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

Department of Chemistry
University of Kentucky
Lexington, KY 40506-0055

The Department of Chemistry, University of Kentucky

presents the

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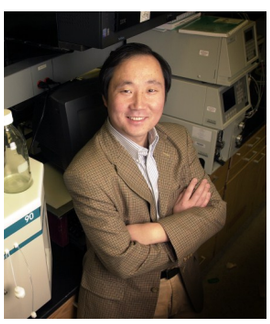
Friday, May 4th, 2012 9:00 a.m.
Auditorium, William T. Young Library

Metals and Proteins

Brian Crane is a professor of Chemistry and Chemical Biology at Cornell University. He received his B.S. degree from the University of Manitoba and his Ph.D. from the Scripps Research Institute under Dr. Elizabeth Getzoff. After a short postdoctoral stay with Dr. John Tainer at Scripps, he trained with Prof. Harry Gray at Caltech as a Helen Hay Whitney Postdoctoral Fellow. Crane studies protein structure and enzymatic mechanism in systems where redox chemistry, photochemistry and cooperative macromolecular interactions are important for cellular function. His specific interests include nitric oxide enzymology, light sensors and oscillators of circadian clocks and the sensory apparatus that mediates bacterial chemotaxis. For this work he has been named a Fellow of the American Association of Arts and Sciences, an Alfred P. Sloan Fellow, and a Searle Scholar. He has received awards that include a Dreyfus New Faculty Award, a Research Innovation Award and most recently, the Cornell Provost Award for Research and Scholarship.



Yi Lu is the Jay and Ann Schenck Professor of Chemistry at the University of Illinois at Urbana-Champaign. He received his B.S. degree from Peking University in 1986, and Ph.D. degree from University of California at Los Angeles in 1992 under Professor Joan S. Valentine. After two years of postdoctoral research in Professor Harry B. Gray's group at the California Institute of Technology, Dr. Lu started his own independent career in the Department of Chemistry at the University of Illinois at Urbana-Champaign in 1994. He is now the Jay and Ann Schenck Endowed Professor of Chemistry and HHMI Professor in the Departments of Chemistry, Biochemistry, Bioengineering and Materials Science and Engineering. He is also a member of the Center for Biophysics and Computational Biology and the Beckman Institute for Advanced Science and Technology. His research interests lie at the interface between chemistry and biology. His group is developing new chemical approaches to provide deeper insight into biological systems. At the same time, they take advantage of recently developed biological tools to advance many areas in chemistry. Specific areas of current interests include a) design and engineering of functional metalloproteins as environmentally benign catalysts in renewable energy generation and pharmaceuticals; b) Fundamental understanding of DNAzymes and their applications in environmental monitoring, medical diagnostics, and targeted drug delivery; and c) Employing principles from biology for directed assembly of nanomaterials and its applications in photonics and sensing. Dr. Lu has received numerous research and teaching awards, including the Fellow of the American Association for the Advancement of Science (2007), Early Career Award, Society of Biological Inorganic Chemistry (2007), Howard Hughes Medical Institute Professor Award (2002), Camile Dreyfus Teacher-Scholar Award (1999), Alfred P. Sloan Research Fellowship (1998), Research Corporation Cottrell Scholars Award (1997), and the Beckman Young Investigators Award (1996).

Harry Gray is the Arnold O. Beckman Professor of Chemistry and the Founding Director of the Beckman Institute at the California Institute of Technology. He received his B.S. degree from Western Kentucky University in 1957. After graduate work at Northwestern University and postdoctoral research at the University of Copenhagen, he joined the chemistry faculty at Columbia University, where in the early 1960s he developed ligand field theory to interpret the electronic structures and substitution reactions of metal complexes. After moving to Caltech in 1966, he began work in biological inorganic chemistry and solar photochemistry, including the development of inorganic systems for energy storage. Working with Ru-modified proteins in the early 1980s, he demonstrated that electrons can tunnel rapidly over long molecular distances through folded polypeptide structures; and, in the years following, he and J. R. Winkler developed laser flash-quench methods that opened the way for experimental investigations that have led to a deeper understanding of the mechanisms of electron flow through proteins that function in respiration and photosynthesis. Dr. Gray has published over 800 research papers and 18 books. He has received the National Medal of Science from President Ronald Reagan (1986); the Pauling Medal (1986); the Linderstrøm-Lang Prize (1992); the Gibbs Medal (1992); the Harvey Prize (2000); the National Academy of Sciences Award in Chemical Sciences (2003); the Benjamin Franklin Medal in Chemistry (2004); the Wolf Prize in Chemistry (2004); the City of Florence Prize in Molecular Sciences (2006); the Welch Award(2009), the Priestley Medal (1991); and 16 honorary doctorates, including ones from Rochester, Northwestern, Pennsylvania, Chicago, Columbia, Toulouse, Florence, Copenhagen, and Edinburgh. He is a member of the National Academy of Sciences; the American Academy of Arts and Sciences; the American Philosophical Society; a foreign member of the Royal Danish Academy of Sciences and Letters; the Royal Swedish Academy of Sciences; the Royal Society of Great Britain; and the Accademia Nazionale dei Lincei. He has been a member of the Board of Directors of the Arnold and Mabel Beckman Foundation since 1994.

For additional information, contact Professor Edith Glazer, Department of Chemistry, ec.glazer@uky.edu.

2012 Committee: Professor Edith Glazer (Chair, Chemistry), Professor Jason DeRouchey (Chemistry), Professor Mark Watson (Chemistry), Professor Anne-Frances Miller, Dean Tim Tracy (College of Pharmacy)

Symposium supported by the Anna S. Naff Endowment Fund