule based on the force field energy calculations. We showed the ΔA landscape represents both the 3-dimensional distribution and the stability of ligand around targeted molecule and is comparable to the experimental ligand distribution extracted from structural database. ΔA landscape has the ability to predict recognition sites of ligand and is useful to understand molecular recognition. In this study, we calculate the ΔA landscape of water dimer using direct ab initio MO-MC. It means energy of the interaction configurations between the two water molecules is calculated by means of the ab initio MO at every 1 step of Monte Carlo simulation. To obtain reliable ΔA landscape, it is important to use reliable energy calculation method. Resulting ΔA landscape is compared to the one using the force field (TIP3P) energy calculation.

<Method> We denote one water molecule as wA and the other as wB. ΔA landscape is obtained by sampling all the possible interaction configurations between the wA and the wB. Energy of the system is calculated by means of the ab initio MO (HF/STO-3G, HF/3-21G, HF/6-31G* level of theory). ΔA landscape is calculated by two steps. First, 10^7 MC sampling of the wA's configuration with the fixed wB's coordinate system is performed. The space around wB is divided into small cubic cells, and relative free energies A_i among cells are calculated from the number of times of wA visited the cells during the simulation. Then, interaction free energy ΔA_{min} at the most frequently visited cell is calculated using the overlapping distribution method [2]. Interaction free energy at the cell i , ΔA_i is obtained by adding A_i and ΔA_{min} . Entire ΔA_i is the ΔA landscape and visualized as isosurface.

<Results> Figure shows the ΔA isosurface using TIP3P and HF/STO-3G. The difference appears in the distribution around the oxygen atom. TIP3P has hemispherical distribution and HF/STO-3G has not. Distribution around the oxygen atom reflects the angle dependency in hydrogen-bonding. The inability of TIP3P potential to produce the angle dependency in hydrogen-bonding is visualized as the difference in the ΔA isosurface.



Fig. ΔA isosurface ($\Delta A = -3.0$ kcal/mol, $T = 300$ K)

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