Quantum Analysis of the Oxygen Reduction Reaction Mechanism at the Mitochondria

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Cytochrome c oxidase is a mitochondrial membrane bounded enzyme which is the fourth complex of the respiratory electron transport chain which catalyzes the respiratory reduction reaction of O_2 to water. Reduction of O_2 takes places at the metallic center of the cytochrome c oxidase. In 1990, Wikström titrated the catalytic cycle of cytochrome c oxidase with a phosphorylation potential, and the results were interpreted as evidence for the thermodynamic linkage of proton translocations [1]. In 2000, Wikström was able to successfully sustain a complete catalytic oxygen reduction reaction of cytochrome c oxidase, $4Fe^{2+} - Cytochrome\ c + 8H^+ + O_2 \longrightarrow 4Fe^{3+} - Cytochrome\ c + 2H_2O + 4H^+$ [2]. In 2009, Collman et al. found the rate-determination step of the catalytic oxygen reduction reaction in cytochrome c oxidase, and synthesize the best mimic structure of cytochrome c oxidae active site [3].

The oxygen reduction reaction was previously studied using first principle calculations based on the density functional theory (DFT) with the B3LYP /6-31G (d, p) method in the Gaussian09 program [4]. The B3LYP method includes a three-parameter hybrid functional, according to Becke, with additional correlation corrections due to Lee, Yang and Parr [5-6]. The simulated parameters are shown in Table 1. It is generally agreed that DFT methods give accurate results for the geometries and vibrational frequencies of transition metals [7-8]. In this study, the simulated the functional model of metallic active site in the respiratory enzyme cytochrome c oxidase is simulated and the output data is used to analyze the reaction energy of oxygen reduction reaction. The metallic active center was calculated with three different multiplicities, singlet, triplet, and quintet.

The computed geometric structure of the mimicked cytochrome c oxidase active site is shown in Fig. 2. According to the results of geometric energy of different multiplicities, we could sum up the reaction center of cytochrome c oxidase be quintet. Figure 3 shows the computed geometric structure of the predicted oxidized cytochrome c oxidase. The reaction energies are defined as $E_{reaction} = E_{O_2} + E_{Cyt\ c\ oxidase} - E_{(Cyt\ c\ oxidase+O_2)}$ and results are shown in Table 3. Metallic ions have different kinds of multiplicity. However, Gaussian09 outputs the most stable state of cytochrome c oxidase ferrous ion as a quintet. It is well known that the electron configuration of O_2 is $(1\sigma)^2(2\sigma)^2(3\sigma)^2(4\sigma)^2(1\pi)^4(5\sigma)^2(2\pi)^2(6\sigma)^0$. The HOMO (the highest occupied molecular orbital) is found to be occupied by two single electrons. The adsorption bond formed by the interaction of the d orbital of the metal and the $2\pi^*$ orbital due to the electrons that exist in the metallic d orbital is predicted.

REFERENCES

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Table 1. Gaussian 09 setup of the cytochrome c oxidase active site.

Software	Gaussian09
Function	Optimization & Frequency
Method	DFT (B3LYP)
Basis set	6-31G (d,p)

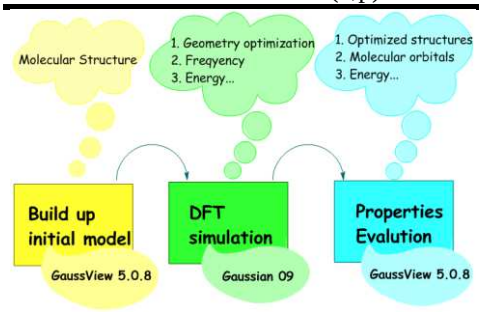

Fig. 1. Simulation Flow Chart of this study.

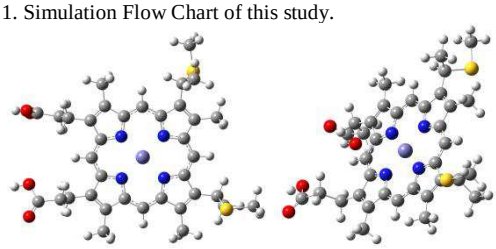

Fig. 2. Optimized structure of the reduced cytochrome c oxidase active site.

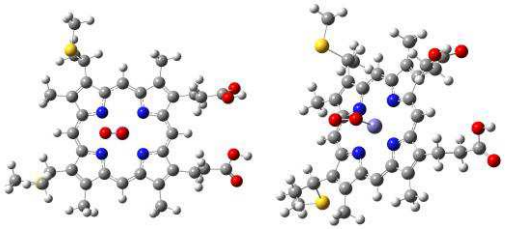

Fig. 3. Optimized structure of the oxidized cytochrome c oxidase active site.

Table 2. Gaussian 09 output summary of the catalytic oxygen reduction reaction at the cytochrome c oxidase active site.

Gaussian09	Energy(eV)
Fe(singlet)	-108188
Fe(triplet)	-108193
Fe(quintet)	-108195

Table 3. Gaussian 09 output summary of the catalytic oxygen reduction reaction at the cytochrome c oxidase active site.

Gaussian09	Energy(eV)	Reaction Energy
O_2	-4071.3	N/A
Fe(quintet)	-108195	N/A
Fe-O-O	-112287	-20.615