# Developments of the Computational Technique to Predict the Binding Enthalpy for Protein-Inhibitor Complex

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**Abstract**

Although recent advances in Japanese original software make it now possible to carry out the quantum chemical calculations of the protein-inhibitor interaction energy, it is still very difficult to calculate the quantum chemical binding free energy ($\Delta G = \Delta H - T\Delta S$), which is directly concerned with the pharmacological activity of inhibitor. However, there is a possibility that the binding enthalpy term ($\Delta H$) is able to calculate with quantum chemical calculation. The aim of the project is developments of the computational technique for the prediction of the binding enthalpy for the protein–inhibitor complex with the quantum chemical calculation on Earth Simulator in order to utilize it for SBDD (Structure Based Drug Design). In fiscal 2009, we have designed the computational technique using DIEM (Difference mean Interaction Energy Matrix) which is defined by the subtraction the interaction energy matrix for hydrated protein from that for hydrated protein–inhibitor complex and the subtraction the interaction energy matrix for hydrated inhibitor from that for pure water. Using DIEM, it is possible to make the molecular system to calculate quantum chemically small. For small protein-inhibitor complex we checked that the binding enthalpy was able to be calculated in realistic time by using the quantum chemical calculation with DIEM method on Earth Simulator. In fiscal 2010, we are going to validate the accuracy of the prediction of this technique for the protein-inhibitor complexes which the binding enthalpy is measured.

**Keywords:** binding enthalpy, Fragment molecular orbital (FMO) method, SBDD, interaction energy matrix