# Quantum Analysis of the Oxygen Reduction Reaction Mechanism at the Mitochondria: the Power Generator of Eukaryotic Organisms

Yu-Chien Ting, and Che-Wun Hong

Department of Power Mechanical Engineering, National Tsing-Hua University, 300 Hsinchu, Taiwan

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 computed geometric structure of the mimicked cytochrome c oxidase active site is shown in Fig. 1. Figure 2 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 2. 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

1. M. Wikström, Nature, **336**, 776, (1989)
2. M. Wikström, Biochemistry, **239**, 3515, (2000)
3. J. P. Collman, et al., J. Am. Chem. Soc, **131**, 5034, (2009)
4. M. J. Frisch, et al., Gaussian, Inc., Wallingford CT, 2010.
5. A. D. Becke, J. Chem. Phys, **98**, 5648, (1993)
6. C. Lee et al., Phys. Rev. B., **37**, 785 (1998)
7. C. W. Bauschlicher et al., Recent Advances in Density Functional Theory, Part II, World Scientific Publ., Singapore, 1997
8. I. Bytheway et al., Chem. Phys. Lett., **282**, 219 (1998)

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

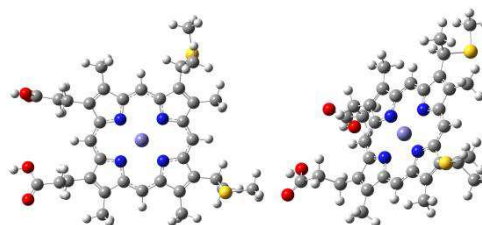| Software | Gaussian09 |
|---|---|
| Function | Optimization & Frequency |
| Method | DFT (B3LYP) |
| Basis set | 6-31G (d,p) |



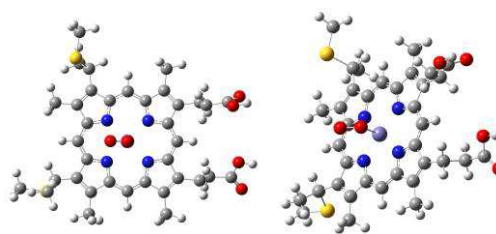Fig. 1. Optimized structure of the reduced cytochrome c oxidase active site.



Fig. 2. 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) | Reaction Energy |
|---|---|---|
| $O_2$ | -4071.3 | N/A |
| Fe | -108195 | N/A |
| Fe-O-O | -112287 | -20.615 |