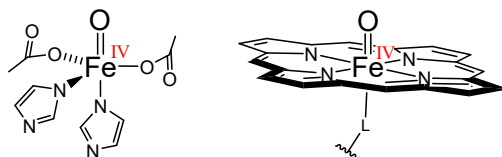
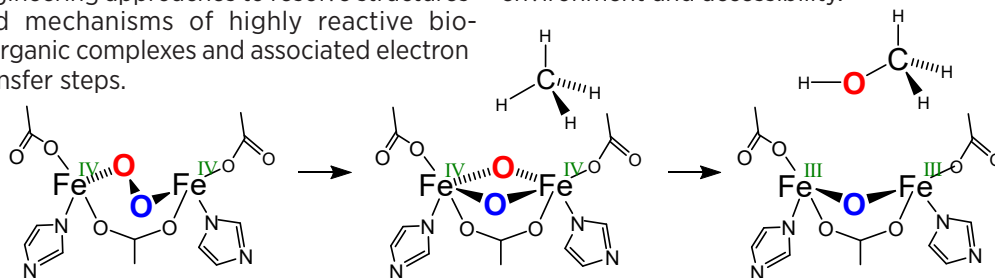


Molecular oxygen, O_2 , is a powerful oxidant, which is kinetically sluggish under ambient conditions. The ability of living cells to overcome this barrier using transition metal enzymes lead to the explosion of aerobic life. We are interested in understanding mechanisms of O_2 activation in biology and their applications from fundamental and industrial chemistry to climate control and biomedical solutions. Working with metalloenzymes, their synthetic analogs, and subcellular organelles, we use a range of spectroscopic, electrochemical, and engineering approaches to resolve structures and mechanisms of highly reactive bio-inorganic complexes and associated electron transfer steps.

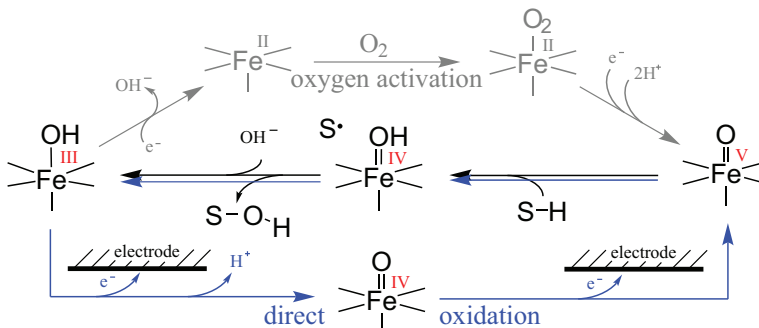


Enzymes use transition metals to overcome spin restrictions of triplet O_2 , which oxidizes the metal/protein complex in a concerted, multi- e^- step. The resulting highly oxidized species, in turn, initiate chemical reactions with specific substrates. Protein moiety tunes reactivity of the metal through coordination environment and accessibility.

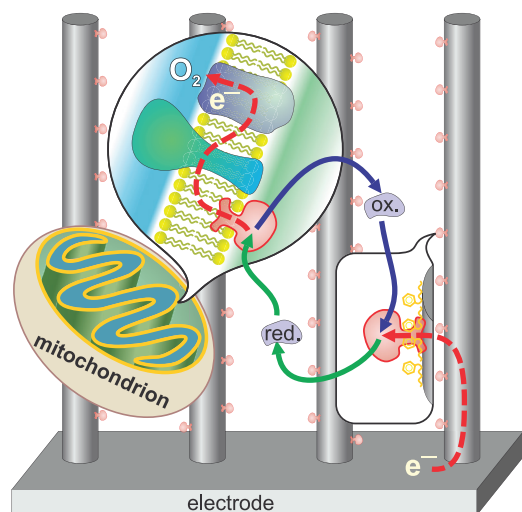


Methane Monooxygenase, an enzyme in methanotropic bacteria, uses a pair of Fe^{IV} ions to accomplish an unrivaled conversion of methane to methanol. This reaction is of major interest for liquid fuels production from natural gas and as an initial step in the industrial synthesis. Using time-resolved laser spectroscopy, we observed this reaction in real time and resolved the mechanism that puzzled the field for the last two decades. Many more analogous enzymes with unresolved mechanisms are awaiting their turn.

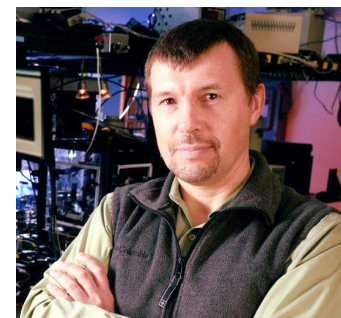
Enzymatic O_2 activation always starts with reduction, followed by metal oxidation yielding formal $Fe^V=O$ state (top path), which activates the substrate SH to transient S^\bullet radical. By reversing the reaction under large positive electrode potential we can generate $Fe^V=O$ directly from water, circumventing the need for O_2 (bottom path) and opening intriguing possibilities for applied catalysis and new analytical methods.



Mitochondria are power plants of the cell: semi-autonomous organelles, which capture the energy of e^- current from food to O_2 to make ATP. A choreographed chain of enzymatic redox



reactions takes place in the impermeable inner mitochondrial membrane, which isolates mitochondria from the cytosol. It makes detection of functional changes in whole mitochondria in such metabolic disorders as diabetes, Alzheimer's disease, etc., difficult. We are developing a fundamentally new method to study intact mitochondria. It is based on dynamic redox equilibrium of natural metabolites, membrane transport, and electrochemistry on specifically modified electrodes. We establish chemically-mediated e^- current from fiber electrodes into mitochondrial enzymes and further to oxygen, mimicking natural metabolic pathways as an artificial "respiration in a tube".



Denis A. Proshlyakov

Biological Redox Chemistry

ASSISTANT PROFESSOR

(b. 1967)

B.S., 1989,

M.S., 1992,

Moscow Medical State Univ.;

Monbusho Scholarship, 1993-95

Ph.D., 1995,

Inst. for Molecular Science,

Okazaki National Research Institutes,

Okazaki, Japan;

Postdoctoral 1995-2001,

Michigan State Univ..

<http://www.bio.cem.msu.edu/>



517-353-1117

SELECTED PUBLICATIONS

FTIR Spectro-Voltammetry and Quantitative Modeling of Analytes in Kinetically Constrained Redox Mixtures, John, C.W., Proshlyakov, D.A., *Anal. Chem.* **2019**, in press; doi.org/10.1021/acs.analchem.9b00859.

Structure of the key species in the enzymatic oxidation of methane to methanol, Banerjee, R., Proshlyakov, Y., Lipscomb, J.D., & Proshlyakov, D.A., *Nature* **2015**, 518, 431.

Apoprotein isolation and activation, and vibrational structure of the Helicobacter mustelae iron urease Carter E.L., Proshlyakov, D.A., Hausinger, R.P., *J. Inorg. Biochem.* **2012**, 111, 195.

Transient iron species in the catalytic mechanism of the archetypal α -ketoglutarate-dependent dioxygenase in iron-containing enzymes: versatile catalysts of hydroxylation reactions in nature, Proshlyakov, D.A., & Hausinger, R.P.; de Visser, S., & Kumar, D., Eds., *RSC*, **2011**.

Equilibrium and Kinetic Behavior of $Fe(CN)_6^{3-/4-}$ and Cytochrome c in Direct Electrochemistry Using a Film Electrode Thin-Layer Transmission Cell, Dai, Y., Zheng, Y., Greg M. Swain, G.M., Proshlyakov, D.A., *Anal. Chem.* **2010**, 83(2), 542.

Insight into the mechanism of an iron dioxygenase by resolution of steps following the $Fe^V=O$ species, Grzyzka, P.K., Appelman, E.H., Hausinger R.P., Proshlyakov, D.A., *Proc. Natl. Acad. Sci. U.S.A.* **2010**, 107(9), 3982.