Effective Intermediate-Spin Iron in O_2-Transporting Heme Proteins

Nils Schuth[1], Stefan Mebs[1], Dennis Huwald[2], Pierre Wrzolek[3], Matthias Schwalbe[3], Anja Hemschemeier[2], Michael Haumann[1*]

[1]Freie Universität Berlin, Department of Physics, 14195 Berlin, Germany
[2]Ruhr-Universität Bochum, Department of Plant Biochemistry, Photobiotechnology, 44801 Bochum, Germany
[3]Humboldt-Universität zu Berlin, Department of Chemistry, 12489 Berlin, Germany
[*]michael.haumann@fu-berlin.de

Proteins carrying an iron-porphyrin (heme) cofactor are essential for biological O_2 management. The nature of the Fe-O_2 bonding in hemoproteins has been debated for long. We used energy-sampling and rapid-scan X-ray Kβ emission and K-edge absorption spectroscopy at synchrotrons as well as quantum chemistry to determine molecular and electronic structures of unligated (**deoxy**), CO-inhibited (**carboxy**), and O_2-bound (**oxy**) hemes in myoglobin (MB) and hemoglobin (HB) solutions and in porphyrin model compounds at 20-260 K. Similar metrical and spectral features revealed analogous heme sites in MB and HB and the absence of low-spin (LS) to high-spin (HS) conversion. Amplitudes of Kβ main-line emission spectra were directly related to the formal unpaired Fe(d) spin count, indicating HS Fe(II) in **deoxy** and LS Fe(II) in **carboxy**. For **oxy**, two effective Fe(d) spins were revealed by our static and kinetic X-ray spectroscopy data, as supported by (TD)DFT and CASSCF calculations. The emerging Fe-O_2 bonding situation includes in essence a ferrous iron center, minor superoxide character of the non-innocent ligand, significant double-bond properties of the interaction, and three-center electron delocalization as in ozone. It resolves the classical and apparently contradictory models of Pauling, Weiss, and McClure/Goddard into a unifying view of O_2-bonding tuned towards reversible oxygen transport in the heme proteins [1].

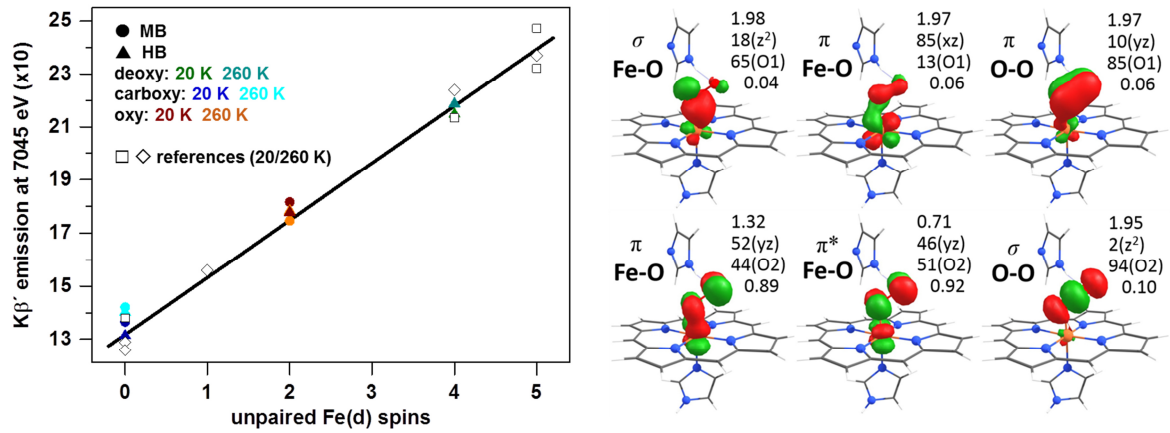

Figure 1: Effective unpaired Fe(d) spins from Kβ emission spectroscopy (left) and molecular orbitals of the Fe-O_2 bonding (right; numbers: spin densities, Fe(d)/O(p) characters, EUEDs).

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[1] N. Schuth, S. Mebs, D. Huwald, P. Wrzolek, M. Schwalbe, A. Hemschemeier, M. Haumann. Effective intermediate spin iron in O_2-transporting heme proteins. Proc. Natl. Acad. Sci. USA 114, 8556-8561 (2017)