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The Adolph C. and Mary Sprague Miller Institute for Basic Research in Science
University of California, Berkeley

Miller Institute News

Miller Fellow Focus: Matthew Francis

Deadline To Note

Monday, February 12: Visiting Miller Professorship nomination deadline (Spring competition). Term of appointment in 2001-2002.

More information for each program is available on the Miller Institute website: http://socrates.berkeley.edu/~4mibrs

All materials are due in the Miller Institute office by 4:00 pm of deadline.

Matt Francis' research involves the development of new methods in synthetic chemistry and the application of diversity-based strategies to problems that lie at the interfaces between chemistry, biology, and material science.

One of Matt's interests is the development of new catalytic reactions involving transition metal ions. A key component of many catalytic systems is an organic ligand that binds to a metal center and controls its reactive properties. By carefully designing these ligands, the reactivity of the metal can be turned to produce a desired reaction product, and this approach has afforded many selective and efficient reactions for organic synthesis. However, the factors controlling this reactivity are interrelated and poorly understood, and as a result the discovery of new catalytic reactions frequently involves a time consuming and empirical optimization process.

In the last decade, combinatorial chemistry has emerged as a powerful method for the exploration of multivariate chemical problems. The key to this approach is the generation of a large collection, or library, of diverse molecules using efficient synthetic methods. The library of molecules is then subjected to a carefully designed screening process that can identify the members that possess desired properties. In the context of small molecule librarties, this process has been used to accelerate the identification of new pharmaceutical compounds and to explore the structural features associated with receptor-ligand interactions. It was envisaged that combinatorial approaches could be similarly useful as a tool for rapid catalyst discovery and optimization.

In order to accomplish this, Matt developed new synthetic techniques that allowed a library of 5,760 metal-ligand complexes to be synthesized in an efficient manner. The complexes were prepared attached to small polystyrene beads (~100 um in size) and varied in terms of the metal ion identity, ligand structure, and counter ions--variables known to have a strong influence on catalytic activity. Furthermore, an efficient screening process was developed in order to ascertain which of the complex-bearing beads produced the desired products for a given reaction. The identification of the associated structures led to the discovery of new catalytic systems for the epoxidation of unfunctionalized olefins with hydrogen peroxide, a reaction potentially useful for the synthesis of pharmaceutical compounds. The new catalytic systems possessed little if any resemblance to

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previously known epoxidation systems, thus validating the power of the method for the discovery of new reactivity.

One of Matt's research areas at UC Berkeley employs a diversity-based approach for the development of new carrier molecules for targeted drug delivery. The beneficial effects of most pharmaceutical compounds arise from their interactions with a limited number of cell types; however, most drug molecules possess the ability to readily traverse cell membranes, and thus can gain access to most of the cells in the patient's body. The exposure of the drugs to inappropriate cell types frequently leads to side effects, toxicity, and premature degradation of the pharmaceutical compounds.

"In the last decade, combinatorial chemistry has emerged as a powerful method for the exploration of multivariate chemical problems"

A potential improvement to this situation could be achieved by [illegible] molecules to polymeric carriers that possess a high molecular weight. Once attached to the carrier, the drug molecules can no longer freely diffuse into inappropriate cell types, and thus are much less toxic in circulation. By incorporating small molecule targeting moieties on the polymer, the carriers can then be directed to specific tissue types, such as solid tumors. Once the carriers have reached these targets, they can enter cells via endocytosis, and the release of the free drug molecules can be triggered using linkers that degrade in the endosomal and lysosomal vesicles. Thus, the drug molecules are delivered only to the targeted cells.

The early stages of this research have focused on the development of well-defined polymers that possess the biocompatibility necessary for these applications. From these studies, non-toxic water-soluble polymers have been identified and converted into carriers for the highly toxic anticancer drug doxorubicin. Furthermore, a modular synthetic approach has been developed that allows these polymers to be prepared with a variety of molecular weights and architectures. Current efforts are underway to explore the effects of these parameters on the pharmacokinetics and biodistribution of these materials, as well as the incorporation of tissue-specific targeting mechanisms.

In Matt's free time, he and his wife, Jennifer enjoy backpacking and other outdoor activities, watching movies, and drinking gin martinis with friends. This fall he has been searching for academic positions, and this spring he will be learning Kung Fu with Miller Fellow Tom Juenger.

News Flash! Miller Fellow Adam Summers will be writing a monthly column for Natural History magazine. The column will focus on biomechanics. After having his research featured in two columns during the past year the editor offered Adam the opportunity to be the regular columnist, providing 10 columns per year to the magazine. Watch for his first contribution to appear in the May 2001 issue.

Recent Miller Institute Awards

Visiting Miller Professorships

The Executive Committee and Advisory Board of the Miller Institute have granted awards to the following Visiting Miller Professors. Terms range from fourteen days to one semester during the 2001-2002 academic year. Additional awards for next year will be made in March. The deadline for nominations is February 12.

Astronomy	Prof. Donald Ekers, Australia National Telescope Facility Prof. Jonathan Lunine, University of Arizona
Chemistry	Prof. Mehran Kardar, MIT (also in Physics) Prof. Mats Larsson, Stockholm University
Earth & Planetary Science	Prof. Philippe Lognonne, University Paris VII and Institut de Physique du Globe de Paris
Mathematics	Prof. Barry McCoy, Institute for Theoretical Physics, New York University
Physics	Prof. Charles Thorn, University of Florida Prof. Dale Van Harlingen, University of Illinois
Statistics/EECS	Prof. Peter Bartlett, Australian National University

Miller Professorships

The Executive Committee and Advisory Board of the Miller Institute have granted awards to the following Miller Professors. Terms are either one or two semesters during the 2001-2002 academic year.

Chemistry	Professor Paul Alivisatos Professor Martin Head-Gordon	***Mathematics***	Professor Craig Evans
Computer Science	Professor Jitendra Malik	***Materials Science &Engineering***	Professor Eugene Haller
Earth & Planetary Science	Professor Walter Alvarez	***Molecular & Cell Biology***	Professor Terry Machen
Economics	Professor Christina Shannon	***Physics***	Professor Kam-Biu Luk Professor Paul Richards
Integrative Biology	Professor Mary Power		

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Selected Recent Publications

Former Miller Fellow Ryosuke Motani wrote an article, "Rulers of the Jurassic Seas" which was featured on the cover of Scientific American, December 2000.

Miller Fellow Deborah Croteau completed a paper during her term (1998-2000) with the Miller Institute: "Mitochondrial DNA Repair Pathways", with R. H Stierum and V. A Bohr, Mutation Research, 434(3): 137-48, 1999.

Visiting Miller Professor Richard Gordon published a paper during his term (Spring 2000) with the Miller Institute: "The Antarctic Connection", Nature, 404, 139-140, 2000.

Miller Professor Costas Grigoropoulos wrote a paper during his term (Fall 1999) with the Miller Institute: "Excimer Laser-Induced Temperature Field in Melting and Resolidifcation of Silicon Thin Films", with M. Hatano, S. Moon and K. Suzuki, Journal of Applied Physics, Vol. 87, pp. 36-43.

Miller Professor Daniel Neumark had a prolific term (Academic Year 1999-2000) with the Miller Institute publishing twelve papers: "Electronic Structure of Indium Phosphide Clusters: Anion Photoelectron Spectroscopy of $In_xPË‰_x$ and $In_{x+1}P^-_x$ (X=1-13) Clusters", with K. R. Asmis and T. R. Taylor, Chem. Phys. Lett. 308, 347, 1999, "Photodissociation of Gas Phase $IË‰_3$ using femtosecond Photelectron spectroscopy", with M. T. Zanni, J. Greenblatt and A. V. Davis, J. Chem. Phys. 111, 2991, 1999, "Photodissociation dynamics of singlet and triplet states of the NCN radical", with R. T. Bise and H. S. Choi, J. Chem. Phys. 111, 4923, 1999, "Anion Photoelectron Spectroscopy of $B_3NË‰$", with K. R. Asmis and T. R. Taylor, J. Chem. Phys. 111, 10491, 1999, "Anion Photoelectron Spectroscopy of $B_3NË‰$", with K. R. Asmis and T. R. Taylor, J. Chem. Phys. 111, 8838, 1999, "Femtosecond Photoelectron Spectroscopy of $I_2Ë‰ (Ar)_n$ Clusters (n=6, 9, 12, 16, 20)", with B. J. Greenblatt and M. T. Zanni, J. Chem. Phys. 111, 10566, 1999, "Anion Photoelectron Spectroscopy of Small Boron Nitride Clusters: Adiabitic Detachment Energies and Vibrational Frequencies of Low-lying Electronic States in B_2N and B_3N", with K. R. Asmis and T. R. Taylor, Eur. Phys. J. D. 9, 257, 1999, "Vibrationally Resolved Anion Photoelectron Spectra of Low Lying Electronic States of $GaP_2Ë‰$, $Ga_2PË‰$, and $Ga_2P_3^-$", with K. R. Asmis , H. Gomez and T. R. Taylor, Eur. Phys. J. D. 9, 317, 1999, "Femtosecond Photoelectron Spectroscopy of $I_2Ë‰ (CO_2)_n$ Clusters (n= 4, 6, 9, 12, 14, 16)", with B. J. Greenblatt and M. T. Zanni, J. Chem. Phys. 112, 601, 2000, "Photodissociation of Linear Carbon Clusters C_n (n= 4-6)", with R. T. Bise , H. S. Choi, A. A. Hoops and D. H. Mordaunt, J. Phys. Chem. A 104, 2025, 2000, "Dynamics of the Charge-Transfer-to-Solvent States in $IË‰(Xe)_n$ Clusters", with M. T. Zanni, C. Frischkorn, and A. V. Davis, J. Phys. Chem. A 104, 2527, 2000, and "Femtosecond Stimulated Emission Pumping: Characterization of the $IË‰_2$ Ground State", with M. T. Zanni, C. Frischkorn, and M. Elhanine, J. Chem. Phys. 112, 8847, 2000.

Awards & Honors

Manuel Cardona, Visiting Miller Professor (Spring '00), of the Max Planck Institute for Solid State Research in Stuttgart won the Mott Medal and Prize in recognition of his broad and important contributions to the detailed understanding of the optical and electronic properties of solids.

Ewine van Dishoeck of the Leiden Observatory in The Netherlands and Visiting Miller Professor (Fall '00), has been awarded the Spinoza Prize, the most prestigious award in Dutch academia.

Former Miller Fellows **Dana Longcope** ('93-'95) of Montana State University and **Jonas Peters** ('98-'99) of The California Insitute of Technology were named by President Clinton as recipients of the fifth annual Presidential Early Career Awards for Scientists and Engineers (PECASE). This is the highest honor bestowed by the United States government on young professionals at the outset of their independent research careers. These awards, established by President Clinton in February 1996, embody the high priority the Administration places on producing outstanding scientists and engineers ready to contribute to all sectors of the economy. Eight Federal departments and agencies join together annually to nominate the most meritorious young scientists and engineers who will broadly advance the science and technology that will be of the greatest benefit to fulfilling the agencies' missions.

Chang-Lin Tien of the Department of Mechanical Engineering at the University of California, Berkeley, was named the Distinguished Alumnus for 2000 by Tau Beta Pi, the engineering honor society. Professor Tien was recognized for his leadership as an educator, committed to expanding opportunities for all, and for serving as a role model and inspiration to young students around the world. Dr. Tien was a Miller Professor in 1967-68.

Obituaries

Former Miller Professor ('71 - '72) **Lucien LeCam** of the Department of Statistics, passed away April 2000 at the Doctor's Medical Center in San Pablo. He was 75.

Former Executive Director (1984-87) and Miller Professor ('68-'69) **Robert Ornduff** of the Department of Integrative Biology, passed away on September 22, 2000 at Alta Bates Medical Center in Berkeley. He was 68.

Former Miller Professor ('60-'66 and '67-'68) **John Reynolds** of the Department of Physics, passed away on November 4, 2000 at his home in Berkeley. He was 77.

Former Miller Professor ('65-'66) **Sherwood Washburn** of the Department of Anthropology passed away April 2000 at Alta Bates Medical Center in Berkeley. He was 88.

Former Miller Professor ('60-'61) **Edmund Laitone** of the Department of Mechanical Engineering, passed away on December 18, 2000 at his home in El Cerrito. He was 85.