A Theoretical Study of Nitric Oxide Reduction in Heme-Copper Oxidase and Nitric Oxide Reductase

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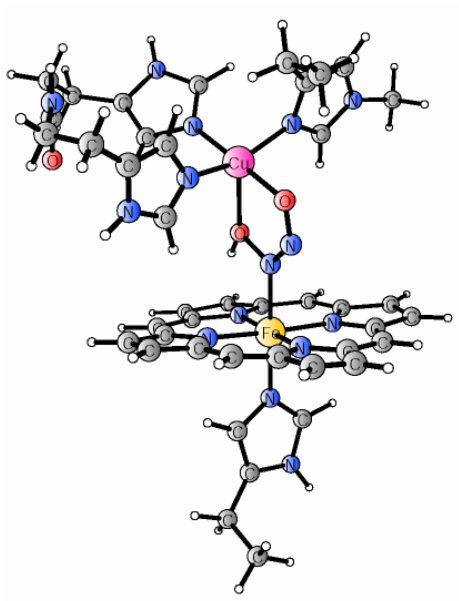
Cytochrome oxidase and the bacterial nitric oxide reductase (NOR) both belong to the heme-copper oxidase superfamily of enzymes. The two enzymes are proposed to have similar structures and are believed to share a common phylogeny. The binuclear center consists of a heme iron and a second metal ion, which is Cu in the oxidases and a non-heme Fe in NOR. The similarity in the structural features of the binuclear centers suggests that the two enzymes can reduce the same substrates, and indeed several cytochrome oxidases have been shown to display nitric oxide reductase activity and one bacterial NOR has been shown to reduce O_2.

The reduction of two NO to N_2O and H_2O in a *ba*$_3$ type heme-copper oxidase has been investigated using density functional theory (B3LYP). The first NO binds to the ferrous heme iron, which slightly reduces NO to a more nitroxyl anion character. In this way nitric oxide is activated toward the reaction with the second NO. A five-membered ring is formed with the two oxygens coordinating to Cu_B whereas the binuclear center is oxidized to Fe(III) and Cu_B(II). A proton has to enter the catalytic cycle at this stage to break the N-O bond forming Cu_B(II)-OH and Fe(III)-N_2O in a rate limiting step.



The structure of NOR is not solved but by using the structural similarities with the cytochrome oxidases qualified guesses of the coordination of the binuclear center can be made. Two models of the binuclear active site of NOR have been used to investigate the coordination of the non-heme iron (Fe_B). Furthermore, the reduction mechanism of NO in the *ba*$_3$ type heme-copper oxidase is compared to the corresponding reaction in NOR.