Chemistry Seminars
Spring, 2012

Tuesdays at 11:00-12:00

Classroom Building 170
Seminar Program

January 17
Robert Bergman
Department of Chemistry, University of California, Berkeley

February 14
James Miranda
Department of Chemistry, California State University, Sacramento

February 21
James Kercher
Department of Chemistry, Hiram College

February 28
Steve Leone
Department of Chemistry, University of California, Berkeley
Lawrence Berkeley National Laboratory

March 13
Jennifer Manilay
School of Natural Sciences, University of California, Merced

March 20
Jonathan Chaires
Department of Biochemistry and Molecular Biology, University of Louisville

March 27
Roshanak Rahimian
Thomas J. Long School of Pharmacy and Health Sciences, University of the Pacific
April 3
Yatin Shukla
*Ralphs Inc, Pharmacy Division, Southern California*

April 10
Lousie Berben
*Department of Chemistry, University of California, Davis*

April 17
Julie Leary
*Department of Molecular and Cellular Biology, University of California, Davis*
Robert Bergman

Department of Chemistry
University of California, Berkeley
Berkeley, CA 94720

January 17, 11:00 AM
Classroom Building 170

Bio: Ph.D.: University of Wisconsin 1966 (with Jerome A. Berson); postdoctoral: Columbia University 1966-67 (with Ronald Breslow). Faculty positions: Assistant professor to Professor, California Institute of Technology (1967-78); Professor, University of California, Berkeley (joint appointment with Lawrence Berkeley National Laboratory) 1978 – 2002; Gerald E.K. Branch Distinguished Professor, UC Berkeley, 2002 - present. Awards include: Sloan Fellowship, Dreyfus Teacher-Scholar Award, American Chemical Society Award in Organometallic Chemistry, election to National Academy of Sciences and American Academy of Arts and Sciences, DOE E.O. Lawrence Award in Chemistry, ACS Arthur C. Cope Award, Royal Society of Chemistry Sir Edward Frankland Prize Lectureship. Research summary: Bergman has long been interested in exploratory and mechanistic studies in organic and organotransition metal chemistry. He is probably best known for his discovery of the thermal cyclization of cis-1,5-hexadiyne-3-enes to 1,4-dehydrobenzene diradicals, later identified as a crucial DNA-cleaving reaction in several antibiotics, discovery of the first soluble organometallic complexes that undergo intermolecular insertion of transition metals into the carbon-hydrogen bonds of alkanes, and the synthesis and cycloaddition reactions of complexes with metal-heteroatom multiple bonds. Other recent interests: application of C-H bond activation in synthetic organic chemistry, nanovessel catalysis; methods for the conversion of biomass to fuels and commodity chemicals.
Selective Stoichiometric and Catalytic Reactions in Water-Soluble Host-Guest Supramolecular Systems

Robert Bergman

January 17, 11:00 AM, Classroom Building 170

In a collaborative study being carried out by the R. G. Bergman and K. N. Raymond research groups, several cationic organic and organometallic compounds have been shown to bind into the cavities of water-soluble chiral clusters or “nanovessels” (constructed earlier by the Raymond group) from metal salts and dicatecholate bridging ligands. Among these are reactive Ir(III) complexes that undergo Ir(III)/Ir(V) C-H oxidative addition reactions (discovered earlier by the R. G. Bergman group) when they are encapsulated in the nanovessel clusters in aqueous solution, leading to the first nanovessel intracavity C-H activation reactions. Substantial size- and shape selectivities have been observed in these reactions. Subsequently, aza-Cope and other pericyclic rearrangements have been found to proceed in the nanovessel cavities; small quantities of the nanovessels have been found to catalyze these reactions with accelerations above 800-fold. Nanovessels have also been found to perturb the acidities of organic bases, and the $pK_a$-shift properties of the nanovessels has provided a way of carrying out acid-catalyzed hydrolyses in strongly basic aqueous solution. For example, the nanovessels strongly catalyze the aqueous hydrolyses of orthoformates and acetals at high pH with even larger accelerations (>3000-fold) than those seen for the aza-Cope rearrangement. The velocities of the hydrolysis reactions mirror the classic rate behavior of enzymes, including adherence to Michaelis-Menten kinetics and exhibition of competitive inhibition by strongly-binding guests. Most recently, nanovessel-catalyzed Nazarov rearrangements have been discovered, proceeding with unprecedented accelerations of up to two million, and enantioselective transformations catalyzed by chiral nanovessels have also been found.
Bio: Dr. James Miranda graduated with a BS in Biochemistry from Cal Poly, San Luis Obispo. He received a master’s degree in Chemistry from Fresno State University and a Ph. D. in Chemistry from UC Santa Barbara. Since 2006, he became an Assistant Professor of Chemistry at Sacramento State University. His research interest primarily lies in developing new methodology for the organic synthesis of biologically active molecules. Usually these complex molecules are not only important in medicinal chemistry as therapeutic agents, but are also interesting from a structural point of view. He also seeks to understand the mechanism of these important new reactions.
Efforts to achieve the electroreductive cyclization (ERC) and the electrohydrocyclization (EHC) reactions using catalytic nickel(II) salen are described. Cyclic voltammetry was used to demonstrate the presence of a catalytic current. Results of the investigation as well as a discussion of reaction mechanism will be presented.\textsuperscript{1} Other various projects will also be discussed as well.

Bio: James P. Kercher graduated with a BS in Chemistry from Gettysburg College and earned a PhD in Physical Chemistry under the direction of Tomas Baer at the University of North Carolina – Chapel Hill. His doctoral studies focused on investigating the unimolecular dissociation dynamics of energy-selected ions in the gas phase using Threshold Photoelectron Photoion Coincidence (TPEPICO) spectroscopy. Dr. Kercher spent two years working with Joel Thornton at the University of Washington – Seattle as a Camille and Henry Dreyfus postdoctoral fellow in the Department of Atmospheric Sciences. During this time, he worked to develop a chemical ionization mass spectrometer (CIMS) for simultaneous, in situ monitoring of trace gases associated with halogen activation from reactive nitrogen oxides. Dr. Kercher is now an Assistant Professor in the Chemistry Department of Hiram College working on the development of a TPEPICO mass spectrometer for undergraduate research.
Chlorine atoms are highly reactive oxidants, affecting the lifetimes of mercury and volatile organic compounds such as methane, at levels 10 – 100x lower than the hydroxyl radical. However, their tropospheric sources and abundance remain highly uncertain. Recently, there has been much interest in nitryl chloride (ClNO₂), formed from the heterogeneous chemistry of dinitrogen pentoxide (N₂O₅), an important nighttime reservoir of nitrogen oxide radicals. ClNO₂ photolyzes within a few hours after sunrise to yield Cl atoms and NO₂. Using existing data sets and our current understanding of ClNO₂ formation, widespread ClNO₂ production is expected globally -- well beyond the polluted marine boundary layer. The consequence is that anthropogenic pollutants may yield a significant fraction of tropospheric chlorine atoms. As such, anthropogenic activities may play a more important role on halogen sources and the troposphere’s oxidizing capacity than currently recognized.
Bio: Dr. Leone was born in New York City on May 19, 1948. He received his B.A. in Chemistry at Northwestern University in 1970 and his Ph.D. in Chemistry at the University of California at Berkeley with Professor C. Bradley Moore in 1974. He was an assistant professor at the University of Southern California from 1974-76. He assumed a position with NIST and the University of Colorado in 1976 and became full professor in 1982. Dr. Leone was a Fellow and staff member of the National Institute of Standards and Technology as well as Adjunct Professor of Chemistry and Biochemistry and Lecturer of Physics at the University of Colorado. In 2002 he became Professor of Chemistry and Physics at Berkeley and Director of Chemical Sciences Division and Chemical Dynamics Beamline at Lawrence Berkeley National Laboratory. His numerous awards and honors include: Fellow of the Optical Society of America, Fellow of the American Physical Society, Fellow of the American Association for the Advancement of Science Alfred P. Sloan Fellow 1977-1981, Department of Commerce Silver Medal Award 1980, American Chemical Society Award in Pure Chemistry 1982, American Chemical Society Nobel Laureate Signature Award for Graduate Education in Chemistry, with D. J. Nesbitt and J. T. Hynes 1983, Coblentz Award for Spectroscopy 1984, Department of Commerce Gold Medal Award 1984, Arthur S. Flemming Award for Government Service 1986, Fellowship, Japanese Society for the Promotion of Science 1986, John Simon Guggenheim Fellow 1988, Herbert P. Broida Prize of the American Physical Society 1989, Visiting Miller Research Professor, University of California, Berkeley 1990, Visiting Professor, Chemistry Research Promotion Center, Taiwan 1992, Samuel Wesley Stratton Award, National Institute of Standards and Technology 1992, Bourke Medal of the Faraday Division of the Royal Society of Chemistry 1995, Member, National Academy of Sciences 1995, Fellow, American Academy of Arts and Sciences 2000, American Chemical Society Peter Debye Award 2005, JILA Fellow Adjoint 2006-2011, Morris Belkin Visiting Professorship, Weizmann Institute 2009, Polanyi Medal of the Gas Kinetics Division of the Royal Society of Chemistry, UK 2010, Miller Professorship, Miller Research Institute 2010, National Security Science, Engineering Faculty Fellowship, Department of Defense 2010, John R. Thomas Endowed Chair in Physical Chemistry 2010, and Irving Langmuir Prize in Chemical Physics 2011, Distinguished Schulich Lectureship Award, Technion – Israel Institute of Technology 2011, Chemical Society Review Lecture Award, Royal Society of Chemistry 2011.

His research interests include ultrafast laser investigations and soft x-ray probing of valence and core levels, attosecond physics and chemistry, state-resolved collision processes and kinetics investigations, nanoparticle fluorescence intermittency, aerosol chemistry and dynamics, probing with near field optical microscopy, and neutrals imaging.
Advanced Light Sources for Analytical Spectroscopy: From X-Rays to Attoseconds  
Steve Leone

February 28, 11:00 AM, Classroom Building 170

Real world applications of planetary atmospheres, combustion, energy production, and aerosols in our environment, as well as fundamental time resolved dynamics are discussed in the context of new sources of light useful for spectroscopy and chemical dynamics.
Bio: Dr. Manilay is an Assistant Professor and Founding Faculty member at UC Merced, the tenth and newest campus of the University of California, which opened in 2005. Dr. Manilay graduated from UC Berkeley and then received her Ph.D. in Immunology at Harvard University, where she studied mechanisms of immunological tolerance in natural killer cells after bone marrow transplantation. As a post-doctoral fellow, she investigated the effects of Notch signaling regulation during early T cell development. She was awarded a Young Investigator Award from the Transplantation Society in 1996, and is a member of the American Association of Immunologists and the International Society for Stem Cell Research. The current research projects in her laboratory are focused at the crossroads of immunology, developmental biology and stem cell biology. In 2008, Dr. Manilay was awarded a $1.5M research grant from the California Institute for Regenerative Medicine.
Hematopoietic stem cells (HSCs) are in direct contact with osteoblasts in the endosteum and trabecular regions of the long bones. Osteoblasts are considered “niche” cells that support HSC self-renewal and maintenance, and can also regulate the differentiation of committed lymphoid and myeloid lineages in the bone marrow. However, the cellular and molecular mechanisms by which osteoblasts mediate this regulation, and the effects of osteoblast cell maturation and differentiation on hematopoietic lineages are unclear. In this seminar, I will present data from ongoing studies in my laboratory that investigate the consequences of osteoblast overactivity and mineralization on hematopoietic differentiation in vitro and in vivo, and offer clinical implications and future directions of this work.
Bio: Jonathan B. Chaires is currently a Professor in the Department of Medicine, University of Louisville Health Sciences Center, and holds the James Graham Brown Chair of Cancer Biophysics. He is also a Senior Scientist in the James Graham Brown Cancer Center, and is a Professor in the Department of Biochemistry and Molecular Biology. Previously he was a Professor in the Department of Biochemistry at the University of Mississippi Medical Center (Jackson, MS), with a joint appointment as Professor of Chemistry in the Department of Chemistry at the University of Mississippi (Oxford, MS). A native of California, Dr. Chaires obtained a B. A. degree in biology from the University of California at Santa Cruz, where he completed his undergraduate research thesis with Dr. Harry Noller. He then obtained a Ph. D. in biophysics from the University of Connecticut under the mentorship of Dr. Gerson Kegeles. He received an NIH Postdoctoral Fellowship for research in the Department of Chemistry at Yale University in the laboratory of Dr. Donald Crothers. Among several honors, Dr. Chaires was a President’s Scholar at the University of California, and received an Alexander von Humboldt Fellowship for research at the Max Planck Institute for Biophysical Chemistry in Gottingen, Germany. Dr. Chaires was named the “Outstanding Chemist” by Mississippi Section of the American Chemical Society for the year 2000. Dr. Chaires’s current research interests are in the physical biochemistry of nucleic acids and their interactions, with particular emphasis on the integration of thermodynamics into the rational drug design process. Dr. Chaires has served on the Biophysics Panel of the National Science Foundation, and the Molecular and Cellular Biophysics Study Section at the National Institutes of Health. He has edited a volume of Advances in DNA Sequence Specific Agents (JAI Press), and special issues of the journals Biopolymers: Nucleic Acid Sciences, Current Medicinal Chemistry, and a recent issue of Biophysical Chemistry in honor of Julian Sturtevant. He edited a volume of Methods in Enzymology devoted to drug-nucleic acid interactions that appeared in 2001. He is currently a member of the Editorial Board of the Biophysical Chemistry, Current Medicinal Chemistry: Anti-Cancer Agents, and Biochimie. In addition to his academic activities, Dr. Chaires is a founder of Louisville Biosciences Inc.
G-Quadruplexes as Drug Targets

Jonathan B. Chaires

March 20, 11:00 AM, Classroom Building 170

G-quadruplexes are unique DNA structures that are highly conserved and which are localized to specific regions in the human genome. G-quadruplexes are thought to be of functional importance in a number of cellular processes, including telomere maintenance and the control of gene expression. This presentation will focus on the structure(s) and stability of G-quadruplexes formed by the human telomere repeat sequence. A novel drug discovery platform developed in my laboratory will be describe that integrates virtual screening and high-throughput experimental validations of “hits”, small molecules that selectively recognize and bind to specific features of G-quadruplexes.

Supported by grants CA35635 and GM077422 from the National Institutes of Health and by the James Graham Brown Foundation.
Bio: Dr. Rahimian earned her doctor of pharmacy from Tehran University of Medical Sciences in 1988, her master of science from the University of Ottawa in 1995, and her doctor of philosophy from the University of British Columbia in 1998. She then completed a three-year post-doctoral fellowship from the Canadian Institute of Health Research (CIHR) before joining Pacific as an assistant professor in 2001. Currently, she is a professor in the Department of Physiology & Pharmacology in the Thomas J. Long School of Pharmacy and Health Sciences. Her research focuses on estrogen-mediated signaling events associated with vascular tone and the changes that occur in diabetes (a project supported by NIH). Dr. Rahimian was the recipient of the 2011 Eberhardt Teacher Scholar award.
Gender Differences in Rat Endothelial Function under Hyperglycemic Conditions, and in Streptozotocin-induced Diabetes

Roshanak Rahimian

March 27, 11:00 AM, Classroom Building 170

Objectives: Several reports suggest that diabetes affect male and female vascular beds differently. However, little is known about the interaction between diabetes and gender in the vasculature. The objectives of our study were to investigate 1) if there is a gender based difference in the endothelium-dependent vasodilation (EDV) of rat aorta after acute exposure to high glucose (HG), and 2) whether there are gender differences in EDV in aortic and mesenteric arteries (MA) of diabetes, and 3) the diabetes and gender alter the relative contributions of endothelium derived relaxing factors including prostacyclin (PGI2), nitric oxide (NO), and endothelium-derived hyperpolarizing factor (EDHF) in modulating vascular reactivity in arteries of rats.

Methods: Relaxation responses to acetylcholine (ACh, $10^{-8}$ to $10^{-5}$ M) were obtained before and after 3 h treatment with Krebs’ solution containing high glucose (46 mM) in aortic rings pre-contracted with phenylephrine (PE, 2 μM) taken from male and female rats. Furthermore, the vascular reactivity of aortic and mesenteric arteries from male and female rats was analyzed at one (1-wk group) or eight (8-wk group) weeks after injection with either streptozotocin (STZ, an inducer of experimental diabetes) or vehicle (citrate buffer). Results: We demonstrated that 1) a 3 h incubation with elevated level of glucose impairs ACh responses to a greater extend in females than in male aortic rings, 2) ACh-induced EDV was significantly impaired in aortic and mesenteric artery from both male and female rats treated with STZ in 8-wk group (vs. that in the respective controls), but not in 1-wk group. Interestingly, the effects of 8 wk diabetes in blunting ACh-mediated vasorelaxation in females were significantly greater than in males. MA taken from diabetic female rats were also characterized by a greater 1) PE concentration-response curve, and 2) potentiation of the PE responses after L-NAME (a nitric oxide synthase inhibitor) compared with other experimental groups in 8-wk group. Finally, our data shows that in females, the role of NO was substantially enhanced, and that of EDHF was significantly reduced after STZ treatment. Conclusion: This study reveals the predisposition of female arteries to vascular injury under hyperglycemic and diabetic conditions. Furthermore, the shift away from EDHF as the major vasodilatory factor in peripheral vessels towards a greater reliance on NO may be directly related to the increased risk for cardiovascular complications in female patients with diabetes mellitus compared with their male counterparts.
**Yatin Shukla**

Ralphs Inc., Pharmacy Division  
Southern California  
*April 3, 11:00 AM*  
*Classroom Building 170*

**Bio:** Dr. Yatin Shukla received his Ph.D. in pharmaceutical sciences with the emphasis on Natural products chemistry from the University of Mississippi, Oxford, MS. His research interests include quality, efficacy and safety studies of botanical supplements and discovery of novel natural products of pharmacological potential. He currently works as a manager with Ralphs Inc.- Pharmacy division in southern California. He is also an associate editor for the journal BIOINFO Natural Products and serves as a consultant for development of Natural Products and botanical monographs for various organizations in the US.
Science Based Authentication of Botanicals: Application of Pharmaceutical Research Techniques for Better Botanical Supplements

Yatin Shukla

April 3, 11:00 AM, Classroom Building 170

Recent years have seen resurgence in the popularity and use of herbal supplements as aid in healthy lifestyle. With the growing demand there have also been a lot of debates about the efficacy, quality and safety of these products, which are available as over the counter supplements in the US market. While a significant compendium of information has been compiled to resolve questions related to the above issues, it is clear that more work needs to be done. Unfortunately, there is no “one-stop shop” method that can authenticate every plant sample or botanical supplement. For each sample, there needs to be a full understanding of the constituents being considered and what method(s) are specifically applicable to that material. However use of common approaches and research techniques should direct the efforts of pharmaceutical scientists working in this field. This presentation will explain applications of such research methodologies using two specific botanicals as examples, *Hoodia gordonii* and *Caralluma fimbriata*. These two succulent plants are used as weight-loss supplements in the United States. Our studies have generated fundamental information about these plants and should enable development of methods for quality control and safety assessment of botanical supplements.
**Bio:** Louise Berben was born in Sydney, Australia. She received a Bachelor of Science degree with 1st class honors from the University of New South Wales in 2000, and in 2005 was awarded a Ph.D. from the University of California Berkeley for research undertaken with Professor Jeffrey Long. In 2006 Louise began postdoctoral research with Professor Jonas Peters at the California Institute of Technology and in July 2007, moved with the Peters research group to the Massachusetts Institute of Technology. In July 2009, Louise joined the faculty at the University of California Davis where her research program focuses primarily on synthetic and physical inorganic chemistry.
Our choice of synthetic target is directed by a desire to investigate the activation of small molecules or interesting electronic states. By addition of redox active ligands to aluminum, we can now access aluminum complexes in five oxidation states including one oxidation state that has two unpaired electrons. Using these complexes we can perform classic transition metal reactions such as one- or two-electron oxidation chemistry, and C-H or CO$_2$ activation.

Electrochemical methods for the production of fuels can be linked to a photovoltaic device that can supply the required electricity as a product of solar radiation. Atom-level understanding of the reaction of acids with metal clusters under electrochemical conditions has been probed to control competing reactions such as hydrogen evolution and CO$_2$ reduction to formic acid. Metal-hydride catalyst intermediates can react with H$^+$ or with CO$_2$ and we endeavor to understand how to selectively direct competing reactions and favor CO$_2$ reduction.
Bio: Julie A. Leary is Professor of Biochemistry in the Department of Molecular and Cellular Biology at the University of California, Davis. Her research efforts focus on the use of mass spectrometry as an important tool in chemical biology. She is particularly interested in developing new analytical methods for analyzing carbohydrate:protein and protein-protein complexes as well as investigating enzyme kinetics and mechanisms of enzyme catalysis using mass spectrometry. After receiving her Ph.D. from the Massachusetts Institute of Technology under the mentorship of Prof. Klaus Biemann, Dr. Leary moved to U.C. Berkeley where she was Director of Analytical Facilities and Adjunct Professor of Chemistry. In 2000, she won the prestigious international award, The Biemann Medal, for her pioneering work on metal-coordinated oligosaccharides and their stereochemical differentiation using mass spectrometry. In 2010 she was elected as Fellow to the American Association for the Advancement of Science. She has been on the editorial board of several journals and has served on numerous NIH study section panels as Chair and reviewer. She is also a member of the Advisory Boards for the Complex Carbohydrate Research Center in Georgia and the Joint Bioenergy Energy Institute at U.C. Berkeley/DOE.
Probing Protein and Protein:Carbohydrate Complexes
Using Ion Mobility Mass Spectrometry

Julie Leary

April 17, 11:00 AM, Classroom Building 170

The integration of ion mobility with mass spectrometry is an emerging technology in structural biology, capable of providing protein’s collision cross-section and delineating the dissociation and/or unfolding processes of protein assemblies using collisional activation. Retention of the native structure in the gas phase is reflected in the strong correlation of experimental collision cross-section with theory and considered as a means in evaluating the ion mobility mass spectrometry (IM-MS) data. The assessment of IM-MS data, however, is currently impeded due to the lack of appropriate structural coordinates to use as input in the \textit{in silico} calculation of theory. To address this issue, this study involves the first use of rapid protein threading predictor (RAPTOR) software to generate three-dimensional structures of closely related monomeric chemokines (MCP-1, MCP-3, MCP-4 and eotaxin), and subsequently, utilize these models to estimate the theoretical values. Experimental collision cross-section of both the model proteins and chemokines correlate well with theory. While all conformations for the lowest charge state ($\zeta = 5+$) of chemokines fall within theory, MCP-4 shows distinct structural changes upon collisional activation. Of the four chemokines, MCP-4 with $z = 6+$ appears to have adopted an extended state, while eotaxin gradually unfolds, and the extended structures of MCP-1 and MCP-3 increase in abundance upon activation. Combining RAPTOR with IM-MS and collisional activation enables us to interrogate the conformations of homologous proteins with very similar tertiary structures. Inclusion of binding partners such as sulfated carbohydrates will be shown as well as their collisional cross sections.