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A Functional Model for the Active site in Cytochrome c Oxidase Catalytically Reduces Oxygen to Water Under Physiological Conditions

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At physiological pH and potential a synthetic model of the active site in the enzyme cytochrome c oxidase (CcO), catalyzes the 4-electron reduction of oxygen. This model is covalently attached to a self-assembled-monolayer (SAM) on a gold electrode. During catalytic oxygen reduction electron delivery through the SAM's liquid-crystalline film is rate limiting, similar to the situation in CcO. The model contains all of the essential components in CcO's active site: an Fe heme ("heme a₃") fitted with a proximal imidazole ligand and an array of three distal imidazoles bound to copper ("Cu-b"). A phenol mimicing "tyrosine 244" is attached to one distal imidazoles. All three redox-active components are required to minimize the production of partially-reduced-oxygen-species (PROS) during oxygen reduction. This functional CcO model demonstrates how CcO itself might tolerate the hormone NO, which is known to diffuse through the mitochondria. It is proposed that Cu-b delivers superoxide to NO bound to Fe in heme a₃ forming peroxynitrite and then nitrate, which diffuses away.

Relevant references: Collman, James P.; Devaraj, Neal K.; Decréau, Richard A.; Yang, Ying; Yan, Yilong; Ebina, Wataru; Eberspacher, Todd A.; Chidsey, Christopher E. D. A Cytochrome c Oxidase Model Catalyzes Oxygen to Water Reduction Under Rate-Limiting Electron Flux. *Science*, **2007**, 315, 1565-1568. Collman, James P.; Dey, Abhishek; Decreau, Richard A.; Yang, Ying; Hosseini, Ali; Solomon, Edward I.; Eberspacher, Todd A. Interaction of Nitric Oxide with a Functional Model of Cytochrome c Oxidase. *Proc. Natl. Acad. Sci. U. S. A.*, **2008**, 105(29), 9892-9896.