2012 PROGRAM

8:00 a.m. Registration & Continental Breakfast
Keeneland Room, W.T. Young Library
8:50 a.m. Welcome — Dr. Eli Capilouto
President, University of Kentucky
9:00 a.m. Dr. Brian Crane
Cornell University
How Metal, Nitric Oxide and Redox Chemistry Coordinate Cellular Responses in Microbes and Men

Nitric oxide (NO) is a small, reactive and diffusible agent produced by the complex redox chemistry of the nitric oxide synthases (NOSs). In mammals, NOSs generate NO as a second messenger for many purposes that include neuronal transmission, regulation of the vasculature and release of hormones. In addition, immune cells produce NO as part of the oxidative burst to combat pathogens and tumor cells. Microbial NOSs are less understood but appear to involve NO in novel mechanisms that include toxin biosynthesis, protection against oxidative damage and the coordination of stress responses. A common theme in this broad spectrum of reactivity is the ability of NO to mediate redox reactions at metalloenzyme centers. The chemistry of NO production and targeting will be discussed as well as emerging roles of this fascinating molecule.

10:00 a.m. Break (refreshments available)
10:30 a.m. Dr. Yi Lu
University of Illinois at Urbana-Champaign
Designing Functional Metalloproteins: Exploring the Roles of Non-covalent Interactions in Conferring and Fine-tuning Enzymatic Activities

Designing metalloproteins is an ultimate test of our knowledge about metalloproteins and can result in new biocatalysts for practical applications. In this presentation, we provide three examples to demonstrate that, while reproducing the primary coordination sphere may be good enough to make structural models of metalloproteins, careful design of the non-covalent secondary coordination sphere interactions is required to create functional metalloproteins. In the first example, we demonstrate the fine-tuning of reduction potentials of azurin a member of cupredoxin family that are involved in long-range electron transfers in many important biological processes such as photosynthesis, to span ~1 V through carefully design of hydrophobicity and hydrogen bonding networks around the primary coordination sphere, and the use of these redox proteins to address fundamental questions in biological electron transfers such as reorganization energy and Marcus inverted region. In the second example, we have shown that the roles of two conserved glutamate in converting myoglobin into nitric oxide reductase, one through binding to a non-heme iron and the other through hydrogen bonding interaction. Finally, we present recent unpublished results that the presence of waters as part of a new hydrogen-bonding network in myoglobin is necessary to confer oxidase activity in reducing O_2 to water with minimum release of other reactive oxygen species and with > 1,000 turnovers.

11:30 a.m. Lunch
1:30 p.m. Poster Session, Gallery, W.T. Young Library
2:30 p.m. Dr. Harry Gray
California Institute of Technology
Electron Flow through Metalloproteins

Electron transfers in photosynthesis and respiration commonly occur between metal-containing cofactors that are separated by large molecular distances. Understanding the underlying physics and chemistry of these biological electron transfer processes is the goal of much of the work in my laboratory. Employing laser flash-quench triggering methods, we have shown that 2-nm, coupling-limited Fe(II) to Ru(III) and Cu(I) to Ru(III) electron tunneling in Ru-modified cytochromes and blue copper proteins can occur on the microsecond timescale both in solutions and crystals. Redox equivalents can be transferred even longer distances by multistep tunneling (hopping) through intervening tyrosines and tryptophans. In recent work, we have found that 2- to 3-nm hole hopping through one or more intervening tryptophans is several orders of magnitude faster than single-step tunneling in Re-modified mutants of Pseudomonas aeruginosa azurin. The lessons we have learned about the control of electron tunneling and hopping are now guiding the design and construction of sensitizer-modified redox metalloenzymes and other molecular machines for the production of fuels and oxygenated hydrocarbons from sunlight and water.

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Thirty-Eighth Annual
Symposium on

Chemistry & Molecular Biology

Established by M. Benton Naff
in memory of Anna S. Naff

Metals and Proteins

SPEAKERS

Dr. Brian Crane
Dr. Yi Lu
Dr. Harry Gray

Friday, May 4th, 2012

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