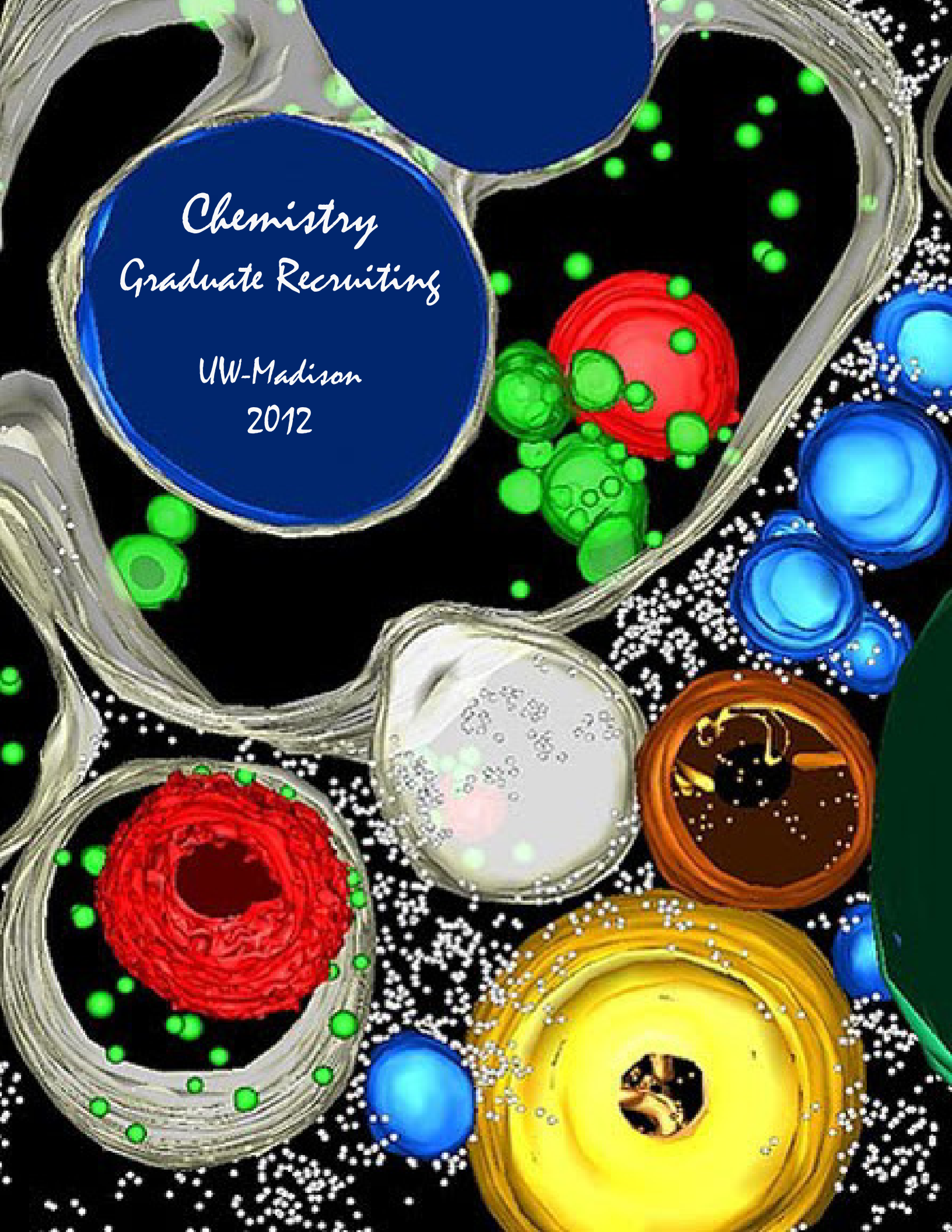
Chemistry
Graduate Recruiting
UW-Madison
2012

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February and March, 2012

Welcome to Prospective Chemistry Grad Students!

You are a large and talented group which has come from all over the U.S. to visit one of the strongest Chemistry Departments in the country. The UW-Madison Chemistry Department is a *great* place to teach and to learn, to carry out exciting research, and to grow intellectually. It is also a warm and welcoming place. Our strength relies not only on our faculty and staff, but also on the outstanding grad students who continually drive the research forward with their talent, motivation, creativity, and hard work. Cutting-edge science is developing all around you in this Department, and we would be very pleased to have you join us in these efforts.

Your goal is to find the graduate school that best suits your needs and career goals. Please use this visit to learn as much as possible about Madison (a great town in which to live), the research in the Department, and what it is like to be a graduate student here. The information sessions and informal social events with both faculty and students are designed to help you explore who we are and how we do science. *Please go out of your way to talk in depth with faculty and grad students about their research.* This is not a burden on anyone—we all *love* to talk about our research and we welcome your questions! And keep an open mind. You may find yourself *absolutely fascinated* by a problem you know nothing about today. *Follow your instincts.*

We have six "paths" leading to the Ph.D. in Chemistry: Analytical Sciences, Chemical Biology (new this year), Inorganic Chemistry, Materials Chemistry, Organic Chemistry, and Physical Chemistry. *Importantly, you can follow any path while working towards the Ph.D. with any research advisor.* The accompanying information sheets give a broad description of each research area, a timeline of events for the first three years, and a list of faculty officially affiliated with each path. The paths differ somewhat in the details, but all six are designed to help you develop into an excellent research scientist with outstanding communication skills.

Let me close by saying that I consider it a privilege to be allowed to make a living by teaching and doing research; few people are so lucky. You stand at the threshold of a great intellectual adventure. I can guarantee trials and tribulations, but if you persist and work hard and *think*, you can experience the thrill that comes from solving a problem for the first time or making a discovery that is uniquely yours. I wish you every success in the exciting years to come.

With best regards,

James C. Weisshaar
Professor and Chair

Welcome to the UW-Madison Department of Chemistry!

Our department is consistently ranked among the top ten chemistry departments in the United States. On the following pages, you will get a glimpse of some of the state-of-the-art research programs here at Wisconsin. You will find that our department is very diverse, with strong programs in all areas of chemistry.

We hope you have an enjoyable and productive time during your visit to Madison! If you have any questions about the graduate program, please feel free to call or contact any of the members of the graduate admissions committee indicated below.

Sincerely,

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FACULTY LISTING BY TOPIC AREA

Atmospheric/Environmental Chemistry: **Keutsch**

Bioanalytical: **Coon**, **Li, Schwartz, Smith**, Hamers

Bioinorganic and Physical Inorganic: **Berry, Brunold, Burstyn**

Biophysical/Biomolecular Structure and Dynamics: **Cavagnero,** Cui, Goldsmith, **Record, Weisshaar**, Yethiraj, Zanni

Bioorganic/Chemical Biology: **Blackwell, Cavagnero, Gellman, Kiessling, Mecozzi, Raines, Strieter**

Chemical Education: Andrew, Landis, McMahon

Laser Spectroscopy and Dynamics: **Crim, Goldsmith,** Keutsch**, McMahon,** Woods, **Wright, Zanni**

Nanomaterials, Polymers, Interfacial Chemistry and Materials for Energy: Andrew, Choi, **Ediger,** Fredrickson**,** Goldsmith**,** Gopalan, **Hamers, Jin**, Lynn, **Mahanthappa,** McMahon, **Nathanson**, Schmidt, Yethiraj, **Yu**

Natural Products: **Burke, Hsung**

Physical-Organic: Andrew, **Gellman, Mecozzi, McMahon, Strieter**

Synthesis: **Andrew, Blackwell, Burke,** Choi, **Gellman, Hsung, Kiessling, Mecozzi, Raines, Yoon, Strieter**

Synthesis/Catalysis: Berry, Choi, **Fredrickson**, Goldsmith, Jin, **Landis,** Mahanthappa, **Stahl, Schomaker**

Theory: **Cui,** Fredrickson**,** Landis, **Schmidt**, **Sibert, Skinner, Yethiraj**

*Boldface indicates primary research focus

FACULTY LISTING BY PRIMARY DIVISIONAL INTERESTS(S)

Analytical: Choi, Coon, Hamers, Jin, Keutsch, Li, Schwartz, Smith, Weisshaar, Wright

ChemBio: Blackwell, Brunold, Burstyn, Cavagnero, Coon, Cui, Gellman, Hamers Jin, Kiessling, Li, Lynn, Mecozzi, Raines, Record, Schwartz, Skinner Smith, Strieter, Weisshaar, Yethiraj, Zanni

Inorganic: Berry, Brunold, Burstyn, Choi, Fredrickson, Jin, Landis, Stahl, Yoon

Materials: Andrew, Choi, Ediger, Goldsmith, Gopalan, Hamers, Jin, Kiessling, Mahanthappa, McMahon, Smith, Wright, Yethiraj, Zanni

Organic: Andrew, Berry, Blackwell, Burke, Cavagnero, Gellman, Gopalan, Hsung, Kiessling, Landis, Lynn, Mahanthappa, McMahon, Mecozzi, Nelsen, Raines, Record, Schomaker, Stahl, Strieter, Yoon

Physical: Andrew, Cavagnero, Choi, Crim, Cui, Ediger, Gellman, Gilbert, Goldsmith, Hamers, Jin, Keutsch, Mahanthappa, McMahon, Nathanson, Record, Schmidt, Sibert, Skinner, Weisshaar, Wright, Yethiraj, Yu, Zanni

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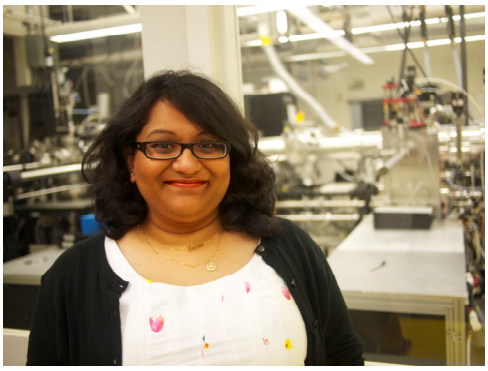
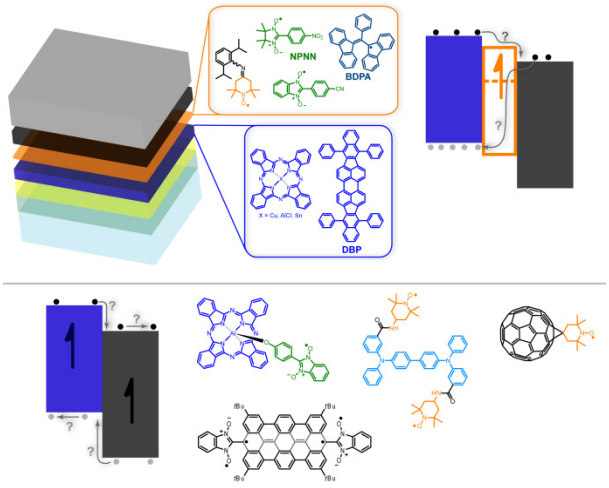


Research

Our research program focuses equally on synthesizing optically- and electronically-interesting materials, and fabricating optoelectronic or spintronic devices using these materials. We are interested in understanding the role of electron spin on organic light-emitting diodes (OLEDs) and photovoltaic cells (OPVs). Additionally, we aim to demonstrate the utility of organic radical-containing materials in magnetic spin valves and magneto-optic devices.

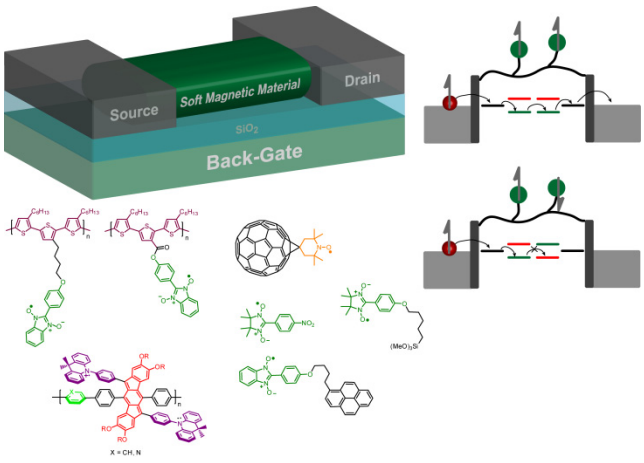
Understanding the Effect of Electron Spin in Optoelectronic Devices

The electronic and morphological factors that affect charge separation events in organic optoelectronic devices have been (and continue to be) widely studied. However, using spin dynamics to control charge transport within individual molecules and thin films has received comparatively less attention. We aim to fabricate simple OLEDs and OPVs containing a redox-active organic radical interlayer and characterize the resulting effects on device metrics. This project involves synthesizing analogs of prevalent small-molecule and polymeric donor materials containing stable radical moieties and studying the effects of electron spin within specific layers of a nanostructured OLED and OPV.



Organic Nanostructured Magnetic and Magneto-Optic Devices

We are interested in studying spin-dependent charge transport in organic thin films. This project involves both the design of interesting, magnetically-active organic materials and the fabrication of appropriate device architectures that take advantage of our unique material systems. Examples of materials include: conjugated polymers containing either pendant or directly-conjugated organic radicals; and small-molecule organic radicals that can either be thermally-evaporated or possess anchoring groups, which will allow adsorption onto SiO_2, metal oxides or carbon nanotubes. We aim to fabricate transistor-like spin valves using these materials to characterize their magnetic properties.



Selected Publications

- 6,6-Dicyanofulvenes as Efficient Fullerene Substitutes in Bulk Heterojunction Solar Cells. Andrew, T. L.; Bulović, V. *ACS Nano*, accepted for publication.
- Improving the Performance of P3HT-Fullerene Bulk Heterojunction Solar Cells with Side-Chain Functionalized Polythiophene Additives: A New Paradigm for Polymer Design. Andrew, T. L.; Lobez, J. M.; Swager, T. M.; Bulović, V. *ACS Nano*, in press.
- Cascaded Energy Transfer for Efficient Broad-Band Pumping of High-Quality Micro-Lasers. Rotschild, C.; Tomes, M.; Mendoza, H.; Andrew, T. L.; Swager, T. M.; Carmon, T.; Baldo, M. A. *Adv. Mater.* **2011**, *23*, 3057-3060.
- Selective Detection of High Explosives Via Photolytic Cleavage of Nitroesters and Nitramines. Andrew, T. L.; Swager, T. M. *J. Org. Chem.* **2011**, *76*, 2976-2993. [editor's selection for feature article]
- Thermally-polymerized rylene nanoparticles. Andrew, T. L.; Swager, T. M. *Macromolecules*, **2011**, *44*, 2276-2281.
- Structure Property Relationships for Exciton Transfer in Conjugated Polymers. Andrew, T. L.; Swager, T. M. *J. Polym. Sci. B*, **2011**, *49*, 476-498.
- The Synthesis of Azaperylene-9,10-dicarboximides. Andrew, T. L.; VanVeller, B.; Swager, T. M. *Synlett*, **2010**, 3045-3048.
- Synthesis, Reactivity, and Electronic Properties of 6,6-Dicyanofulvenes. Andrew, T. L.; Cox, J. R.; Swager, T. M. *Org. Lett.* **2010**, *12*, 5302-5305.
- Confining Light to Deep Subwavelength Dimensions to Enable Optical Nanopatterning. Andrew, T. L.; Tsai, H.-Y.; Menon, R. *Science*, **2009**, *324*, 917-921.
- Anionic Oxidative Polymerization: The Synthesis of Poly(phenylenedicyanovinylene) (PPCN2V). Moslin, R. M.; Andrew, T. L.; Kooi, S. E.; Swager, T. M. *J. Am. Chem. Soc.* **2009**, *131*, 20-21.
- Reduced Photobleaching of Conjugated Polymer Films Through Small Molecule Additives. Andrew, T. L. and Swager, T. M. *Macromolecules,* **2008**, *41*, 8306-8308.
- A Fluorescence Turn-On Mechanism to Detect the High Explosives RDX and PETN. Andrew, T. L. and Swager, T. M. *J. Am. Chem. Soc.* **2007**, *129*, 7254-7255.

Awards

- L'Oréal USA Fellowship for Women in Science, 2011
- Wyeth Scholar, 2009
- Chesonis Foundation Solar Revolution Project Fellow, 2008
- Corning Foundation Graduate Fellow, 2007
- Merck Index Award, 2005
- Mary Gates Research Scholar, 2003
- Zahlia Jencks Rowe Scholar in Chemistry, 2003
- Hyp Dauben Award for Excellence in Organic Chemistry, 2003

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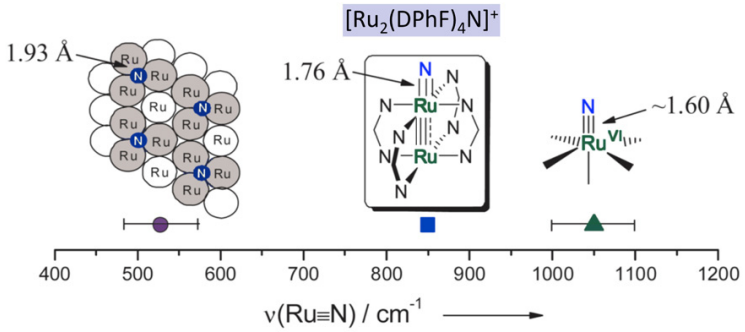
Research

Coordination chemistry - synthesis, structures, spectroscopy, and electronic structure of new types of transition metal complexes; isolation and characterization of highly-reactive high-oxidation state intermediate species; redox catalysis, especially of reactions involving multiple electron transfers; metal-ligand and metal-metal multiple bonding; heterobimetallic complexes.

Some of the most important - yet difficult to control - catalytic processes are those that add heteroatoms (e.g., N, O) to unfunctionalized organic molecules. These reactions often involve the intermediacy of species having metal-oxygen or metal-nitrogen multiple bonds, which are often unobservable because they are highly reactive. The Berry group's interest is in synthesizing and characterizing such elusive intermediate species in order to elucidate their electronic structure, and thereby the electronic effects that govern their reactivity.

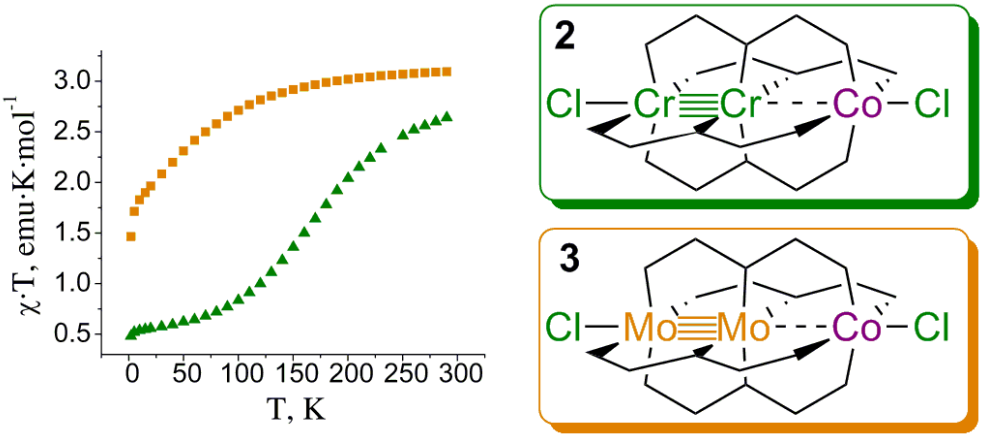
For example, compounds with a linear M–M≡E structure are key intermediates in rhodium-catalyzed reactions that directly functionalize unreactive C–H bonds; prior to our work no M–M≡E intermediates of this type have ever been isolated. We have succeeded in the low-temperature synthesis and characterization of an unprecedented new compound that has delocalized sigma and pi bonding throughout a linear Ru–Ru≡N chain. This remarkable electron delocalization causes the Ru≡N bond to be weaker and longer than in mononuclear Ru-nitrido compounds. In fact, the bond strength of the Ru–Ru≡N species, as measured by the Ru≡N stretching frequency, appears to be intermediate between mononuclear Ru(VI)-nitrido species and nitrogen atoms bound to a bulk Ru metal surface.



Other projects in our group involve the synthesis of heterometallic complexes of geometrically constrained porphyrin ligands or tripodal ligands. These complexes are designed to facilitate multi-electron transfer reactions relevant to energy conversion. Our goals are to develop new catalytic processes for important multi-electron reactions such as CO_2 reduction and various oxidations.

Heterometallic Electronic Effects

Many metalloenzymes use a heterometallic active site ($M_A \cdots M_B$) to catalyze reactions that are essential for life. We are interested in finding out how the presence of M_A affects the electronic structure of M_B, and, thereby, its reactivity. When both M_A and M_B are first row transition metals, the effects that we want to probe are complicated by spin-spin interactions. We have therefore initiated a study of linear M_A–$M_A \cdots M_B$ compounds that have a strong M_A–M_A metal-metal bond. This renders the M_A–M_A group diamagnetic, and it is therefore possible to probe the electronic structure of M_B by traditional spectroscopic and magnetic measurements. For example, we have found in recent work that a neighboring Cr≡Cr bonded group has a significant impact on the redox potential of an Fe(II) ion, lowering the potential for oxidation to Fe(III). Also, we have found that the spin state of a Co(II) ion strongly depends on the nature of its heterometallic neighbor. As shown below, a Cr≡Cr···Co complex is low-spin at temperatures below ~ 100 K, but the corresponding Mo≡Mo···Co species is high-spin.



Selected Publications

- Manni, G. L.; Dzubak, A.; Mulla, A.; Brogden, D. W.; Berry, J. F.; Gagliardi, L., *Chem. Eur. J.* **2012**, *18*, 1737-1749.
- Timmer, G. H.; Berry, J. F. *Comptes Rendus Chimie* **2012**, *15*, 192-201.
- Kornecki, K. P., Berry, J. F. *Eur. J. Inorg. Chem.* **2012**, 562-568.
- Berry, J. F. *Dalton Trans.* **2012**, *41*, 700-713.
- Nippe, M.; Turov, Y.; Berry, J. F. *Inorg. Chem.* **2011**, *50*, 10592-10599.
- Long, A. K. M.; Timmer, G. H.; Pap, J. S.; Snyder, J. L.; Yu, R. P.; Berry, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 13138-13150.
- Nippe, M.; Bill, E.; Berry, J. F. *Inorg. Chem.* **2011**, *50*, 7650-7661.
- Kornecki, K. P.; Berry, J. F. *Chem. Eur. J.* **2011**, *17*, 5827-5832.
- Nippe, M.; Goodman, S. M.; Fry, C. G.; Berry, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 2856-2859.
- Nippe, M.; Wang, J.; Bill, E.; Hope, H.; Dalal, N. S.; Berry, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 14261-14272.
- Piccoli, P. M. B.; Berry, J. F. *J. Cluster Sci.* **2010**, *21*, 351-359.
- Long, A. K. M.; Yu, R. P.; Timmer, G. H.; Berry, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 12228-12230.
- Berry, J. F. *Chem. Eur. J.* **2010**, *16*, 2719-2724.

Selected Awards

- NSF CAREER Award, 2008-2013
- Ernst Haage Preis des Max-Planck-Institüt für Bioanorganische Chemie (First Recipient), 2006
- Alexander von Humboldt Forschungsstipendium, MPI-Mülheim, 2004-2006
- Association of Former Students Graduate Assistant Award for Research, Texas A&M, 2004
- Celanese, Ltd. Outstanding Graduate Student Award, Texas A&M, 2004

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Research

Organic chemistry is in the unique position to provide molecular level insights into biological processes. Renewed appreciation for the power of small molecules as tools to explore living systems has fueled an explosion of interest in chemical biology. Within this broad context, our research program is focused on the development of new synthetic methodology to expedite the discovery of biologically active molecules. We are strategically combining elements of microwave-assisted organic chemistry, solid-phase synthesis, and combinatorial chemistry to provide access to new classes of chemical probes. In turn, we are applying these small molecule tools to bacterial communication and host/microbe interactions, previously unexamined areas of chemical biology. We seek to understand how both plants and animals sense and respond to invasion by pathogenic microbes. The ability of bacteria to communicate with each other and function as a group is a critical step in the development of infectious disease. The reliance of bacteria on a language of small molecules places organic chemists in a unique position to discover the fundamental principles underlying this communication network and design tools to modulate it at the molecular level.

All aspects of our multidisciplinary research program are synergistic with one another. The chemical component drives biological inquiry, and the biological outcomes dictate new avenues for chemical methodology development. Current research projects in our laboratory and their interconnections are outlined below:

-We are making contributions in the area of **microwave-assisted organic chemistry**. Microwave irradiation is seeing increasing use as an alternate heating source for chemical reactions, due to dramatic reductions in reaction times and increases in product yields and purity. We predict that the use of microwave irradiation to expedite solid-phase organic reactions will greatly facilitate the application of combinatorial chemistry to biological problems. We are currently examining the scope and limitations of microwave-assisted solid-phase organic reactions, with particular attention focused on diversity-generating reactions that do not proceed at an appreciable rate under standard thermal conditions, e.g., selected multicomponent, cyclization, and condensation reactions. We have recently used this methodology to synthesize new classes of peptidomimetics (i.e., **peptoids**).

-Our methodological work is enabling us to develop a powerful and accessible solid-phase synthesis platform for the rapid generation of focused, small molecule libraries. We have engineered a synthesis platform that allows modest sized (100-500 member) libraries to be prepared routinely in one day. The platform consists of functionalized planar polymeric supports and library synthesis is performed in a spatially addressable manner to generate **small molecule macroarrays**. The application of microwave irradiation (see above) to selected reactions during macroarray construction permits diverse chemical libraries to be generated at unprecedented rates. The use of our synthesis platform is accelerating the pace at which new biologically active compounds are discovered (see below).

-With the development of our synthesis platform well underway, we are designing, preparing, and screening focused collections of small molecules to ask important questions in bacteriology. Specifically, we seek to uncover compounds that modulate key protein-protein interactions involved in bacterial communication pathways. At present, we are trying to intercept the binding of bacterial LuxR-type proteins to their cognate autoinducer ligands and subsequent homodimerization, which are pivotal events in Gram-negative **bacterial quorum sensing circuits**. Compounds uncovered in these screens will be the first to reveal molecular level features essential for autoinducer-regulated quorum sensing. Quorum sensing regulated behaviors in bacteria account for greater than 50% of all crop disease and 80% of

human infections, therefore, active compounds emerging from our research could serve as scaffolds for agricultural agents and therapeutics with unprecedented modes of action. Our unique ability to rapidly manipulate the chemical structures of these molecules using microwave-assisted reactions will streamline their development as powerful tools in the laboratory, in the clinic, and in the field. Using this approach, we recently identified a set of quorum sensing antagonists that are among the most potent reported to date. On-going work is focused on further developing these compounds as probes, designing the first quorum sensing "super agonists", and applying our integrated research approach to examine the alternate quorum sensing pathways used by Gram-positive bacterial pathogens.

Selected Recent Publications

- J. A. Crapster, J. R. Stringer, I. A. Guzei, and **H. E. Blackwell**. "Design and Conformational Analysis of Peptoids Containing *N*-Hydroxy Amides Reveals a Unique Sheet-Like Secondary Structure." *Biopolymers* **2011**, in press.
- M. E. Mattmann, N. J. Heth. P. M. Shipway, and H. E. Blackwell. "Potent and Selective Synthetic Modulators of a Quorum Sensing Repressor in Pseudomonas aeruginosa Identified from Second-Generation Libraries of *N*-Acylated L-Homoserine Lactones." *ChemBioChem* **2011**, in press.
- J. R. Stringer, M. D. Bowman, B. Weisblum, and **H. E. Blackwell.** "An Improved Small-Molecule Macroarray Platform for the Rapid Synthesis and Discovery of Antibacterial Chalcones." *ACS Comb. Sci.* **2011**, in press.
- G. Palmer, E. Streng, K. A. Jewell, and **H. E. Blackwell. "**Quorum Sensing in Bacterial Species that Use Degenerate Autoinducers Can Be Tuned Using Structurally Identical Non-Native Ligands." *ChemBioChem*, **2011**, 12, 138–147.
- S. Breitbach, A. H. Broderick, C. M. Jewell, S. Gunasekaran, Q. Lin, D. M. Lynn, and **H. E. Blackwell**. "Surface-Mediated Release of a Synthetic Small-Molecule Modulator of Bacterial Quorum Sensing: Gradual Release Enhances Activity." *Chem. Commun.* **2011**, *47*, 370-372.
- R. Borlee, G. D. Geske, **H. E. Blackwell**, and J. Handelsman. "Identification of Synthetic Inducers and Inhibitors of the Quorum Sensing Regulator LasR in *Pseudomonas aeruginosa* by High-Throughput Screening." *Appl. Environ. Microbiol.* **2010**, *76*, 8255-8258.
- J. R. Stringer, J. A. Crapster, I. A. Guzei, and **H. E. Blackwell.** "Construction of Peptoids with All Trans-Amide Backbones and Peptoid Reverse Turns via the Tactical Incorporation of N-Aryl Side Chains Capable of Hydrogen Bonding." *J. Org. Chem.* **2010**, *75*, 6068–6078.
- R. Frei and **H. E. Blackwell.** "Small Molecule Macroarray Construction *via* Palladium-Mediated Carbon-Carbon Bond Forming Reactions: Highly Efficient Synthesis and Screening of Stilbene Arrays." *Chem. Eur. J.* **2010**, *16*, 2692-2695.
- J. Campbell, G. D. Geske, Q. Lin, and **H. E. Blackwell**. "New and Unexpected Insights into the Modulation of LuxR-type Quorum Sensing by Cyclic Dipeptides." *ACS Chem. Biol.* **2009**,*4*, 1051–1059.
- C. Gorske, J. R. Stringer, B. L. Bastian, S. A. Fowler, and **H. E. Blackwell**. "New Strategies for the Design of Folded Peptoids Revealed by a Survey of Noncovalent Interactions in Model Systems." *J. Am. Chem. Soc.* **2009**, *131*, 16555–16567.
- J. Campbell and **H. E. Blackwell**. "Construction of Diketopiperazine Macroarrays Through a Cyclative-Cleavage Strategy and Their Evaluation as Luminescence Inhibitors in the Bacterial Symbiont *Vibrio fischeri*." *J. Comb. Chem.* **2009**, *11*, 1094–1099.
- T. Praneenararat, G. D. Geske, and **H. E. Blackwell**. "Efficient Synthesis and Evaluation of Quorum Sensing Modulators Using Small Molecule Macroarrays." *Org. Lett.* **2009**, *11*, 4600–4603.

Awards

- 2010 ACS Arthur C. Cope Scholar Award
- 2009 Iota Sigma Pi Agnes Fay Morgan Research Award
- 2007 Popular Science Magazine "Brilliant 10" Award
- 2007 UW–Madison Department of Chemistry James W. Taylor Excellence in Teaching Award
- 2007 Camille Dreyfus Teacher-Scholar Award
- 2007 DuPont Young Professor Award
- 2007 3M Non-Tenured Faculty Award
- 2006 W. M. Keck Foundation Distinguished Young Scholars in Medical Research Award
- 2006 Burroughs Wellcome Fund Investigator in Pathogenesis of Infectious Disease Award

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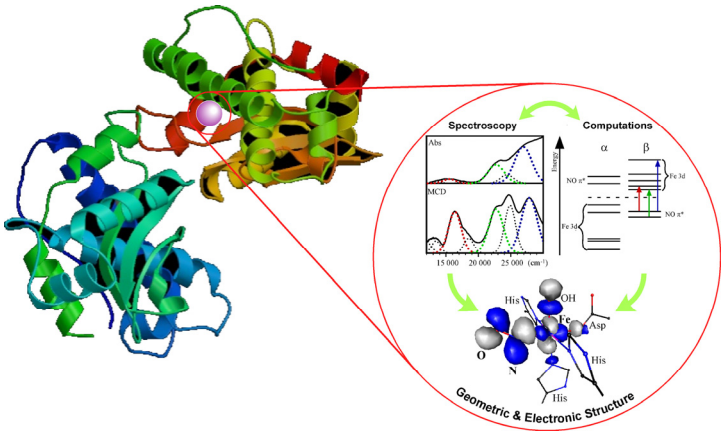
Research

The research carried out in my laboratory is aimed at elucidating the geometric and electronic properties, and ultimately the reactivity, of metal centers in proteins and cofactors through combined spectroscopic and computational studies of key enzymatic states and synthetic inorganic model complexes. The spectroscopic techniques used in this research include electronic absorption, circular dichroism, magnetic circular dichroism, resonance Raman, and electron paramagnetic resonance. These experimental techniques are complemented by density functional theory and combined quantum mechanics/molecular mechanics electronic structure calculations to develop experimentally validated bonding descriptions. With this combined spectroscopic/computational approach we can selectively probe the geometric and electronic properties of catalytically active metal centers in proteins and model complexes and also explore the natures of catalytic intermediates that are inaccessible to structural studies using X-ray crystallography.

One area of research in my laboratory is devoted to the study of enzymes utilitizng **bio-organometallic cofactors**, which include the enzymatically active forms of vitamin B_{12}, adenosylcobalamin and methylcobalamin, and the Ni-containing F_{430} species. While structurally related to the well-characterized hemes, these cofactors employ macrocyclic ligands (termed corrin and hydrocorphin, respectively) that are substantially more reduced than the porphyrin ring, offering them considerably more conformational freedom. The mechanistic significance of this increased flexibility in the catalytic cycles of B_{12}- and NiF_{430}-dependent enzymes remains a subject of intense debate.

A second project pursued in my laboratory aims at exploring the geometric and electronic prerequisites for the high catalytic activities of Ni-, Fe-, and Mn-dependent **superoxide dismutases** (SODs) that protect aerobic organisms from oxidative damage mediated by the superoxide radical anion. The Ni-dependent enzyme has only recently been isolated from some *Streptomyces* species, and X-ray crystallographic data have revealed that NiSOD is structurally unrelated to the other SODs. Conversely, the Fe- and MnSODs from *E. coli* possess virtually identical protein folds and active-site geometries; however, they are strictly metal specific. Though small differences in the second coordination spheres (comprising amino acid residues that are not directly bound to the active-site metal ion) do exist between these two enzymes, their relationship to this extraordinary metal-ion specificity remains incompletely understood.



A third major research focus of my laboratory is directed toward elucidating the electronic properties and catalytic mechanisms of enzymes possessing **polynuclear NiFeS active-site clusters**, including ACS and CODH that catalyze the reversible oxidation of CO to CO_2 and the synthesis of acetyl-CoA from CO, CoA, and a methyl group, respectively. While high-resolution X-ray structures have recently been solved for CODH and bifunctional ACS/CODH enzymes, fundamental questions concerning the redox states, substrate binding sites, and the natures of catalytically relevant reaction intermediates of these highly elaborate polynuclear active sites have yet to be answered.

Selected Publications

- Conrad, K. S.; Brunold, T. C. "Spectroscopic and Computational Studies of Glutathionylcobalamin: Nature of Co–S Bonding and Comparison to Co–C bonding in Coenzyme B_{12}", *Inorg. Chem*. **2011**, *70*, 6313–6324.
- Gardner, J. D.; Pierce, B. S.; Fox. B. G.; Brunold, T. C. "Spectroscopic and Computational Characterization of Substrate-Bound Mouse Cysteine Dioxygenase: Nature of the Ferrous and Ferric Cysteine Adducts and Mechanistic Implications", *Biochemistry* **2010**, *49*, 6033-6041.
- Van Heuvelen, K. M.; Cho, J.; Dingee, T.; Riordan, C. G.; Brunold, T. C. "Spectroscopic and Computational Studies of a Series of High-Spin Ni(II) Thiolate Complexes", *Inorg. Chem*. **2010**, *69*, 6535-6544.
- Van Heuvelen, K. M.; Cho, J.; Riordan, C. G.; Brunold, T. C. "Spectroscopic and Computational Studies of a μ-η^2:η^2-Disulfido-Bridged Dinickel(II) Species, [{(PhTt^{tBu})Ni}$_2$(μ-η^2:η^2-S_2)]: Comparison of Side-on Disulfido and Peroxo Bonding in $(Ni^{2+})_2$ and $(Cu^{2+})_2$ Species", *Inorg. Chem*. **2010,** *49*, 3113-3120.
- Van Heuvelen, K. M.; Kieber-Emmons, M. T.; Riordan, C. G.; Brunold, T. C. "Spectroscopic and Computational Studies of a *Trans*-μ-1,2-Disulfido-Bridged Dinickel Species, [{(tmc)Ni}$_2$(S_2)](OTf)$_2$: Comparison of End-on Disulfido and Peroxo Bonding in $(Ni^{2+})_2$ and $(Cu^{2+})_2$ Species", *Inorg. Chem*. **2010,** *49*, 3104-3112.
- Liptak, M.D.; Van Heuvelen, K.M., Brunold, T.C. "Computational Studies of Bioorganometallic Enzymes and Co-factors" in Sigel, A.; Sigel, H.; Sigel, R.K.O., Eds.; "Metal Ions in Life Sciences", the Royal Society of Chemistry, Cambridge, UK, 6, 417-460 (Invited Article) (**2009**).
- Liptak, M.D.; Fleischhacker, A.S.; Matthews, R.G.; Telser, J.; Brunold, T.C. "Spectroscopic and Computational Characterization of the Base-off Forms of Cob(II)alamin", *J. Phys. Chem. B, 113*, 5245-5254, (**2009**).
- Brunold, T.C., Conrad, K.; Liptak, M.D.; Park, K. "Spectroscopically Validated Density Functional Theory Studies of the B12 Co-factors and their Interactions with Enzyme Active Sites", *Coord. Chem., 253*, 779-794 (Invited Article) (**2009**).
- Liptak, M. D.; Datta, S.; Matthews, R.; Brunold, T. C. "Spectroscopic Study of the Cobalamin-Dependent Methionine Synthase in the Activation Conformation: Effects of the Y1139 Residue and S-Adenosylmethionine on the B_{12} Cofactor", *J. Am. Chem. Soc., 130*, 16374-16381 (**2008**).
- Park, K.; Mera, P.; Escalante-Semerena, J. C.; Brunold, T. C. "Kinetic and Spectroscopic Studies of the ATP:Corrinoid Adenosyltransferase PduO from *Lactobacillus reuteri*: Insights into Substrate Specificity and Mechanism of Co(II)corrinoid Reduction", *Biochemistry* , *47*, 9007-9015 (**2008**).
- Grove, L. E.; Xie, J.; Yikilmaz, E.; Karapetyan, A.; Miller, A.-F.; Brunold, T. C. "Spectroscopic and Computational Insights into Second Sphere Amino Acid Tuning of Substrate Analogue/Active Site Interactions in Iron(III) Superoxide Dismutase", *Inorg. Chem*., *47*, 3993-4004 (**2008**).
- Liptak, M. D.; Fleischhacker, A. S.; Matthews, R.; Brunold, T. C. "Probing the Role of the Histidine 759 Ligand in Cobalamin-Dependent Methionine Synthase", *Biochemistry*, *46*, 8024-8035 (**2007**).
- Fiedler, A. T.; Brunold, T. C. "Spectroscopic and Computational Studies of Ni^{3+} Complexes with Mixed S/N Ligation: Implications for the Active-Site of Ni Superoxide Dismutase", *Inorg. Chem*., *46*, 8511-8523 (featured on cover) (**2007**).

Selected Awards

- Division of University Housing's Honored Instructors Award, 2009, 2010, 2011
- Graduate Student Faculty Liaison Committee Mentor Award, 2009
- Romnes Award, University of Wisconsin-Madison, 2009
- National Science Foundation CAREER Award, 2003
- Sloan Foundation Fellow, 2003
- Swiss Chemical Society: Alfred Werner Award, 2003
- University of Bern, Switzerland: Theodor Kocher Award, 2000
- Research Corporation Innovation Award, 2000
- University of Bern, Switzerland: Faculty Award for Ph.D. Thesis, 1997

STEVEN D. BURKE

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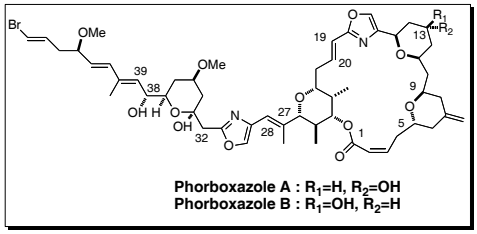
Research

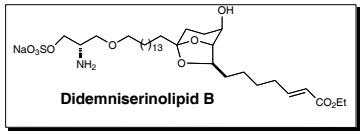
Our primary research interests focus on synthetic organic chemistry, with an emphasis on the efficient synthesis of natural products (and analogues thereof) with potent biological activity. Development of synthetic methods and novel strategies in response to the demands of complex molecule construction are key elements of our approach to target-oriented synthesis. Exemplifying this is our ongoing exploitation of symmetry for simplification of synthetic sequences, with the accompanying need for methods to efficiently break symmetry. Recently completed syntheses of such diverse structural types as phorboxazole B, thromboxane B_2, didemniserinolipid B, squamocin N, and dictyostatin illustrate common themes that have been developed in our group. Included among these themes are Pd(0)-mediated asymmetric double cycloetherification, ketalization/ring-closing metathesis, asymmetric double hetero Diels-Alder cycloaddition, and kinetically-controlled Meerwein-Ponndorf-Verley reduction.

RECENT BURKE GROUP TOTAL SYNTHESES



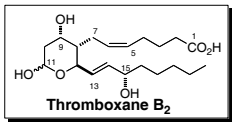
Phorboxazole A : R_1=H, R_2=OH
Phorboxazole B : R_1=OH, R_2=H

Brian Lucas, Laura Wysocki *Angew. Chem. Int. Ed.* **2007**, *46*, 769.
Featuring: Catalytic asymmetric double cycloetherification.
Shortest reported synthesis of a phorboxazole.



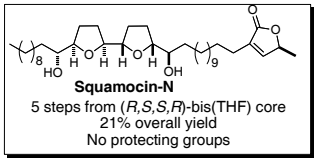
Didemniserinolipid B

Chris Marvin *Org. Lett.* **2007**, *9*, 5357;
J. Org. Chem. **2008**, *73*, 8452.
Featuring: Ketalization/Ring-Closing Metathesis.
Shortest reported synthesis of didemniserinolipid B.



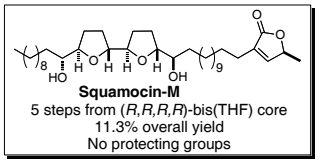
Thromboxane B_2

Chris Marvin *Org. Lett.* **2007**, *9*, 5353.
Featuring: Ketalization/Ring-Closing Metathesis



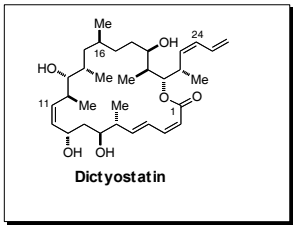
Squamocin-N
5 steps from (*R,S,S,R*)-bis(THF) core
21% overall yield
No protecting groups

Matt Dodge
Manuscript in preparation.
Featuring: RO/CM/asymmetric double cycloetherification core synthesis in two steps; synthesis ompleted in only 7 steps total.
Shortest reported syntheses of annonaceous acetogenins.



Squamocin-M
5 steps from (*R,R,R,R*)-bis(THF) core
11.3% overall yield
No protecting groups

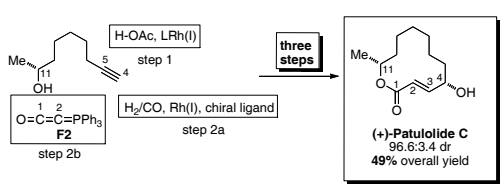
Matt Dodge
Manuscript in preparation.
Featuring: RO/CM/asymmetric double cycloetherification core synthesis in two steps



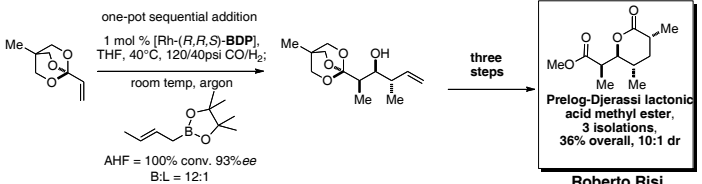
Dictyostatin

Andrew Dilger *J. Am. Chem. Soc.* **2007**, *129*, 16273. **Manuscript describing total synthesis in preparation.** Featuring: Ultrasound-accelerated double hetero D.-A. and kinetically-controlled Meerwein-Ponndorf-Verley reduction, affording ten asymmetric centers (>200:1 e.r) in three steps.
Shortest reported synthesis of dictyostatin.

Expeditious Synthesis of Natural Products via Catalytic Asymmetric Hydroformylation



Roberto Risi
Org. Lett. **2012**, ASAP



Roberto Risi
Manuscript in preparation.

A substantial portion of our current efforts are directed at developing Rh-catalyzed asymmetric hydroformylations (AHF) in tandem with compatible C-C and C-X bond forming reactions. We are pursuing this endeavor in collaboration with the Landis group, seeking to explore the possibility of using the chiral bis(diazaphospholane) ["BDP"] ligand/Rh(I) catalysts in complex molecule synthesis. The perfectly atom-economical AHF procedure delivers branched, chiral aldehydes in high enantiomeric excess from achiral alkenes, CO, and H_2, with very low catalyst loadings. Illustrative examples of the

power of these tandem processes to facilitate complex natural product synthesis is shown at the bottom of the scheme, detailing a three step total synthesis of the 12-membered antibiotic lactone patulolide C (see ASAP paper below) and a 4-step synthesis of the C1-C7 subunit of the methynolide antibiotics, represented by the Prelog-Djerassi lactone. Beginning with the AHF of the known vinyl ortho ester shown, the branched aldehyde formed is directly reacted with the indicated *E*-crotylboronate to afford a polypropionate stereotriad in a highly enantio- and diastereoselective manner in a single step. Three more steps provided the targeted Prelog-Djerassi lactone..

Selected Publications

- "Synthesis of (+)-Patulolide C via an Asymmetric Hydroformylation/Macrocyclization Cascade," Risi, R. M.; Burke, S. D. *Org. Lett*. (in press) DOI http://dx.doi.org/10.1021/ol2034299
- "A Citric Acid-Derived Ligand for Modular Functionalization of Metal Oxide Surfaces via "Click" Chemistry**,"** Bishop, L. M.; Yeager, J. C.; Chen, X.; Wheeler, J. N.; Torelli, M. D.; Benson, M. C.; Burke, S. D.; Pedersen, J. A.; Hamers, R. J. *Langmuir*, **2012**, *28*, 1322-1329.
- "Synthesis of Didemniserinolipid B: Application of a 2-Allyl-4-fluorophenyl Auxilliary for Relay Ring-Closing Metathesis," Marvin, C. C.; Voight, E. A.; Suh, J. M.; Paradise, C. L.; Burke, S. D. *J. Org. Chem*. **2008**, *73*, 8452-8457.
- "Total Synthesis of Phorboxazole B," Lucas, B. S.; Gopalsamuthiram, V.; Burke, S. D. *Angew. Chem. Int. Ed.* **2007**, *46*, 769-772.
- "Synthesis of Thromboxane B_2 via Ketalization/Ring-Closing Metathesis," Marvin, C. C.; Clemens, A. J. L.; Burke S. D. *Org. Lett*. **2007**, *9*, 5353-5356.
- "Synthesis of (+)-Didemniserinolipid B: Application of a 2-Allyl-4-fluorophenyl Auxilliary for Relay Ring-Closing Metathesis," Marvin, C. C.; Voight, E. A.; Suh, J. M.; Paradise, C. L.; Burke, S. D. *J. Org. Chem*. **2008**, *73*, 8452-8457.
- "Stereochemically General Approach to Adjacent Bis(tetrahydrofuran) Cores of Annonaceous Acetogenins," Wysocki, L. M.; Dodge, M. W.; Voight, E. A.; Burke, S. D. *Org. Lett*. **2006**, *8*, 5637-5640.
- "A Two-Directional Approach to a (-)-Dictyostatin C11-C23 Segment: Development of a Highly Diastereoselective, Kinetically-Controlled Meerwein-Ponndorf-Verley Reduction," Dilger, A. K.; Gopalsamuthiram, V.; Burke, S. D. *J. Am. Chem. Soc*. **2007**, *129*, 16273-16277.
- "Macrocyclic Scaffold for the Collagen Triple Helix," Horng, J.-C.; Hawk, A. J.; Zhao, Q.; Benedict, E. A.; Burke, S. D.; Raines, R. T. *Org. Lett*. **2006**, *8*, 4735-4738.
- "Halichondrin B: Synthesis of the C1-C22 Subunit," Lambert, W. T.; Hanson, G. H.; Benayoud, F. Burke, S. D. *J. Org. Chem*. **2005**, *70*, 9382-9398.
- "Total Synthesis of Rhizoxin D," Jiang, Y.; Hong, J.; Burke, S. D. *Org. Lett*. **2004**, *6*, 1445-1448.
- "Synthesis of Sialic Acids via Desymmetrization by Ring-Closing Metathesis," Voight, E. A.; Rein, C.; Burke, S. D. *J. Org. Chem*. **2002**, *67*, 8489-8499.

Awards

- Emil Steiger Distinguished Teaching Award, 2004 (UW-Madison, University-wide)
- Pharmacia & Upjohn Teaching Award, 1998-99
- Vilas Associate Award, UW-Madison, 1996-97
- Pfizer Research Award for Synthetic Organic Chemistry, 1993-96
- Merck Academic Development Program Award, 1993-94
- Alumni Distinguished Service Award, University of Wisconsin-Eau Claire, 1987
- NSF-Presidential Young Investigator Award, 1984-89
- Alfred P. Sloan Fellow, 1984-88
- Outstanding Young Man of America Award, 1980
- Andrew Mellon Predoctoral Fellow, 1975-78
- NSF-URP Traineeship, 1971
- L. L. Phillips Scholar, 1969-73
- Wisconsin Honor Scholar, 1969-70

JUDITH N. BURSTYN

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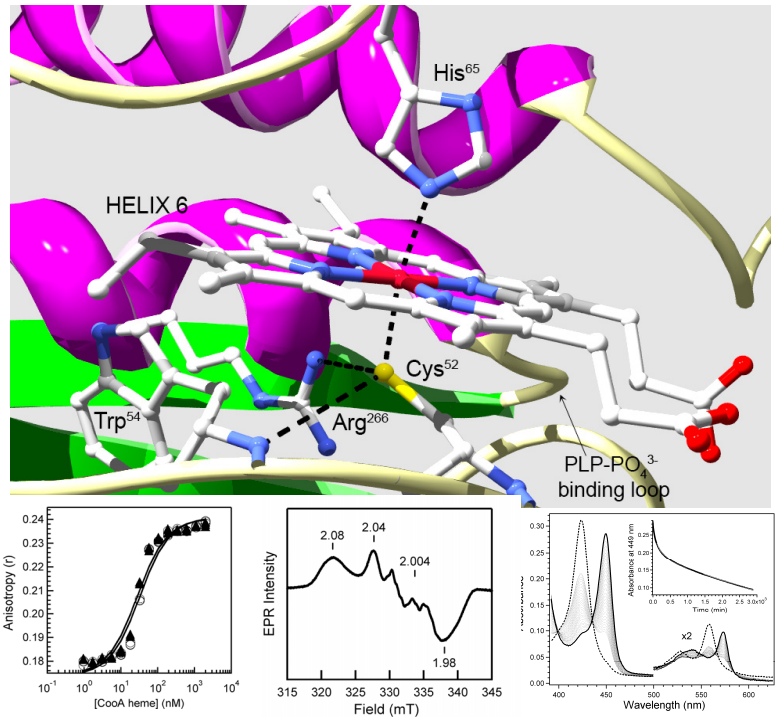
Research

Bioinorganic chemistry, Allostery in gas sensing metalloproteins, Metallosensor design

Our group studies gas-sensing metalloproteins, specifically how the interaction of a gas molecule with a metal center alters protein structure and function. Metalloproteins serve as sensors and signal transducers in a number of important biological processes. For example, NO regulates your blood pressure by interacting with heme containing soluble guanylyl cyclase. Bacteria use metalloproteins to sense gases such as O_2, CO, and NO in their environment, and plants use copper to detect ethylene, a hormone that regulates plant development. In our laboratory, research efforts are directed towards understanding how gas sensing occurs at a metal center, and how changes in the coordination chemistry at the metal center are coupled to allosteric conformational changes in the protein.

Through our studies of the mammalian NO-sensor soluble guanylyl cyclase and the bacterial CO-sensor CooA, we learned that interaction of gas molecules with the heme centers induces changes in the coordination geometry, and these changes correlate with functional changes in the proteins. Our current work aims to elucidate the mechanisms by which the coordination changes are communicated through the protein. To this end we study several gas-responsive transcription factors, including newly discovered heme-containing gas sensors that regulate microRNA processing and circadian rhythm.



Another project investigates why cystathionine-β-synthase (CBS), an enzyme that controls metabolism of sulfur amino acids, contains heme. CBS is a fascinating enzyme whose regulatory mechanisms are poorly understood. Through our studies, we are learning how heme is involved in controlling the stability of the protein. My lab uses a variety of biochemical and biophysical methods, including enzyme kinetics, protein modification and mutagenesis, EPR, electronic absorption, MCD, resonance Raman, CD and fluorescence spectroscopies to probe the structure-function relationships. Our group is highly interactive and interdisciplinary, with active collaborations at UW and other institutions.

Selected Publications

- "Ferric, Not Ferrous, Heme Activates DGCR8 for Primary microRNA Processing" Ian Barr, Aaron T. Smith, Yanqiu Chen, Rachel Senturia, Judith N. Burstyn, Feng Guo, *Proc. Natl. Acad. Sci.* **2012**, *109*, 1919-1924.
- "Cobalt Cystathionine β-Synthase: A Cobalt-Substituted Heme Protein With a Unique Thiolate Ligation Motif" Aaron T. Smith, Tomas Majtan, Katherine M. Freeman, Judith N. Burstyn, Jan P. Kraus *Inorganic Chemistry*, **2011**, *50*, 4417–4427.
- "Purification and characterization of cystathionine beta-synthase bearing a cobalt protoporphyrin" Tomas Majtan, Katherine M. Freeman, Aaron T. Smith, Frank E. Frerman, Judith N. Burstyn, Jan P. Kraus *Arch. Biochem. Biophys*. **2011**, *508*, 25–30.
- "DiGeorge Critical Region 8 (DGCR8) Is a Double-Cysteine-Ligated Heme Protein" Ian Barr, Aaron T. Smith, Rachel Senturia, Yanqiu Chen, Brooke D. Scheidemantle, Judith N. Burstyn, Feng Guo *J. Biol. Chem*. **2011**, *286*, 16716-16725.
- "Nitric Oxide Photogeneration from *trans*-Cr(cyclam)$(ONO)_2^+$ in a Reducing Environment. Activation of Soluble Guanylyl Cyclase and Arterial Vasorelaxation" Alexis D. Ostrowski, Sherine J. Deakin, Bilal Azhar, Thomas W. Miller, Nestor Francoleon, Melisa M. Cherney, Andrea Lee, Judith N. Burstyn, Jon M. Fukuto, Ian L. Megson, Peter C. Ford, *J. Med. Chem.* **2010**, *53*, 715–722 715.
- "The effects of nitroxyl (HNO) on soluble guanylyl cyclase activity: Interactions at ferrous heme and cysteine thiols" Thomas W. Miller, Melisa M. Cherney, Andrea J. Lee, Nestor E. Francoleon, Patrick J. Farmer, S. Bruce King, Adrian J. Hobbs, Katrina M. Miranda, Judith N. Burstyn, Jon M. Fukuto, *Journal of Biological Chemistry*, **2009**, *284*, 21788-21796.
- "Nuclear receptors *Homo sapiens* Rev-erbβ and *Drosophila melanogaster* E75 are thiolate-ligated heme proteins, which undergo redox-mediated ligand switching and bind CO and NO" Katherine A. Marvin, Jeffrey L. Reinking, Andrea J. Lee, Keith Pardee, Henry M. Krause, Judith N. Burstyn, *Biochemistry*, **2009**, *48*, 7056–7071.
- "Guanidine Hydrochloride-Induced Unfolding of the Three Heme Coordination States of the CO-Sensing Transcription Factor, CooA" Andrea J. Lee, Robert W. Clark, Hwan Youn, Sarah Ponter, Judith N. Burstyn, *Biochemistry*, **2009**, *48*, 6585-6597.
- "Synthesis and DNA Cleavage Activity of a Bifunctional Intercalator-Linked Copper(II) Macrocycle" Ta-Sheng Andrew Tseng, Judith N. Burstyn, *Chem. Commun.* **2008**, 6209-6211
- "The CO-activated transcription regulator RcoM-2 from *Burkholderia xenovorans* is a cysteine-ligated hemoprotein that undergoes a redox-mediated ligand switch" Katherine A. Marvin, Robert L. Kerby, Hwan Youn, Gary P. Roberts, Judith N. Burstyn, *Biochemistry*, **2008**, *47*, 9016-9028.
- "Ferrous Human Cystathionine Beta-synthase Loses Activity During Enzyme Assay Due to a Ligand Switch Process" Melisa M. Cherney, Samuel Pazicni, Nina Frank, Katherine A. Marvin, Jan P. Kraus, Judith N. Burstyn, *Biochemistry*, **2007**, *46,* 13199-13210.
- "DNA Binding by an Imidazole-Sensing CooA Variant is Dependent on the Heme Redox State" Robert W. Clark, Hwan Youn, Andrea J. Lee, Gary P. Roberts, Judith N. Burstyn, *J. Biol. Inorg. Chem.* **2007**, *12*, 139-146.

Awards

- Fellow of the American Association for the advancement of Science, 2009
- Vilas Associates Award 2005-2006
- Doris Slesinger Award for Excellence in Mentoring 2005
- Fellow of UW-Madison Teaching Academy 2004
- Women in Engineering Program Award 2001 (Women in Science and Engineering Residential Program, UW-Madison, Co-Directors Judith N. Burstyn & Wendy C. Crone)
- Alfred P. Sloan Foundation Fellow 1996-1998
- Dave McClain Research Award, American Heart Association, Wisconsin Affiliate 1994
- American Cancer Society Postdoctoral Fellow 1987-1989

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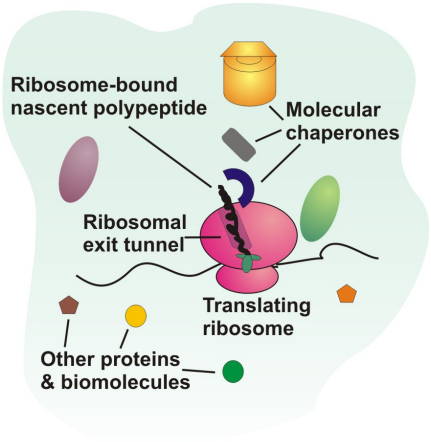
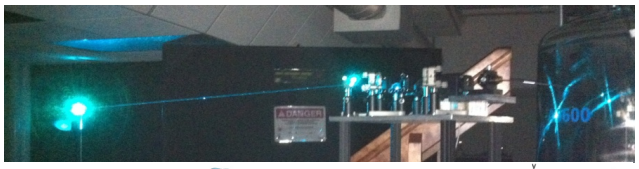
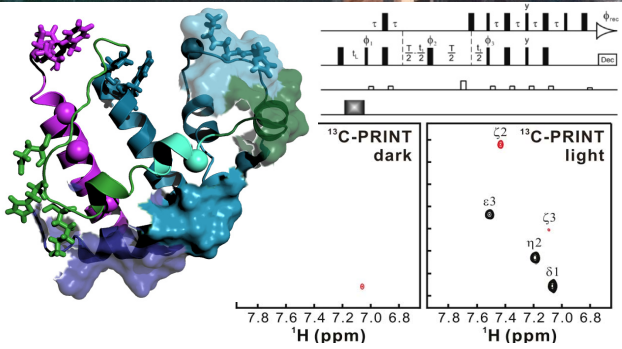
Research

Protein folding in the cell and Biomolecular spectroscopy. How does a protein with a given amino acid sequence manage to achieve its amazingly organized three-dimensional structure? This process, known as protein folding, is one of the most fundamental yet poorly understood events in chemistry and biology. Most studies performed in the past have focused on the *in vitro* folding of full-length biopolymers starting from unfolded states generated by high concentrations of denaturants or high temperature. However, these types of unfolded states rarely exist in living cells! Moreover, polypeptide chains start sampling conformational space (and possibly even fold) way before the protein amino acid sequence has been fully synthesized, during a process known as translation. In order to fully understand protein folding, it is therefore important to take the cellular context into account. This is even more important in the case of protein *mis*folding, i.e., folding gone wrong, which leads to protein aggregation and several deadly neurodegenerative and brain disorders such as Alzheimer's disease, spinocerebellar ataxia and Huntington's chorea. Thus, understanding protein folding and misfolding will lead to both fundamental knowledge and long-term benefits to human health.







The Cavagnero group specializes in the high resolution understanding of the fundamental principles of protein folding and misfolding in the cell. We place particular emphasis on understanding folding as nascent proteins emerge from the molecular machine responsible for their biosynthesis, the ribosome. All the studies are performed under physiologically relevant conditions in crowded aqueous media.

Fundamental questions in protein folding. Our group is involved in the study of fundamental questions in protein folding, including the role of water and hydrophobic collapse *in vitro* and in the cell, the effect of amino acid sequence on structure, the role of the protein's C terminus in folding, kinetic trapping events across the folding energy landscape, the thermodynamic balance between protein folding, misfolding and interaction with molecular chaperones.

Protein folding *in vivo*: conformation and dynamics of ribosome-bound nascent polypeptides. The earliest stages of a protein's life are crucial for its ability to function in the cell. Our group is doing pioneering studies on the folding of proteins as they emerge from the ribosome by a combination of time-resolved fluorescence, NMR, mass spectrometry-detected H/D exchange and biological assays. In addition, we are developing novel approaches to study protein folding and translation rates in living cells.

The role of molecular chaperones in protein folding and aggregation. All the aboveresearch directions are pursued in the absence and presence of cotranslationally- active chaperones. We are also performing model

studies with purified chaperones such as Hsp70, to specifically explore whether chaperones act merely by preventing misfolding or play an active role in the folding of their substrate. This work is carried out primarily by multidimensional NMR on ^{15}N- and ^{13}C-enriched polypeptide substrates and involves both high resolution kinetics and structural/dynamic analysis.

Method development in laser-enhanced NMR spectroscopy. We are developing novel methodologies to enhance the power NMR spectroscopy for the analysis of protein folding. Our efforts include laser-enhances approaches to boost NMR sensitivity, new radio-frequency pulse schemes to overcome undesired NMR resonance line-broadening due to conformational exchange in the intermediate chemical shift timescale, and methods to site-specifically study the role of water in protein folding. Exciting new developments include laser-driven techniques based on photochemically-enhanced dynamic nuclear polarization (photo-CIDNP) and its application to heteronuclear correlation NMR in ^{15}N and ^{13}C isotopically enriched samples.

Selected Publications

- Sekhar, A., Santiago, M., Cavagnero, S. 'Transient Interactions of a Slow-Folding Protein with the Hsp70 Chaperone Machinery' submitted (**2012**).
- Lee, J.H., Sekhar, A., Cavagnero, S. '^{1}H-detected ^{13}C Photo-CIDNP as a Sensitivity Enhancement Tool in Solution NMR' *J. Am. Chem. Soc.* **133**, 8062-8065 (**2011**).
- Armstrong, B.D., Choi, J., López, C., Wesener, D.A., Hubbell, W., Cavagnero, S.*, Han, S.* 'Site-Specific Hydration Dynamics in the Nonpolar Core of a Molten Globule by Dynamic Nuclear Polarization of Water' *J. Am. Chem. Soc.* **133**, 5987-5995 (**2011**), (*) corresponding authors.
- Fedyukina, D.V., Cavagnero, S. 'Protein Folding at the Exit Tunnel' *Annu. Rev. Biophys.* **40**, 337-359 (**2011**).
- Rajagopalan, S., Kurt, N., Cavagnero, S. 'High Resolution Conformation and Backbone Dynamics of a Soluble Aggregate of Apomyoglobin$_{119}$' *Biophys. J.* **100**, 747-755 (**2011**), cover article.
- Fedyukina, D.V., Rajagopalan, S., Sekhar, A., Fulmer, E.C., Eun, Y.-J., Cavagnero, S. 'Contribution of Long-Range Interactions to the Secondary Structure of an Unfolded Globin' *Biophys. J.* **99**, L37-L39 (**2010**), cover article.
- Weinreis, S.A., Ellis, J.P., Cavagnero, S. 'Dynamic Fluorescence Depolarization: A Powerful Tool to Explore Protein Folding on the Ribosome' *Methods* **52**, 57-73 (**2010**).
- Ellis, J.P., Culviner, P.H., Cavagnero, S. 'Confined Dynamics of a Ribosome-Bound Nascent Globin: Cone Angle Analysis of Fluorescence Depolarization Decays in the Presence of Two Local Motions' *Protein Sci.* **19**, 1600 (**2010**).
- Ziehr, D.R., Ellis, J.P., Culviner, P.H., Cavagnero, S. 'Ribosome Release by Hydroxylamine Produces Newly Synthesized Proteins with Optimal Physical Properties' *Analyt. Chem.* **82**, 4637-4643 (**2010**).
- Sekhar, A., Cavagnero, S. EPIC- and CHANCE-HSQC: Two ^{15}N Photo-CIDNP-Enhanced Pulse Sequences for the Sensitive Detection of Solvent-Exposed Tryptophan, *J. Magn. Reson.* **200**, 207-213 (**2009**)
- Ellis, J.P., Culviner, P.H., Cavagnero, S. Confined Dynamics of a Ribosome-Bound Nascent Globin: Cone Angle Analysis of Fluorescence Depolarization Decays in the Presence of Two Local Motions, *Protein Sci.* **18**, 2003-2015 (**2009**)
- Sekhar, A., Cavagnero, S. 1H Photo-CIDNP Enhancements in Heteronuclear Correlation NMR Spectroscopy *J Phys. Chem. B.*, **113**, 8310-8318 (**2009**)
- Mounce, B., Kurt, N., Ellison, P.A., Cavagnero, S. 'Nonrandom Distribution of Intramolecular Contacts in Native Single-Domain Proteins' *Proteins, Struct. Funct. Bioinf.* **75**, 404-412 (**2009**).
- Ellis, J.P., Bakke, C.K., Kirchdoerfer, R.N., Jungbauer, L.M., Cavagnero, S. 'Chain Dynamics of Nascent Polypeptides Emerging from the Ribosome' *ACS Chem. Biol. 3*, 555-566 (**2008**), cover article.
- Kurt, Cavagnero, S. 'Nonnative Helical Motif in a Chaperone-Bound Protein Fragment' *94***,** 48-50 *Biophys. J.* (**2008**).

Awards

- Vilas Associates Award 2009
- ACS PROGRESS/Dreyfus Lectureship Award, 2007
- Research Corporation Research Innovation Award, 2001
- Shaw Scientist Award, 2001
- Best Poster Award, 6th Johns Hopkins University Folding Meeting, 2001
- Wills Foundation Postdoctoral Fellowship, 1998-1999
- Italian national Research Council (CNR) Postdoctoral Fellowship (declined), 1998
- American Association of University Women Postdoctoral Fellowship, 1996-1997
- Fulbright Fellowship, 1988-1992
- Soroptimist Award, 1981

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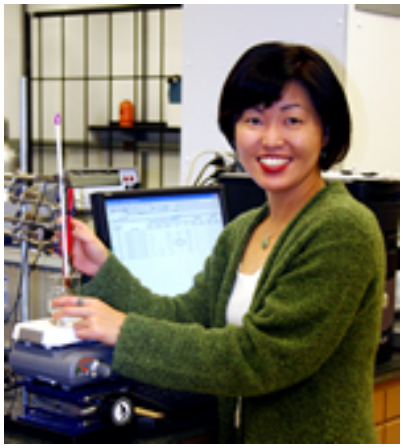
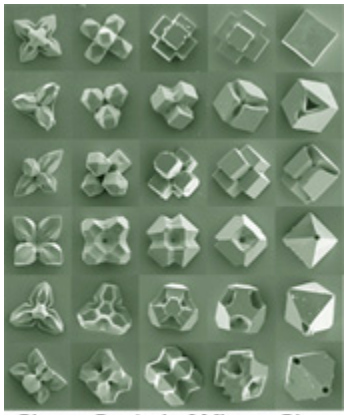


Research

Research in the Choi group focuses on design, synthesis, and characterization of semiconducting and metallic crystals and thin film-type electrodes with controlled micro- and nano-structures for use in electrochemical and photoelectrochemical devices (e.g. photoelectrochemical cells, fuel cells, and rechargeable batteries, and sensors). This research combines disciplines of inorganic chemistry, solid state chemistry, electrochemistry, materials chemistry, and nano-scale science.

When electrochemical and photoelectrochemical devices contain polycrystalline electrodes or catalysts, variances of particle shapes, sizes, orientations, and interconnections significantly affect the chemical and physical factors that define the energetics and kinetics of these electrodes or catalysts. Therefore, controlling and understanding the effects of micro- and nano-structural features at the interface on functional properties are the keys to producing highly efficient, cost effective, and lightweight devices.

In order to accomplish these tasks our group develops new electrochemical synthetic strategies that can make a significant advancement in constructing polycrystalline electrode materials. We achieve this by combining compositionally versatile electrodeposition methods with various new synthetic concepts/techniques that can allow for precise morphological control at various length scales (e.g. electrochemical interfacial supramolecular templating, controlled electrocrystallization). Since electrodeposition is based on a low-temperature solution-based method with many synthetic variables that can be precisely and freely controlled, our approach allows for the assembly of a broad range of inorganic electrodes with systematically varying micro- and nano-structural features (e.g. mesoporous films, nano- and micro-scale crystal engineering).



Shape Control of Micron-Size Cu_2O Crystals

The functional properties we currently investigate in conjunction with morphological variation include optical, electrochemical, photoelectrochemical, and photo-/electro-catalytic properties. By pursuing an in-depth atomic level understanding of structure-property relationships as well as efficiency enhancement by interfacial engineering, we attempt to bridge the gap between chemistry and materials engineering.

Selected Publications

- Seabold, J. A.; Choi, K.-S. "Efficient and Stable Photo-Oxidation of Water by a Bismuth Vanadate Photoanode Coupled with an Iron Oxyhydroxide Oxygen Evolution Catalyst" *J. Am. Chem. Soc.*, **2012**, *134,* 2186–2192.
- McDonald, K. J.; Choi, K.-S. "Synthesis and Photoelectrochemical Properties of $Fe_2O_3/ZnFe_2O_4$ Composite Photoanodes for Use in Solar Water Oxidation" *Chem. Mater.* **2011**, *23*, 4863-4869.
- McDonald, K. J.; Choi, K.-S. "Photodeposition of Co-Based Oxygen Evolution Catalysts on □-Fe_2O_3 Photoanodes" *Chem. Mater.* **2011**, *23*, 1686–1693.
- Spray, R. L. McDonald, K. J.; Choi, K.-S. "Enhancing Photoresponse of Nanoparticulate □-Fe_2O_3 Electrodes by Surface Composition Tuning" *J. Phys. Chem C.* **2011**, 115, 3497-3506.
- Seabold, J. A.; Choi, K.-S. "Effect of a Cobalt-Based Oxygen Evolution Catalyst on the Stability and the Selectivity of Photo-Oxidation Reactions of a WO_3 Photoanode" *Chem. Mater.* **2011**, *23*, 1105–1112.
- McShane. C. M.; Siripala, W. P.; Choi, K.-S. "Effect of Junction Morphology on the Performance of Polycrystalline Cu_2O Homojunction Solar Cells" *J. Phys. Chem. Lett.* **2010**, *1*, 2666–2670.
- Shankar K.;Basham, J. I.;Allam, N. K.;Varghese, O. K.;Mor, G. K.;Feng, X. J.;Paulose, M.;Seabold, J. A.;Choi, K. S.;Grimes, C. A., Recent Advances in the Use of TiO2 Nanotube and Nanowire Arrays for Oxidative Photoelectrochemistry. *Journal of Physical Chemistry C* **2009,** 113, 6327-6359.
- McShane C. M.;Choi, K. S., Photocurrent Enhancement of n-Type Cu2O Electrodes Achieved by Controlling Dendritic Branching Growth. *Journal of the American Chemical Society* **2009,** 131, 2561-2569.
- Mor G. K.;Varghese, O. K.;Wilke, R. H. T.;Sharma, S.;Shankar, K.;Latempa, T. J.;Choi, K. S.;Grimes, C. A., p-type Cu-Ti-O nanotube arrays and their use in self-biased heterojunction photoelectrochemical diodes for hydrogen generation. *Nano Letters* **2008,** 8, 1906-1911.

Selected Awards

- 2011-2016 University Faculty Scholar, 2011
- 2011 Chair, ACS-Division of Inorganic Chemistry, Solid State Subdivision, 2010
- 2012 Vice Chair-Elect, Gordon Research Conference-Electrodeposition, 2010
- Iota Sigma Pi Agnes Fay Morgan Research Award, 2010
- Materials Research Society Bulletin 2011 Volume Organizer, 2009
- College of Science Outstanding Undergraduate Teaching by an Assistant Professor Award, 2008
- ExxonMobil Solid State Chemistry Faculty Fellowship, 2007
- ACS PROGRESS/Dreyfus Lectureship Award, 2006
- Alfred P. Sloan Research Fellow, 2006

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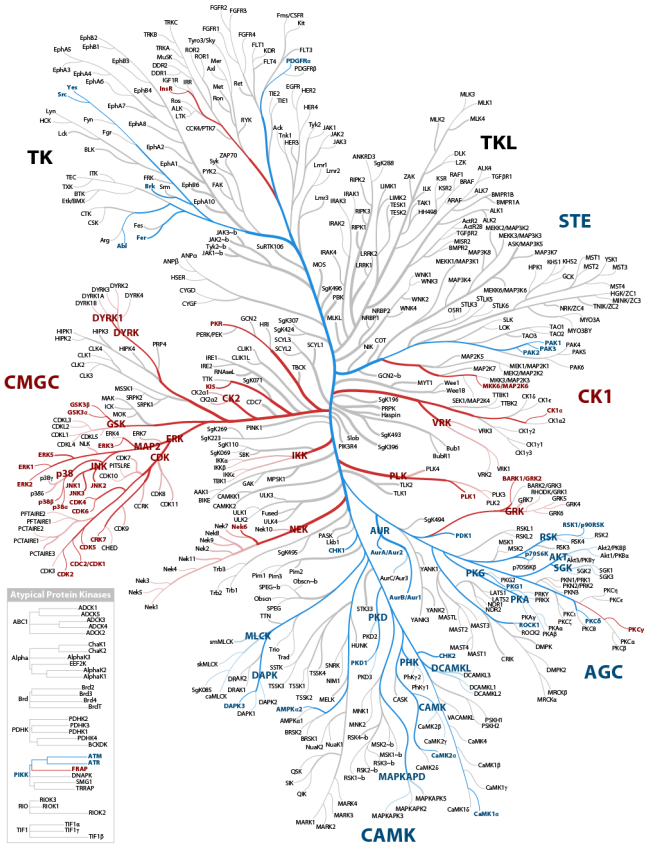
Quantitative Biology, Chemical Biology, Mass Spectrometry, Proteomics

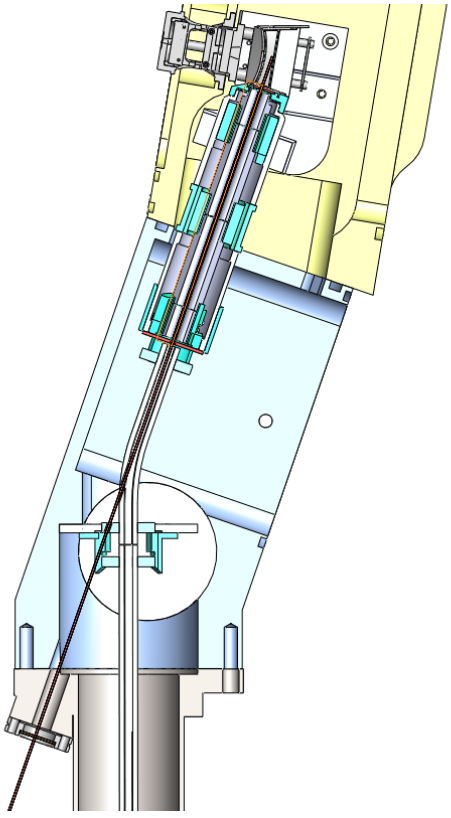
Awards

- Biemann Medal (ASMS, 2012)
- Arthur F. Findeis Young Analytical Scientist Award (ACS, 2011)
- Philip R. Certain Dean's Distinguished Faculty Award (2010)
- The Pittsburgh Conference Achievement Award (2010)
- Ken Standing Award (2009)
- National Science Foundation CAREER Award (2008)
- Eli Lilly and Company Young Investigator (2008)
- Beckman Young Investigator (2007)
- American Society of Mass Spectrometry Research Award (2006)
- Named one of "Tomorrow's PIs" by *Genome Technology* magazine (2006)

QUANTITATIVE BIOLOGY



CHEMICAL INSTRUMENTATION



Branches of the kinome active in human embryonic stem cells as mapped by mass spectrometry (left). Design for a dedicated ion/ion reactor within an orbitrap mass spectrometer (right).

Overview

My research group aims to catalyze evolution in the rapidly developing field of proteomics and to use these technologies to address fundamental problems in biology. With an emphasis on ion chemistry and instrumentation, we develop and apply new, enabling mass spectrometry-based (MS) proteomic technologies. Past successes in instrumentation include: the coupling electron-transfer dissociation to an Orbitrap mass analyzer, the addition of a high resolution mass filter over an ion trap to increase throughput and isolation fidelity, the development of both collision- and photon-activated methods to boost ETD efficiency (ETcaD and AI-ETD, respectively), and the use of ETD reagents for spectral calibration to eliminate mass accuracy drift. Such cutting-edge tools allow us to examine, for example, the molecular events that commit human embryonic stem cells (hES cells) to exit the pluripotent state with unprecedented chemical detail and sensitivity. Here we are focused on intracellular signaling, the epigenetic regulation of pluripotency, and interpreting and monitoring epigenetic codes. Coupled with instrumentation, new methodology is a vital component in accomplishing our overarching goal. In this vein, we have led the way in using intelligent data acquisition logic (Decision Tree) ETD with collision-activated dissociation (CAD), using ETD with isobaric tagging for protein quantification, and using ETD with various proteases other than trypsin to increase proteome coverage. Finally, our informatics team works on unique spectra pre-processing routines, an ETD-specific search algorithm called zCore (now commercially available), and an open platform for ETD spectral processing (COMPASS).

Active projects

Research projects include: (1) instrumentation development, (2) data analysis software design, (3) fundamental ion chemistry studies, and (4) biological applications: global identification of protein post-translational modification (specifically phosphorylation), quantitative analysis of protein phosphorylation (i.e., comparative analysis of two cellular states), and cancer biomarker discovery, among others.

Selected Publications (12 of 72)

- Wenger CW, Lee MV, Phanstiel DP, Westphall MS, **Coon JJ**. *Gas-phase purification enables accurate, multiplexed proteome quantification with isobaric tagging*. Nature Methods, **2011**, 8 (11), 933-935. Citation count [1]
- Phanstiel DH, Brumbaugh J, Wenger CD, Tian S, Probasco MD, Bailey DJ, Swaney DL, Tervo MA, Bolin JM, Ruotti V, Stewart S, Thomson JA, **Coon JJ**. *Proteomic and phosphoproteomic comparison of human ES and iPS cells*. Nature Methods, **2011**, 8, 821–827. PMID: 21983960. Citation count [3]
- Lee MV, Topper SA, Hubler SL, Wenger CW, **Coon JJ**, Gasch A. *A dynamic model of proteome changes reveals new roles for transcript alteration in yeast*. Molecular Systems Biology, **2011**, 7 (514). PMCID: PMC3159980. Citation count [2]
- Wenger CD, McAlister GC, Xia Q, Coon JJ. *Sub-part-per-million precursor and product mass accuracy for high-throughput proteomics on an electron transfer dissociation-enabled orbitrap mass spectrometer.* Molecular & Cell Proteomics, **2010**, 9 (5): 754-763. Citation count [9]
- Swaney DL, Wenger CD, Coon JJ. *Value of using multiple proteases for large-scale mass spectrometry-based proteomics.* Jouurnal of Proteome Research, **2010**, 9 (3): 1323-1329. Citation count [27]
- Ledvina AR, Beauchene NA, McAlister GC, Syka JE, Schwartz JC, Griep-Raming J, Westphall MS, Coon JJ. *Activated-ion electron transfer dissociation improves the ability of electron transfer dissociation to identify peptides in a complex mixture*. Analytical Chemistry, **2010**, 82 (24): 10068-10074. Citation count [2].
- McAlister GC, Phanstiel DH, Wenger CD, Lee MV, Coon JJ. *Analysis of tandem mass spectra by FTMS for improved large-scale proteomics with superior protein quantification*. Analytical Chemistry, **2010**, 82 (1): 316-22. Citation count [12]
- Ledvina AR, McAlister GC, Gardener MW, Smith SI, Madsen JA, Schwartz JC, Stafford GC Jr, Syka JEP, Brodbelt JS, and Coon JJ. *Infrared Photo-Activation Reduces Peptide Folding and Hydrogen Atom Migration Following ETD Tandem Mass Spectrometry*. Angewandte Chemie, **2009**, 48 (45): 8526-8528. Citation count [9]
- Swaney DL, Wenger CD, Thomson JA, Coon JJ. *Human embryonic stem cell phosphoproteome revealed by electron transfer dissociation tandem mass spectrometry*. Proceedings of the National Academy of Sciences of the United States of America, **2009**, 106 (4): 995-1000. Citation count [64]
- Swaney DL, McAlister GC, Coon JJ. "*Decision Tree Driven Tandem Mass Spectrometry for Shotgun Proteomics*." Nature Methods, **2008,** 5, 11, 959-964. Citation count [88]
- McAlister GC, Berggren WT, Griep-Raming J, Horning S, Makarov A, Phanstiel D, Stafford GC, Swaney DL, Syka JEP, Coon JJ. "*A Proteomics Grade ETD-enabled Linear Ion Trap-Orbitrap Hybrid Mass Spectrometer.*" Journal of Proteome Research, **2008**, 7 (8), 6388-6394. Citation count [56]
- Phanstiel D, Brumbaugh J, Berggren WT, Feng X, Levenstein ME, Thomson JA, Coon JJ. "*Mass Spectrometry Identifies and Quantifies 74 Unique Histone H4 Isoforms in Differentiating Human Embryonic Stem Cells".* Proceedings of the National Academy of Sciences of the United States of America, **2008**, 105, 11, 4093-4098. Citation count [63]
- Good DM, McAlister GC, Phanstiel D, Coon JJ. "*Performance Evaluation of Electron Transfer Dissociation.*" Molecular and Cellular Proteomics, **2007**, 6, 11, 1942-51. Citation count [125]
- McAlister GC, Phanstiel D, Good DM, Berggren WT, Coon JJ. "*Implementation of Electron Transfer Dissociation on a Hybrid Linear Ion Trap-Orbitrap Mass Spectrometer.*" Analytical Chemistry, **2007**, 79, 10, 3525-3534. Citation count [76]

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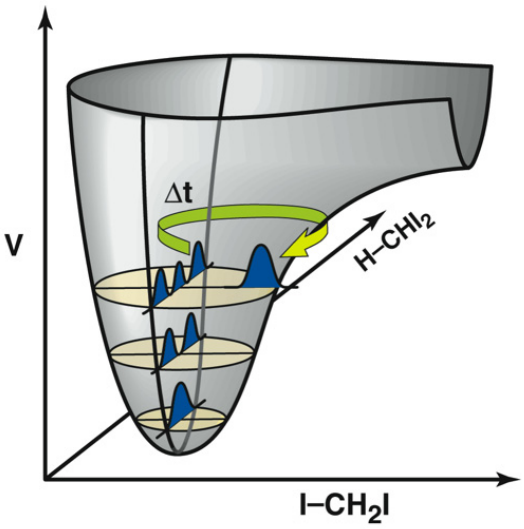
Research Interests

Our group is studying the dynamics of reaction and photodissociation with the goal of understanding the essential features of chemistry in both gases and liquids. The unifying theme of our research is connecting chemical reaction dynamics occurring in gases to those in liquids. We use both high resolution lasers and ultrafast lasers, and the key to all of our experiments is preparing molecules in vibrationally excited states and spectroscopically monitoring their subsequent behavior.

Vibrational excitation is crucial in many chemical reactions because motion of the atoms relative to each other carries the system through the transition state that lies atop the barrier to reaction. Because laser excitation is a particularly attractive means of preparing molecules in specific internal states, our strategy is to excite molecules with a laser pulse and use time-resolved spectroscopy to follow their subsequent behavior. We use high resolution lasers in some experiments and ultrafast lasers, which produce pulses of less than 100 fs duration, in others. The two approaches often provide complementary information and allow us to study some of the same reactions in isolated molecules and in liquids. In the former case, laser excitation prepares a molecular eigenstate that does not evolve in time and whose properties we exploit to control the course of a chemical reaction. In the later case, the short laser pulse prepares a state that does evolve in time and that we intercept at different points in its evolution. This good time resolution allows us to observe processes that occur during a time that is comparable to the interval between the interactions in solution.



We use a variety of excitation and detection techniques, such as resonant multiphoton ionization with ion imaging in molecular beams and time-resolved transient absorption or non-linear spectroscopy in liquids. The molecular beam experiments provide an extremely detailed view of the chemical dynamics of isolated, well-characterized molecules. We have exploited our understanding of the behavior of vibrationally excited molecules to control the course of a chemical reaction, and we have used laser excitation to cleave a particular bond selectively in both photodissociation and bimolecular reaction. The ultrafast laser techniques now allow us to follow the flow of energy within a molecule directly and to study vibrationally driven reactions in liquids. Discovering the controlling aspects of chemical reactions at a fundamental level is the focus of our research. The listing on the next page gives a few representative publications. There is a current list of all publications at our group website, *http://www.chem.wisc.edu/~crim/*.

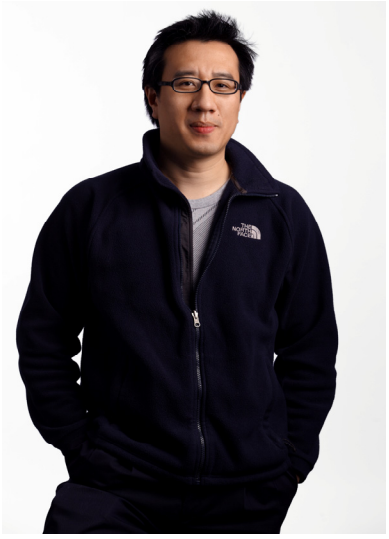
Selected Publications

- "Formation and Relaxation Dynamics of iso-CH_2ClI in Cryogenic Matrices." Thomas J. Preston, Maitreya Dutta, Brian J. Esselman, Aimable Kalume, Lisa George, Robert J. McMahon, Scott A. Reid, and F. Fleming Crim, J. Chem. Phys. *135*, 114503 (**2011**).
- "Dissociation Energy and Vibrational Predissociation Dynamics of the Ammonia Dimer." Amanda S. Case, Cornelia G. Heid, Scott H. Kable, and F. Fleming Crim, J. Chem. Phys. *135*, 084312 (**2011**).
- "Reaction Dynamics and Vibrational Spectroscopy of CH_3D Molecules with Both C-H and C-D Stretches Excited." Christopher J. Annesley, Andrew E. Berke, and F. Fleming Crim, *J. Phys. Chem*. A *112*, 9448 (**2008**).
- "Vibrationally Mediated Photodissociation of Ammonia: The Influence of N-H Stretching Vibrations on Passage through Conical Intersections." Michael L. Hause, Y. Heidi Yoon, and F. Fleming Crim, *J. Chem. Phys. 125*, 174309 (**2006**).
- "Mode- and Bond-selective Reaction of $Cl(^2P_{3/2})$ with CH_3D Excited in the C-H Stretch Overtone Region." Robert J. Holiday, Chan-Ho Kwon, Christopher J. Annesley, and F. Fleming Crim, *J. Chem. Phys*. *125*, 133101 (**2006**).
- "Connecting Chemical Dynamics in Gases and Liquids." Christopher G. Elles and F. Fleming Crim*, Annu. Rev. Phys. Chem***.** 57, 273 (**2006**).
- "A Time-Resolved Spectroscopic Study of the Reaction Cl + n-C_5H_{12} → HCl + C_5H_{11} in Solution, Leonid Sheps." Andrew C. Crowther, Stacey L. Carrier, and F. Fleming Crim, *J. Phys. Chem*. A *110*, 3087 (**2006**).
- "Recombination Dynamics and Hydrogen Abstraction Reactions of Chlorine Radicals in Solution." Leonid Sheps, Andrew C. Crowther, Christopher G. Elles, and F. Fleming Crim, *J. Phys. Chem*. A 109, 4296 (**2005**).
- "Vibrational Relaxation of CH_3I in the Gas Phase and in Solution." Christopher G. Elles, M. Jocelyn Cox, and F. Fleming Crim, *J. Chem. Phys*. *120*, 6973 (**2004**)
- "The Relative Reactivity of the CH_3D molecules with Excited Symmetric and Antisymmetric Stretching Vibrations." Sangwoon Yoon, Robert J. Holiday, Edwin L. Sibert III, and F. Fleming Crim, *J. Chem. Phys*. *119*, 9568 (**2003**)
- "Competition between Adiabatic and Nonadiabatic Pathways in the Photodissociation of Vibrationally Excited Ammonia." Andreas Bach, J. Matthew Hutchison, Robert J. Holiday, and F. Fleming Crim, *J. Phys. Chem* A, *107*, 10490 (**2003**).
- "Control of Bimolecular Reactions: Bond-Selected Reaction of Vibrationally Excited CH_3D with $Cl(^2P_{3/2})$." Sangwoon Yoon, Robert J. Holiday, and F. Fleming Crim, *J. Chem. Phys*. *119*, 4755 (**2003**)
- "Vibrational Relaxation of CH_2I_2 in Solution: Excitation Level Dependence." Christopher G. Elles, Dieter Bingemann, Max M. Heckscher, and F. Fleming Crim, *J. Chem. Phys*., *118* 5587 (**2003**)
- "Relaxation of the C-H Stretching Fundamental Vibrations of CHI_3, CH_2I_2, and CH_3I in Solution." Max M. Heckscher, Leonid Sheps, Dieter Bingemann, and F. Fleming Crim, *J. Chem. Phys*. *117*, 8917 (**2002**)
- "Transient Electronic Absorption of Vibrationally Excited CH_2I_2: Watching Energy Flow in Solution." Dieter Bingemann, Andrew M. King, and F. Fleming Crim, *J. Chem. Phys*. *113*, 5018 (**2000**)
- "Vibrational State Control of Bimolecular Reactions: Discovering and Directing the Chemistry." F. Fleming Crim, *Acc. Chem. Res*. *32*, 877 (**1999**)
- "Bond-Selected Chemistry: Vibrational State Control of Photodissociation and Bimolecular Reaction." F. Fleming Crim, *J. Phys. Chem*. *100*, 12725 (**1996**) (Centennial Issue)
- "Vibrationally Mediated Photodissociation: Exploring Excited State Surfaces and Controlling Decomposition Pathways." F. Fleming Crim, *Ann. Rev. Phys. Chem*. *44*, 397 (**1993**)

Selected Awards

- ACS Fellow, Inaugural Class, 2009
- Silver Medal and Centenary Lectureship, Royal Society of Chemistry, London, 2008
- Irving Langmuir Award in Chemical Physics, American Chemical Society, 2006
- Member, National Academy of Sciences, 2001
- Earl K. Plyler Prize for Molecular Spectroscopy, American Physical Society, 1998
- Fellow, American Academy of Arts and Sciences, 1998
- Fellow, Japan Society for the Promotion of Science, 1995
- Fellow, American Association for the Advancement of Science, 1995
- Max Planck Research Award (with Juergen Troe), 1993
- Upjohn Teaching Award, Department of Chemistry, University of Wisconsin, 1992
- Chancellor's Award for Excellence in Teaching, University of Wisconsin, 1991
- Fellow, American Physical Society, 1989

QIANG CUI



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Research Interests
Enzyme catalysis, macromolecular machines, ion transport, membrane remodeling, computational biophysics, electronic structure, bio-materials

Understanding complex molecular systems using experiments alone is difficult. Computer simulations based on physical and chemical principles can complement experiments and provide novel insights into the behavior of these systems at an atomic level. Our research targets the development and applications of state-of-the-art computational tools that explore the underlying mechanisms of complex molecular systems. Enzymes and other biological macromolecules, along with bio-inorganic ligands, are of primary interest.

Developing computational techniques and theoretical models for complex systems: A substantial amount of research activity in our group is geared toward developing novel computational techniques to make the simulation of complex biomolecular systems possible. One major area involves improving the efficiency and accuracy of combined quantum mechanical and classical mechanical methods, such that bond-breaking and bond-formation (chemistry!) can be studied in detail for realistic biological environments. Another area is related to the development of coarse-grained models for proteins and membranes, such that insights into the driving force of conformational transitions in proteins, protein/peptide aggregation and membrane remodeling processes (e.g., membrane fusion) can be obtained computationally. In these coarse-grained model developments, we explore both particle and continuum mechanics based models, and integration with not only atomistic simulations but also experimental observables such as thermodynamics data for complex solutions.

Simulation of complex molecular machines in bio-energy transduction: Biological systems involve many fascinating "molecular machines" that transform energy from one form to the other. Important examples are F1-ATP synthase and proton pumps, the former utilizes the proton motive force to synthesize ATP, while the latter employs the free energy of chemical reactions (e.g., oxygen reduction) to generate the proton motive force across the membrane. With the recent developments in crystallography, cyro-EM and single molecule spectroscopy, the working mechanisms of these nano-machines are being discovered. In order to understand the energy transduction process at an atomic level, our group is developing and applying state-of-the-art computational techniques to analyze the detailed mechanisms of several large molecular complexes including: myosin, DNA repair enzymes and the cytochrome c oxidase. Questions of major interest include: (i). What are the functionally relevant motions of these complexes? (ii). How are the chemical events (e.g., ATP binding and hydrolysis) coupled to the mechanical (e.g., conformational transition) process? (iii). How is the efficiency and vectorial nature of energy transduction regulated?

Understanding the catalytic mechanism of enzymes: Enzymes overshadow most chemical catalysts because they are extremely efficient and highly reaction-specific. Our group is developing and applying novel computational methods to explore the physical and chemical mechanisms behind the catalytic efficiency and specificity of several fascinating enzymatic systems. These include enzymes that exploit transition metal ions (phosphatases) and radical intermediates (DNA repair enzymes). In addition to their important biological implications, an underlying theme for these systems is catalysis modulated by protein motion. Our studies will not only provide insights into the fundamental working mechanisms of enzymes, but may also lead to the rational design of proteins/enzymes (e.g., metal ion activated transcription factors) with improved or even altered functions.

Interfacing biology and material science: The last decades have seen the thrilling developments in the science of materials at the nanometer scale. Nano-materials with tailored electrical, optical or mechanical properties have been synthesized. An exciting direction that has been recently recognized is that biomolecules can be used to provide control in organizing technologically important (non-biological) objects into functional nano-materials. The interaction between biomolecules and inorganic materials is fundamental to these applications, and we are using computational techniques to investigate this aspect. These studies are expected to play a guiding role in the design of novel hybrid materials, new sensors for biological molecules, as well as in understanding the fascinating process of biomineralization.

Selected Publications

- Large-scale motions in the adenylate kinase solution ensemble: coarse-grained simulations and comparison with solution X-ray scattering, M. Daily, L. Makowski, G. N. Phillips, Jr. and Q. Cui, *Chem. Phys.* In press (**2012**)
- A new coarse-grained force field for membrane-peptide simulations, Z. Wu, Q. Cui* and A. Yethiraj*, *J. Chem. Theo. Comp.* 11, 3793-3802 (**2011**)
- Proton storage site in bacteriorhodopsin: new insights from QM/MM simulations of microscopic pKa and infrared spectra, P. Goyal, N. Ghosh, P. Phatak, M. Clemens, M. Gauss, M. Elstner and Q. Cui, *J. Am. Chem. Soc*. 133, 14981-14997 (**2011**)
- "Electronic properties and desolvation penalties of metal ions plus protein electrostatics dictate the metal binding affinity and selectivity in the Copper efflux Regulator", L. Rao, Q. Cui and X. Xu, *J. Am. Chem. Soc*. 132, 18092 (**2010**)
- "Iron-Catalyzed Oxidation Intermediates Captured in A DNA Repair Monooxygenase", C. Yi, G. Jia, G. Hou, Q. Dai, G. Zheng, X. Jian, C. G. Yang, Q. Cui, and C. He, *Nature*, 468, 330-333 (**2010**)
- "An implicit solvent model for SCC-DFTB with Charge-Dependent Radii", G. Hou, X. Zhu and Q. Cui, *J. Chem. Theo. Comp*. 6, 2303-2314 (**2010**)
- "Evaluating Elastic Network Models of Crystalline Biological Molecules with Temperature Factors, Correlated Motions, and Diffuse X-Ray Scattering", D. Riccardi, Q. Cui and G. N. Phillips, Jr, *Biophys. J*. 99, 2616-2625 (**2010**)
- "Many low-barrier local motions cooperate to produce the adenylate kinase conformational transition", M. Daily, G. N. Phillips, Jr. and Q. Cui, *J. Mol. Biol*., 400, 618-631 (**2010**)
- "Curvature Generation and Pressure Profile in Membrane with lysolipids: Insights from coarse-grained simulations", J. Yoo and Q. Cui, *Biophys. J*. 97, 2267-2276 (**2009**)
- "A combined continuum mechanics and continuum electrostatics (CM/CE) computational framework for macromolecules: application to the salt concentration dependence of DNA bendability", L. Ma, Y. Tang, A. Yethiraj, X. Chen and Q. Cui, *Biophys. J.* 96, 3543-3554 (**2009**)
- "Amino acids with an intermolecular proton bond as the proton storage site in bacteriorhodopsin." P. Phatak, N. Ghosh, H. Yu, Q. Cui and M. Elstner, *Proc. Natl. Acad. Sci*. USA, *105*, 19672-19677 (**2008**)
- "Proton transfer in Carbonic Anhydrase is controlled by electrostatics rather than the orientation of the acceptor." D. Riccardi, P. Konig, H. Guo and Q. Cui, Biochem., *47*, 2369-2378 (**2008**)
- "Gating Mechanisms of Mechanosensitive Channels of Large Conductance Part II: Systematic Study of Conformational Transitions." Y. Tang, J. Yoo, A. Yethiraj, Q. Cui and X. Chen, *Biophys. J*., *95*, 581-596 (**2008**) (Cover)
- "Extensive conformational changes are required to turn on ATP hydrolysis in myosin." Y. Yang, H. Yu and Q. Cui, *J. Mol. Biol*., *381*, 1407-1420 (**2008**)
- "Mechanochemical coupling in myosin motor domain, II. Analysis of critical residues." H. Yu, L. Ma, Y. Yang and Q. Cui, *PLoS Comput. Biol., 3*, 0214 (**2007**)
- "The activation mechanism of a signaling protein at atomic resolution from advanced computations." L. Ma, Q. Cui, *J. Am. Chem. Soc*., *129*, 10261-10268 (**2007**)
- "Improving the Self-Consistent-Charge Tight-Binding-Density-Functional method for proton affinities and hydrogen bonding interactions." Y. Yang, H. Yu, D. York, Q. Cui, M. Elstner, *J. Phys. Chem. A*, *111*, 10861-10873 (**2007**)
- "Development of effective quantum mechanical/molecular mechanical (QM/MM) methods for complex biological processes." D. Riccardi, et al., M. Elstner, and Q. Cui, *J. Phys. Chem. B* Feature Article, *110*, 6458-6469 (**2006**)

Selected Awards

- H.I. Romnes Faculty Fellowship (2010)
- Alfred P. Sloan Research Fellowship (2004)
- CAREER Award, National Science Foundation (2004)
- Research Innovation Award, Research Corporation (2003)
- Lester Award, Emory University (1996)
- Osborn R. Quayle Award, Emory University (1995)

MARK EDIGER

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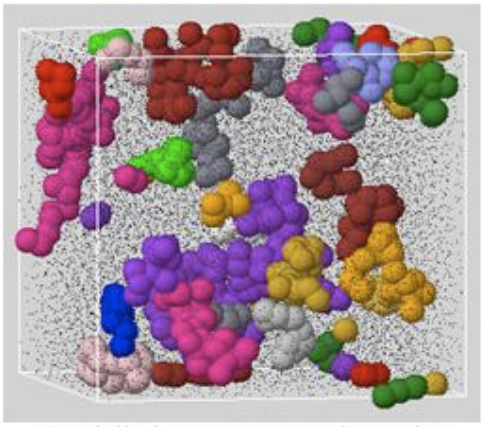
Research

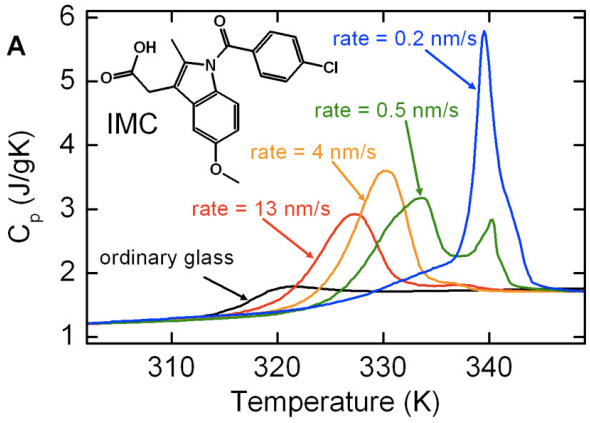
The properties of materials depend to a considerable extent upon the dynamics of the atoms and molecules that comprise them. Our research attempts to develop a molecular-level understanding of dynamics in polymeric materials and low molecular weight glass formers. What is it about the structure of the material and the potentials which govern the interaction of the atoms which makes dynamics fast or slow in a given system? How does the presence of a nearby interface alter the dynamics? How can we utilize interfacial mobility to prepare new materials?



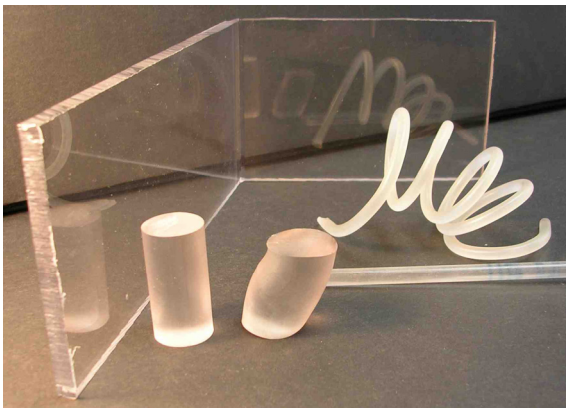
Spatially heterogeneous dynamics
Simulation by Glotzer group (U. of Michigan)

Supercooled liquids/diffusion in thin films. As the glass transition is approached, dynamics become increasingly spatially heterogeneous, i.e., the dynamics in one region of the sample may be orders of magnitude faster than the dynamics a few nanometers away. Our current work involves vapor deposition of thin films of deuterated and hydrogenous glass formers onto a cold substrate, followed by subsequent thermal cycling leading to inter-diffusion. SIMS experiments have extended the range of measured diffusion coefficients by 6 orders of magnitude and shown that diffusion near the glass transition is qualitatively different than in "normal" liquids. We have prepared some glasses that are so tightly packed that diffusion can only occur at the outer surfaces and the glass falls apart from the outside, qualitatively like a melting ice cube.

Creation of exceptionally stable glasses. Using vapor deposition, we have prepared what are very likely the most stable glasses ever made in a laboratory. In an afternoon, we can make glasses that would require at least 4000 years to prepare using any published methodology. Our glasses have useful material properties. For example, because they are more dense and energetically more stable than ordinary glasses, they resist crystallization and water uptake. These stable glasses may have immediate technological relevance, e.g., in organic electronics.



More fundamentally, as compared to ordinary glasses, our glasses are much deeper in the energy landscape that controls the thermodynamics and kinetics of an amorphous system. Our stable glasses are ideal for exploring fundamental issues such as the Kauzmann entropy crisis. Ongoing work focuses on characterization of stable glasses by nanocalorimetry, ellipsometry, and dielectric relaxation.



Dynamics during the deformation of polymer glasses and nanocomposites. Consider polycarbonate (the polymer used in safety glasses) as a representative polymer glass. When polycarbonate is stretched slightly (less than 1%) at room temperature, it responds like a very stiff, ideal spring. When the force is released, the material returns to its original state. At larger deformation, polycarbonate "yields" and can be pulled without further increase of the applied force. We wish to understand the microscopic mechanism that allows polymer glasses to “flow” (deform) under conditions where mobility is otherwise absent. We have built an apparatus to measure the deformation-induced mobility of polymer glasses and nanocomposites. We have observed large increases in mobility (more than a factor of 1000) during deformation over a range of temperatures (from Tg-10 K to Tg-30 K), with larger changes at lower temperatures. These results qualitatively explain the yield behavior of polymer glasses; deformation causes a glass to transform into a viscous liquid that can flow and dissipate large amounts of energy without breaking.

Selected Publications

- H-N. Lee, K. Paeng, S.F. Swallen, and M.D. Ediger, Direct measurement of molecular mobility in actively deformed polymer glasses, Science 323, 231-4 (2009).
- S.F. Swallen, K. Traynor, R.J. McMahon, M.D. Ediger, and T.E. Mates, Stable glass transformation to supercooled liquid via surface-initiated growth front, Phys. Rev. Lett. 102, 065503 (2009).
- K.J. Dawson, K.L. Kearns, L. Yu, W. Steffen, and M.D. Ediger, Physical vapor deposition as a route to hidden amorphous states, Proc. Nat’l. Acad. Sci. USA 106, 15165-170 (2009).
- R.A. Riggleman, H.-N. Lee, M.D. Ediger, and J.J. de Pablo, Heterogeneous dynamics during deformation of a polymer glass, Soft Matter 6, 287-91 (2010).
- K.L. Kearns, T. Still, G. Fytas, and M.D. Ediger, High modulus organic glasses prepared by physical vapor deposition, Adv. Mater. 22, 39-42 (2010).
- Y. Sun, H. Xi, M.D. Ediger, R. Richert, and L. Yu, Diffusion-Controlled and “Diffusionless” Crystal Growth Near the Glass Transition: Relation Between Liquid Dynamics and Growth Kinetics of Seven ROY Polymorphs, Journal of Chemical Physics 131, 074506 (2009).
- K.L. Kearns, M.D. Ediger, H. Huth, C. Schick, One micron length scale controls kinetic stability of low energy glasses, J. Phys. Chem. Lett. 1, 388-92 (2010).
- Y. Sun, L. Zhu, K. Kearns, M.D. Ediger, and L. Yu, Glasses crystallize rapidly at free surfaces by growing crystals upward, Proc. Nat’l. Acad. Sci. USA 108, 5990-5995 (2011).
- K. Paeng, S.F. Swallen, and M.D. Ediger, Direct measurement of molecular motion in freestanding polystyrene thin films, J. Am. Chem. Soc. 133, 8444-7 (2011).
- L. Zhu, C. Brian, S.F. Swallen, P. Straus, M.D. Ediger, and L. Yu, Surface diffusion of an organic glass, Phys. Rev. Lett. 106, 256103 (2011).

Selected Awards

- Fellow, American Association for the Advancement of Science (AAAS), 2010
- University Housing Honored Instructor Award (UW-Madison), 2008
- Kellett Mid-Career Faculty Researcher Award, UW-Madison, 2008
- National Science Foundation, Special Creativity Award, Division of Materials Research, 2006
- James W. Taylor Excellence in Teaching Award, 2003
- Helfaer Professor, 2001
- Fellow, American Physical Society, 1998

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Research

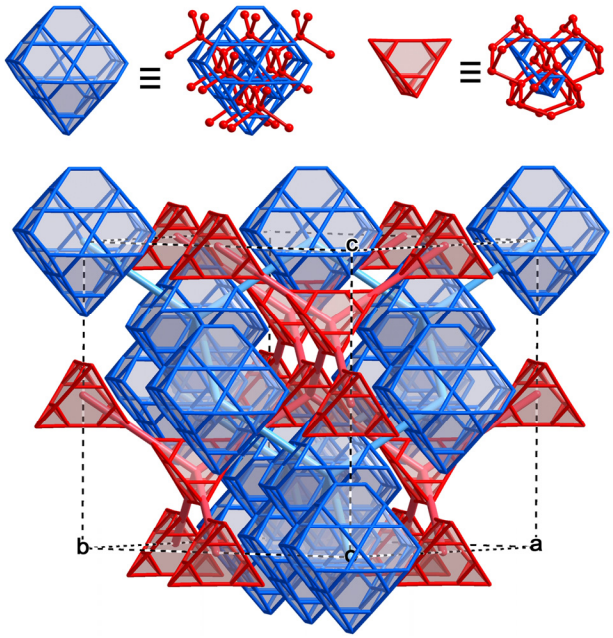
Solid state chemistry - Crystallography - Chemical Bonding Theory - Materials

The focus of our research is the elucidation of the chemical principles underlying the structures of the solid state compounds that form upon alloying metals together: inter-metallic compounds. In 1923, Linus Pauling's X-ray diffraction examinations of $NaCd_2$ revealed inter-metallics to be a realm of incredible complexity. While Na(s) and Cd(s) both form in crystal structures typical of metals (body-centered cubic and hexagonal close-packed lattices, respectively, each with just 2 atoms per unit cell), mixing them in a simple 1:2 ratio yields a giant 31 Å cubic unit cell, containing more than 1000 atoms (top, right). Extensive families of inter-metallic compounds with rivalling complexity have since been discovered, and as X-ray diffraction technology and crystallographic methods continue to advance, we continue to find new layers of intricacy in the structures of inter-metallics. Examples include the Nowotny chimney ladder phases, a family of compounds formed from the threading of helices of Sn, Ga, or other main group elements through the insides of transition metal helices; and the icosahedral quasi-crystals, such as $YbCd_6$, whose structures are perhaps most easily comprehended via models in 6D space.

Our aim is to reveal the chemical origins of these beautiful structures, with the ultimate goal of gaining some degree of synthetic control of this structural diversity. With this knowledge in hand, we hope to use the atomic structures of these phases as parameters for the optimization of a variety materials properties important for energy technology, including superconductivity, thermoelectricity, and catalysis.

In our research, we combine quantum mechanical calculations with solid-state synthesis and advanced crystallographic methods. Students working in our group can adjust the balance between these theoretical and experimental components to best suit their interests and goals. Below you may find each of these aspects of our work described in more detail.

Empirical observations and earlier quantum mechanical calculations have drawn intriguing connections between inter-metallic phases and molecular chemistry. Electron-counting rules, atomic size effects and electronegativity differences all appear to be at work in these compounds. We are exploring these connections, using electronic structure calculations--ranging from the orbital-based extended Hückel method to density functional calculations--to build theoretical schemes for understanding the chemical driving forces behind the structures of inter-metallics. To this end, we are seeking new ways of extracting chemical stories from the vast arrays of numbers resulting from electronic structures calculations.



Our theoretical efforts are currently directed toward exploring a common theme that has emerged over the course of calculations of several families of structures: complex structures are built at the electronic level from fragments or slabs of

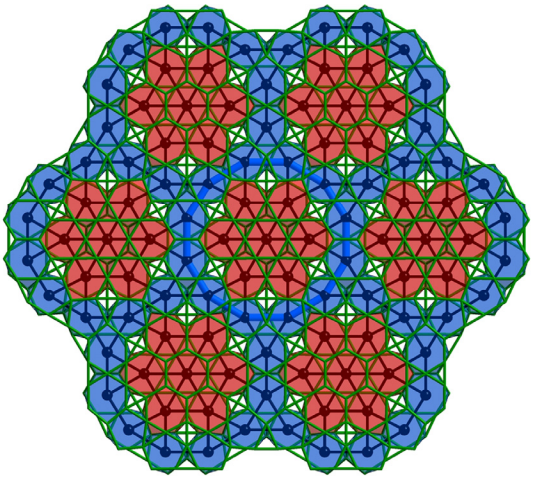
simpler ones fused together in new ways. The $NaCd_2$ structure is a shimmering example of this. Model calculations reveal it to consist of nanometer-sized blocks matching the much simpler structure of $MgCu_2$. $NaCd_2$ is, in essense, a crystal of nanometer-sized crystallites of the $MgCu_2$ structure (below). We are working now to developing this theme of complexity as a perturbation on simple periodicity into a predictive theoretical framework.

Structure solution and description of complex alloy phases

The synthesis and structure determination of new intermetallic structures provides both input for our theoretical calculations and mode of expression of our new conceptual understanding of their bonding. Synthesizing these beautiful structures follows standard routes of solid-state synthesis, often requiring little more than cooling of a molten mixture of metals.

Their structure determinations, on the other hand, pose exciting crystallographic problems: Superstructures, incommensurate modulations, twinning, and quasi-crystalline order are just some of the issues we face in revealing the atomic arrangements in these compounds. To face these challenges, we employ state-of-the-art crystallographic methods, such as super-space modeling, in which complex structures are viewed as cross-sections of simpler structures in four or more dimensions. One project in this area is the structure determination of dodecagonal quasi-crystals. A hint of the geometrical features within these structures is illustrated below with the approximant structure solved previously by Shoemaker and Shoemaker.

$Mn_{81.5}Si_{18.5}$
dodecagonal approximant



Optimization of materials properties through structural variation

In addition to their often breath-taking structures, inter-metallics are attractive for their materials properties. Complex magnetic ordering, superconductivity, thermoelectricity, and hydrogen storage are examples of the properties observed in this family of compounds. Unfortunately, the discovery of new materials exhibiting one of these phenomena is largely a matter of serendipity. This means that once one has exhausted the possibilities for optimizing an existing material through elemental substitutions and additives, one must start from scratch in the search for materials with improved properties. One long-term goal of our work is to examine how structural variations in inter-metallics may supplement compositional tuning. In mastering the synthetic control of geometry, we hope to introduce a new variable--the structure--in the optimization of materials properties. One of our first ventures into this will be attempts to introduce structural variations into the superconductor Nb_3Ge.

Selected Publications

- D. C. Fredrickson; S. Lidin; G. Venturini; B. Malaman; J. Christensen. "Origins of superstructure ordering and incommensurability in stuffed CoSn-type phases." *J. Am. Chem. Soc.* **2008**, *130*, 8195-8214.
- D. C. Fredrickson; S. Lee; R. Hoffmann. "Interpenetrating polar and non-polar sublattices in intermetallics: the NaCd2 structure" *Angew. Chem. Int. Ed.*, **2007**, *46*, 1958-1976.
- J. T. Schmidt; S. Lee; D. C. Fredrickson; M. Conrad; J. Sun; B. Harbrecht. "$Pd_{21.3}Cd_{78.7}$ and $Pd_{23.5}Cd_{76.5}$ Structures: Their long c axis and compositive crystals, chemical twinning and atomic site preferences" *Chem. Eur. J.*, **2007**, *13*, 1394-1410.
- P. M. Clark; S. Lee; D. C. Fredrickson. "Transition Metal AB3 Intermetallics: Structure Maps Based on Quantum Mechanical Stability." *J. Solid State Chem.*, **2005**, *178*, 1269-1283.
- D. C. Fredrickson; S. Lee; R. Hoffmann. "The Nowotny Chimney Ladder Phases: Whence The 14 Electron Rule?" *Inorg. Chem.*, **2004**, *43*, 6159-6167.

Selected Awards

- NSF Career Award, 2009
- National Science Foundation MPS Distinguished International Research Fellowship, 2005-2007
- Wentink Prize, Cornell University, 2005
- Hy J. Dauben Award in Organic Chemistry, University of Washington, 1999

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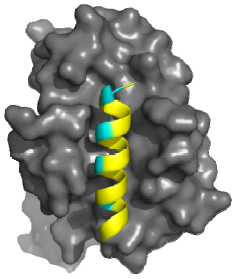
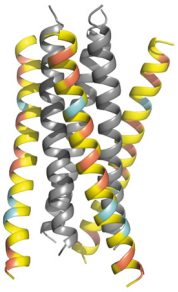
Research

We focus on the design, synthesis and evaluation of new types of molecules intended to display interesting structures and functions; many of our goals focus on targeted biological activities. In addition, we seek to understand how proteins, the most diverse class of biomolecules, perform their natural functions. Our efforts require a wide range of experimental tools, including asymmetric organic synthesis, high-resolution NMR and crystallographic analysis of molecular structure, protein expression and biochemical assays. Many projects involve extensive collaboration with other laboratories at UW-Madison and around the world.

***Foldamers**:*
Nature teaches us that folded oligomers can be very powerful molecular machines, as exemplified by proteins and nucleic acids. "Foldamers" are unnatural oligomers that adopt compact, specific and predictable shapes. The foldamer approach represents a new strategy for designing molecules that display specific functions. We are interested in developing foldamers that mimic the shapes of natural peptides or proteins, for biomedical applications, and in foldamers that adopt unprecedented shapes. We have learned a great deal about oligomers of beta-amino acids ("beta-peptides") and oligomers containing both alpha- and beta-amino acid residues ("alpha/beta-peptides"), which makes these systems suitable for goal-oriented design efforts. We have shown that properly designed helix-forming foldamers can disrupt protein-protein interactions associated with viral infection or cancer, and we are now targeting many other interactions of biomedical interest. Long-term goals include generating foldamers with specific tertiary folding patterns and catalytic activities.



Crystal structure of a foldamer bound to Bcl-x_L (Boersma et al. *J. Am. Chem. Soc.* 134:315 (2012))



Crystal structure of an anti-HIV foldamer co-assembled with a fragment of viral entry protein gp41 (Horne et al. *Proc. Natl. Acad. Sci.* 105.14751(2009))

"Evaluation of Diverse α/β Backbone Patterns for Functional α-Helix Mimicry: Analogues of the Bim BH3 Domain," M. D. Boersma, H. S. Haase, K. J. Peterson-Kaufman, E. F. Lee, O. B. Clarke, P. M. Colman, B. J. Smith, W. S. Horne, W. D. Fairlie and S. H. Gellman *J. Am. Chem. Soc.* **2012**, *134*, 315.

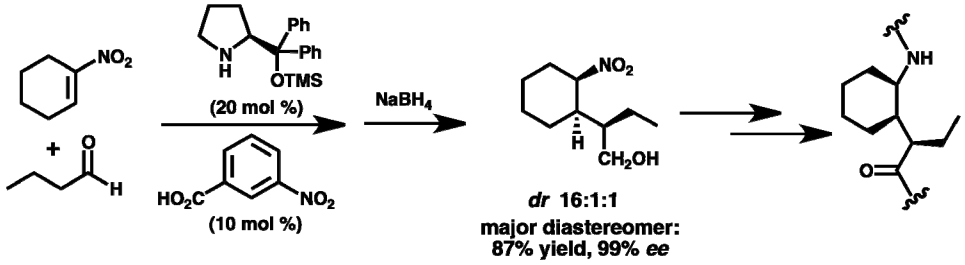
"Broad Distribution of Energetically Important Contacts Across an Extended Protein Interface," L. M. Johnson, W. S. Horne and S. H. Gellman *J. Am. Chem. Soc.* **2011**, *133*, 10038.

"Structural and Biological Mimicry of Protein Surface Recognition by α/β-Peptide Foldamers," W. S. Horne, L. M. Johnson, T. J. Ketas, P. J. Klasse, M. Lu, J. P. Moore and S. H. Gellman *Proc. Natl. Acad. Sci. USA* **2009**, *106*, 14751.

"A Rationally Designed Aldolase Foldamer," M. M. Müller, M. A. Windsor, W. C. Pomerantz, S. H. Gellman and D. Hilvert *Angew. Chem. Int. Ed.* **2009**, *48*, 922.

"Foldamers with Heterogeneous Backbones," W. S. Horne and S. H. Gellman *Acc. Chem. Res.* **2008**, *41*, 1399.

Our foldamer research includes a substantial synthetic effort. Currently we seek efficient asymmetric routes to gamma-amino acid building blocks; one recent success is illustrated below. A number of challenging targets remain.



"Structural Mimicry of the α-Helix in Aqueous Solution with an Isoatomic α/β/γ-Peptide Backbone," T. Sawada and S. H. Gellman *J. Am. Chem. Soc.* **2011**, *133*, 7336.

"Stereospecific Synthesis of Conformationally Constrained γ-Amino Acids: New Foldamer Building Blocks that Support Helical Secondary Structure," L. Guo, Y. Chi, A. Almeida, I. A. Guzei, B. Parker and S. H. Gellman *J. Am. Chem. Soc.* **2009**, *131*, 16018.

New tools for studying the origins of protein folding preferences

We want to understand how the sequence of a protein determines the folding pattern adopted by the polypeptide chain. Our approaches to this widely-studied area involve the development and application of distinctive chemical tools. We have recently developed a new method for probing protein conformational stability, "backbone thioester exchange," which is proving useful for studying helix-helix interactions. In addition, we have developed unique tools for studying parallel beta-sheet structure.

"Parallel β-Sheet Secondary Structure is Stabilized and Terminated by Inter-Strand Disulfide Crosslinking," A. M. Almeida, R. Li and S. H. Gellman *J. Am. Chem. Soc.* **2012**, *134*, 75.

"Impact of Strand Length on the Stability of Parallel β-Sheet Secondary Structure," F. Freire, A. M. Almeida, J. D. Fisk, J. D. Steinkruger and S. H. Gellman *Angew. Chem. Int. Ed.* **2011***, 50*, 8735.

"Side-Chain Pairing Preferences in the Parallel Coiled-Coil Dimer Motif: Insight on Ion-Pairing Between Core and Flanking Sites," J. D. Steinkruger, D. N. Woolfson and S. H. Gellman *J. Am. Chem. Soc.* **2010**, *132*, 7586.

Design of biologically active polymers

We are exploring materials generated via ring-opening polymerization of beta-lactams. The resulting poly-beta-peptides (also known as nylon-3 polymers) have a protein-like backbone, which should make them biocompatible. We have recently shown that co-polymers in this class can mimic the selective antibacterial activity of natural peptide antibiotics. We are currently exploring polymers in this class as antimalarial agents, antifungal agents, lung surfactant mimics and scaffolds for tissue engineering. This work is highly collaborative.

"C-Terminal Functionalization of Nylon-3 Polymers: Effects of C-Terminal Groups on Antibacterial and Hemolytic Activities," J. Zhang, M. J. Markiewicz, B. P. Mowery, B. Weisblum, S. S. Stahl and S. H. Gellman *Biomacromolecules* **2012**, in press.

"Biophysical Mimicry of Lung Surfactant Protein B by Random Nylon-3 Copolymers," M. T. Dohm, B. P. Mowery, A. M. Czyzewski, S. S. Stahl, S. H. Gellman and A. E. Barron *J. Am. Chem. Soc.* **2010**, *132*, 7957.

"Nylon-3 Co-Polymers that Generate Cell-Adhesive Surfaces Identified by Library Screening," M.-r. Lee, S. S. Stahl, S. H. Gellman and K. S. Masters *J. Am. Chem. Soc.* **2009**, *131*, 16779.

"Structure-Activity Relationships Among Random Nylon-3 Copolymers that Mimic Antibacterial Host-Defense Peptides," B. M. Mowery, A. M. Lindner, B. Weisblum, S. S. Stahl and S. H. Gellman *J. Am. Chem. Soc.* **2009**, *131*, 9735.

Selected Awards

- Member, American Academy of Arts & Sciences, 2010
- Phi Beta Kappa Teaching Award (University of Wisconsin), 2008
- Ralph F. Hirschmann Award in Peptide Chemistry (American Chemical Society), 2007
- Vincent du Vigneaud Award (American Peptide Society), 2006

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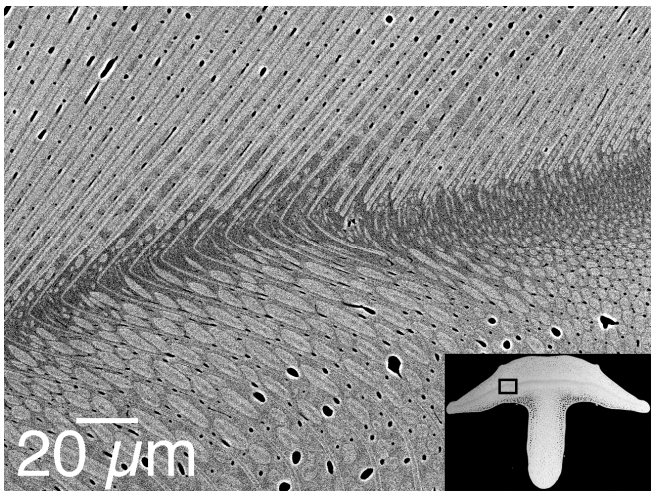
Research Field: Biomineralization

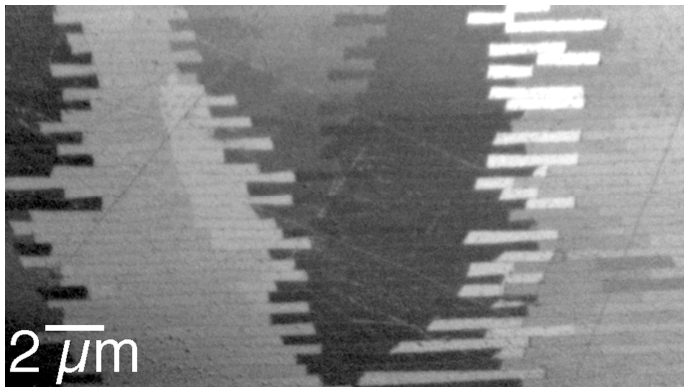
Sea urchin teeth

The teeth of sea urchins are among the most complicated structures in the natural world. They can grind rocks, and self-sharpen with use. We studied these fascinating biominerals, revealed their complex crystal arrangement[1], discovered how they co-orient all their nanocrystals[2], and how they self-sharpen with use[3]. The inset in the image on the left shows the cross section of one tooth, which looks a bit like a mushroom. In the higher magnification image, you can appreciate the details of imbricated minerals: the elongated structures are plates (the rounded ones are fibers) and these both are entirely made of calcite. The space between fibers and plates is completely filled by high-Mg calcite nanoparticles 10 nm in size.



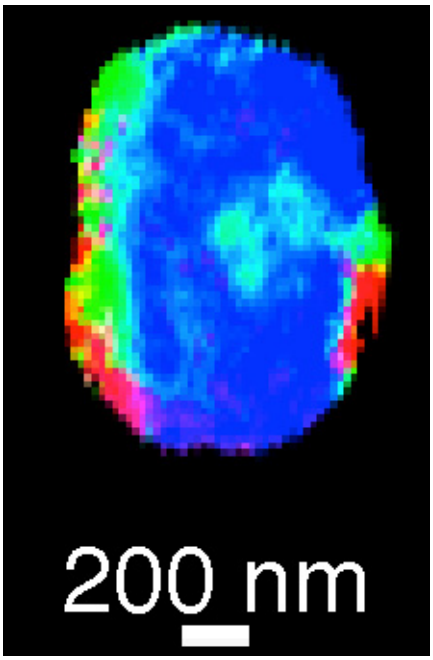
Mollusk shell nacre

Nacre, or mother-of-pearl, is the layer at the inner surface of some mollusk shells and pearls (see image on the right). It has a fracture resistance 3000x greater than aragonite, the mineral of which it is composed. The toughening effect is due to well-defined nanolayers of organics at the interfaces between micro-tablets of aragonite.



Nacre formation is poorly understood at the molecular level, and this piqued our interest in this material, joining the interdisciplinary community of scientists around the world tackling this problem. It is our opinion that the key to nacre formation mechanisms lies at the organic-mineral interface. Understanding the role of that interface is thus pivotal to the development of new biomimetic materials. We desire to understand the fundamental mechanisms leading to the formation of these beautiful, extraordinarily efficient, self-assembling natural structures. We recently introduced a new imaging modality, termed Polarization-dependent Imaging Contrast (PIC) mapping, which is based onx-ray linear dichroism[4-8]. PIC-mapping revealed that immediately adjacent stacks of co-oriented tablets are finite in height, have very different crystallographic c-axis orientations, and consequently the nacre growth direction cannot be identified with the c-axis. In the PIC-map displayed here 400-nm thick nacre tablets show dramatically different gray levels due to their differing c-axis orientations. The appearance of the columns also inspired new models for the formation mechanism of nacre [6].

Amorphous precursor in sea urchin spicules



One of the most fascinating aspects of calcite biominerals is their intricate and curved morphology, quite different from the rhombohedral crystal habit of geologic calcite. These morphologies, as well as space-filling and greater resistance to fracture, are achieved via amorphous precursor mineral phases [9]. We have shown that in sea urchin larval spicules two distinct phase transitions occur, 1→2 and 2→3 [10]. Both transitions are regulated by inhibiting proteins, which introduce activation barriers between states otherwise spontaneously transforming because they are energetically downhill [11].

Left: Cross-section of a spicule, freshly extracted from a 48-h sea urchin embryo, caught in the act of transforming from amorphous $CaCO_3$ (R,G) to crystalline calcite (B), and imaged with XANES-PEEM spectromicroscopy. Notice the crystalline phase at the center, and the amorphous phases at the left and right edges of the spicule. Each pixel is 20 nm. Data from ref.[11].

Selected Publications

(1) Ma, Y. R.; Aichmayer, B.; Paris, O.; Fratzl, P.; Meibom, A.; Metzler, R. A.; Politi, Y.; Addadi, L.; Gilbert, P. U. P. A.; Weiner, S. *Procs Natl Acad Sci USA* **2009**, *106*, 6048.

(2) Killian, C. E.; Metzler, R. A.; Gong, Y. T.; Olson, I. C.; Aizenberg, J.; Politi, Y.; Addadi, L.; Weiner, S.; Wilt, F. H.; Scholl, A.; Young, A.; Coppersmith, S. N.; Gilbert, P. U. P. A. *J Am Chem Soc* **2009**, *131*, 18404.

(3) Killian, C. E.; Metzler, R. A.; Gong, Y. U. T.; Churchill, T. H.; Olson, I. C.; Trubetskoy, V.; Christensen, M. B.; Fournelle, J. H.; De Carlo, F.; Cohen, S.; Mahamid, J.; Wilt, F. H.; Scholl, A.; Young, A.; Doran, A.; Coppersmith, S. N.; Gilbert, P. U. P. A. *Adv Funct Mater* **2011**, *21*, 682.

(4) Metzler, R. A.; Abrecht, M.; Olabisi, R. M.; Ariosa, D.; Johnson, C. J.; Frazer, B. H.; Coppersmith, S. N.; Gilbert, P. *Phys. Rev. Lett.* **2007**, *98*, 268102.

(5) Metzler, R. A.; Zhou, D.; Abrecht, M.; Chiou, J. W.; Guo, J. H.; Ariosa, D.; Coppersmith, S. N.; Gilbert, P. U. P. A. *Phys Rev B* **2008**, *77*, 064110.

(6) Gilbert, P. U. P. A.; Metzler, R.; Zhou, D.; Scholl, A.; Doran, A.; Young, A.; Kunz, M.; Tamura, N.; Coppersmith, S. *J. Am. Chem. Soc.* **2008**, *130*, 17519.

(7) Gilbert, P. U. P. A.; Young, A.; Coppersmith, S. N. *Proc Natl Acad Sci USA* **2011**, *108*, 11350.

(8) Olson, I. C.; Gilbert, P. U. P. A. *submitted* **2012**.

(9) Politi, Y.; Metzler, R. A.; Abrecht, M.; Gilbert, B.; Wilt, F. H.; Sagi, I.; Addadi, L.; Weiner, S.; Gilbert, P. U. P. A. *Procs Natl Acad Sci USA* **2008**, *105*, 17362.

(10) Radha, A. V.; Forbes, T. Z.; Killian, C. E.; Gilbert, P. U. P. A.; Navrotsky, A. *Procs Natl Acad Sci USA* **2010**, *107*, 16438.

(11) Gong, Y. U. T.; Killian, C. E.; Olson, I. C.; Appathurai, N. P.; Amasino, A. L.; Holt, L. J.; Wilt, F. H.; Gilbert, P. U. P. A. *under review* **2012**.

Awards

- Chancellor's Distinguished Teaching Award, UW-Madison (6 awards/year, selected among ~2000 professors at UW), January 2011, Award ceremony April 27th, 2011.
- Fellow of the American Physical Society, Division of Condensed Matter Physics (DCMP), November 2010.
- Elected Vice-Chair, Chair-Elect, Chair, Pst-Chair of the Division of Biological Physics (DBIO) of the American Physical Society (APS), 2010-2014.
- American Competitiveness and Innovation (ACI) fellowship 2008-2010, nominated (without Gilbert knowing about it) by the NSF program officer David Brant, and awarded by the NSF-Division of Materials Research.
- George and Pamela Hamel Faculty Fellow, UW-Madison, 2008-2012.
- Vilas Associate Award, UW-Madison, 2006-2007.
- H. I. Romnes Award, UW-Madison, 2002.
- Cavaliere della Repubblica (Knight of the Italian Republic), appointed by President Carlo Azeglio Ciampi, 2000.
- Gert Rempfer "New Millennium Guiding Light Award" 2000.

RANDALL GOLDSMITH

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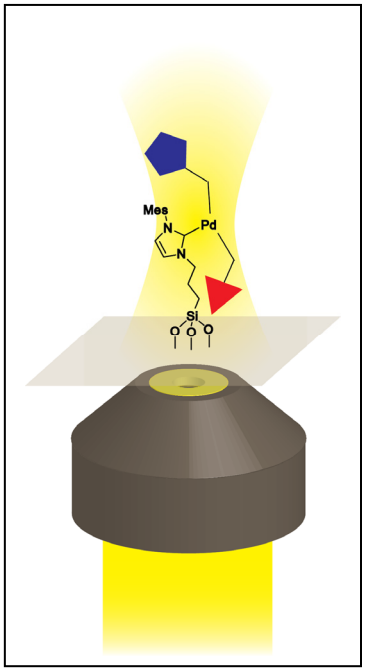
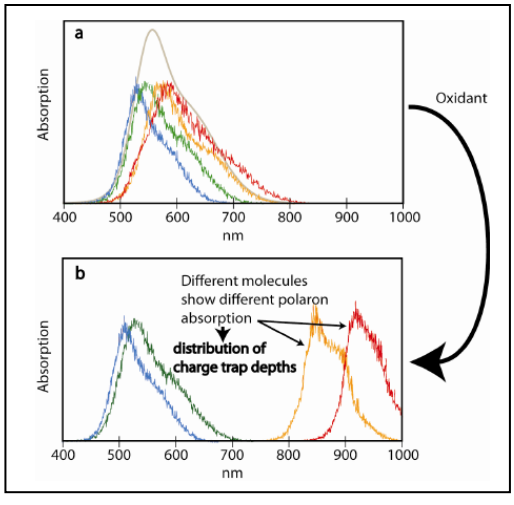
Research

Performing measurements on individual molecules, single-molecule spectroscopy, opens a profoundly informative window into the behavior and properties of chemical systems by revealing heterogeneity in molecular properties and critical unsynchronized dynamics that are obscured in ensemble measurements. We aim to develop new single-molecule techniques and apply them to outstanding and socially relevant problems in chemistry, materials science, and biophysics. Research targets will include novel mechanistic studies of homogeneous catalysts, investigation of electronic properties of conjugated polymers relevant for organic photovoltaic devices, and analysis of protein conformational dynamics. Our efforts will employ creative combinations of fluorescence microscopy, nanophotonics, and chemical synthesis to find the best means of studying our chemical systems of interest.



Watching individual homogeneous catalysts in action. Homogeneous catalysis relies on an intricate series of bond forming and breaking reactions. Production of more active, selective, and easily recyclable (ie., "greener") catalysts is necessary for the availability of next generation drugs, fuels, and materials. Mechanistic study informs the design of better catalysts, and single-molecule spectroscopy is a powerful tool for mechanistic study because it allows unsynchronized or rare processes to be directly observed.

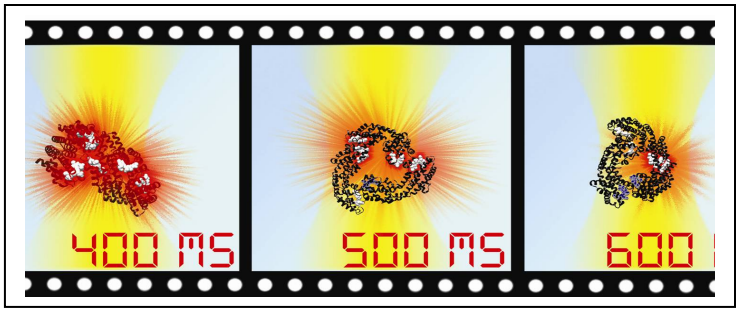
We will look for dynamic and static heterogeneity in the catalyst population, behavior that has been previously seen in enzymes. These dynamics likely come from changes in coordination environment and are unsynchronized across the catalyst population and many cannot be observed in ensemble-averaged experiments. We will search for this heterogeneity, quantify transition kinetics, and vary ligand and substrate properties to establish structure-behavior relationships. The goal is to build a detailed understanding of the microscopic events in homogeneous catalysis through revolutionary new observations of individual catalysts in operation. We will observe reaction intermediates that have so far been only speculated upon or indirectly inferred and quantify the lifetimes of those intermediates in active catalysts, not analogs.



Mapping the energy landscape in organic photovoltaics Optical characterization of single molecules is nearly universally attained via fluorescence. However,

fluorescence has many disadvantages, including the reliance upon covalently bound dye molecules with limited photostability and the loss of information about the fascinating molecular photophysics that precede fluorescence. These deficiencies are particularly hindering in the study of organic materials for molecular electronics and organic photovoltaics, where a molecular assembly optimized for functional charge transfer will generally not be fluorescent.
We will fabricate and develop nanophotonic tools to characterize the energy landscape of organic electronic materials, ultimately pushing toward single-molecule resolution. These tools will be employed to characterize structural and electronic heterogeneity in individual organic chromophores and charge transporting polymers to learn how conformation affects wasteful charge trapping in organic photovoltaics. By varying polymer globule size and composition, electronic heterogeneity can be studied at the many important length scales of a functioning organic photovoltaic device.

Conformational dynamics of proteins in crowded environments In their cellular environment, proteins must perform their function in the presence of dissolved macromolecules exceeding 200g/L, a condition that is ignored in most biochemical assays though it may have significant effects on protein dynamics and activity. Molecular crowding has been shown to increase enzyme-substrate binding efficiencies, affect drug pharmacological response, and increase the rate of misfolding of prion proteins and the rate of aggregation of proteins implicated in Alzheimer's disease. However, a protein's individual folding trajectory, which contains crucial information about its energy landscape that is lost in ensemble experiments, has not been studied in the presence of crowding agents.



We will examine protein folding and enzyme activity at the single-molecule level under crowded conditions. Critical to this approach is avoiding surface-attachment, as this practice has been shown to alter protein folding dynamics. We can avoid this difficulty with a specialized microfluidic device that uses electroosmotic flows to cancel Brownian motion of single fluorescent molecules in solution.

Selected Publications

- Goldsmith, R.H., Tabares L.C., Kostrcz, D., Dennison, C., Aartsma, T.J., Canters, G.W., Moerner, W.E. "Redox cycling and kinetic analysis of single molecules of solution-phase Nitrite Reductase ," *Proc. Natl. Acad. Sci. U. S. A.,* 2011, *108*, 17269.
- Goldsmith, R.H., and Moerner, W.E. "Watching conformational- and photodynamics of single fluorescent proteins in *solution", Nature Chem., 2010, 2, 179. Featured on cover, Highlighted in Nature Chemistry, News and Views, "Best of First Year" list, Nature Chemistry*
- *Goldsmith, R.H.; Vura-Weis,* J.A.; Scott, A.M.; Borkar, S.; Sen, A.; Ratner, M.A.; Wasielewski, M.R. "Unexpectedly similar charge transfer rates through benzo-annulated bicyclo[2.2.2]octanes," *J. Am. Chem. Soc.*, 2008, 130, 7659.
- Goldsmith, R.H.; Sinks, L.E.; Kelley, R.F.; Betzen, L.J.; Liu, W.H.; Weiss, E.A.; Ratner, M.A.; Wasielewski, M.R. "Wire-like charge transport at near constant bridge energy through fluorene oligomers," *Proc. Natl. Acad. Sci. U. S. A.,* 2005, *102*, 3540.

Awards

- ACS PHYS section Postdoctoral Research Award 2010
- Dan David Prize Scholarship in Materials Science 2006
- Link Energy Foundation Graduate Fellowship 2005
- Donald E. Smith Award for Excellence in Advanced Teaching 2004

PADMA GOPALAN

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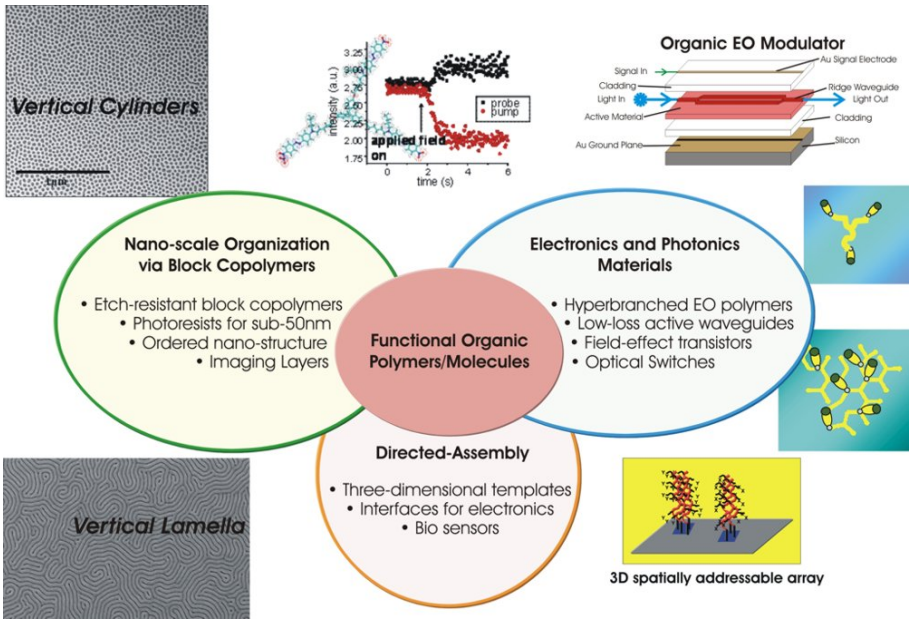
Research

Our group research interests involve the molecular design, synthesis, and characterization of novel functional organic/polymeric materials directed towards electro-optic, photonic and biological applications. Efforts are targeted towards developing versatile synthetic strategies, which would enable the control of nano- functionality, structure and property. Our current research focus is in three major areas: new synthetic strategies towards organic photonic and electronic materials, self-assembly of rod-coil block copolymers with conducting/liquid crystalline segments and directed assembly of biological, mesogenic and nonmesogenic molecules using polymeric templates.

Our goal is to design novel materials by using the advances made in polymer chemistry and organic chemistry for photonic and biological applications. One such example is elecro-optic materials for high - speed modulators. Compared to lithium niobate based modulators, organic materials have advantages in terms of fast response time, low dielectric constant and low dispersion in index of refraction from dc to optical frequencies hence minimizing the velocity mismatch. Our efforts are too design new materials with most of the desirable properties using elegant chemistry and demonstrate their viability in photonic devices. Fundamental understanding of the organic-inorganic interface and tailoring these interfaces is a critical component towards successful design of such materials.



The second area of emphasis is self-assembly and directed-assembly of block copolymers. Self-assembly of block copolymers can result in organization on length scales ranging from few nanometers to micron size scale. Our interest is in designing block copolymers with nanometer size self-assembled structures. These block copolymers are those containing functional units such as liquid crystalline or conducting domains. Understanding the factors governing the phase separation process in these complex rod-coil block copolymers and predicting the morphologies is the key motivation in this area. Directed-assembly of various organic, inorganic and biological molecules using templates of functional polymeric brushes is another area of interest. In the last few years the area of surface anchored polymeric brushes has grown tremendously. Polymeric brushes provide a uniform, high surface density of the desired functionality, which makes them attractive for biosensor applications and as interfaces to impart specific properties such as biocompatibility.

Selected Publications

- "Synthesis and Characterization of Silicon-containing Block Copolymers from Nitroxide-mediated Living Free Radical Polymerization" Fukukawa, K.; Zhu, L.; **Gopalan**, P.; Ueda, M.; Yang, S.; *Macromolecules*, 38(2),**2005**,263.

- Star-Shaped Azo-Based Dipolar Chromophores: Design, Synthesis, Matrix Compatibility, and Electro-optic Activity. **Gopalan, P.**; Katz, H. E.; McGee., D. J.; Erben, C.; Zielinski, T.; Bousquet, D.; Muller, D.; Grazul, J.; and Olsson, Y.; *JACS* **2004**, 126, 1741.

- Mesophase Transitions, Surface Functionalizaiton, and Growth Mechanism of Semiconducting 6PTTP6 Films from Solution Katz, H. E.; Siegrist, T.; Lefenfeld, M.; **Gopalan, P.**; Mushrush, M.; Ocko, B.; Gang, O.; Jisrawl, N.; *J. Phys. Chem. B.*; **2004**, 108(25), 8567-8571.

- Synthesis and Characterization of Silicon-Containing Block Copolymers from Nitroxide-Mediated Living Free Radical Polymerization Fukukawa, K.; Zhu, L.; **Gopalan, P.**; Ueda, M.; Yang, S.; *Macromolecules*, **2005**, 38(2), 263-270.

- Liquid Crystalline Rod-Coil Block Copolymers by Stable Free Radical Polymerization: Synthesis, morphology, and rheology. **Gopalan, P.**; Yuanming Zhang, Xuefa Li, Christopher K. Ober, Ulrich Weisner, Ober, C. K.; *Macromolecules*, **2003**, 36, 3357.

- Broadband Modulation of Light Using an Electro-optic Polymer. Lee, M.; Katz, H. E.; Erben, C.; Gill, D. M.; **Gopalan, P.**; Heber, J. D.; Mc Gee, D. J.; *Science*, **2002**, 298, 1401.

- Fluorinated Mesogen Jacketed Liquid Crystalline Polymers as Low Surface Energy Materials. **Gopalan, P.;** Andruzzi, L.; Li, X.; *Macromolecular Chem & Physics*, **2002**, 203(10-11) 1573.

- Synthesis, Characterization and Redox Reactivity of Novel Quinone Containing Polymers. Takada, K.; **Gopalan, P.**; Ober, C. K.; Abruna, H. D.; *Chemistry of Materials*, **2001**, 13(9), 2928.

- Highly Reactive 2,5-disubstituted Styrenic Liquid Crystalline Monomer Under SFRP Conditions. **Gopalan, P.**; Li, X.; Ober, C. K.; *Macromolecules*, **2001**, 34, 5120.

Awards

- NSF CAREER AWARD 2005

- Member of American Chemical Society, Materials Research Society

ROBERT J. HAMERS

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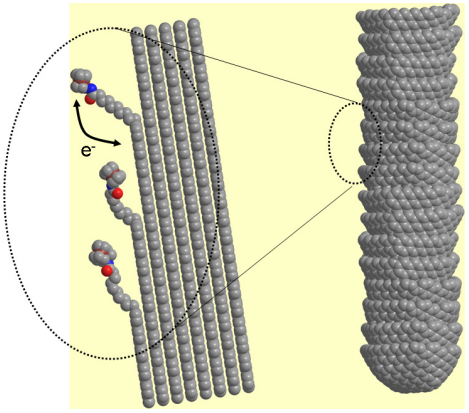
Research

Research in the Hamers group lies at the intersection of chemistry, materials science, and nanotechnology. We are interested in developing and exploiting new types of surface chemistry to create and improve next-generation devices for renewable energy, and are interested in understanding the potential environmental and health effects associated with nanomaterials. Our work spans the range from very fundamental, experimental and computational studies of surfaces, all the way to using surface chemistry to control the formation and properties of devices such as next-generation solar cells, photocatalysts, batteries, and environmental safety of nanomaterials. The group is multidisciplinary and highly collaborative.

Our interest in surfaces is driven by the fact that the most important chemical and physical phenomena are often controlled by surfaces and/or interfaces between materials. This is particularly true with nanoscale materials, where a substantial fraction of the total atoms are located at their surfaces. Surfaces have their own, very unique chemistry because the atoms are typically in very unusually, highly asymmetric geometries. Most of our current work addresses surface chemistry issues relevant to renewable energy and/or nanotechnology and couples state-of-the-art surface chemistry with the electrochemical and/or photo-electrochemical properties of materials.

Interface Chemistry for Renewable Energy



This is the largest area of research in the group, with several complementary projects. Renewable energy technologies such as photovoltaic energy conversion, photocatalysis, and electrochemical energy storage all hinge on being able to control the transfer of electrons across interfaces between different materials. One major effort is to develop new "ultra-stable" surface chemistries to control chemical selectivity and electron-transfer properties at interfaces. Carbon-based materials (diamond, carbon nanofibers) and metal oxide semiconductors (TiO_2, ZnO, SnO_2) play especially important roles because of their intrinsically high stability and the fact that their semiconducting properties facilitate charge separation. By coupling these materials to molecules that can harvest light or catalyze reactions, we aim to develop "smart" materials with a high degree of functionality. In our own labs and through collaborations, we are investigating the dynamics of electron-transfer processes on time scales from seconds to femtoseconds. An expanding area of interest is the use of electrochemical and photochemical methods to produce energy-rich fuels from inexpensive and/or starting materials such as CO_2. All of these projects hinge on a central theme of understanding how surface chemistry impacts charge-transfer processes at surfaces.

Electrochemical Energy Storage: . Because solar and wind power are highly variable, renewable energy can only be truly effective if we can develop new and improved methods for *storing* energy. Increased interest in hybrid and all-electric vehicles as well as increasing reliance on portable electronics are driving a need for improved energy storage on all scales, from the iPod nano to the entire electrical power grid. We are engaged in research investigating the materials science and interface chemistry associated with next-generation lithium-ion batteries. Current-generation batteries are plagued by safety problems associated with the use of highly flammable organic electrolytes. One aspect of our research is to develop safer batteries using new organosilicon-based electrolytes. A second aspect involves research on new anode and cathode materials that have the potential to store nearly 10 times as much

energy per unit weight as today's batteries. These projects involve a complex interplay of materials science, interface chemistry, and electrochemistry, and are largely performed in collaboration with industrial partners, including Silatronix, Inc. (co-founded by RJH in 2007) and Dow Chemical.

Environmental Impact of Nanomaterials: The explosion of interest in nanotechnology also raises questions about the possible environmental safety and health issues surrounding the potential release of engineered nanoparticles into the environment. Nanoparticles are often stabilized by surface ligands; these ligands strongly impact their stability and bioavailability in the environment. As part of a multidisciplinary collaboration with several groups we are investigating how the surface chemistry of nanoparticles affects bioavailability and toxicology. Even nominally non-toxic materials such as TiO_2 can be highly toxic in nanoscale form through photocatalytic effects, such as generation of superoxide (O_2^{-}) ions and hydroxyl radicals from water in the presence of sunlight. In this collaboration, zebrafish are used as a model system because in the embryonic stage they are transparent, allowing one to directly view how nanoparticles influence embryonic organ development; transgenic fish and other state-of-the-art molecular biology methods are being used to achieve a molecular understanding of nanoparticle toxicity.

Our group spans a range from very fundamental studies of surface chemical reactions and reaction mechanisms, to the practical applications of these materials to important problems in renewable energy and biomaterials. The work is interdisciplinary in scope, and students from all areas of chemistry, materials science and related fields are welcome.

Selected Publications (252 publications total)

- Allison C. Cardiel, Michelle C. Benson, Lee M. Bishop, Kacie M. Louis, Joseph C. Yeager, Yizheng Tan, and Robert J. Hamers, Chemically directed assembly of photoactive metal oxide nanoparticle heterojunctions via the copper-catalyzed azide-alkyne cycloaddition "click" Reaction", ACS Nano, **2012** (accepted)
- Lee M. Bishop, Joseph C. Yeager, Xin Chen, Jamie Wheel,er Marco Torelli, Michelle C. Benson, Stephen D. Burke, Joel Pedersen, and Robert J. Hamers, "A citric acid-derived ligand for modular functionalization of metal oxide surfaces via "click" chemistry", Langmuir, **2012**.
- Michelle C. Benson, Rose E. Ruther, James B. Gerken, Matthew L. Rigsby, Lee M. Bishop, Yizheng Tan, Shannon S. Stahl, and Robert J. Hamers, "modular "click" chemistry for electrochemically and photoelectrochemically active molecular interfaces to tin oxide surfaces", **2011**, ACS Applied Materials and Interfaces, 3, 3110-3119.
- Ofek Bar-Ilan, Kacie M. Louis, Sarah P. Yang, Joel A. Pedersen, Robert J. Hamers, Richard E. Peterson, and Warren Heideman, "Titanium dioxide nanoparticles produce phototoxicity in the developing zebrafish", Nanotoxicology, accepted **2011**.
- Rose E. Ruther, Matthew L. Rigsby, James B. Gerken, Stephanie R. Hogendoorn, Elizabeth C. Landis, Shannon S. Stahl*, and Robert J. Hamers , "Highly stable redox-active molecular layers by covalent grafting to conductive diamond", *Journal of the American Chemical Society*, **2011**, .
- Jixin Chen, Ryan Franking, Rose E. Ruther, Yizheng Tan, Xueying He, Stephanie R. Hogendoorn, and Robert J. Hamers, "Formation of molecular monolayers on TiO_2 surfaces: a surface analog of the Williamson Ether Synthesis", Langmuir **2011**, 27, 6879-6889.
- Lingzhi Zhang, Leslie J. Lyons, Jocelyn Newhouse, Zhengcheng Zhang, Megal Straughan, Zonghai Chen, Khalil Amine, Robert J. Hamers, and Robert West, "Synthesis and characterization of alkylsilane ethers with oligo(ethylene oxide) substituents for safe electrolytes in lithium ion batteries", *J. Materials Chemistry*, **2010**, *20*, 8224-8226

Awards

- ACS National Award in Colloid and Surface Chemistry, 2012
- Medard Welch Award, AVS Science and Technology Society, 2009
- International Semiconductor Surfaces, Interfaces and Nanostructures Prize, Weimar, Germany, 2009
- Wisconsin Alumni Research Foundation Named Professorship, 2008
- Wisconsin Distinguished Professor (Univ. of Wisconsin-System), 2007-present
- Fellow of the American Association for the Advancement of Science (AAAS), 2005
- Arthur Adamson Award of the American Chemical Society, 2005
- "Highly-Cited Researcher" (field of Materials Science), Institute for Scientific Information, 2002

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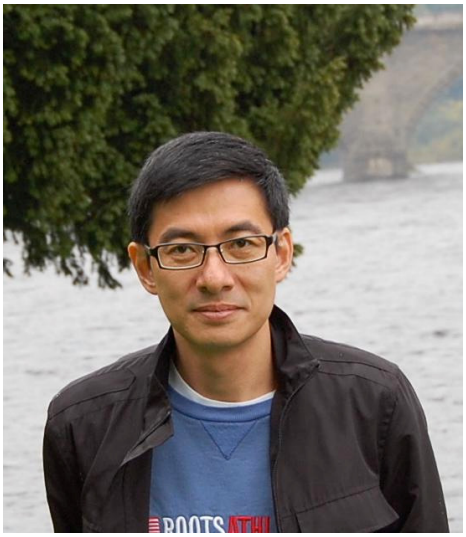
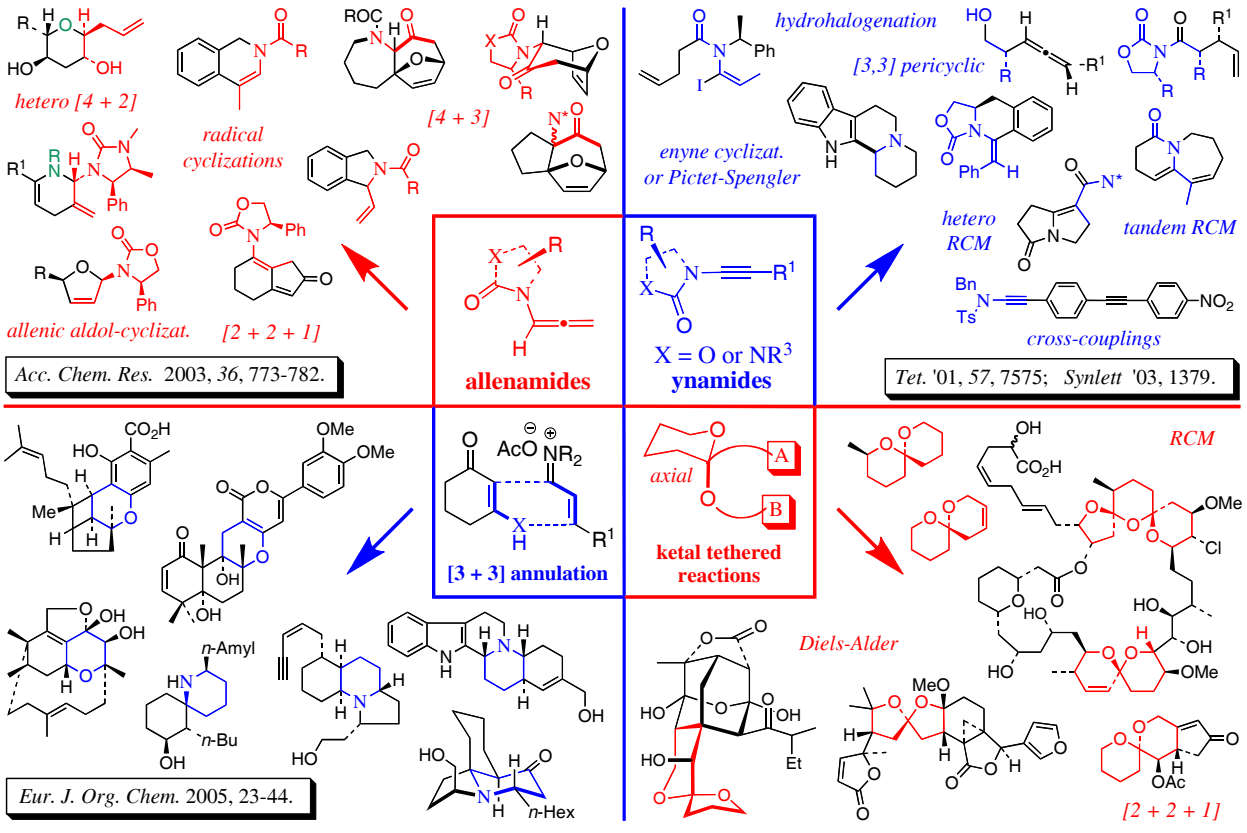


Research Description

Our research efforts consist of 50% total syntheses of natural products and 50% methodological development, and we are fortunate to be involved in 7 major areas: 1) Cycloadditions using chiral *allenamides*; 2) synthetic methods using *ynamides* as building blocks; 3) new chemistry of *enamides*; 4) a [3 + 3] annulation strategy for natural product total syntheses; 5) cationic cycloadditions of vinyl acetals; 6) cyclic acetal-tethered intramolecular reactions for constructing spiroketals containing natural products, and 7) most recently, asymmetric catalysis employing *de novo* chiral amino alcohols.



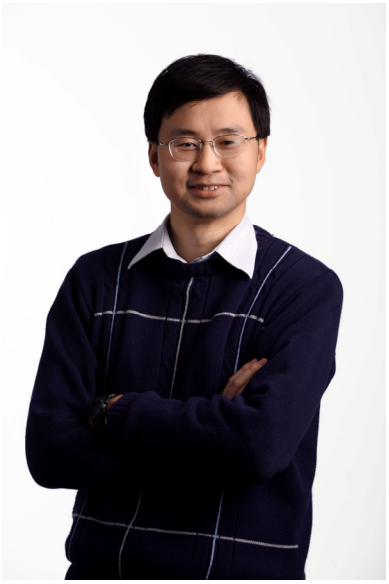
Selected Publications

- "A Tandem 1,3-H-Shift–6p-Electron Pericyclic Ring-Closure–Intramolecular Diels-Alder Cycloadditions Approach to BCD-Ring of Atropurpuran." Hayashi, R.; Ma, Z.-X.; Hsung, R. P. *Organic Lett.* **2012**, *13*, 252–255.
- "Development of An Intramolecular Gassman's [2 + 2] Cycloaddition." Feltenberger, J. B.; Ko, C.; Deng, J.; Ghosh, S. K.; Hsung, R. P. *Heterocycles* **2012**, *84*, 843–878. [*Special Issue Dedicated to Professor Albert Padwa's 75th Birthday*]
- "Challenges in Constructing the Architecturally Distinctive ABD-Tricycle via An Intramolecular *Oxa*–[3 + 3] Annulation Strategy." Buchanan, G. S.; Cole, K. P.; Li, G.; Tang, Y.; You, L.; Hsung, R. P. *Tetrahedron* **2011**, 67, 10105–10118. *[Tetrahedron-Symposium-In-Print Dedicated to Professor Gilbert Stork's 90th Birthday].*
- "Introducing the New Class of *N*-Phosphoryl Ynamides via Cu(I)-Catalyzed Amidations of Alkynyl Bromides." DeKorver, K. A.; Walton, M. C.; North, T. D.; Hsung, R. P. *Organic Lett.* **2011**, *13*, 4862–4865.
- "An Asymmetric *Aza*-[3 + 3] Annulation in the Synthesis of Quinolizidine Alkaloids: An Unexpected Reversal of Regiochemistry." Buchanan, G.; Dai, H.; Hsung, R. P.; Gerasyuto, A.; Schienebeck, C.; *Organic Lett.* **2011**, *13*, 4402–4405.
- "Stereoselectivities and Regioselectivities of (4+3) Cycloadditions Between Allenamide-Derived Chiral Oxazolidinone-Stabilized Oxyallyls and Furans: Experiment and Theory." Antoline, J.; Krenske, E.; Lohse, A.; Hsung, R. P.; Houk, K. N. *J. Am. Chem. Soc.* **2011**, *133*, 14443–14451.
- "Total Synthesis of (±)-Phomactin A. Lessons Learned from Respecting a Challenging Structural Topology." Buchanan, G. S.; Cole, K. P.; Tang, Y.; Hsung, R. P. *J. Org. Chem.* **2011**, *76*, 7027–7039.
- "Oppolzer-Type Intramolecular Diels-Alder Cycloadditions via Isomerizations of Allenamides." Feltenberger, J. B.; Hsung, R. P. *Organic Lett.* **2011**, *13*, 3114–3117.
- "*N*-Allyl-*N*-Sulfonyl Ynamides as Synthetic Precursors to Amidines and Vinylogous Amidines. An Unexpected 1,3-Sulfonyl Shift in Nitrile Synthesis." DeKorver, K. A.; Johnson, W. L.; Zhang, Y.; Hsung, R. P.; Dai, H.; Deng, J.; Lohse, A. G.; Zhang, Y.-S. *J. Org. Chem.* **2011**, *76*, 5092–5103.
- "Resveratrol Metabolites Do Nor Elicit Early Pro-Apoptotic Mechanisms in Neuroblastoma Cells." Kenealey, J. D.; Subramanian, L.; Van Ginkel, P. R.; Darjatmoko, S.; Lindstrom, M. J.; Somoza,V.; Ghosh, S. K.; Song, Z.; Hsung, R. P.; Kwon, G. S.; Eliceiri, K.; Albert, D. M.; Polans, A. S. *J. Agric. Food. Chem.* **2011**, *59*, 4979–4986.
- "Developing a Diastereoselective Intramolecular [4 + 3] Cycloaddition of Nitrogen-Stabilized Oxyallyl Cations Derived from *N*-Sulfonyl-Substituted Allenamides." Lohse, A. G.; Hsung, R. P.; Leider, M. D.; Ghosh, S. K. *J. Org. Chem.* **2011**, *76*, 3246–3257.
- "An Efficient and Practical Entry to 2-Amido-Dienes and 3-Amido-Trienes from Allenamides Through Stereoselective 1,3-Hydrogen Shifts." Hayashi, R.; Feltenberger, J. B.; Lohse, A. G.; Walton, M. C.; Hsung, R. P. *Beil. J. Org Chem.* **2011**, *7*, 410–420. [*A Thematic Issue on Recent Advances in Chemistry of Allenes*]
- "(+)-Arisugacin A: Computational Evidence of a Dual Binding Site Covalent Inhibitor of Acetylcholinesterase." Al-Rashid, Z. F.; Hsung, R. P. *Bioorg. Med. Chem. Lett.* **2011**, 2687–2691. [*Symposium-In-Print Issue on Recent Advances in Medicinal Chemistry in Recognition of the Journal's 20 Years of Service to Medicinal Chemistry Community*]
- "A Cyclic Acetal Tethered Intramolecular Diels-Alder Cycloaddition. Studies Directed Toward a Total Synthesis of (±)-Fusidilactone C." Ghosh, S. K.; Wei, Y.; Gerasyuto, A. I.; Feltenberger, J. B.; Wang, J.; Hsung, R. P. *Heterocycles* **2011**, *82*, 1379–1409. [*A Special Issue Dedicated to Professor Albert Eschenmoser's 85th Birthday*]
- "Two Remarkable Epimerizations Imperative for the Success of an Asymmetric Total Synthesis of (+)-Aigialospirol." Figueroa, R.; Feltenberger, J. B.; Guevarra, C. C.; Hsung, R. P. *Science: China Chem.* **2011**, *54*, 31–42. [*An Invited Article and The Journal Cover: Special Issue on The Frontiers of Chemical Biology and Synthesis: The Sixth Sino-US Chemistry Professors Conference*]

Awards

- Vilas Associate Award, 2010
- Visiting Professor at Tianjin University [P. R. China], 2005 - 2007
- The Camille Dreyfus Teacher-Scholar, 2001
- McKnight Faculty Award**,** 2001 - 2003
- National Science Foundation Early Career Development Award, 2001 - 2006
- RW-Johnson Pharmaceutical Research Institute Faculty Award, 1998 - 2000
- National Institutes of Health Postdoctoral Fellow, 1996 - 1997

SONG JIN



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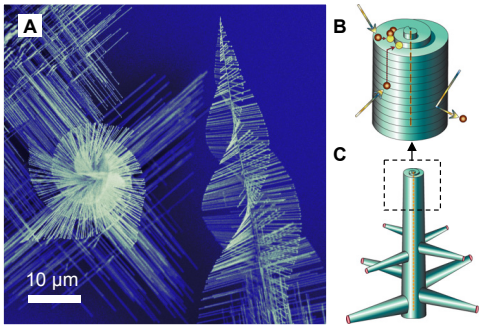
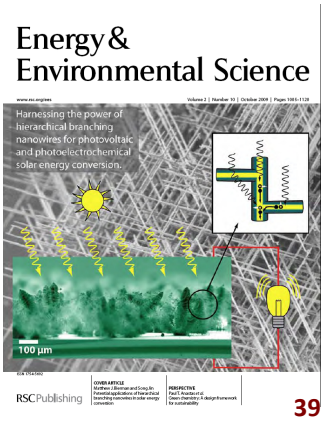
Research

Our research is centered on the chemistry and physics of nanoscale materials. We develop rational strategies for chemical synthesis, assembly and integration of nanomaterials, investigate fundamental synthesis-structure-property relationships, and explore them for ***renewable* energy** applications, such as photovoltaic and photoelectrochemical energy conversion, thermoelectric energy conversion, and electrochemical energy storage. We also work on nanospintronics and biological applications of nanomaterials. Highlighted below are some of our on-going research areas:

Nanomaterials formation mechanism driven by screw dislocations. We have discovered a nanowire (NW) and nanotube (NT) growth mechanism driven by axial screw dislocations that is fundamentally different from the traditional vapor-liquid-solid (VLS) or analogous catalyst-driven mechanisms. The self-perpetuating steps of a screw dislocation spiral provide the fast crystal growth front under low supersaturation during crystal growth (Fig. B) to enable the anisotropic crystal growth of one-dimensional (1D) NWs. The fast growing NWs driven by dislocation, when combined with epitaxial overgrowth of NW branches formed via the slower VLS mechanism, result in unprecedented "Christmas tree" nanostructures (Fig. A). These rotating branches are the clearest demonstration of "Eshelby twist". We have further elucidated the growth of single-crystal nanotubes due to screw dislocations with large Burgers vectors. We have confirmed that this mechanism occurs in many materials grown from both vapor and solution phase in many more materials, such as CdS, ZnO, FeOOH, Cu, Cu_2O. This growth mechanism also provides the general and unifying concepts for many nanomaterial morphologies that are commonly observed but unconvincingly explained so far, such as 2D nanoplates and helices. Dislocation-driven nanowire growth is a general mechanism that has been greatly under appreciated. Our discoveries and continuing fundamental study will create a new dimension in the rational design and synthesis of nanomaterials. The general understanding on promoting dislocation-driven nanomaterial growth is opening up the exploitation of *large scale/low cost solution growth* for rational catalyst-free synthesis of 1D nanomaterials for a variety of large-scale applications, such as those for renewable energy (solar energy, battery electrode materials, thermoelectric materials).



Solar energy conversion using earth-abundant semiconductors and nanomaterials. The success of solar photovoltaic (PV) or photoelectrochemical (PEC) technologies depends not only on achieving highly efficient devices, but also on dramatically reduced cost. The enormous scale and significance of the energy challenges demands materials that are more abundant and less expensive, and processes that are less energy-intensive and costly. We investigate earth-abundant semiconductor materials, such as ***iron pyrite*** (FeS_2, fool's gold) and ***hematite*** (α-Fe_2O_3), and improve them for potential high performance photovoltaics (solar cell) and photoelectrochemical (solar water splitting) applications. Particularly, nanotechnology offers new approaches to solar energy conversion that promise higher efficiencies and lower costs. We utilize our understanding of the screw-dislocation driven NW growth to develop nanomaterials of earth-abundant semiconductor materials that can be carried out on a large scale in an economical manner. Furthermore, the complex hierarchical nanowire structures we have made can be promising candidates for effectively



harvesting solar energy because the scattering improves light absorption and the dendritic structure optimizes carrier collection. We are exploring various approaches to utilize such nanostructures for photovoltaics and photoelectrocatalysis.

From a more fundamental perspective, we collaborate with Prof. John Wright and Prof. Robert Hamers to investigate coherent charge transport across quantum confined nanoscale heterostructures mimicking the coherent processes in photosynthesis and dye-sensitizer solar cells. We have developed methods to grow heteroepitaxial quantum dots directly from wide band gap oxide semiconductor nanowires. Our collaboration hopes to provide the fundamental understandings required to make coherent transport a ubiquitous feature of solar energy conversion nanostructures with arbitrarily complex shapes, compositions, and dimensionalities.

Chemical synthesis of metal silicide nanomaterials for enhancing thermoelectric performance. Nanomaterials extensively studied so far are usually made of elements or prototypical compound semiconductors with simple stoichiometries. In contrast, intermetallic silicides have multiple and unpredictable stoichiometries and complex phase behavior, making them challenging to synthesize and rarely explored so far. However, novel NW materials of silicides have significant applications in nanoelectronics, nanospintronics, and thermoelectrics. We develop general synthetic approaches to silicide NWs using chemical vapor deposition (CVD) of single source organometallic precursors (SSPs) and complementary chemical vapor transport (CVT) methods to enable the chemical synthesis of silicide NWs. We are working on elucidating the detailed NW growth mechanism and the chemical rules governing the formation of the nanoscale intermetallic phases, towards the goal of rational synthesis of nanomaterials of any pure or alloyed metal silicides. NWs of those semiconducting silicides with complex crystal structures, such as $MnSi_{1.8}$, are very promising as improved thermoelectric materials because the reduced dimensions suppress thermal conductivity. We are investigating how nanoscale dimensions in these nanomaterials impact their fundamental thermal properties. We are also developing and investigating bulk nanostructured abundant silicide thermoelectric materials for automobile waste heat recovery.

Selected Publications

- Li, L.; Yu, Y.; Meng, F.; Tan, Y.; Hamers, R. J.; Jin, S.; "Facile Solution Synthesis of α-$FeF_3 \cdot 3H_2O$ Nanowires and Their Conversion to α-Fe_2O_3 Nanowires for Photoelectrochemical Application" *Nano Lett.* **2012,** *12*, 724-731.
- Meng, F.; Morin, S. A.; Jin, S.; "Rational Solution Growth of α-FeOOH Nanowires Driven by Screw Dislocations and Their Conversion to α-Fe_2O_3 Nanowires" *J. Am. Chem. Soc.* **2011,** *133,* 8408-8411.
- Morin, S. A.; Bierman, M. J.; Tong, J.; Jin, S.; "Mechanism and Kinetics of Spontaneous Nanotube Growth Driven by Screw Dislocations" *Science* **2010**, *328,* 476-480.
- Jin, S.; Bierman, M. J.; Morin, S. A.; "A New Twist on Nanowire Formation: Screw Dislocation-Driven Growth of Nanowires and Nanotubes" *J. Phys. Chem. Lett.* **2010**, *1,* 1472-1480.
- Lau, Y. H. A.; Chernak, D. J.; Bierman, M. J.; Jin, S. "Formation of PbS Nanowire Pine Trees Driven by Screw Dislocations" *J. Am. Chem. Soc.* **2009**, *131*, 16461-16471.
- Schmitt, A. L.; Higgins, J. M.; Szczech, J. R.; Jin, S. "Synthesis and Applications of Metal Silicide Nanowires" *J. Mater. Chem.* **2010**, *20,* 223-235. (Invited Feature Article, featured on front cover)
- Morin, S. A.; La, Y.-H. Liu, C. C.; Streifer, J. A.; Hamers, R. J.; Nealey, P. F.; Jin, S. "Self-Assembly of Nanocrystal Arrays via Block Copolymer Directed Nucleation" *Angew. Chem. Intl. Ed.*, **2009**, *48,* 2135-2139.
- Bierman, M. J.; Lau, Y. H. A.; Kvit, A. V.; Schmitt, A. L.; Jin, S.; "Dislocation Driven Nanowire Growth and Eshelby Twist" *Science* **2008**, *320*, 1060.
- Higgins, J. M.; Schmitt, A. L.; Guzei, I. A.; Jin, S. "Higher Manganese Silicide Nanowires of Nowotny Chimney Ladder Phase", *J. Am. Chem. Soc.* **2008**, *130*, 16086.

Selected Awards

- Research Corporation SciaLog Award for Solar Energy Conversion (2011)
- Sloan Research Fellowship (2009)
- ExxonMobil Solid State Chemistry Fellowship (2008)
- Research Corporation Cottrell Scholar Award (2007)
- DuPont Young Professor (2007)
- NSF CAREER Award (2006-2011)
- 3M Nontenured Faculty Award (2006)
- MIT Technology Review TR35 (35 Young Innovators under the age of 35) (2006)

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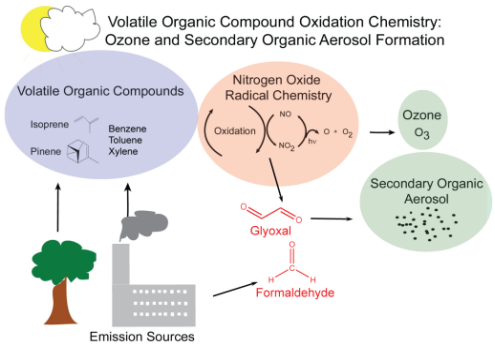
Research

Research in the Keutsch group is aimed at improving our understanding of photochemical oxidation processes of volatile organic compounds (VOCs) that produce tropospheric ozone and are central to secondary organic aerosol (SOA) formation. O_3 and aerosol affect human health and climate, and uncertainties in the radiative effects of aerosol comprise the largest uncertainties in current estimates of anthropogenic forcing of climate. Our scientific approach builds on enabling new field observations of key VOC oxidation intermediates (OVOCs) via instrumentation and method development. Formaldehyde and α-dicarbonyls are examples of target species we have selected that are directly relevant to O_3 and SOA formation, but can also act as powerful indicators for overall VOC oxidation processes. We combine these field observations, taken during collaborative field campaigns, with laboratory studies of kinetics that provide new detailed chemical information, in order to test and improve existing atmospheric chemistry models. The field observations and scientific analysis are then made available to the wider atmospheric sciences community.

VOC photochemistry and ozone and SOA formation

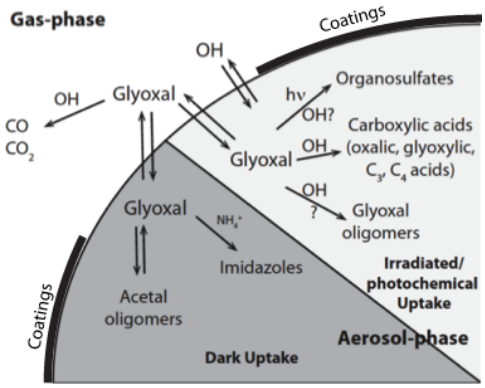


Photochemical oxidation of biogenic (e.g., isoprene, terpenes) and anthropogenic (benzene, toluene) VOCs is tied to both tropospheric O_3 and SOA formation. Although much research has been conducted in this area the ability to model ozone away from urban centers and SOA formation in general is limited. Measurement of higher generation OVOCs, such as α-dicarbonyls, together with formaldehyde, an important first generation OVOC, allows a more detailed means of studying a larger part of the oxidative fate of VOCs. Comparison of field measurements of VOC oxidation chemistry with model results provides a means for testing and improving models of O_3 and SOA formation, as these are a result of this oxidative chemistry. Improved models are necessary for regulators and policy makers to make informed decisions as they seek to reduce pollution levels, especially of O_3 and SOA.

Field Campaigns

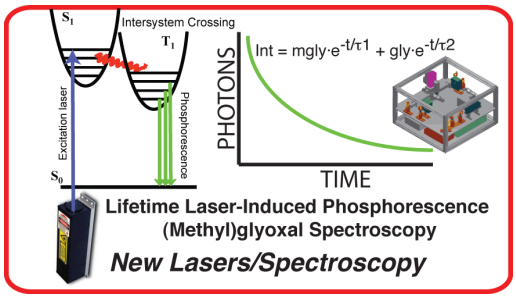
Collaborative field campaigns, in which a number of groups make coordinated measurement of key species such as VOCs, OVOCs, NO_x and ozone, are the backbone of atmospheric chemistry as they provide the only means of testing the accuracy of models. The scientific goal of the Keutsch Group in such campaigns is to test and improve our understanding of VOC oxidation processes and SOA formation. We are particularly interested in (1) rapid VOC oxidation in forest canopies, for which formaldehyde flux measurements can provide valuable insight, (2) contribution of biogenic vs. anthropogenic VOC precursors to α-dicarbonyl concentrations, and (3) influence of other anthropogenic emissions (e.g. NO_x) on biogenic VOC oxidative chemistry and α-dicarbonyl concentrations. Our interests also extend to aircraft studies and studies in urban and maritime regions. In addition, we are interested in providing validation of satellite retrievals of glyoxal, the smallest α-dicarbonyl, and formaldehyde.

Laboratory Studies



The Keutsch Group conducts laboratory studies of processes that are central to the uptake and fate of α-dicarbonyls in aerosol. These studies address the uptake mechanism, rate, reversibility, dependence on photo-chemical processes, and products formed in the aerosol phase. Our studies are the first to observe formation of imidazoles from reaction of glyoxal with ammonium sulfate aerosol and first to show formation of organosulfates during glyoxal uptake only occurs under irradiated conditions. Chamber studies of glyoxal uptake on aerosol seed are undertaken in collaboration with other research groups; in our laboratory we study the kinetics of formation of α-dicarbonyl reaction products (especially those bearing nitrogen) and synthesize organosulfate standards. Our goal is to implement the results of these studies into models of SOA formation.

Instrument development Instrument development in the Keutsch Group employs ultra high sensitivity spectroscopic techniques, such as Laser-Induced-Fluorescence (LIF) and cavity-ringdown spectroscopy, combined with cutting edge technology to enable new and improved measurements of key atmospheric species.



LIF is an established atmospheric field measurement technique for NO_2 and OH. The Keutsch Group has successfully applied LIF to measure HCHO with sensitivity as good as 15 ppt/min. The instrument also takes advantage of a novel pulsed fiber laser, which is lighter and more compact and requires only a fraction of the power drawn by a Ti:Sapphire—all highly desirable in any field instrument, especially for aircraft based measurements. This instrument is also the first to have the capability of HCHO flux measurements via eddy correlation. We are currently extending fiber laser instrumentation to other atmospherically relevant species.

We have also developed the first instrument for direct, highly specific, *in situ* measurement of glyoxal. The instrument is the first atmospheric field instrument to use laser induced phosphorescence (LIP), taking advantage of the unusually efficient intersystem crossing in α-dicarbonyls. The long timescale of phosphorescence compared to scattering and fluorescence from possible interferants makes it virtually background free, and the precision of 1 ppt/min allows fast measurement of glyoxal even in clean environments. We are extending the LIP technique to other α-dicarbonyls and have successfully observed methylglyoxal. We are also developing measurement capabilities for aerosol phase α-dicarbonyls as well as the uptake rate of glyoxal into aerosols under ambient conditions.

Selected Publications

- S.B. Henry, A. Kammrath, F.N. Keutsch, "Quantification of gas-phase glyoxal and methylglyoxal via the Laser-Induced Phosphorescence of (methyl)GLyOxal Spectrometry (LIPGLOS) Method," Atmos. Meas. Techn. 5, 181-192 (**2012**).
- M.M. Galloway, A.J. Huisman, L. D. Yee, A.W.H. Chan, C.L. Loza, J.H. Seinfeld, F.N. Keutsch, "Yields of oxidized volatile organic compounds during the OH radical initiated oxidation of isoprene, methyl vinyl ketone, and methacrolein under high-NOx conditions," Atmos. Chem. Phys. 11, 10779–10790 (**2011**).
- J.P. DiGangi, E.S. Boyle, T. Karl, P. Harley, A. Turnipseed, S. Kim, C. Cantrell, R.L. Mauldin III, W. Zheng, F. Flocke, S.R. Hall, K. Ullmann, Y. Nakashima, J.B. Paul, G.M. Wolfe, A.R. Desai, Y. Kajii, A. Guenther, and F.N. Keutsch, "First direct measurements of formaldehyde flux via eddy covariance: implications for missing in-canopy formaldehyde sources," Atmos. Chem. Phys. 11, 10565–10578 (**2011**).
- M.M. Galloway, C.L. Loza, P.S. Chhabra, A.W.H. Chan, L.D. Yee, J.H. Seinfeld, F.N. Keutsch, "Analysis of photochemical and dark glyoxal uptake: Implications for SOA formation," Geophys. Res. Lett. 38, L17811, (**2011**).
- G. Yu, A. Bayer, M.M. Galloway, K.J. Korshavn, C.G. Fry, F.N. Keutsch "Glyoxal in Aqueous Ammonium Sulfate Solutions: Products, Kinetics and Hydration Effects," Environ. Sci. Technol. 45, 6336-6342, (**2011**).
- C.N. Olson, M.M. Galloway, G. Yu, C.J. Hedmann, M.R. Lockett, T.P. Yoon, E.A. Stone, L.M. Smith, F.N. Keutsch, "Hydroxycarboxylic Acid-Derived Organosulfates: Synthesis, Stability and Quantification in Ambient Aerosol," Environ Sci. Technol. 45, 6468-6474, (**2011**).
- A.J. Huisman, J.R. Hottle, M.M. Galloway, J. P. DiGangi, K.L. Coens, W. Choi, I.C. Faloon, J.B. Gilman, W.C. Kuster, J. de Gouw, N.C. Bouvier-Brown, A.H. Goldstein, B.W. LaFranchi, R.C. Cohen, G.M. Wolfe, J.A. Thornton, K.S. Docherty, D.K. Farmer, M.J. Cubison, J.L. Jimenez, J. Mao, W. Brune, F.N. Keutsch "Photochemical modeling of glyoxal at a rural site: observations and analysis from BEARPEX 2007," Atmos. Chem. Phys. 11, 8883-8897 (**2011**).

LAURA L. KIESSLING

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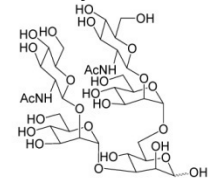
Research

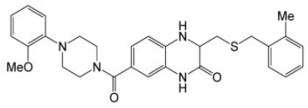
Our group develops and implements synthetic methods to access biologically-active compounds for hypothesis-driven and discovery-driven research. This important foundation of our program offers chemically-oriented researchers new opportunities to develop and apply their synthetic skills. Biochemically- and biologically-oriented researchers benefit from access to unique biologically active ligands. Some representative questions that drive our interdisciplinary research program follow.

I. *What are the biological roles of carbohydrates?* Carbohydrates can influence protein stability and protein trafficking; they also are important in recognition and can act as signals. Illuminating the biological roles of carbohydrates stands as a major scientific forefront. Chemical synthesis is uniquely poised to address this challenge. In our initial forays, we focused on synthesizing carbohydrates and glycoconjugates to explore their roles. These studies led to new discoveries about how sulfation influences carbohydrate recognition and the role of carbohydrate-binding proteins in embryo implantation. More recently, we are focused on finding non-carbohydrate inhibitors. These compounds can be used to block important protein-carbohydrate inter-actions or to inhibit specific carbohydrate biosynthetic enzymes. Examples of targets of interest are shown in Figure A.

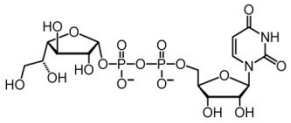
A



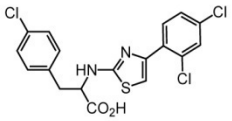
natural DC-SIGN ligand



nonnatural antagonist
(1000-fold more potent than natural ligand)

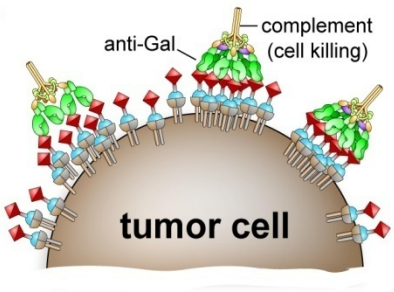


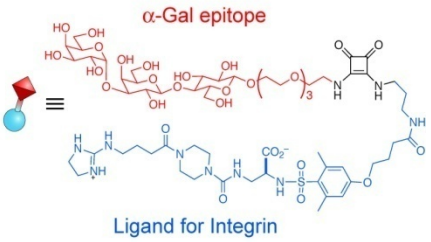
natural UGM ligand



UGM inhibitor

B





II. *Can we exploit carbohydrate recognition for new purposes?* We used the properties of carbohydrate recognition to devise a strategy to mediate selective killing of tumor cells. Our approach exploits the features of tumor cells, which are often distinguished from normal cells by their higher levels of particular cell surface receptors. We used a chemically-synthesized, small-molecule composed of two distinct motifs: (1) a ligand that binds tightly (K_d ~ 10^{-9} M) to a_vb_3 integrins, and (2) a carbohydrate (galactosyl-a(1-3)galactose or a-Gal epitope), which is recognized by human anti-a-galactosyl antibodies (anti-Gal). Importantly, anti-Gal antibodies are recruited when the bifunctional conjugate decorates a tumor cell possessing a high level of the target receptor (the a_vb_3 integrin); anti-Gal then triggers cell killing. Tumor cell lines with high levels of the integrin receptor are killed (Figure B). Our results have implications for the treatment of cancer and other diseases.

III. *How do cells detect and respond to stimuli in the environment?* The view from the surface of a cell reveals a complex milieu composed of membrane-associated proteins, lipids and carbohydrates. This surface of molecules is a remarkable conduit of information. The molecules on the surface have the critical role of reporting to the interior on extracellular conditions (e.g., presence of nutrients or toxins), so that the cell can respond appropriately. We have been designing chemical probes to understand the mechanisms underlying how molecular signals are processed.

Selected Publications

- Li L, Orner BP, Huang T, Hinck AP, Kiessling LL. (2010) Peptide ligands that use a novel binding site to target both TGF-β receptors. Mol Biosyst. 6(12): 2392-402.
- Klim JR, Li L, Wrighton PJ, Piekarczyk MS, Kiessling LL. (2010) A defined glycosaminoglycan-binding substratum for human pluripotent stem cells. Nat Methods 7(12): 989-94.
- Jiarpinitnun C, Kiessling LL. (2010) Unexpected enhancement in biological activity of a GPCR ligand induced by an oligoethylene glycol substituent. J Am Chem Soc. 132(26): 8844-5.
- Splain RA, Kiessling LL. (2010) Synthesis of galactofuranose-based acceptor substrates for the study of the carbohydrate polymerase GlfT2. Bioorg Med Chem. 18(11): 3753-9.
- Derda R, Musah S, Orner BP, Klim JR, Li L, Kiessling LL. (2010) High-throughput discovery of synthetic surfaces that support proliferation of pluripotent cells. J Am Chem Soc. 132(4): 1289-95.
- Kiessling LL, Splain RA. (2010) Chemical approaches to glycobiology. Annu Rev Biochem. 79: 619-53.
- May JF, Splain RA, Brotschi C, Kiessling LL (2009) A tethering mechanism for length control in a processive carbohydrate polymerization. Proc Natl Acad Sci USA 106(29): 11851-6.
- Gruber TD, Borrok MJ, Westler WM, Forest KT, Kiessling LL. (2009) Ligand binding and substrate discrimination by UDP-galactopyranose mutase. J Mol Biol. 391(2): 327-40.
- Kolonko EM, Pontrello JK, Mangold SL, Kiessling LL. (2009) General synthetic route to cell-permeable block copolymers via ROMP. J Am Chem Soc. 131(21): 7327-33.
- Dykhuizen EC, Kiessling LL. (2009) Potent ligands for prokaryotic UDP-galactopyranose mutase that exploit an enzyme subsite. Org Lett. 11(1): 193-6.
- Courtney AH, Puffer EB, Pontrello JK, Yang ZQ, Kiessling LL. (2009) Sialylated multivalent antigens engage CD22 in trans and inhibit B cell activation. Proc Natl Acad Sci USA 106(8): 2500-5.
- Borrok MJ, Zhu Y, Forest KT, Kiessling LL. (2009) Structure-based design of a periplasmic binding protein antagonist that prevents domain closure. ACS Chem Biol. 4(6): 447-56.
- Allen MJ, Wangkanont K, Raines RT, Kiessling LL. (2009) ROMP from ROMP: A new approach to graft copolymer synthesis. Macromolecules 42(12): 4023-7.

Awards

- Guggenheim Fellowship, 2008
- Member, Wisconsin Academy of Sciences, Arts and Letters, 2008
- Wilbur Cross Award, Yale University, 2008
- Member, National Academy of Sciences, 2007
- Member, American Academy of Microbiology, 2007
- Francis P. Garvan-John M. Olin Medal, American Chemical Society, 2006
- Tetrahedron Young Investigator Award, 2005
- Harrison-Howe Award, Rochester ACS, 2005
- Member, American Academy of Arts & Sciences, 2003
- Fellow, American Association for the Advancement of Science, 2003
- Carbohydrate Research Award, 2001
- Romnes Faculty Fellowship, University of Wisconsin-Madison, 2001
- Horace Isbell Award, Carbohydrate Division of the American Chemical Society, 2000
- MacArthur Foundation Fellowship, 1999-2004
- Selected as one of the 50 top R & D stars to watch by Industry Week, 1999
- John D. and Catherine T. MacArthur Foundation Fellowship, 1999
- Arthur C. Cope Scholar Award, 1999
- National Science Foundation, National Young Investigator Award (NYI), 1993-98
- Alfred P. Sloan Foundation Fellowship, 1997-99

CLARK LANDIS

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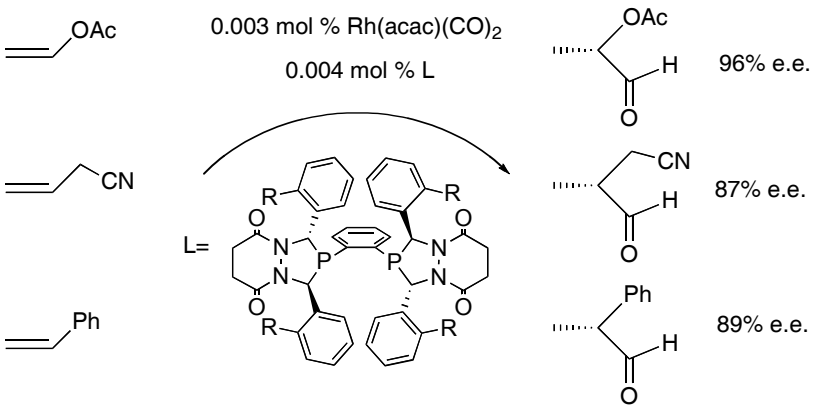
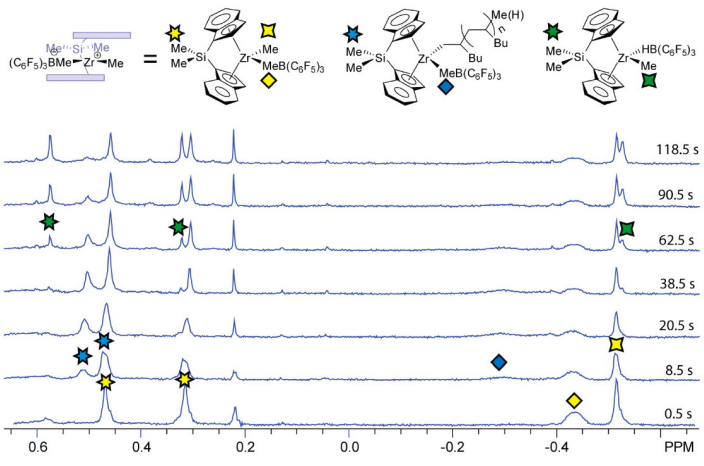


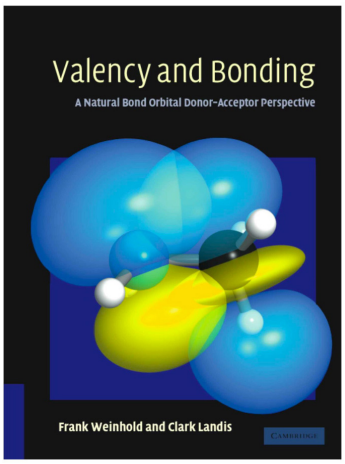
Research

Our research centers on catalysis involving transition metal complexes. The approach is multidisciplinary: synthesis, kinetics, development of novel instrumentation, sophisticated NMR spectroscopy, theory, and computations all are brought to bear on contemporary issues in homogeneous catalysis. Themes in our current research include the creation of highly selective and active catalysts for asymmetric transformations, mechanistic studies of important catalytic processes, and simple approaches to understanding electronic structure throughout the periodic table.

Mechanisms of Catalytic Reactions: One of the largest commercial applications of homogeneous catalysts is the metallocene-catalyzed polymerization of simple alkenes to make polyethene, polypropene, polystyrene, etc. New homogeneous metallocenes catalysts based on Ti and Zr have revolutionized this industry, making possible new polymeric materials through exquisite control of polymer molecular weights and microstructure. Surprisingly, characterization of rate laws for the fundamental steps (initiation, propagation, and termination) of metallocene-catalyzed polymerization and a fundamental understanding of how various activators and co-catalysts affect the rates, stereospecificity, and molecular weights of catalytic polymerizations are underdeveloped. Our research encompasses new approaches to determining the number of catalyst sites that are producing polymers (i. e., active site counting), new chromatographic and mass spectrometric methods for obtaining mechanistic information, and new approaches to probing the influence of ion-pairing dynamics on the polymerization activity. An offshoot of this development work has been the development of new stopped-flow NMR methods and probes. The goal of this work is to exploit the high information content of NMR spectroscopy in the determination of fast reaction kinetics.



Chiral Ligands for Enantioselective Catalysis: The key attribute of homogeneous catalysts is selectivity. The potential of harnessing such selectivity for cost effective, sustainable manufacturing of pharmaceuticals and fine chemicals drives modern research in homogeneous catalysis. We have developed a new class of phosphine ligands, 3,4-diazaphospholanes, that are chiral, rapidly synthesized, and readily expanded into diverse collections. When bound to rhodium, bis-3,4-diazaphospholanes effect enzyme-like rates and enantioselectivities for the hydroformylation of a variety of alkenes. Catalytic hydroformylation effects the conversion of an alkene, carbon monoxide, and dihydrogen into aldehydes. Effective, practical enantioselective hydroformylation enables the production of chiral aldehydes that serve as important synthons in the production of pharmaceuticals and fine chemicals. We are actively expanding the range of chiral diazaphospholanes and their applications. More recently we have embarked on detailed studies of the hydroformylation mechanism.



Computation and Theory in Catalysis: Computations are a valuable complement to both catalyst design and mechanistic studies. Our goals are to develop a "Valence Bond" perspective of bonding in transition metal complexes and to apply high level, hybrid quantum mechanics/molecular mechanics methods to explore the origin of selectivity control in homogeneous catalysis. In addition to understanding fundamental issues concerning electronic structure, we recently have initiated a computational exploration of the mechanism of asymmetric hydroformylation.

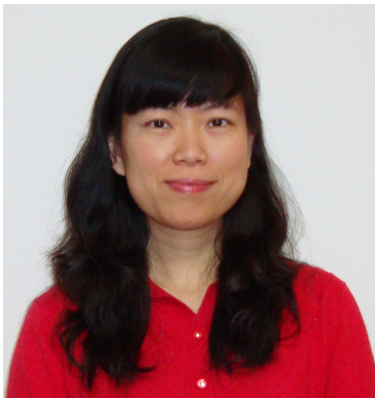
Selected Publications

- 'Highly Active, Regioselective, and Enantioselective Asymmetric Hydroformylation with Rhodium Catalysts Ligated by Bis-3,4-Diazaphospholanes' Thomas P. Clark, R. Landis, Susan Freed, Jerzy Klosin, Khalil A. Abboud *J. Am. Chem. Soc.* **2005**, *127,* 5040-5042.
- 'Origin of trans-Bent Geometries in Maximally-Bonded Transition Metal and Main Group Molecules' Clark R. Landis, Frank Weinhold *J. Am. Chem. Soc.* **2006**, *128*, 7335-7345.
- 'Trigonal Pyramids: Alternative Ground-State Structures for Sixteen-Electron Complexes' Detlev Ostendorf, Clark Landis, and Hansjörg Grützmacher *Angew. Chemie Int. Ed. Engl.* **2006**, *118*, 5293-5297.
- 'Metallocene Catalyzed Alkene Polymerization and the Observation of Zr-Allyls' Matthew Christianson and Clark R. Landis, *Proceedings of the National Academy of Science*, **2006**, *103,* 15349-15354.
- 'Generalized Treatment of NMR Spectra for Rapid Chemical Reactions' Matthew Christianson and Clark R. Landis, *Concepts in Magnetic Resonance Part A,* **2007**,*30A*, 165-183.
- 'High Bond Orders in Metal-Metal Bonding' Frank Weinhold and Clark R. Landis *Science* **2007**, *316*, 61-63.
- 'Valence and Extra-Valence Orbitals in Main-Group and Transition Metal Bonding' Clark R. Landis and Frank Weinhold, *Journal of Computational Chemistry*, **2007**, *28*, 198-203.
- 'Highly Enantioselective Hydroformylation of Aryl Alkenes with Diazaphospholane Ligands', A. L. Watkins, B. G. Hashiguchi, C. R. Landis, *Organic Letters*, **2008**, *10*, 4553-4556.

Awards

- Fellow, American Academy for the Advancement of Science
- Dow Lecturer in Inorganic Chemistry, UC-Berkeley
- Hutchison Lecturer, University of Rochester
- Fellow of the Japan Society for the Promotion of Science

LINGJUN LI



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Research Emphasis: Bioanalytical Chemistry, Mass Spectrometry, Microseparations, Proteomics & Peptidomics, Neurochemistry

Research

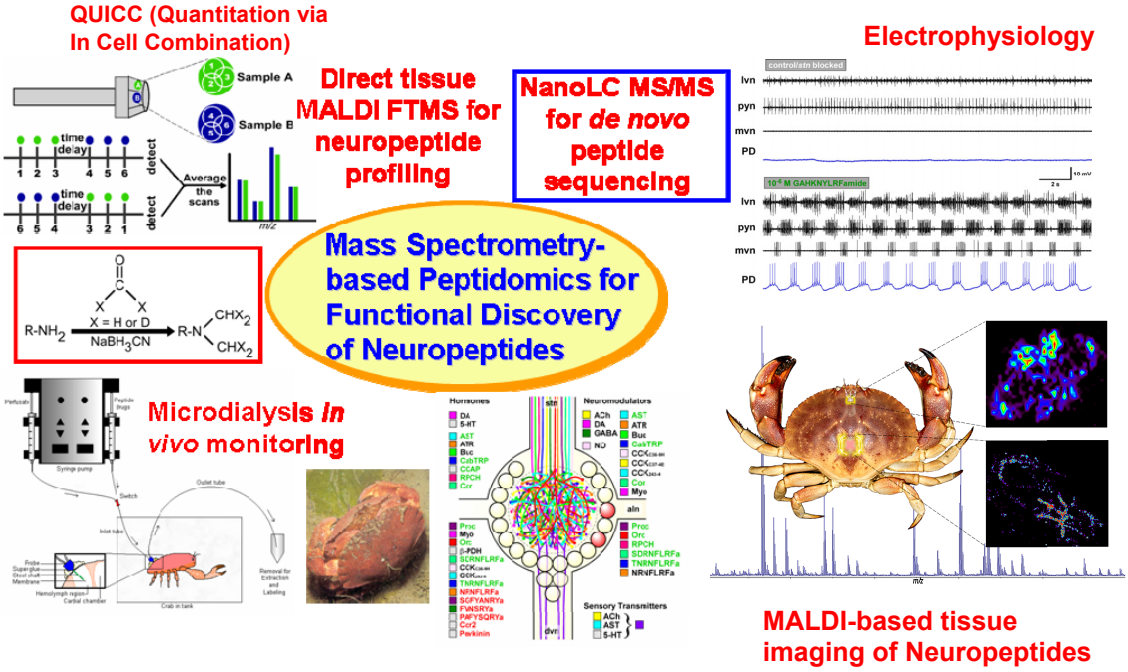
Research in my laboratory focuses on developing and implementing an array of novel mass spectrometry based strategies to answer questions about the most complex and elusive set of signaling molecules, the neuropeptides, and gain new insights into the roles of peptide hormones and neurotransmitters play in the plasticity of neural circuits and behavior. While significant effort has been directed to analytical technique and method development, it is the biomedical importance of understanding the neuropeptidergic system that drives our research to continuously refine and improve the analytical capabilities to address challenging neuroscience problems. A large body of research strongly suggests that an imbalance of chemical messengers is associated with various neurological disorders. However, compared to classical neurotransmitters such as amines, the functional roles of many neuropeptides are still poorly understood. This is, in part, due to the lack of analytical capabilities to measure and identify these low abundance endogenous signaling molecules in a complex microenvironment. Clearly, development of highly sensitive and selective analytical tools for neuropeptide identification and quantitation is in great demand. Specifically, we are interested in understanding the roles that neuropeptides play in food intake, neural network development and response to environmental stresses.

We have chosen to work with a simpler and well-defined crustacean nervous system to both facilitate technology development and address fundamental neuroscience problems related to neuromodulation and network plasticity. We are developing a multi-faceted mass spectrometry-based analytical platform to probe peptidergic signaling with enhanced sensitivity and selectivity. A wide range of MS instruments are available for the study. By combining chemical labeling, micro-scale separation (capillary electrophoresis and nanoLC), and tandem mass spectrometry sequencing techniques, we have discovered a large number of novel neuropeptides in crustacean nervous systems. The physiological effects of these new peptides at the cellular and network levels are evaluated in collaboration with neurophysiologists in the field. Furthermore, both mass spectrometric imaging technology and *in vivo* microdialysis sampling tools have been implemented to follow neuropeptide distribution and secretion with unprecedented details. Finally, a differential display strategy in conjunction with isotopic labeling technique is being developed to allow functional discovery of neuropeptides in response to various physiological changes.

While the technology is developed using crustacean model system as a test-bed, the technology advancement resulting from our research is widely applicable to the large-scale analysis of peptides and proteins in many biological systems, including those of mammalian and humans. Towards this end, we have established several exciting collaborations targeted at neurochemical analysis in more complex systems. These collaborative projects include biomarker discovery in various neurodegenerative diseases and ovarian cancer, peptide analysis and neuromodulation in mammalian rhythmic neural network, proteomic analysis of human embryonic stem cell derived astrocytes, and proteomic study of dioxin-induced cardiotoxicity in developing zebrafish.

These synergistic projects span analytical mass spectrometry, capillary separations, peptide chemistry, bioinformatics, neurochemistry, and neurobiology. The improved analytical method development enables biological discovery, and the emerging biological questions require further advancement of analytical tools.

Li Lab Overview – An Integrated Approach for Neuropeptide Discovery



Selected Publications (out of 111 peer-reviewed publications)

- J. Wang, H. Ye, Z. Zhang, F. Xiang, G. Girdaukas, and L. Li* (**2011**). MALDI imaging for capillary electrophoresis separation of neuropeptides. *Analytical Chemistry 83*, 3462-3469.
- F. Xiang, H. Ye, R. Chen, Q. Fu, and L. Li* (**2010**). N,N-dimethyl leucines as novel isobaric tandem mass tags for quantitative proteomics and peptidomics. *Analytical Chemistry*, *82*, 2817-2825.
- X. Wei, C. Dulberger, and L. Li* (**2010**). Characterization of murine brain membrane glycoproteins by detergent assisted lectin affinity chromatography (DALAC). *Analytical Chemistry*, *82*, 6329-6333.
- R. Chen, L. Hui, S.S. Cape, J. Wang, and L. Li* (**2010**). Comparative neuropeptidomic analysis of food intake via a multi-faceted mass spectrometric approach. *ACS Chemical Neuroscience*. *1*, 204-214
- J. Wang, Y. Zhang, F. Xiang, Z. Zhang, and L. Li* (**2010**). Combining capillary electrophoresis-MALDI mass spectrometry and stable isotope labeling techniques for comparative crustacean peptidomics. *Journal of Chromatography A*, *1217*, 4463-4470
- R. Chen, X. Jiang, I. Mohtashemi, M. P. Conaway, L. Hui, R. Viner, and L. Li* (**2010**). Mass spectral analysis of neuropeptide expression and distribution in the nervous system of the lobster *Homarus americanus*. *Journal of Proteome Research*, *9*, 818-832
- J.A. Dowell, J.A. Johnson, and L. Li* (**2009**). Identification of astrocyte secreted proteins with a combination of shotgun proteomics and bioinformatics. *Journal of Proteome Research*, *8*, 4135-4143
- M. Ma, J. Wang, R. Chen, and L. Li* (**2009**). Expanding the crustacean neuropeptidome using a multi-faceted mass spectrometric approach. *Journal of Proteome Research*, *8*, 2426-2437
- R. Chen, L. Hui, R. Sturm, and L. Li* (**2009**). Three dimensional mapping of neuropeptides and lipids in crustacean brain by mass spectral imaging. *Journal of American Society for Mass Spectrometry*, *20*, 1068-77.
- M. Ma, R. Chen, Y. Ge, H. He, A.G. Marshall, and L. Li* (**2009**). Combining bottom-up and top-down mass spectrometric strategies for *de novo* sequencing of the crustacean hyperglycemic hormone (CHH) from *Cancer borealis*. *Analytical Chemistry,* **81**, 240-247.
- A. Herbst, S. McIlwain, J. J. Schmidt, J. M. Aiken, C. D. Page, and L. Li* (**2009**). "Prion disease diagnosis by proteomic profiling." *Journal of Proteome Research*, *8*, 1030-1036. DOI: **10**.1021/pr800832s.

Selected Awards

- Pittsburgh Conference Achievement Award
- H. I. Romnes Faculty Fellowship
- Vilas Associate Award
- Alfred P. Sloan Research Fellowship
- National Science Foundation CAREER Award
- American Society for Mass Spectrometry (ASMS) Research Award

DAVID M. LYNN

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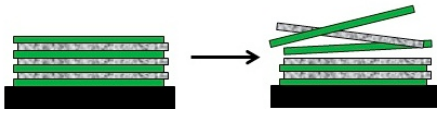
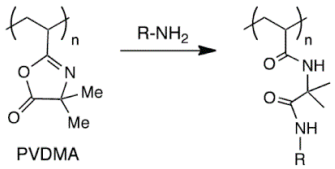
Research

Research in our laboratory is focused broadly on **(i) the design and synthesis of functional organic materials** and **(ii) the fabrication and physical characterization of macromolecular assemblies, nanoscale materials, and interfaces**, with particular interests in the design of functional polyelectrolytes, reactive polymers, and developing solutions to problems of biomedical and biotechnological importance. Our research is conducted in a highly interdisciplinary and collaborative training environment that provides opportunities for students with backgrounds and interests in chemistry, engineering, biology, materials science, medicine, and the pharmaceutical sciences. Brief summaries of ongoing research efforts are described in the sections below.

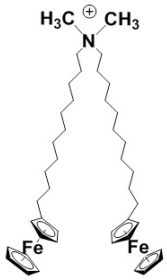
Layer-by-Layer Assembly of Thin Films and Coatings: Surface-Mediated Drug Delivery and Other Applications. We have developed 'layer-by-layer' approaches to the fabrication of thin polymer films that provide control over the release of DNA and other agents (including siRNA, proteins, peptides, and small-molecule drugs) from surfaces. These efforts are made possible, in part, by the design and synthesis of new cationic polymers that can be used to promote the controlled disruption of these ionically-crosslinked assemblies. These materials provide a unique 'multilayered' approach to the localized delivery of agents from the surfaces of film-coated objects both *in vitro* (e.g., in cell culture environments) and *in vivo* (e.g., from the surfaces of implantable objects). Methods for layer-by-layer (LbL) assembly play important roles in many other aspects of our research.

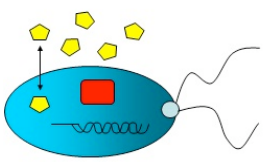


Azlactone-Functionalized Polymers: Reactive Platforms for the Design of Advanced Materials. We have exploited the reactivity of azlactone-functionalized polymers to develop new approaches to (i) the rapid/modular synthesis of side-chain functionalized polymers, and (ii) the fabrication of reactive surfaces and interfaces. An important outcome of these efforts has been the elaboration of methods for the 'reactive' layer-by-layer assembly of crosslinked polymer multilayers in organic solvents. This 'reactive' approach provides a general platform for the post-fabrication introduction of chemical and biological functionality to film-coated surfaces (e.g., by the treatment of azlactone-containing films with a range of functional nucleophiles).



Redox-Based Control of DNA Delivery Using Ferrocene-Containing Cationic Lipids. We are developing approaches to active control over the structures and functional properties of lipid/DNA aggregates ('lipoplexes') by using ferrocene-containing cationic lipids with redox states that can be addressed chemically or electrochemically. We have used this approach to develop methods for redox -based control over the internalization and processing of DNA by cells (e.g., to 'activate' otherwise inactive lipoplexes toward transfection by the controlled addition of reducing agents, etc.). This approach to control of cell transfection is without precedent and has the potential to provide new levels of control over the delivery of DNA to cells *in vitro* and *in vivo*.





Surfaces that Prevent Bacterial Communication and Biofilm Growth. We are developing materials-based approaches to the control of bacterial behavior that differ fundamentally from conventional approaches based on the use bactericidal agents. These approaches are based on the fabrication of surfaces that promote the release of small-molecule inhibitors of bacterial 'quorum sensing' (or the means by which some bacteria communicate and organize into 'biofilms' or activate virulence pathways). Inhibition of quorum sensing as a means of modulating virulence presents a new paradigm for the treatment or prevention of infection. Materials that inhibit quorum sensing at or near the surfaces of objects have the

potential to reduce fouling and/or prevent infection in numerous biomedical, commercial, and industrial contexts.

'Charge-Shifting' Polymers: New Approaches to Control of Ionic Interactions in Polyelectrolyte Assemblies. We have developed new classes of 'charge-shifting' polymers that provide tunable control over ionic interactions between oppositely charged polymers in solution and at surfaces/interfaces. This work based on the design of polyelectrolytes with hydrolyzable side chains that promote dynamic changes in polymer charge densities upon side chain cleavage. These materials represent a departure from the design of conventional cationic and anionic polymers (for which changes in charge density generally occur upon changes in pH, etc.). We are applying these new materials in two arenas: (i) to control the assembly and disassembly of nanoscale DNA 'polyplexes' in solution (to promote more efficient cell transfection), and (ii) to promote the release of DNA and other agents from surfaces coated with multilayered polyelectrolyte films (PEMs).

Selected Recent Publications

- M. E. Buck, A. S. Breitbach, S. K. Belgrade, H. E. Blackwell, and D. M. Lynn, "Chemical Modification of Reactive Multilayered Films Fabricated from Poly(2-Alkenyl Azlactone)s: Design of Surfaces that Prevent or Promote Mammalian Cell Adhesion and Bacterial Biofilm Growth." *Biomacromolecules* **2009**, *10*, 1564-1574.
- M. E. Buck and D. M. Lynn, "Reactive Layer-by-Layer Assembly of Suspended Thin Films and Semi-Permeable Membranes at Interfaces Created Between Aqueous and Organic Phases." *Advanced Materials* **2010**, *22*, 994-998.
- B. Sun, X. Liu, M. E. Buck, and D. M. Lynn, "Azlactone-Functionalized Polymers as Reactive Templates for Parallel Polymer Synthesis: Synthesis and Screening of a Small Library of Cationic Polymers in the Context of DNA Delivery." *Chemical Communications* **2010**, *46*, 2016-2018.
- M. E. Buck and D. M. Lynn, "Functionalization of Fibers Using Azlactone-Containing Polymers: Layer-by-Layer Fabrication of Reactive Thin Films on the Surfaces of Hair and Cellulose-Based Materials." *ACS Applied Materials and Interfaces* **2010**, *2*, 1421-1429.
- A. J. Karlsson, R. M. Flessner, S. H. Gellman, D. M. Lynn, and S. P. Palecek, "Polyelectrolyte Multilayers Fabricated from Antifungal b-Peptides: Design of Surfaces that Exhibit Antifungal Activity Against *Candida albicans*." *Biomacromolecules* **2010**, *11*, 2321-2328.
- M. E. Buck and D. M. Lynn, "Freestanding and Reactive Thin Films Fabricated by Covalent Layer-by-Layer Assembly and Subsequent Lift-Off of Azlactone-Containing Polymer Multilayers." *Langmuir* **2010**, *26*, 16134-16140.
- M. E. Buck, S. C. Schwartz, and D. M. Lynn, "Superhydrophobic Thin Films Fabricated by Reactive Layer-by-Layer Assembly of Azlactone-Functionalized Polymers." *Chemistry of Materials* **2010**, *22*, 6319-6327.
- E. M. Saurer, D. Yamanouchi, B. Liu, and D. M. Lynn, "Delivery of Plasmid DNA to Vascular Tissue *in vivo* using Catheter Balloons Coated with Polyelectrolyte Multilayers." *Biomaterials* **2011**, *32*, 610-618.
- A. T. Breitbach, A. H. Broderick, C. M. Jewell, S. Gunasekaran, Q. Lin, D. M. Lynn, and H. E. Blackwell, "Surface-Mediated Release of a Synthetic Small-Molecule Modulator of Bacterial Quorum Sensing: Gradual Release Enhances Activity." *Chemical Communications* **2011**, *47*, 370-372.
- S. L. Bechler and D. M. Lynn, "Design and Synthesis of a Fluorescently End-Labeled Poly(b-amino ester): Application to the Characterization of Degradable Polyelectrolyte Multilayers." *Journal of Polymer Science – Part A: Polymer Chemistry* **2011**, *49*, 1572–1581.
- A. H. Broderick, S. M. Azarin, M. E. Buck, S. P. Palecek, and D. M. Lynn, "Fabrication and Selective Functionalization of Amine-Reactive Polymer Multilayers on Topographically Patterned Microwell Cell Culture Arrays." *Biomacromolecules* **2011**, *12*, 1998-2007.
- R. M. Flessner, C. M. Jewell, D. G. Anderson, and D. M. Lynn, "Degradable Polyelectrolyte Multilayers that Promote the Release of siRNA." *Langmuir* **2011**, *27*, 7868-7876.
- M. E. Buck and D. M. Lynn, "Azlactone-Functionalized Polymers as Reactive Platforms for the Design of Advanced Materials: Progress in the Last Ten Years." *Polymer Chemistry* **2012**, *3*, 66-80.
- A. H. Broderick, M. R. Lockett, M. E. Buck, Y. Yuan, L. M. Smith, and D. M. Lynn, "*In situ* Synthesis of Oligonucleotide Arrays on Surfaces Coated with Crosslinked Polymer Multilayers." *Chemistry of Materials* **2012**, In press.

Selected Awards

- MIT Technology Review TR100 Award: 'Top 100 Young Innovators in the World', 2003
- Arnold and Mabel Beckman Foundation Young Investigator Award, 2003
- 3M Corporation Non-Tenured Faculty Award, 2005
- Alfred P. Sloan Research Fellow, Alfred P. Sloan Foundation, 2007-2009
- Vilas Associate Award, University of Wisconsin - Madison (2010-2012)
- Edward C. Nagy New Investigator Award, National Institute of Biomedical Imaging & Bioengineering, 2011

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Research

The central goal of my research program is to discover new chemical methods for manipulating the self-assembly of both small molecules and macromolecules to produce functional organic materials with unusual chemical and physical properties. We synthesize well-defined organic materials *and* physically characterize how their specific molecular attributes influence their supramolecular self-assembly, in order to gain fundamental insights into their ultimate bulk properties. We are specifically working (1) to develop molecular structure-property relationships in new classes of (bio)degradable polymers, (2) to understand how molecular polydispersity influences the self-assembly behavior of novel functional block copolymers, and (3) to gain fundamental insights into ion transport through nanoporous polymeric media, toward the development of selective ion transporting membranes for electrical energy storage and utilization.

Vinyl Esters: A New Monomer Palette for Degradable Block Copolymers. The development of economical, degradable plastics and polymer surfactants that can replace non-degradable, commodity polymers is a major challenge in polymer science. Known degradable polymers (*e.g.*, poly(lactic acid)) generally exhibit thermal and mechanical properties that limit their widespread applications. As an alternative, we have developed the synthetic polymer chemistry of vinyl esters as a new monomer palette for constructing block copolymers (BCPs) with tunable physical properties and degradation profiles. Comprised of two or more chemically dissimilar homopolymer segments, BCPs self-assemble into periodic nanostructures that nonlinearly combine their constituent homopolymer properties. Based on our studies of controlled vinyl ester polymerizations, we have synthesized the first poly(vinyl ester) block copolymers. While studying their mechanical properties, we also developed new insights and methods for toughening poly(vinyl ester) BCPs. Contrary to the conventional wisdom in block copolymer design, our studies demonstrate that nanoscale BCP self-assembly is not necessary for increased mechanical toughness and elasticity. In a related effort, we have also synthesized new multiblock copolymer surfactants (“soaps”) comprised of hydrophobic poly(vinyl ester) (PVE) and hydrophilic poly(vinyl alcohol) (PVA) segments. We are studying the properties of these amphiphiles in dilute aqueous solutions and as new hydrogel materials for potential biomedical applications.

Molecular Polydispersity in Block Copolymer Self-Assembly. Advanced polymerization methodologies enable the enchainment of new, functional monomers into block copolymers (BCPs) that exhibit unusual thermal, optical, electronic, and permselective properties. However, use of these new BCP syntheses often introduces significant molecular polydispersity or chain length heterogeneity into one or more of the copolymer blocks. Conventional wisdom stipulates that chain length uniformity (“monodispersity”) is a prerequisite for the useful periodic nanoscale self-assembly of BCPs. Few studies have questioned the validity and stringency of this preconceived notion. We have studied the self-assembly of three classes of polydisperse ABA triblock copolymers, in which a polydisperse B block is flanked by monodisperse A end blocks. Contrary to conventional wisdom, polydisperse ABA BCPs also assemble into a rich array of periodic nanoscale structures with unexpectedly *greater* thermodynamic stabilities as compared to their monodisperse analogs. Our fundamental insights into the effects of polydispersity on nanoscale self-assembly unleash new opportunities to develop designer soft materials derived from functional yet polydisperse homopolymers. On this foundation, we are currently studying the physical properties of new classes of ion conducting, polydisperse block copolymers toward next-generation fuel cell and lithium-ion battery materials.

Lyotropic Liquid Crystal-based Ion Exchange Membranes. Polymer electrolyte membranes (PEMs) that selectively transport H^+ or OH^- are essential components in acidic and alkaline fuel cells, respectively, which use both $H_2(g)$ and alcohol fuels. While commercially available PEMs transport H^+/OH^- through polymers with water-filled pores ~5-6 nm diameter that are decorated with highly acidic functionalities, improved ionic conductivities have been noted in materials with even smaller pores (diameters ~2-5 nm). These observations raise fundamental questions: Why does ion transport depend

on pore diameter and pore functionality? Does ionic conductivity continue to increase with decreasing pore diameters?

To probe these fundamental yet technologically important questions, we have developed a new surfactant platform that exhibits an unusual tendency to self-assemble in water into bicontinuous liquid crystalline phases comprised of interpenetrating aqueous and hydrophobic domains, which percolate over macroscopic lengthscales with tunable nanopore diameters (~0.6-6 nm) and well-defined pore functionalities. Using these self-assembling systems, we have produced a model set of nanoporous membrane materials that we are studying for fuel cell, water desalination, and selective chemical separations applications. In the future, we plan plan to use these materials as an experimental platform to probe fundamental mechanisms of H^+/OH^- transport in water-filled nanoporous media and to elucidate the structure of water in soft, ionic nanoconfinement using neutron scattering.

Summary. Through the interplay of materials synthesis and characterization, my research group uses chemical synthesis as a tool to manipulate the self-assembly of organic molecules into materials with well-defined supramolecular morphologies that exhibit unusual and useful bulk properties. Each project area emphasizes this molecular approach in addressing significant challenges in the development of sustainable materials and materials for energy storage and utilization, while uncovering fundamental chemical principles that will guide the design of new functional organic materials.

Selected Publications

- "Poly(vinyl acetate-*b*-vinyl alcohol) Surfactants Derived from Poly(vinyl ester) Block Copolymers," Repollet-Pedrosa, M. H.; Weber, R. L.; Schmitt, A. L; Mahanthappa, M. K., *Macromolecules,* **2010**, *43,*7900-7902.
- "Poly(vinyl ester) Block Copolymers Synthesized by Reversible Addition Fragmentation Chain Transfer Polymerizations," Lipscomb, C. E.; Mahanthappa, M. K., *Macromolecules*, **2009**, *42*, 4571-4579.
- "Unexpected Consequences of Center Block Polydispersity in ABA Triblock Copolymer Self-Assembly," Schroeder, J. M.; Schmitt, A. K.; Schmitt, A. L.; Im, K.; Mahanthappa, M. K *J. Amer. Chem. Soc., in press* and online as DOI:10.1021/ja210548e.
- "Polydispersity-driven Formation of Football-shaped Micelles," Schmitt, A. L.; Mahanthappa, M. K. *revision submitted to ACS Macro Letters,* **2012**, *1*, 300-304.
- "Polydispersity-Driven Shift in the Lamellar Meosphase Composition Window of OBO Triblock Copolymers," Schmitt, A. L.; Mahanthappa, M. K. *Soft Matter*, **2012**, *8*, 2294-2303.
- "Thermal and Ion Transport of Hydrophilic and Hydrophobic Polymerized Styrenic Imidazolium Ionic Liquids" Weber, R. L.; Ye, Y.; Banik, S. M.; Elabd, Y. A.; Hickner, M. A.; Mahanthappa, M. K. *J. Polym. Sci. Part B: Polym. Phys.,* **2011**, *49*, 1287-1296.
- "Effects of Nanoscale Morphology on the Ionic Conductivity of Polymerized Ionic Liquid Block Copolymers," Weber, R. L.; Ye, Y.; Schmitt, A. L.; Banik, S. M.; Elabd, Y. A.; Mahanthappa, M. K. *Macromolecules*, **2011**, *44*, 5727-5735.
- "Unusually Stable Aqueous Lyotropic Gyroid Phases from Gemini Dicarboxylate Surfactants," Sorenson, G. P.; Coppage, K. L.; Mahanthappa, M. K. *J. Amer. Chem. Soc.,* **2011**, *133*, 14928-14931.

Awards

- Emil H. Steiger Distinguished Teaching Award, 2010
- James W. Taylor Award for Excellence in Teaching, 2009
- National Science Foundation CAREER Award, 2008
- 3M Non-Tenured Faculty Award, 2008
- Fannie and John Hertz Foundation Graduate Fellowship, 1997-2003
- NSF Graduate Fellowship (declined)
- Boettcher Foundation Fellowship, 1993-1997
- 7th Place Westinghouse Science Talent Search Award, 1993

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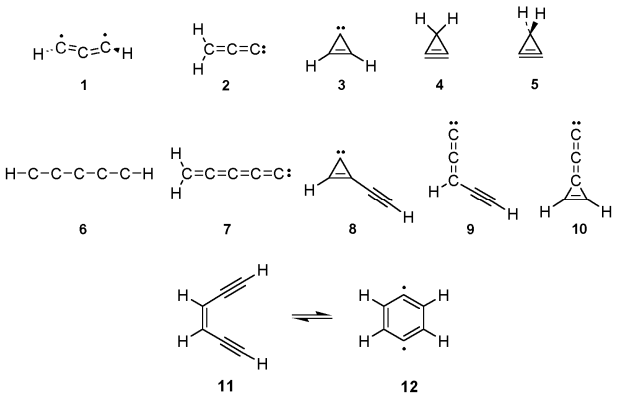
Research

Our research program focuses on bringing physical-organic insights and physical and analytical methods to bear on important problems in chemistry. Our interests range from mechanistic organic and organometallic chemistry to the fundamental chemistry underlying important problems in material science.

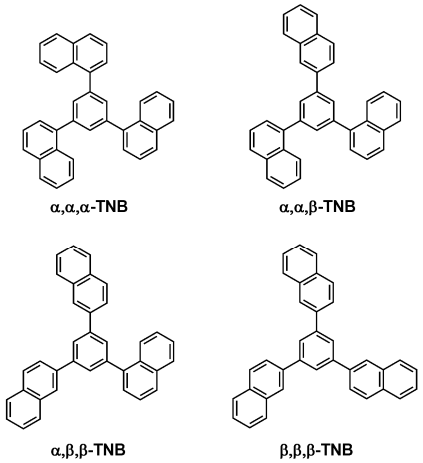
Reactive Intermediates and Astrochemistry

We continue a longstanding interest in studying highly reactive organic species using both experimental and computational methods. Our recent research efforts focus on elucidating the structure, photochemistry, and spectroscopy of organic species that are relevant to combustion chemistry, the formation of fullerenes, nanotubes, and soot, and the chemistry of the interstellar medium. Understanding the *organic chemistry* of interstellar clouds represents a significant challenge in mechanistic organic chemistry - both in terms of identifying new organic species in the clouds and in terms of investigating the chemical processes that govern the formation and destruction of these organic species.



Materials Chemistry of Organic Glasses and Supercooled Liquids

In collaboration with Prof. Mark Ediger's research group, we have been engaged in the study of fundamental physical properties of organic materials that form glasses and supercooled liquids. Glassy phases are poorly understood because of their amorphous composition. Yet they are extremely important in a variety of technological applications – from dielectric thin films that are used to insulate electrical circuitry in semiconductor devices, to the formulation of pharmaceuticals. We synthesized the first series of glass-forming materials in which it is possible to relate bulk physical properties, such as the glass transition temperature, to molecular properties of the glass-forming material. Our ability to prepare these materials, and tailor their properties through chemical synthesis, enables a range of important studies of their bulk properties.



tris-naphthyl-benzene (TNB) isomers

Selected Publications

- Photochemistry of Benzylallene: Ring-closing Reactions to form Naphthalene, Joshua A. Sebree, Nathanael M. Kidwell, Talitha M. Selby, Brent K. Amberger, Robert J. McMahon, Timothy S. Zwier, *J. Am. Chem. Soc.* **2012**, *134*, 1153−1163.
- Effects of Ethynyl Substitution on Cyclobutadiene, Brian J. Esselman and Robert J. McMahon, *J. Phys. Chem. A* **2012**, *116*, 483–490.
- Photochemistry of $CpMn(CO)_3$ and Related Derivatives: Spectroscopic Observation of Singlet and Triplet $CpMn(CO)_2$, Carl R. Kemnitz, Eric S. Ball, Robert J. McMahon, *Organometallics* **2012**, *31*, 70-84.
- Formation and Relaxation Dynamics of *iso*-CH_2ClI in Cryogenic Matrices, Thomas J. Preston, Maitreya Dutta, Brian J. Esselman, Robert J. McMahon, Scott A. Reid, F. Fleming Crim, *J. Chem. Phys.* **2011**, *135*, 114503.
- On the Trimerization of Cyanoacetylene: Mechanism of Formation of Tricyanobenzene Isomers and Laboratory Detection of their Radio Spectra, Henning Hopf, Cornelia Mlynek, Robert J. McMahon, Jessica L. Menke, Alberto Lesarri, Michael Rosemeyer and Jens-Uwe Grabow, *Chem. Eur. J.* **2010**, *16*, 14115-14123.
- Synthesis of Some Simple Diynals, Diynones, Their Hydrazones, and Diazo Compounds: Precursors to a Family of Dialkynyl Carbenes ($R^1{-}C{\equiv}C{-}C{-}C{\equiv}C{-}R^2$), Nathan P. Bowling, Nicola J. Burrmann, Robert J. Halter, Jonathan A. Hodges, Robert J. McMahon, *J. Org. Chem.* **2010**, *75*, 6382-6390.
- Attempted Isolation and Characterization of Diazirinone (N_2CO), Christopher J. Shaffer, Brian J. Esselman, Robert J. McMahon, John F. Stanton, R. Claude Woods, *J. Org. Chem.* **2010**, *75*, 1815-1821.
- Structure of Triplet Propynylidene (HCCCH) as Probed by IR, UV/vis, and EPR Spectroscopy of Isotopomers, Randal A. Seburg, Eric V. Patterson, Robert J. McMahon, *J. Am. Chem. Soc.* **2009**, *131*, 9442-9455.
- Organic Glasses with Exceptional Thermodynamic and Kinetic Stability, Stephen F. Swallen, Kenneth L. Kearns, Marie K. Mapes, Yong Seol Kim, Robert J. McMahon, M. D. Ediger, Tian Wu, Lian Yu, Sushil Satija, *Science* **2007**, *315*, 353-356.
- Enediyne Isomers of Tetraethynylethene, Nathan P. Bowling and Robert J. McMahon, *J. Org. Chem.* **2006**, *71*, 5841-5847. [selected as feature article for journal cover]

Awards

- JILA Visiting Fellow – NIST, University of Colorado, 2010
- Fellow, American Association for the Advancement of Science, 2003
- Vilas Associate, UW-Madison, 2000-02
- NSF Award for Special Creativity, 1996-98
- Research Fellow - Alfred P. Sloan Foundation, 1994-96
- Departmental Teaching Award, 1992
- NSF Presidential Young Investigator, 1989-94
- Sigma Xi Scientific Research Society, 1989
- UCLA Distinguished Scholar, 1984-85
- Winstein Dissertation Award, 1984
- IBM Corporation Graduate Fellow, 1983-84
- NSF Graduate Fellow, 1980-83
- Phi Kappa Phi Honor Society, 1979
- Phi Lambda Upsilon Honorary Chemical Society, 1979

SANDRO MECOZZI

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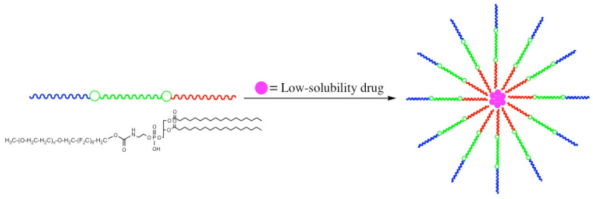
Research

Our research efforts focus on fundamental studies of non-covalent interactions and the application of the resulting findings to biochemical and biomedical problems. We use the predictive value of advanced computational techniques in conjunction with the power of chemical synthesis to generate molecules that are able to recognize each other through intermolecular forces. The study of these complexes allows us to explore a variety of different chemical and biological phenomena. These include the nature of specific intermolecular forces, the origin of the peculiar fluorous phase behavior in highly fluorinated materials, targeted drug delivery through semi-fluorinated functional materials, and the recognition properties of RNA.

The Fluorous Phase: The introduction of fluorine substituents into an organic molecule can radically change the physico-chemical properties of that molecule. High performance materials and polymers, vectors for drug delivery, anesthetics, fluorine-containing drugs, perfluorinated solvents for organic reactions are only a few examples of the practical uses of fluorinated molecules. Extensive perfluorination of organic molecules generates a new phase of liquid matter known as the fluorous phase. This phase does not mix with either polar or non-polar hydrogenated phases. The formation of a fluorous phase is at the basis of the unusual behavior of heavily fluorinated molecules and polymers. While the applications and the uses of fluorinated compounds are constantly increasing, the origin of their unusual properties is currently not completely understood. It is not known what exactly drives the formation of a fluorous phase.

We are currently investigating the nature of the fluorous phase by synthesizing and analyzing several self-assembling fluorinated amphiphilic molecules bearing water solubilizing groups and variously fluorinated functionalities.



Targeted drug delivery of anticancer drugs can be achieved through triblock copolymers forming hyper-stable micelles in aqueous solution.

We are also taking advantage of the large energetics associated with the formation of a fluorous phase to generate thermodynamically stable (micelles) and kinetically stable (nanoemulsions) nanoaggregates that can be used for the efficient and selective intravenous delivery of general anesthetics to the brain. To this purpose, we have designed and synthesized a number of novel, semifluorinated di- and triblock copolymers. The use of specific FDA-approved additives allows us to switch from thermodynamic to kinetically stable aggregates with the corresponding change in the delivery properties of the nanoparticles. We use a similar approach for the selective delivery of powerful anticancer therapeutics.

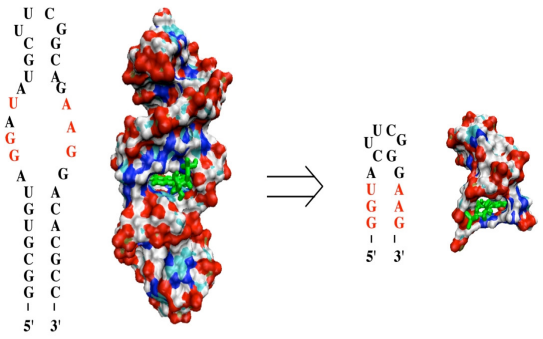
We are also performing molecular dynamics simulations on mixtures involving water, hydrocarbons, and a variety of fluorinated molecules. The purpose of these simulations is to establish first what kind of intermolecular forces can explain the formation of three phases and then identify the minimum number of fluorine atoms that are necessary for generating a fluorous phase under different conditions.

The Nature of Intermolecular Interactions:

We focus our studies on understanding the basic principles behind weak, yet biologically and energetically significant non-covalent forces. Our most recent studies have focused on using the recognition events between enzymes and their inhibitors to study the energetics of specific intermolecular interactions. This approach can be fruitfully used to study a variety of different intermolecular interactions and, at the same time, to achieve a deeper understanding of the enzymes' inner machinery. These experimental studies are complemented by high level *ab initio* calculations on simple complexes.

Short RNA-Small Molecules Complexes:

Our research in this field focuses on finding the minimal RNA sequences able to bind small organic molecules with high selectivity and affinity. Our own approach starts from the analysis of the crystal structure of RNA aptamer-small molecule complexes. We then computationally model these complexes to study the effect of nucleotide deletion and spatial rearrangement on the overall energetics. This approach allows us to computationally design short RNAs that are able to specifically bind small molecules. Using this methodology, we have been able to identify the minimum sequence requirements for the binding of molecules like theophylline, flavin mononucleotide, and aminoglycosides. All computational results have been confirmed experimentally. The current emphasis in this project is on the study of ribonucleoprotein complexes. We are also pursuing a dynamic combinatorial approach to RNA recognition.



Identification of the minimum sequence requirements for the binding of flavin mononucleotide to an RNA aptamer

Selected Publications

- J. P. Fast, M. G. Perkins, R. A. Pearce, S. Mecozzi “Fluoropolymer-based Emulsions for the Intravenous Delivery of Sevoflurane” *Anesthesiology* 2008, *109*, 651-656.
- O. M. Martin and S. Mecozzi “Synthesis and ph-Dependent Self-Assembly of Semifluorinated Calix[4]arenes” *Tetrahedron* 2007, *63*, 5539-5547.
- J. M. Slaughter, K. Schmidt, S. Mecozzi “Synthesis and Self-Assembly Properties of a Novel Poly(ethylene glycol)-Fluorocarbon-Phospholipid Triblock Copolymer” *Tetrahedron Lett.* 2007, *48*, 3879-3882.
- P. C. Anderson and S. Mecozzi “Computational Identification of a Small RNA Duplex that Recognizes and Binds Paromomycin with High Affinity” *Biopolymers*, 2007, *86*, 95-111.

Awards

- Department of Defense BCRP – Concept Award, 2005.
- Best poster. Gordon Conference on Nucleic Acids, 2005.
- NASA Postdoctoral Fellow (NSCORT program) 1997-1999

GILBERT M. NATHANSON

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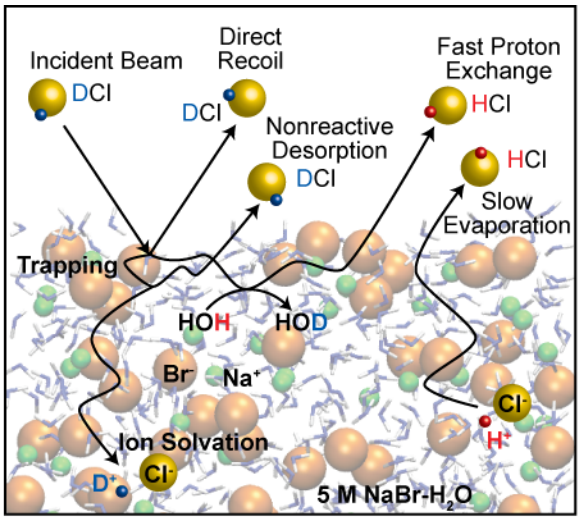
Research

Molecular beam scattering experiments have blossomed into a universal technique for understanding and controlling reactions in the gas phase and on solid surfaces. Our research confronts a third frontier: reactions at the surfaces of pure liquids, solutions, and monolayer films. We use gas-liquid scattering experiments to explore collisions and reactions of gas molecules with liquids ranging from crude oils and liquid metals to pure and salty glycerol, sulfuric acid, and molten sodium hydroxide and sodium carbonate. These liquids are important industrially and in the atmosphere, where sulfuric acid aerosols play a role in ozone destruction. We are now embarking on experiments employing liquid microjets, which open up the possibility of investigating reactions with high vapor pressure liquids including hydrocarbon fuels and water itself.

The questions we ask are simple: what does the surface of a liquid "look like" atom by atom and "feel like" during the short time scale of a gas-liquid collision? How does an acidic molecule such as HCl dissolve and dissociate in protic liquids such as glycerol, sulfuric acid, or salty water? What are the interfacial analogs of hydrogen bonding, the "like dissolves like" rule, oxidation-reduction, acid-base reactions, and electron solvation?

Molecular beam scattering experiments can answer these questions. We direct a highly collimated and nearly monoenergetic beam of molecules at the surface of a continuously renewed, low vapor pressure liquid inside a vacuum chamber. These gases range from inert atoms and organic molecules to HCl, SO_2, and alkali atoms. After striking the liquid, the molecules either scatter from the liquid or stick and dissolve, perhaps reacting with solvent molecules in the interfacial region of the liquid. A fraction of the reaction products may then desorb into the vacuum. The identity of the recoiling and desorbing molecules and their direction and velocity are monitored by a mass spectrometer. In many cases, we also measure interfacial and bulk reaction probabilities and the residence times of the gas molecules in the liquid. The data allow us to develop a true "blow-by-blow" description of the ways in which these gas molecules bounce off, dissolve in, and react with each liquid.

One example is shown in the animation on the right, which depicts collisions of DCl molecules with salty water. These collisions lead to the dissolution of this acidic gas and its dissociation into solvated ions. Our most surprising discovery is a pathway that occurs in collisions of DCl with salty glycerol: for this liquid, a small fraction of the DCl molecules undergo rapid DCl→HCl exchange in the top few monolayers of the solution and then desorb as HCl before they dissolve in the bulk. This is one instance in which an interfacial reaction competes with bulk dissolution.



Our studies bring together the most recent advances in reaction dynamics and theories of liquid structure and reactivity. By carrying out controlled collisions between a gaseous solute molecule and a liquid solvent, we are helping to construct an intimate picture of chemical reactions at gas-liquid interfaces.

Selected Publications

- "Reactions of Solvated Electrons Initiated by Sodium Atom Ionization at the Vacuum-Liquid Interface", William A. Alexander, Justin P. Wiens, Timothy K. Minton, and Gilbert M. Nathanson, In Press in *Science*, 2012.

- Interfacial Acid Dissociation and Proton Exchange Following Collisions of DCl with Salty Glycerol and Salty Water" Logan P. Dempsey, Susan M. Bradstad, and Gilbert M. Nathanson, Perspective in *Journal of Physical Chemistry Letters*, **2**, 522 (2011).

- "Molecular Beam Studies of HCl Dissolution and Dissociation in Cold Salty Water" Susan M. Bradstad and Gilbert M. Nathanson, *Physical Chemistry Chemical Physics*, **13**, 8245 (2011).
- Reactions of HCl and D_2O with Molten Alkali Carbonates, Thomas Krebs and Gilbert M. Nathanson, *Journal of Physical Chemistry A*, in press (**2010**).
- Reactive Collision of Sulfur Dioxide with Molten Carbonates, Thomas Krebs and Gilbert M. Nathanson, *Proceedings of the National Academy of Sciences*, **107**, 6622, (**2010**).
- HCl Uptake through Films of Pentanoic Acid and Pentanoic Acid/Hexanol Mixtures at the Surface of Sulfuric Acid, Daniel K. Burden, Alexis M. Johnson, and Gilbert M. Nathanson, *Journal of Physical Chemistry A*, **113**, 14131 (**2009**).
- Collisions of DCl with a Solution Covered with Hydrophobic and Hydrophilic Ions: Tetrahexylammonium Bromide in Glycerol, Susan M. Brastad, Daniel R. Albert, Mingwei Huang, and Gilbert M. Nathanson, *Journal of Physical Chemistry A*, **113**, 7422, (**2009**).
- "Surfactant Control of Gas Transport and Reactions at the Surface of Sulfuric Acid." Seong-Chan Park, Daniel K. Burden, and Gilbert M. Nathanson, *Accounts of Chemical Research*, *42*, February issue (**2009**).
- "Scavenging by F^- in Collisions of DCl with KF-Glycerol Solutions: Evidence for Formation of Interfacial $[ClDF]^-$." Jennifer L. DeZwaan, Susan M. Brastad, and Gilbert M. Nathanson, *Journal of Physical Chemistry C*, *112*, 15449 (**2008**).
- "The Roles of Salt Concentration and Cation Charge in Collisions of Ar and DCl with Salty Glycerol Solutions of NaI and CaI2." Jennifer L. DeZwaan, Susan M. Brastad, and Gilbert M. Nathanson, *Journal of Physical Chemistry C*, *112*, 3008 (**2008**).
- "The Inhibition of N_2O_5Hydrolysis in Sulfuric Acid by 1-Butanol and 1-Hexanol Surfactant Coatings." Seong-Chan Park, Daniel K. Burden, and Gilbert M. Nathanson, *Journal of Physical Chemistry A*, *111*, 2921 (**2007**).
- "Interfacial Interactions of DCl with Salty Glycerol Solutions of KI, NaI, LiI, and NaBr." Annabel H. Muenter, Jennifer L. DeZwaan, and Gilbert M. Nathanson, *Journal of Physical Chemistry C*, *111*, 15043 (**2007**).
- "Collisions of DCl with Pure and Salty Glycerol: Enhancement of Interfacial D→H Exchange by Dissolved NaI." Annabel H. Muenter, Jennifer L. DeZwaan, and Gilbert M. Nathanson, *Journal of Physical Chemistry B*, *110*, 4881 (**2006**).
- "Evaporation of Water and Uptake of HCl and HBr through Hexanol Films at the Surface of Supercooled Sulfuric Acid." Samuel V. Glass, Seong-Chan Park, and Gilbert M. Nathanson, *Journal of Physical Chemistry A*, *110*, 7593 (**2006**).
- "Collisions and Reactions of n-Propanol with Molten NaOH/KOH." David J. Castro, Sonia M. Dragulin, Michelle Manning, and Gilbert M. Nathanson, *Journal of Chemical Physics*, *125*, #144715 (**2006**).

Awards

- University of Wisconsin Chancellor's Distinguished Teaching Award, 2006
- Fellow, American Association for the Advancement of Science, 2005
- Chair, Gordon Research Conference on Dynamics at Surfaces, 2005
- Closs Lecturer, Department of Chemistry, University of Chicago, 2003
- Fellow of the American Physical Society, 2002
- NSF Grant Continuation Award for Special Creativity, 2000
- University of Wisconsin Romnes Faculty Fellowship, 1998
- Welch Foundation Lecturer, Conference on Chemical Dynamics, 1994
- Presidential Young Investigator Award, 1990-94
- Upjohn Teaching Award, Department of Chemistry, University of Wisconsin, 1993
- Camille and Henry Dreyfus Teacher-Scholar Award, 1992
- Camille and Henry Dreyfus Young Faculty Award, 1988

RONALD T. RAINES

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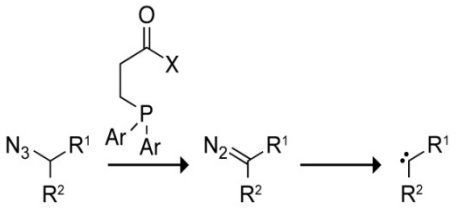
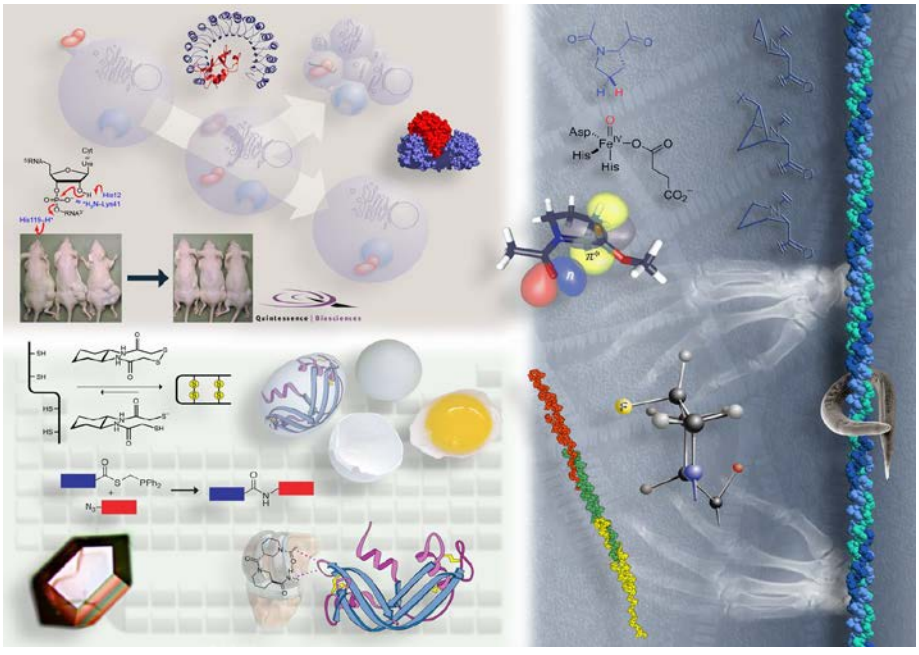
Research

The amino-acid sequences of proteins encode their three-dimensional structures, and these structures engender life. Using techniques that range from synthetic chemistry to cell biology, we are illuminating in atomic detail both the chemical basis and the biological purpose for protein structure and protein function. Our efforts are leading to insights into the relationship between amino-acid sequence and protein function (or dysfunction), as well as to the creation of novel proteins and small molecules with desirable properties. We are now focused on the following problems.

Protein Chemistry. Proteins produced by recombinant DNA technology are limited to twenty or so alpha-amino acids. We have developed a new chemical reaction—the traceless Staudinger ligation—as a means to assemble synthetic peptides into proteins and thereby escape from the tyranny of the genetic code. We are also seeking to use other chemoselective reactions in biological contexts, such as this gentle means to convert an azide into a carbene:



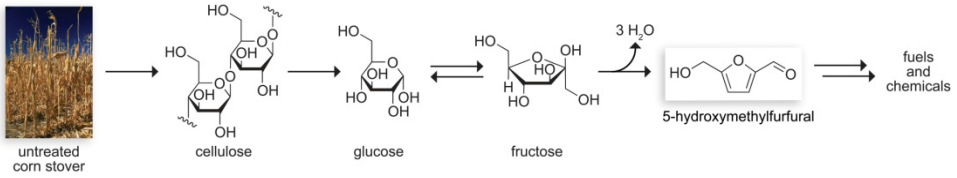


Protein Folding. Nearly ¼ of human proteins contain disulfide bonds, which are formed by the oxidation of the sulfhydryl groups of cysteine residues. We are creating new organocatalysts for this important, and often problematic, process.

Protein Stability. We have discovered that stereoelectronic effects stabilize folded proteins. By exploiting this effect, we have synthesized simple derivatives of collagen that are far more stable than any natural collagen. We have also used molecular self-assembly to produce collagen triple helices that are far longer than any natural one. These discoveries are spawning new materials for biomedicine and nanotechnology.

Protein Function. By catalyzing the cleavage of RNA, ribonucleases can be cytotoxic. Most notably, a human ribonuclease variant discovered by our group is now in clinical trials as a cancer chemotherapeutic agent. We are using both chemical and biological tools to reveal the mechanism by which this remarkable toxin kills cancer cells specifically.

Green Chemistry and Biofuels. We are developing chemical processes to convert crude lignocellulosic biomass (such as corn stover and pine sawdust) into useful fuels and chemicals. In particular, we are exploring and exploiting this reaction scheme, which we can effect in one step with nearly 50% yield:



Our research projects are designed to reveal how biological phenomena can be explained and manipulated by using chemical principles. Our hypotheses are far-reaching, and testing them requires the use of techniques and ideas from diverse disciplines. This broad/deep training is appropriate for scientists who want to perform innovative and meaningful research at the widening chemistry-biology interface.

Selected 2011 Publications (out of 21)

- Functional and structural analyses of *N*-acylsulfonamide–linked dinucleoside inhibitors of bovine pancreatic ribonuclease. Thiyagarajan, N.; Smith, B. D.; Raines, R. T.; Acharya, K. R. *FEBS J.* **2011**, *278*, 541–549.
- Synthesis and utility of fluorogenic acetoxymethyl ethers. Lavis, L. D.; Chao, T.-Y.; Raines, R. T. *Chem. Sci.* **2011**, *2*, 521–530.
- Conversion of fructose to 5-(hydroxymethyl)furfural in sulfolane. Caes, B. R.; Raines, R. T. *ChemSusChem* **2011**, *4*, 353–356.
- Tunable, post-translational hydroxylation of collagen domains in *Escherichia coli*. Pinkas, D. M.; Ding, S.; Raines, R. T.; Barron, A. E. *ACS Chem. Biol.* **2011**, *6*, 320–324.
- Quantum mechanical origin of the conformational preferences of 4-thiaproline and its *S*-oxides. Choudhary, A.; Pua, K. H.; Raines, R. T. *Amino Acids* **2011**, *41*, 181–186.
- Synthesis of conformationally constrained 5-fluoro- and 5-hydroxymethanopyrrolidines. Ring-puckered mimics of *gauche*- and *anti*-3-fluoro- and 3-hydroxypyrrolidines. Krow, G. R.; Shoulders, M. D.; Edupuganti, R.; Gandla, D.; Yu, F.; Sender, M.; Sonnet, P. E.; Zdilia, M. J.; DeBrosse, C.; Cannon, K. C.; Ross, III, C. W.; Choudhary, A.; Raines, R. T. *J. Org. Chem.* **2011**, *76*, 3626–3634.
- Signature of $n \rightarrow \pi^*$ interactions in α-helices. Choudhary, A.; Raines, R. T. *Protein Sci.* **2011**, *20*, 1077–1081.
- Separable fluorous ionic liquids for the dissolution and saccharification of cellulose. Caes, B. R.; Binder, J. B.; Blank, J. J.; Raines, R. T. *Green Chem.* **2011**, *13*, 2719–2722.
- Mechanism of ribonuclease A endocytosis: Analogies to cell-penetrating peptides. Chao, T.-Y.; Raines, R. T. *Biochemistry* 2011, *50*, 8374–8382.
- An $n \rightarrow \pi^*$ interaction in aspirin: Implications for structure and reactivity. Choudhary, A.; Kamer, K. J.; Raines, R. T. *J. Org. Chem.* 2011, *76*, 7933–7937.

Awards

- Repligen Award in Biological Chemistry, American Chemical Society, 2010
- Kellett Mid-Career Faculty Researcher Award, University of Wisconsin-Madison, 2009–2014
- Welch Lecturer, Welch Foundation, 2008
- Rao Makineni Lectureship Award, American Peptide Society, 2007
- Fellow, Royal Society of Chemistry, 2006
- Emil Thomas Kaiser Award, Protein Society, 2005
- Arthur C. Cope Scholar Award in Organic Chemistry, American Chemical Society, 2004
- Vilas Associates Award, University of Wisconsin–Madison, 2002–2004
- H. I. Romnes Faculty Fellowship, University of Wisconsin–Madison, 1998–2003
- Fellow, American Association for the Advancement of Sciences, 2002
- Guggenheim Fellowship, J. S. Guggenheim Memorial Foundation, 2001–2002
- Pfizer Award in Enzyme Chemistry, American Chemical Society, 1998

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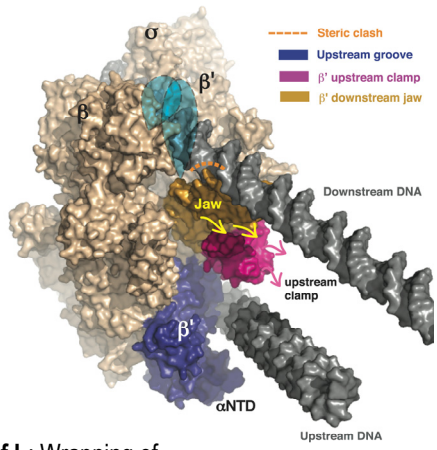
http://www.biochem.wisc.edu/record/index.html

Research

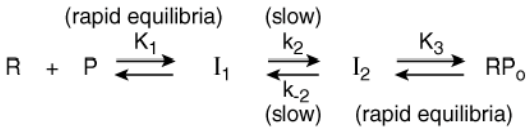
Protein-nucleic acid interactions, including kinetics and mechanism of transcription initiation, characterization of DNA wrapping in protein DNA complexes, development of small molecule solutes as thermodynamic and mechanistic probes of protein and DNA conformational changes.

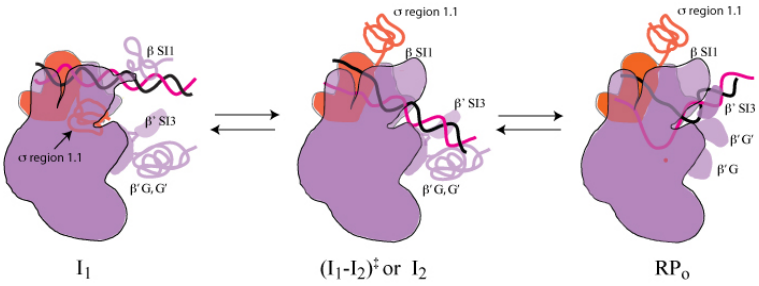
Protein-Nucleic Acid Interactions (PNAI): Protein-DNA interactions are central to all DNA processes, including the storage, replication, and expression of genetic information in the cell. The Record lab has pioneered the use of quantitative physical biochemical approaches to describe these interactions both experimentally and theoretically. Current PNAI projects in the lab involve characterization of the assembly and function of: E. coli RNA polymerase-promoter DNA open complexes in transcription initiation; and wrapped/bent DNA complexes formed with the histone-like proteins Integration Host Factor and HU. All these systems are unified by a common theme: large conformational changes and other coupled processes in the proteins and/or their target DNA sites occur in binding. To study these processes, we use chemical and enzymatic DNA footprinting, microcalorimetry, circular dichroism, fluorescence, nitrocellulose filter binding, rapid mix-quench kinetics, and structural modeling.



Model of I_1: Wrapping of upstream DNA around RNAP opens the downstream jaw, allowing the DNA containing the transcription start site to enter the active site channel. Davis et al. *PNAS* 104: 7833-38, 2007

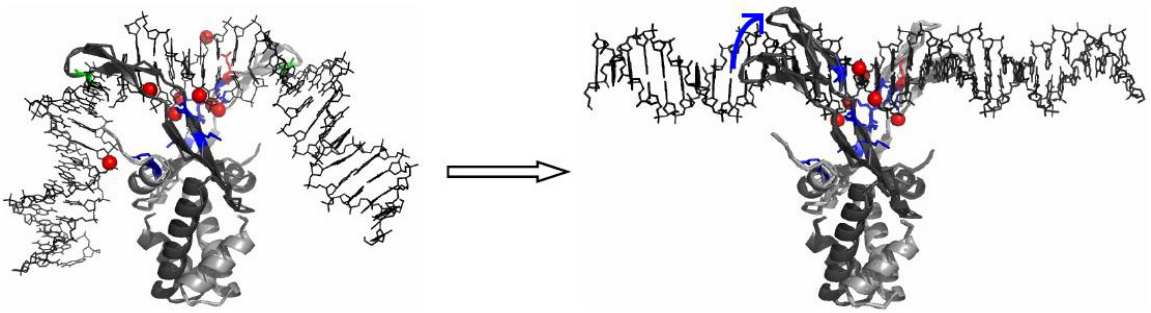
1. RNAP-Promoter Open Complex Formation. How and when is DNA opened in the initial steps of transcription initiation? What roles do the different domains of polymerase play during this highly regulated process? We are using fast footprinting and rapid quench methods to answer these questions; current results summarized in the figures below.





Mechanism of Open Complex (RP_o) Formation & Proposed Series of Large-Scale Conformational Changes
Kontur et al. *Biochemistry* 45: 2161-2177, 2006

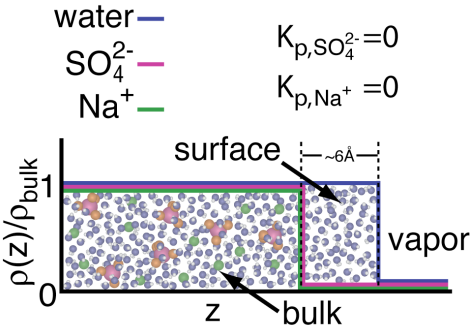
2. IHF/HU-DNA interactions: model systems for the study of coupled folding and DNA wrapping. These two structurally homologous proteins play key roles in organizing the bacterial nucleoid and are involved in numerous DNA transactions (transcription, replication, repair). To gain insight into their functions, we are studying their specific and nonspecific binding modes and how these modes are influenced by solution variables.



34 bp mode 10 bp mode

Model of the transition from a 34 bp DNA binding mode to 10 bp mode as the molar ratio of HU to DNA increases. The shift to a smaller binding mode pulls the beta arms of HU out of the DNA minor groove. The U-shaped DNA bend is lost with the removal of the two proline "levers" (green). Strikingly, the two modes have a similar number of contacts between positively charged side chains (blue) with negatively charged DNA phosphate oxygens (red), consistent with the observation that changes in salt concentration affect the binding affinity of both modes to the same extent. (Koh et al., in preparation, 2009).

Structural Interpretation and Predictions of the Effects of Solutes and Hofmeister Salt Ions on Biopolymer Processes: Interactions of solutes and salts with biopolymer surfaces play a large role in determining the kinetics and thermodynamics of biopolymer processes such as folding, assembling, binding and crystallization. Recent research in the Record lab has focused on the development of a model and molecular thermodynamic analysis to interpret and predict these effects quantitatively in terms of structural information. This can be done using the Solute Partitioning Model (SPM), a two-state model that interprets the effects of a solute on a biopolymer process in terms of the change in water accessible surface of the biopolymer and a partition coefficient K_p quantifying the local concentration of the solute in the water of hydration of that surface, relative to its bulk concentration. A database of partition coefficients for salt ions and solutes is being established from analysis of experiments with biopolymers and model compounds. With this database and structural information about the interface formed in a protein-protein or protein-nucleic acid complex, for the first time one will be able to predict the effect of a solute or Hofmeister salt on the thermodynamics and kinetics of protein and nucleic acid processes, and interpret differences between predicted and observed solute effects in terms of coupled processes (e.g. large-scale conformational changes coupled to binding).



The salt-ion partitioning model superimposed over an idealized representation of molecular dynamics simulation results showing exclusion of Na_2SO_4 from the air–water interface. Pegram and Record, *Chem. Phys. Lett.* 467, 1-8 (2008).

J.R. SCHMIDT

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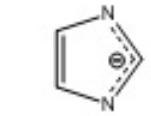
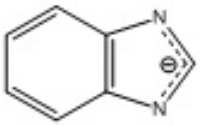
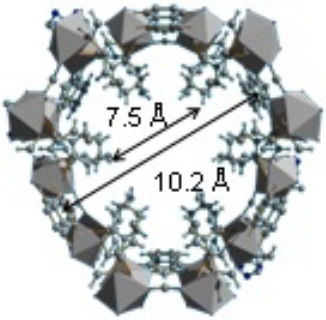
Research

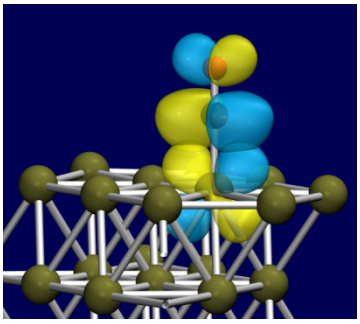
The Schmidt group applies a diverse set of computational approaches to study complex materials, often with direct applications to problems of relevance to energy / fuels. Our research spans the areas of statistical mechanics, electronic structure theory, and dynamics. We utilize both established and novel computational methodologies, including: atomistic molecular dynamics simulations, high-level electronic structure, energy decomposition analysis, QM/MM approaches, path-integral techniques, etc. Current areas of application include nano-porous materials for flue gas separation, enabling energy-efficient CO_2 sequestration; and heterogeneous catalytic conversion of biomass to liquid fuel.

One are of research focus is on CO_2 adsorption and gas separation on porous metal-organic hybrid compounds known as zeolitic imidazolate frameworks (ZIFs), which have shown great promising in absorbing CO_2, and also for separating CO_2 from other gases such as N_2 that are frequently found in the exhaust streams of coal power plants. We using high-level ab initio symmetry adapted perturbation theory calculations to develop physically-motivated force fields to enable a predictive understanding of the relationship between ZIF functionalization of the CO2 adsorption capacity and selectivity in these materials. We are also developing advanced simulation methods to enable order-of-magnitude increase in simulation throughput, thus facilitating high-throughput materials screenings.



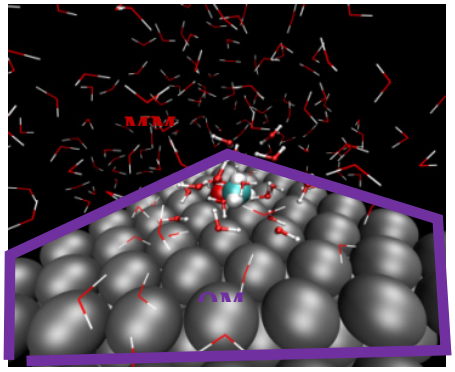






We are also working to develop new theoretical tools to facilitate a predictive understanding of heterogeneous catalyst systems. We recently developed an extension of the existing Natural Bond Orbital (NBO) orbital localization procedure (which has been tremendously successful in elucidating chemical reactivity in small-molecule systems) to solid-state periodic systems and surface models. The resulting NBO analysis yields a chemically-intuitive “general chemistry” Lewis-like picture of bonding between catalysts / adsorbate in terms of localized orbitals. We are exploring applications to catalytic screening, including new NBO-based catalyst “descriptors”.

We are also developing novel QM/MM-like approaches to facilitate computational studies of solution-phase heterogeneous catalysis. Such systems are becoming increasing relevant, particularly in the transformation of biomass to usable liquid fuel. Here many open questions remain regarding the role of solvent in modulating the activity / selectivity of the catalysts. Unfortunately, no existing computational approaches are able to address these systems due to the complex metal/adsorbate/solvent interface and the need to sample over many solvent configurations. Here we are developing several mixed QM/MM approaches to allow us to address this new class of systems.



Research in the group will offer opportunities for students in a variety of areas, including the use of existing simulation and computational programs and the design of novel computational algorithms. Students will not only learn to utilize existing codes to understand interesting phenomena, but also learn to extend existing methodology by implementing the algorithms that we will design.

Other research interests include the continued development and educational applications of the WebMO software package (www.webmo.net). WebMO provides an easy-to-use, web-based interface to many computational chemistry packages for both research and teaching applications. In the future I hope to integrate WebMO into several of the lecture and laboratory classes within the department.

Selected Publications

- Dunnington, B.; Schmidt, J. R., Generalization of Natural Bond Orbital Analysis to periodic systems: Applications to solids and surfaces via plane-wave density functional theory. *J. Chem. Theory Comput.* **2012, submitted**.
- Yu, K.; Schmidt, J. R., Many-Body Effects are Essential in a Physically-Motivated CO_2 Force Field. *J. Chem. Phys* **2012, 136**, 034503.
- McDaniel, J. G.; Yu, K.; Schmidt, J. R., Ab Initio, Physically Motivated Force Fields for CO2 Adsorption in Zeolitic Imidazolate Frameworks. *J. Phys. Chem. C* **2012,** 116, 1892-1903.
- Yu, K.; Schmidt, J. R., Elucidating the Crystal Face- and Hydration-Dependent Catalytic Activity of Hydrotalcites in Biodiesel Production. *J. Phys. Chem. C* **2011,** 115, 1887-1898.
- Yu, K.; McDaniel, J.; Schmidt, J. R., Physically-motivated, robust, ab inito force fields for CO_2 and N_2. *J. Phys. Chem. B* **2011,** 115, 10054-10063.

Awards

- UW Honored Instructor, 2010
- Graduate Research Excellence Award, University of Wisconsin, 2006
- Fannie and John Hertz Foundation Graduate Fellowship, 2001-2006
- Albert E. Lampen Mathematics Prize, Hope College, 2001
- Almon T. Godfrey Prize in Chemistry, Hope College, 2001
- Barry Goldwater Scholarship, 2000
- Beckman Scholar's Research Fellowship, 1999-2000

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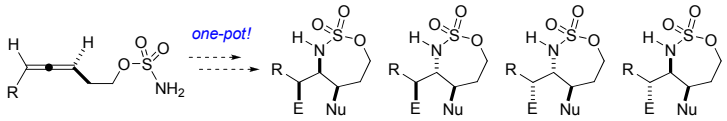
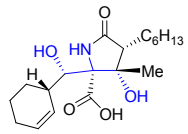
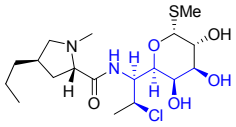
Research Research in the Schomaker group is driven by the need for more efficient methods to transform simple hydrocarbons and gaseous small molecules into more complex building blocks for synthesis. Our program encompasses catalyst development and optimization, elucidation of reaction mechanisms and applications of new methodologies to the synthesis of natural products and other useful molecules. Projects in our group are designed to offer students the ability to gain skills that will serve them well throughout their scientific careers, whether in an academic, government or industrial setting.

Allene oxidation methods for the synthesis of densely functionalized amines. The oxidation of alkenes is a common method to introduce heteroatoms into unsaturated substrates. However, if more than two contiguous heteroatom-bearing stereocenters are desired, typical olefin oxidation methods are not always ideal. The aziridination of an allene to a strained bicyclic methylene aziridine can transform a simple enantioenriched hydrocarbon to many valuable synthetic motifs that contain flexible combinations of three or more contiguous carbon-heteroatom bonds. Exploration of the reactivity of these unusual heterocycles provides many exciting opportunities for both methodology development and applications to total synthesis.

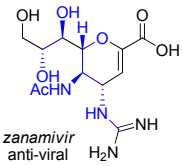




cinnabaramide E
protease inhibitor, anti-cancer



lincomyin analogue
antibiotic



zanamivir
anti-viral

New methods to incorporate gaseous molecules into unsaturated substrates. CO_2 is inexpensive, relatively non-toxic, non-flammable and can display high atom economy. However, the kinetic and thermodynamic stability of CO_2 represent a challenge for organometallic chemists. We are designing methods and catalysts to incorporate CO_2 into simple unsaturated substrates, including alkenes, alkynes and allenes. We hope to reveal new mechanistic avenues for the activation of CO_2 while providing routes to high-value starting materials used in the pharmaceutical, polymer, agricultural and electronic markets. Three areas of current interest are oxidative carboxylation reactions, the conversion of olefins directly to acrylic acids and the development of new methods for asymmetric carboxylation.

New Cu catalysts for cross-coupling under mild conditions. Pd-catalyzed reactions are powerful tools for C-C and C-heteroatom bond formations, yet the high cost of Pd can be problematic. Cu is an inexpensive and abundant 1st-row transition metal (approximately 1/4000 of the price of Pd on a molar basis) that can catalyze many of the same reactions as Pd. However, current conditions are often harsh, employ inconvenient polar aprotic solvents and exhibit poor functional group tolerance. Our group has recently uncovered a mild cross-coupling reaction of aryl halides that utilizes a directing group effect to access a key Ar-Cu intermediate. Studies in this new area in our group hold exciting promise for developing efficient Cu-catalyzed versions of many Pd-catalyzed transformations.

Total synthesis of natural products via nitrogen-centered radical cascade chemistry. The total synthesis of natural products offers students a chance to develop strategic and tactical expertise in the construction of complex molecules, skills that will serve them well throughout their entire scientific careers. Obviously, interesting molecular architectures and the ability to stimulate new reaction development and highlight existing reaction methodologies are valid reasons for choosing a target. We are exploring the chemistry of nitrogen-centered radicals to yield complex, polycyclic ring systems. These new methods will be applied to the total synthesis of bioactive natural products.

Selected Publications

- "Olefins as directing groups for Cu-catalyzed halogen transposition/cross-coupling reactions." Van Hoveln, R.; Grigg, R.D.; Schomaker, J.M. *Manuscript in preparation.*
- "Flexible stereotriad synthesis *via* allene oxidation." Adams, C.S.; Boralsky, L.A.; Schomaker, J.M. *Manuscript in preparation.*
- "Facile generation of benzyl carbanions from styrenes." Grigg, R.D.; Rigoli, J.W.; Van Hoveln, R.; Neale, S.; Schomaker, J.M. *Manuscript submitted,* Feb. **2012**.
- "Stereocontrolled synthesis of 1,3-diamino-2-ols from allenes." Weatherly, C.D.; Rigoli, J.W.; Schomaker, J.M. *Manuscript submitted*, Feb. **2012**.
- "1,4-Diazaspiro[2.2]pentanes as a platform for the synthesis of diamine-bearing stereotriads." Rigoli, J.W.; Boralsky, L.A.; Hershberger, J.C.; Meis, A.R.; Guzei, I.A.; Schomaker, J.M. *J. Org. Chem. in press* Feb. **2012**.
- "Synthesis of Propargylic and Allenic Carbamates via the C-H Amination of Alkynes." Rigoli, J.W.; Grigg, R.D.; Pearce, S.D.; Schomaker, J.M. *Org. Lett.* **2012**, *14*, 280.
- "Organometallics Roundtable 2011." Gladysz, J.; Ball, Z.; Bertrand, G.; Blum, S.A.; Dong, V.M.; Dorta, R.; Hahn, F.E.; Humphrey, M.G.; Jones, W.D.; Klosin, J.; Manners, I.; Marks, T.J.; Mayer, J.M.; Rieger, B.; Ritter, J.C.; Sattelberger, A.P.; Schomaker, J.M.; Yam, V.W. *Organometallics* **2012**, *31*, 1.
- "α,β-Unsaturated imines via Ru-catalyzed coupling of allylic alcohols and amines." Rigoli, J.W.; Moyer, S.A.; Pearce, S.D.; Schomaker, J.M. *Org. Biomol. Chem.* **2012**, *10*, 1746.
- "Efficient Processes to Prepare Asymmetric, Heteroatom-Bearing Stereotriads *via* Allene Oxidation." Schomaker, J.M.; Boralsky, L.A.; Rigoli, J.W.; Hershberger, J.C. U.S. Patent Disclosure, filed June, **2011** through the WARF.
- "C-H amination/cyclocarbonylation of allene carbamates: a versatile platform for the synthesis of α,β-unsaturated γ-lactams." Grigg, R.D.; Schomaker, J.M.; Timokhin, V. Invited paper for the "*Tetrahedron Young Investigator Symposium-in-Print*", **2011**, *67*, 4318.
- "Allene Functionalization via Bicyclic Methylene Aziridines." Boralsky, L.A.; Marston, D.; Grigg, R.D.; Hershberger, J.C.; Schomaker, J.M**.** *Org. Lett.* **2011**, *13*, 1924.
- "Polymorphism of 5-(pyridin-2-ylmethylene)-3-phenyl-2-methylthio-3,5-dihydro-4*H*-imidazole-4-one." Guzei, I.A.; Gunn, E.M.; Spencer, L.C.; Schomaker, J.M.; Rigoli, J.W. *CrystEngComm*, **2011**, *13*, 3444-3450.
- Kulshrestha, A.; Schomaker, J.M.; Holmes, D.; Staples, R.J.; Jackson, J.E.; Borhan, B. "Addition of Organometallic Reagents to Aziridine-2-Carboxyaldehydes: Selectivity with Different Protecting Groups and Substitution Patterns." *Chem. Eur. J.* **2011**, *17*, 12326.
- Boyd, W.C.; Crimmin, M.; Rosebrugh, L.; Schomaker, J.M.; Bergman, R.G.; Toste, F.D. "Cobalt-Mediated, Enantioselective Synthesis of C2 and C1 Dienes." *J. Am. Chem. Soc.* **2010**, *132*, 16365.
- J.M. Schomaker, F.D. Toste, and R.G. Bergman, "Cobalt-Mediated [3 + 2]-Annulation Reaction of Alkenes with α,β-Unsaturated Ketones and Imines" *Org. Lett.* **2009**, *11(16)*, 3698-3700.
- J.M. Schomaker and B. Borhan, "Total Syntheses of Haterumalides NA and NC via a Chromium-Mediated Macrocyclization." *J. Am. Chem. Soc.* **2008***, 130*, 12228-12229.
- J.M. Schomaker, W.C. Boyd, I.C. Stewart, F.D. Toste, and R.G. Bergman, "Cobalt Dinitrosoalkane Complexes in the C-H Functionalization of Olefins." *J. Am. Chem. Soc.* **2008**, *130*, 3777-3779.
- J.M. Schomaker, A.R. Geiser, R. Huang, and B. Borhan, "Tetrasubstituted Pyrrolidines via a Tandem Aza-Payne/Hydroamination Reaction." *J. Am. Chem. Soc.* **2007**, *129*, 3794-3795.
- J.M. Schomaker, S. Bhattacharjee, J. Yan, and B. Borhan, "Diastereomerically and Enantiomerically Pure 2,3-Disubstituted Pyrrolidines from 2,3-Aziridin-1-ols Using a Sulfoxonium Ylide: A One-Carbon Homologative Relay Ring Expansion." *J. Am. Chem. Soc.* **2007**, *129*, 1996-2003.

Awards

- Thieme Chemistry Journal Award 2010
- Ruth L. Kirschstein National Research Service Award Research Training Grant (NIH) 2007-2009
- American Chemical Society, Division of Organic Chemistry Graduate Fellowship sponsored by Eli Lilly 2004-2005
- Michigan State University Distinguished Graduate Fellowship 2001-2005
- Dow Chemical Company Foundation Graduate Fellowship 2004
- Association for Women in Science Educational Foundation Predoctoral Fellowship 1999
- Outstanding Thesis and Dissertation Award, Central Michigan University 1998
- Dow AgroSciences Inventor Award 1997
- DowElanco Inventor's Award 1993, 1994, 1996
- Dow Chemical Company Special Recognition Award, Agricultural Chemicals and Process Research 1992, Organic Chemicals and Polymers 1991

DAVID C. SCHWARTZ

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LMCG:

Scientists: Steve Goldstein, Ph.D., Mathematics; Louise Pape, Ph.D., Biological Sciences; Shiguo Zhou, Ph.D., Plant Pathology & Evolutionary Biology
Postdoc: Prabu Ravindran
Graduate Students: Aditya Gupta (Biophysics), Kristy Kounovsky-Shafer (Chem), Mohana Ray (Chem), Tim Schramm (Chem), Brian Teague (CMB)
Undergraduates: Emerald Nelson**,** Andrea Slavney, Allison Verre
Laboratory Administrator: Dena Clark
Computational Staff: Nathan Panike
Instrumentation Innovators: Gus Potamousis, Michael Place
Research Specialists: Mike Bechner

Research

Our laboratory creates functional systems for many types of genome analysis engendering large data sets for providing scalable biological insights. For this purpose we investigate the biochemical and physical attributes of individual molecules or complexes because reduction of experimental scale terminates at the level of a single molecule. Single molecules are the ultimate analyte since they represent the pinnacle of miniaturization and, when systematically analyzed as ensembles, offer the greatest advantages for generation of large-scale data sets. Such large and often complex data sets are the currency of modern biological analysis requiring extensive statistical and informatic components for revealing biological stories. In this regard, we have incorporated these components into our single molecule systems allowing us to discover novel human genome polymorphisms and to know the detailed architecture of cancer genomes. The new systems we are developing are pushing us to understand molecular nanoconfinement in ways fostering development of fluidic devices that, when combined with novel molecular labeling or detection schemes, will power personal genomics and offer new routes for grappling with the complexity inherent to all biological systems.

Selected Publications

- Sarkar, D., Goldstein, S., Schwartz, D. C. and Newton, M. A. Statistical significance of optical map alignments. *J. Comp. Biol*., accepted, 2011.
- Young, N.D., *et al*. The *Medicago* genome provides insight into the evolution of rhizobial symbioses, *Nature*, 480, 520–524, 2011.
- Kim, K., Choi, B., Kounovsky, K. L., Chang, R., Jung, G. Y., Jo, K., and Schwartz, D. C. Nanochannel Confinement: DNA Stretch Approaching Full Contour Length. *Lab on a Chip,* 2011 May 21;11(10):1721-9. Epub 2011 Mar 23 (featured on the cover)
- Schwartz, D.C. and M.S. Waterman. "New Generations: Sequencing Machines and Their Computational Challenges." *Journal of Computer Science and Technology*, 25(1): p. 3-9, **2010**.

- Teague, B., M.S. Waterman, S. Goldstein, K. Potamousis, S. Zhou, S. Reslewic, D. Sarkar, A. Valouev, C. Churas, J.M. Kidd, S. Kohn, R. Runnheim, C. Lamers, D. Forrest, M.A. Newton, E.E. Eichler, M. Kent-First, U. Surti, M. Livny, and D.C. Schwartz. "High-resolution human genome structure by single-molecule analysis." *Proceedings of the National Academy of Science USA*, 107(24): 10848-53, **2010**.
- Antonacci, F., J.M. Kidd, T. Marques-Bonet, B. Teague, M. Ventura, S. Girirajan, C. Alkan, C.D. Campbell, L. Vives, M. Malig, J.A. Rosenfeld, B.C. Ballif, L.G. Shaffer, T.A. Graves, R.K. Wilson, D.C. Schwartz, and E.E. Eichler. "A large and complex structural polymorphism at 16p12.1 underlies microdeletion disease risk." *Nat Genet*, 42(9): p. 745-50, **2010**.
- Yu, H., K. Jo, K.L. Kounovsky, J.J. de Pablo, and D.C. Schwartz. "Molecular propulsion: chemical sensing and chemotaxis of DNA driven by RNA polymerase." *J Am Chem Soc*, 131(16): p. 5722-3 **2009**.
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- Zhou, S., F. Wei, J. Nguyen, M. Bechner, K. Potamousis, S. Goldstein, L. Pape, M.R. Mehan, C. Churas, S. Pasternak, D.K. Forrest, R. Wise, D. Ware, R.A. Wing, M.S. Waterman, M. Livny, and D.C. Schwartz. "A single molecule scaffold for the maize genome." *PLoS Genet*, 5(11): p. e1000711, **2009**.
- Schnable, P.S., D. Ware, R.S. Fulton, … D.C. Schwartz, …,and R.K. Wilson. "The B73 maize genome: complexity, diversity, and dynamics." *Science*,. 326(5956): p. 1112-5, **2009**.
- Jo, K., Y.L. Chen, J.J. de Pablo, and D.C. Schwartz. "Elongation and migration of single DNA molecules in microchannels using oscillatory shear flows." *Lab on a Chip*, 9(16): p. 2348-55, **2009**.
- Sambriski, E.J., D.C. Schwartz, and J.J. de Pablo. "Uncovering pathways in DNA oligonucleotide hybridization via transition state analysis." *Proceedings of the National Academy of Science USA*, 106(43): p. 18125-30, **2009**.
- Kidd, J.M., Cooper, G.M., …Schwartz, D.C., …, et.al. "Mapping and sequencing of structural variation from eight human genomes." *Nature 453*: 56-64, **2008**.
- Izmitli, A., Schwartz, D.C., Graham, M.D., and de Pablo, J.J. "The effect of hydrodynamic interactions on the dynamics of DNA translocation through pores." *Journal Physical Chemistry 128*: 085102 1-7, 2008.
- Zhou, S., Bechner, M.C., Place, M., Churas, C.P., Pape, L., Leong, S.A., Runnheim, R., Forrest, D.K., Goldstein, S., Livny, M. and Schwartz, D.C. "Validation of rice genome sequence by optical mapping." *BMC Genomics* **8**:278, **2007**.
- Li., H., Valouev, A., Schwartz, D.C., Waterman, M.S. and Li, L.M. "A quantile method for sizing optical maps." *Journal of Computational Biology 14*: 255-266, **2007**.
- Knotts, IV, T.A., Rathore, N., Schwartz, D.C., de Pablo, J.J. "A coarse grain model for DNA." *J. Chem Phys*., *126***:** 084901 1-12, **2007**.
- Jo, K., Dhingra, D.M., Odijk, T., de Pablo, J.J., Graham, M.D., Runnheim, R., Forrest, D., and Schwartz, D.C. "A single-molecule barcoding system using nanoslits for DNA analysis." *Proceedings of the National Academy of Science USA 104*:2673-2678, **2007**.
- Wu, T., and Schwartz, D.C. "Transchip: Single-molecule detection of transcriptional elongation complexes." *Analytical. Biochemistry 361*: 31-46, **2007**.
- Valouev, A., Schwartz, D.C., Zhou, S. and Waterman, M.S. "An algorithm for assembly of ordered restriction maps from single DNA molecules." *Proceedings of the National Academy of Science USA 103***:** 15770-15775, **2006**.
- Schwartz, D.C., "The new biology." in *The Markey Scholars Conference*, G.R. Reinhardt, Editor. National Academies Press: Puerto Rico. p. 73-79, **2003**.

Awards

- Vilas Associate (2009-2011)
- Kellett Mid-Career Award (2002-2007)
- American Society for Biochemistry and Molecular Chemistry Amgen Prize (1995)
- Beckman Young Investigator Award, from the Arnold and Mable Beckman Foundation (1993)
- Presidential Young Investigator Award, from the National Science Foundation (1990)
- *Biochemical Analysis* Prize from the German Society of Clinical Chemistry, presented at Biotechnica, 1988 and awarded jointly with Dr. Charles Cantor (1988)
- Lucille P. Markey Award (1988)

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Research

The long term goal of our research is to develop predictive theories for the dynamics of small molecules in order that we may determine both the products and rates of laser initiated chemical events. Working towards this goal our current research focuses on theoretically describing the dynamics and spectroscopy of polyatomic molecules in both the gas and condensed phases. In the gas phase, we are primarily interested in understanding and elucidating the mechanisms and pathways of intramolecular energy flow of hydrogen bonded species and systems where nonadiabatic effects are at play. In the liquid phase we are investigating vibrational relaxation of CH and OH stretches due to the interplay of solvent-solute interactions and intramolecular couplings.

At low energies the dynamics in the gas phase is well understood. The rotational and vibrational motions are separable, and the vibrations consist of independent normal mode harmonic oscillators. At higher energies, that are relevant to chemical dynamics, the coupling between these motions becomes appreciable, mixing occurs as Fermi and Coriolis resonance interactions become prevalent. The resultant energy flow between the normal modes can be both rapid and complex. At yet higher energies, descriptions of the dynamics once again can be simplified, and statistical descriptions such as random matrix theory can be used.

The exact quantum mechanical solutions to the dynamics over a wide range of energies, using standard basis set methodologies, are intractable for systems with more than three degrees-of-freedom, hence alternative routes to their solutions must be explored and developed. One approach, that we have successfully pursued, is the implementation of perturbation theory to reduce the complexity of the problem. This approach not only allows us to describe many experimental spectra, but it also enables us to understand the spectra in terms of features in the classical phase space structures. With these methods we have begun to understand the dynamics of molecules whose energies span from the normal mode regime to the statistical region.

Vibrational relaxation in the condensed phase is relevant to many aspects of chemistry, physics, and biology. It is involved in thermal chemistry, shock-induced chemistry, electron transfer, photochemistry, and biological processes such as vision and photosynthesis. Moreover, vibrationally excited solute molecules relax due to solvent-solute interactions, hence the rate of energy transfer can be used as a probe of these interactions. At present we are investigating the role of the CH stretch relaxation in neat chloroform in order to unravel the multiple relaxation pathways that are available to this molecule and to develop the theoretical tools that will enable us to combine quantum descriptions of the solvent with classical descriptions of the solute.

Strongly correlated electronic and nuclear motions are central to many chemical processes. When present, these correlations can influence a wide variety of chemical observables. A clear example of such correlated motion is simultaneous proton and electron transfer. On a more practical level, a significant challenge of molecular electronics is that the passage of electrons is often substantially coupled to nuclear degrees of freedom, and these couplings strongly affect electrical properties ranging from resistance to Kondo temperatures. In this area of strongly correlated electron-nuclear motion, we are

studying three systems. The first is that of proton transfer in the tunneling regime in the condensed phase. Here, due to significant charge redistribution during the transfer process, the solvent reorientational motion plays a central role. The second and third systems are the open shell methoxy/ hydroxymethyl $CH_3O \leftrightarrow CH_2OH$ system and the NO_2 molecule. The study of these systems requires one to go beyond the Born-Oppenheimer approximation and inlcude the mixing of manifolds of vibrational states belonging to different electronic surfaces.

For more information, about our group and our research see our web page at sibert.chem.wisc.edu.

Selected Publications

- Carlos Baiz, Kevin Kubarych, Eitan Geva, and Edwin L. Sibert, A Local-Mode Approach to Modeling Multidimensional Infrared Spectra of Metal Carbonyls, J. Phys. Chem. A. **115** ,5354-5363 **(2010)**.
- Jayashree Nagesh and Edwin L. Sibert, Vibrational Dynamics around the Conical Intersection: a Study of Methoxy Vibrations, J. Chem. Chem. Phys. **12**, 8250-8259 **(2010**).
- Ruomu Jiang and Edwin L. Sibert, How Do Hydrogen Bonds Break in Small Alcohol Oligomers? *J. Phys. Chem. A*. **113**, 7275-7285 (**2009**).
- George G. Barnes, Shane M. Squires and Edwin L. Sibert. Symmetric Double Proton Tunneling in Formic Acid Dimer: A Diabatic Basis Approach. *J. Phys. Chem*. B **112**, 595-603 (**2008**).
- Edwin L. Sibert, Eduardo Vergini, Rosa M. Benito, Florentino Borondo. Quantum Localization through Interference on Homoclinic and Heteroclinic Circuits. *New J. Phys*. **10**, 053016 (**2008**).
- Edwin L. Sibert, Sai G. Ramesh, and Tolga S. Gulmen. Vibrational Relaxation of OH and CH Fundamentals of Polar and Nonpolar Molecules in the Condensed Phase. *J. Phys. Chem*. A, **112** (45), 11291 **(2008).**
- Sai G. Ramesh and Edwin L. Sibert. Time Scales and Pathways of Vibrational Energy Relaxation in Liquid $CHBr_3$ and $CDBr_3$. *J. Chem. Phys*. **125,** 244512 (**2006**).
- Edwin L. Sibert and Martin Gruebele. Molecular Vibrational Energy Flow and Dilution Factors in an Anharmonic State Space. *J. Chem. Phys*. **124**, 024317 (**2006**).
- Tolga S. Gulmen and Edwin L. Sibert. Vibrational Energy Relaxation of the OH(D) Stretch Fundamental of Methanol in Carbon Tetrachloride. *J. Chem. Phys*. **122**, 194306 (**2005**).
- Edwin L. Sibert and Jairo Castillo. Theoretical Studies of the Potential Surface and Vibrational Spectroscopy of CH_3OH and its Deuterated Analogues. *J. Chem. Phys*. **122**, 194306 (**2005)**.

Awards

- Villas Associate, University of Wisconsin, 2002-2003
- James W. Taylor Excellence in Teaching Award, University of Wisconsin, 2002
- NSF Presidential Young Investigator, University of Wisconsin, Madison, 1989-94
- Miller Research Fellowship at the University of California, Berkeley, 1985-86
- University of Colorado Research and Creative Work Award, 1983
- University of Colorado Graduate Student Foundation Award, 1983
- University of Colorado Fellowship, 1982
- Award for Outstanding work as Teaching Assistant, 1979 & 1980
- McGregory Prize, Colgate University, 1979
- Award as outstanding graduating chemistry major, Colgate University, 1978
- Graduated cum laude with high honors in chemistry, Colgate University

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Research

Theoretical Chemistry
Non-equilibrium statistical mechanics; condensed phase spectroscopy; relaxation processes; crystals, glasses, interfaces, liquids, supercritical fluids, proteins.

My group is interested in the structure and dynamics of condensed phase systems, and in particular, in the theory of time-dependent phenomena in liquids, supercritical fluids, crystalline and amorphous solids, on surfaces, and in proteins. We typically use the methods of classical and quantum non-equilibrium statistical mechanics to investigate these phenomena.

Experimentally, one important avenue for determining the structure and dynamics of condensed matter involves vibrational and optical spectroscopy. Typically, such spectroscopy contains information about local molecular environments, whose extraction, however, usually requires theoretical models and their solutions. For some time we have been developing theoretical models for molecular spectroscopy in crystals, amorphous solids, liquids, and in proteins, and have performed calculations on specific systems for comparison with a number of different types of experiments. Examples include: single-molecule spectroscopy in crystals, glasses and biopolymers, hole-burning spectroscopy in proteins, and conventional and ultrafast vibrational spectroscopy in liquids, supercritical fluids and proteins, and at interfaces.

Relaxation processes are important for the understanding of chemical reaction dynamics, electron transfer reactions, NMR spectroscopy, solid-state laser design, and many other fields. We been involved with developing theories of relaxation processes in condensed phases. Our interests range from fundamental issues in non-equilibrium quantum statistical mechanics, to calculations of multi-phonon relaxation in crystals, and to theories of vibrational energy relaxation in liquids.

Selected Publications

- Vibrational spectroscopy of water in hydrated lipid multi-bilayers. I. FTIR spectra and ultrafast pump-probe observables, S. M Gruenbaum and J. L. Skinner, J. Chem. Phys. **135**, 075101 (2011).
- Interpretation of the water surface vibrational sum-frequency spectrum, P. A. Pieniazek, C. J. Tainter, and J. L. Skinner, J. Chem. Phys. **135**, 044701 (2011).
- Hydrogen bonding at the water surface revealed by isotopic dilution spectroscopy, I. V. Stiopkin, C. Weeraman, P. A. Pieniazek, F. Y. Shalhout, J. L. Skinner, and A. V. Benderskii, Nature **474**, 192 (2011).
- Robust three-body water simulation model, C. J. Tainter, P. A. Pieniazek, Y.-S. Lin, and J. L. Skinner, J. Chem. Phys. **134**, 184501 (2011).
- Development and validation of transferable amide I vibrational frequency maps for peptides, L. Wang, C. T. Middleton, M. T. Zanni, and J. L. Skinner, J. Phys. Chem. B **115**, 3713 (2011).
- Stable and metastable states of human amylin in solution, A. S. Reddy, L. Wang, S. Singh, Y. Ling, L. Buchanan, M. T. Zanni, J. L. Skinner, and J. J. de Pablo, Biophys. J. **99**, 2208 (2010).
- Vibrational spectroscopy and dynamics of water confined inside reverse micelles. P. A. Pieniazek, Y.-S. Lin, J. Chowdhary, B. M. Ladanyi, and J. L. Skinner, J. Phys. Chem. **113**, 15017 (2009).

- Gating mechanism of the influenza A M2 channel revealed by 1 and 2D IR spectroscopies, J. Manor, P. Mukherjee, Y.-S. Lin, H. Leonov, J. L. Skinner, M. T. Zanni, and I. T. Arkin, Structure **17**, 247 (2009).
- Infrared and Raman spectra of liquid water: Theory and interpretation, B.M. Auer and J.L. Skinner, J. Chem. Phys. **128**, 224511 (2008).
- Hydrogen bonding and Raman, IR, and 2DIR spectroscopy of dilute HOD in liquid D2O, B. M. Auer, R. Kumar, J. R. Schmidt and J. L. Skinner, PNAS **104**, 14214 (2007).
- Hydrogen bonding definitions and dynamics in liquid water, R. Kumar, J. R. Schmidt and J. L. Skinner, J. Chem. Phys. **126**, 204107 (2007).
- Pronounced non-Condon effects in the ultrafast vibrational spectroscopy of water, J. R. Schmidt, S. A. Corcelli, and J. L. Skinner, *J. Chem. Phys.* **123**, 044513 (2005).
- Vibrational spectroscopy of HOD in liquid D2O. III. Spectral diffusion, and hydrogen-bonding and rotational dynamics, C. P. Lawrence, and J. L. Skinner, *J. Chem. Phys.* **118**, 264 (2003).
- Quantum dynamics and vibrational relaxation, S. A. Egorov, K. F. Everitt, and J. L. Skinner, *J. Phys. Chem. A* **103**, 9494 (1999).
- Two-state dynamics of single biomolecules in solution, E. Geva and J. L. Skinner, *Chem. Phys. Lett.* **288**, 225 (1998).
- Molecular theory of electronic spectroscopy in nonpolar fluids: Ultrafast solvation dynamics and absorption and emission lineshapes, M. D. Stephens, J. G. Saven, and J. L. Skinner, *J. Chem. Phys.* **106**, 2129 (1997).
- Theory of single molecule optical line shape distributions in low temperature glasses, E. Geva and J. L. Skinner, *J. Phys. Chem. B* **101**, 8920 (1997).

Selected Awards

- ACS Irving J. Langmuir Award in Chemical Physics, 2012
- ACS Physical Chemistry Division Award in Theoretical Chemistry, 2011
- WARF Named Professorship, 2010
- Noyes Memorial Lecturer, University of Rochester, 2008
- Fellow, American Academy of Arts and Sciences, 2006
- Kohler Lecturer, UC Riverside, 2005
- Fellow, American Assoc. for the Advancement of Science, 2003
- University of Wisconsin Chancellor's Distinguished Teaching Award, 2003
- Reilly Lecturer, University of Notre Dame, 2003
- Student Hosted Colloquium Speaker, Stanford University, 2003
- Student Invited Seminar Speaker, MIT, 2002
- Pharmacia Teaching Award, Department of Chemistry, University of Wisconsin, 2000
- Hascoe Distinguished Lecturer, University of Connecticut, 1998
- Fellow, American Physical Society, 1997
- Graduate Student Invited Speaker, University of California, Berkeley, 1997
- Closs Lecturer, University of Chicago, 1997
- Davidson Lecturer, University of Kansas, 1995
- University of Wisconsin Mid-Career Award, 1995
- Humboldt Foundation Senior Scientist, 1993-96
- Guggenheim Fellow, 1993-94

LLOYD M. SMITH

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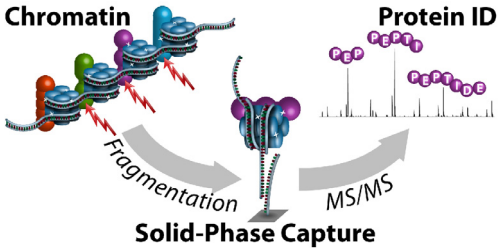
Research in the Smith group is directed at the development of powerful new technologies to drive biological research. The work is multi-faceted and highly interdisciplinary and collaborative in nature. A recent effort in understanding gene regulation builds upon two of our long-standing areas of expertise and interest: 1) surface capture and analysis using biomolecule arrays and 2) mass spectrometry of biological molecules. An emerging area of interest is the high-throughput development of affinity reagents, a cornerstone of modern biotechnology.

Tools for understanding gene regulation. The successful completion of sequencing the human genome and other genomes ushered in a new era in biological research. A strong focus now is identifying regulatory mechanisms that turn genes on or off, and then understanding how such gene regulation is altered by critical biological processes, diseases, or environmental factors such as drugs. We recently established the Wisconsin Center of Excellence in Genomic Sciences, where together with collaborators at the Medical College of Wisconsin, we are developing novel technologies to identify the proteins that bind to particular DNA regions because such regulatory proteins determine, to a large extent, which genes are expressed. Briefly the technology involves (1) chemical cross-linking of proteins to DNA, (2) fragmentation of the chromatin (long strands of DNA wrapped around proteins), (3) capture of these fragments onto surfaces in a DNA-sequence-specific manner, and (4) mass spectrometry to identify and quantify the proteins.

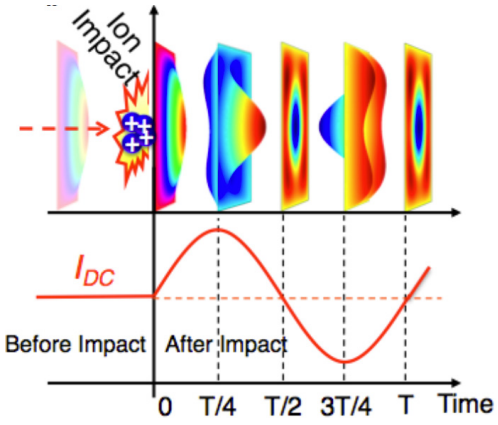


Surfaces. The advent of high-density DNA arrays in the early '90s demonstrated the power of the array concept for genome-wide analyses of biological systems. Our group has a Maskless Array Synthesizer (MAS), which allows any high-density DNA array of interest (up to 786,000 individual DNA features) to be designed and fabricated overnight. We developed a novel lamellar substrate for such DNA array fabrication, consisting of a thin layer of amorphous carbon deposited on a gold thin film over glass. The gold thin film allows the technique of surface plasmon resonance (SPR) imaging to be utilized for label-free detection on these carbon surfaces. Carbon attachment chemistry that we have developed over the last several years permits biomolecule arrays of unprecedented chemical stability to be made on these surfaces. We are actively exploring applications of these new materials for the parallel analysis of DNA:DNA, DNA:RNA and DNA:protein interactions.

Mass Spectrometry. With thousands of genome sequences now readily accessible in databases, research paradigms have fundamentally changed. One of the best examples is in the field of proteomics, where tandem mass spectrometric analyses of complex protein mixtures depend upon whole genome database search algorithms to identify proteins. This approach exploits synergies between genome analysis, bioinformatics, and rapidly evolving instrumentation and chemistries for mass spectrometry.

As powerful as this technology has become, we believe that the field of biological mass spectrometry is still in its infancy. Mass spectrometry as it currently exists is a relatively inefficient process, in which typically only one out of 10^7 to 10^{10} molecules in a sample being analyzed actually give rise to a detection event. This is because of ion losses that occur throughout a mass spectrometry system—in the ion source, the mass analyzer, and at the detector. Our group is interested in addressing the fundamental issues that limit biological mass spectrometry. We have active projects to improve ionization processes, reduce ion suppression and matrix effects, develop a new generation of highly sensitive ion detectors, and develop approaches for the determination of accurate masses of proteins in complex mixtures.

For example, we have collaborated with Robert Blick (Engineering, UW-Madison) to create a novel approach to detection of large ions, based upon the mechanical deformation and vibration of a nanomembrane. The operating principle of the nanomembrane detector is based on the transduction of kinetic energy of the ions into mechanical oscillations of the nanomembrane, which are then detected through their effect upon field emission current. In principle, the nanomembrane detector has no upper mass limit, in contrast to conventional ion detectors. Initial studies have showed that this mode of ion detection offers potential for improved sensitivity in the mass analysis of large ions and complex protein mixtures.



We are also actively engaged in proteomics collaborations encompassing a variety of areas, such as human embryonic stem cells (Prof. Thomson, Morgridge Institute for Research), the proteasome complex in *Arabidopsis* (Prof. Vierstra, Dept. of Genetics, UW-Madison), vocal chord function (Prof. Welham, Dept. of Surgery, UW-Madison), breast cancer (Prof. Gould, UW Comprehensive Cancer Center), and several others. These real-world projects keep us at the cutting edge of the rapidly evolving world of biological mass spectrometry, while helping to provide important information essential to understanding these fascinating and important biological systems.

Affinity reagents. Numerous biotechnology experiments and methods rely heavily upon reagents that specifically interact with a biological molecule of interest. These affinity reagents include antibodies and more recently aptamers (comprised of nucleic acids). Unfortunately, creating such reagents is limited by high cost, lengthy development time, and often inadequate affinity. The current demand for high performance (i.e. strong affinity and specificity) affinity reagents far exceeds the rate at which they can be produced. We are collaborating with Prof. Soh (UC-Santa Barbara) and Prof. Thomson (Morgridge Institute for Research) to create a new affinity reagent development platform consisting of three distinctly novel technologies—microfluidic selection, next-generation aptamer sequencing, and aptamer array imaging. This platform will generate specific aptamers with sub-nanomolar affinities (Kd) for a wide range of protein targets, then identify a pool of the best candidates by next generation DNA sequencing and bioinformatic analysis, and finally home in on the optimal aptamer sequence by parallel synthesis and measurement of the affinities of thousands of aptamer candidates. This integrated approach offers an opportunity to revolutionize the process of aptamer generation for use as affinity reagents for biological research.

Selected Publications

- Liu, Q., Wang, L., Frutos, A., Condon, A., Corn, R.M. and Smith, L.M. 2000. DNA computing on surfaces. Nature, **403**, 175-179.
- Smith, L.M., Shortreed, M. R., Olivier, M. 2011. To understand the whole, you must know the parts: Unraveling the roles of protein-DNA interactions in genome regulation. Analyst, **136** (15), 3060 – 3065.
- Westphall, M.W., Jorabchi, K. and Smith, L.M. 2008. Mass spectrometry of acoustically levitated droplets, Analytical Chemistry, **80** (15), 5847-5853, PMC2561267.
- Lockett, M., Weibel, S., Phillips, M., Shortreed, M., Sun, B., Corn, R., Hamers, R., Cerrina, F. and Smith, L.M. 2008. Carbon-on-metal films for surface plasmon resonance detection of DNA arrays, J. Am. Chem. Soc., **130** (27), 8611-8613, PMC2527731..
- Chen, S., Smith, L.M. 2009. Photopatterned thiol surfaces for biomolecule immobilization. Langmuir, **25** (20), 12275-12282.
- Park, J., Qin, H., Scalf, M., Hilger, R. T., Westphall, M. S., Smith, L.M. and Blick, R., 2011. A Mechanical Nanomembrane Detector for Time-of-Flight Mass Spectrometry. Nano Letters, **11** (9), 3681-4.
- Wu, C.H., *et al.*, 2011. Sequence-Specific Capture of Protein-DNA Complexes for Mass Spectrometric Protein Identification. PLoS ONE, **6** (10):e26217. Epub 2011 Oct 20. PMC3197616.

Selected Awards

- Fellow of the American Association For the Advancement of Science
- Pittsburgh Analytical Chemistry Award
- Member of the Faculty of 1000
- American Chemical Society Award in Chemical Instrumentation
- John D. MacArthur Professorship, University of Wisconsin-Madison
- Association of Biomolecular Resource Facilities Award for development of automated DNA sequencing

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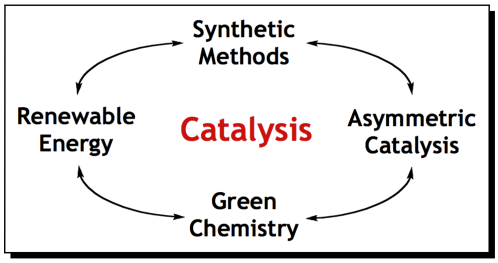
Research

Our research focuses on the field of CATALYSIS, and our work draws upon and impacts a number of areas of chemistry, including synthetic and mechanistic aspects of:

- Organometallic Chemistry
- Organic Chemistry
- Inorganic Chemistry



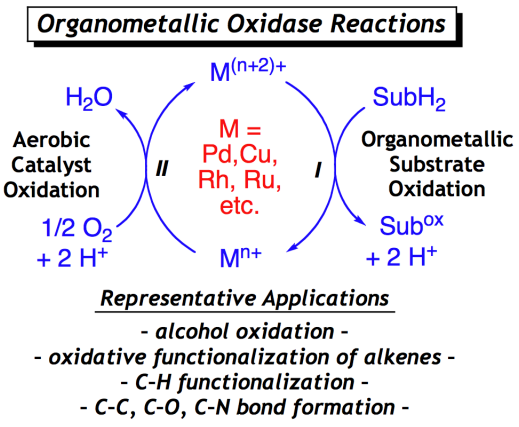
Many of the exciting new methods in organic synthesis consist of catalytic reactions. Furthermore, advances in catalysis research are critical to address many of the major challenges facing our nation and world, including (*i*) reducing the contribution of human activities to global warming, (*ii*) identifying sustainable energy sources and (*iii*) minimizing the environmental impact of chemical synthesis (i.e., green chemistry).

Our interests in the field of catalysis encompass many of these topics, and projects in the lab range from the development of useful synthetic methods for organic chemistry (synthetic organic chemistry) to the elucidation of mechanistic principles that underlie various catalytic transformations (physical organic, inorganic and organometallic chemistry). Mechanistic studies often include the preparation of key catalytic intermediates (synthetic inorganic and organometallic chemistry) and investigation of their fundamental reactivity through the use of kinetic studies, isotope effects, spectroscopic methods, high-level DFT computations and other mechanistic tools. Electrochemical methods are commonly employed in the study of catalysts and metal complexes relevant to the development of new energy-conversion technologies. Two prominent areas of research in our lab are surveyed below.

Aerobic Oxidation Catalysis

There is a dramatic need for environmentally benign oxidation chemistry in the pharmaceutical and chemical industries. Molecular oxygen represents an ideal alternative to commonly used stoichiometric oxidants such as CrO_4^{2-} and MnO_4^-; however, the scope of dioxygen-coupled oxidation reactions is presently quite limited. Our research has been focused on the development and mechanistic characterization of "organometallic oxidase" reactions. Over the past ten years, this class of oxidation reactions has become the most versatile approach for selective aerobic oxidation of organic molecules. Reactions of this type enable selective dehydrogenation (e.g., alcohol oxidation), oxidative carbonylation, and C–H functionalization, including C–C, C–O and C–N bond-forming reactions.

The "oxidase" term reflects the fact that these reactions proceed by a two-stage catalytic cycle that resembles the mechanism of biological oxidases (see graphic). The two stages of the catalytic mechanism feature (1) oxidation of an organic molecule by a transition-metal center, such as Pd^{II} or Cu^{II}, via an organometallic pathway (Stage I) and (2) oxidation of the reduced catalyst by molecular oxygen (Stage II). The mechanistic versatility of organometallic chemistry enables a broad range of oxidative transformations to be achieved with molecular oxygen as the stoichiometric oxidant.

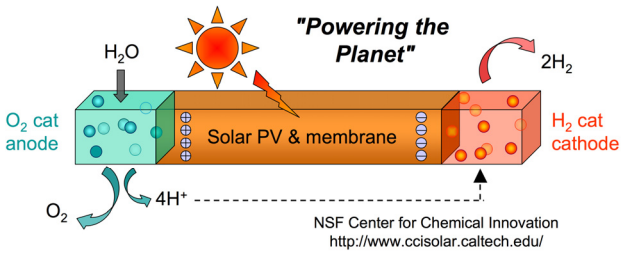


Organometallic oxidase reactions represent the consummate "playground" for chemists with an interest in synthetic and/or mechanistic organometallic, organic and inorganic chemistry, and for those who seek to have an impact on environmentally responsible chemical synthesis. Advances in the synthetic applications of these reactions are closely linked to the elucidation of new fundamental principles of chemical reactivity, for example, new organometallic transformations and reactions of molecular oxygen with transition metal centers. Our group has several active projects in this area:

(1) Development of Pd- and Cu-catalyzed synthetic methods for aerobic oxidative functionalization of alkenes and C–H bonds
(2) Elucidation of catalytic mechanisms of Pd- and Cu-catalyzed organometallic oxidase reactions
(3) Investigation of novel organometallic reactions involving Pd and Cu that are relevant to aerobic oxidation methods
(4) Investigation of fundamental reactions between molecular oxygen and transition-metal complexes

Catalysis for Solar Energy Conversion

The Stahl group is an active participant in the "Powering the Planet" NSF Center for Chemical Innovation (CCI Solar: http://www.ccisolar.caltech.edu). This collaborative team is exploring the fundamental chemistry that underlies one of the most profound challenges of the 21st century: the efficient conversion of solar energy into chemical fuels, such as H_2 or CH_3OH. The CCI investigators ultimately envision a three-component solar water splitting system that features three components: (*i*) a membrane-supported assembly that captures sunlight and efficiently separates electrons and holes with sufficient chemical potential to drive the water-splitting reactions; (*ii*) a two-electron catalyst to facilitate reduction of water to H_2 at the cathode; and (*iii*) a four-electron catalyst for water oxidation to O_2 at the anode (see graphic). Our group is investigating metal-based catalysts and fundamental mechanisms involved in the anodic oxidation of water to O_2. This chemical transformation is formally the microscopic reverse of O_2 reduction reactions involved in the organometallic oxidase reactions described above.



Selected Publications

- Campbell, A. N.; Stahl, S. S. *Acc. Chem. Res.* **2012**, *45*, ASAP. "Overcoming the 'Oxidant Problem': Strategies to Use O_2 as the Oxidant in Organometallic C–H Oxidation Reactions Catalyzed by Pd (and Cu)."
- Izawa, Y.; Pun, D. Stahl, S. S. *Science* **2011**, *333*, 209-212. "Palladium-Catalyzed Aerobic Dehydrogenation of Substituted Cyclohexanones to Phenols."
- Hoover, J. M.; Stahl, S. S. *J. Am. Chem. Soc.* **2011**, *133*, 16901–16910. "Highly Practical Copper(I)/TEMPO Catalyst System for Chemoselective Aerobic Oxidation of Primary Alcohols."
- Gerken, J. B. et al. *J. Am. Chem. Soc.* **2011**, *133*, 14431–14442. " Electrochemical Water Oxidation with Cobalt-Based Electrocatalysts from pH 0–14: The Thermodynamic Basis for Catalyst Structure, Stability and Activity"
- Wendlandt, A. E.; Suess, A. M.; Stahl, S. S. *Angew. Chem., Int. Ed.* **2011**, *50*, 11062-11087. Copper-Catalyzed Aerobic Oxidative C–H Functionalizations: Recent Trends and Mechanistic Insights.
- Ye, X.; Yates, M. H.; Diao, T.; Johnson, M. D.; Stahl, S. S. *Green Chem.* **2010**, *12*, 1180-1186. "Development of a Safe and Scalable Flow-Based Method for Homogeneous Palladium-Catalyzed Aerobic Oxidation Reactions."
- Konnick, M. M.; Stahl, S. S. *J. Am. Chem. Soc.* **2008**, *130,* 5753-5762. "Mechanistic Study of the Reaction of a Pd^{II}–Hydride with Molecular Oxygen to Produce a Pd^{II}–Hydroperoxide."

Awards

- Fellow, American Association for the Advancement of Science 2010
- Alexander von Humboldt Senior Research Award 2010
- Hamel Family Faculty Fellow, UW-Madison 2008-2012
- Moore Faculty Scholar, California Institute of Technology 2008
- H. I. Romnes Faculty Fellowship, University of Wisconsin-Madison, 2007
- Outstanding Mentor Award - UW-Madison, Dept of Chemistry (inaugural award), 2007
- Pfizer Michigan Green Chemistry Award, 2006
- Camille Dreyfus Teacher-Scholar Award 2003-2008
- Alfred P. Sloan Research Fellowship 2002-2004
- National Science Foundation CAREER Award 2001-2005

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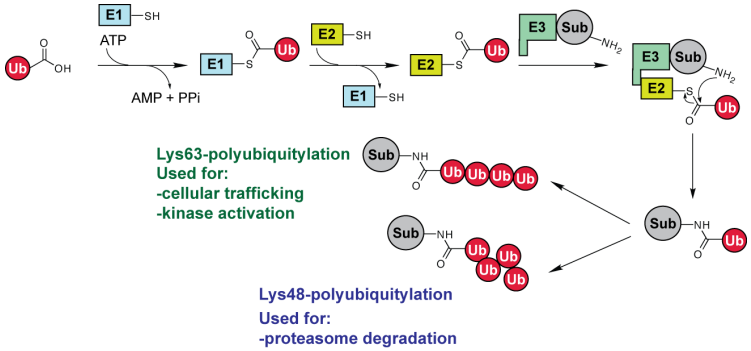
Research

In a very broad sense, my group is interested in combining the tools of synthesis, molecular biology, microbiology, and enzymology to understand how natural products regulate events associated with protein degradation. Our focus is truly at the interface of chemistry and biology and we approach biological problems from the perspective of deciphering chemical mechanisms.

The cell cycle involves rapid and responsive protein turnover, allowing cells to respond immediately to environmental changes. In eukaryotes, protein degradation is catalyzed by the ATP-dependent 26S proteasome, which recognizes substrates marked by the covalent attachment of a polymeric ubiquitin chain. Ubiquitin chains dictate nearly all aspects of proteolytic and non-proteolytic cell cycle regulation; the enzymatic conjugation of ubiquitin to a substrate relies on the sequential and tightly regulated activity of three enzymes (E1, E2, E3), resulting in an isopeptide bond between ubiquitin and the target substrate. Ubiquitin, bearing seven lysines, can then serve as a scaffold upon which the ubiquitin chain can be extended by rounds of enzymatic activity. Distinct chain topologies serve distinct functions: it has been demonstrated that ubiquitin chains comprised of four or more ubiquitin monomers linked through lysine-48 target the substrate for proteasomal degradation, whereas chains linked through lysine-63 do not mediate destruction and are important signaling events in a diverse array of cellular functions.



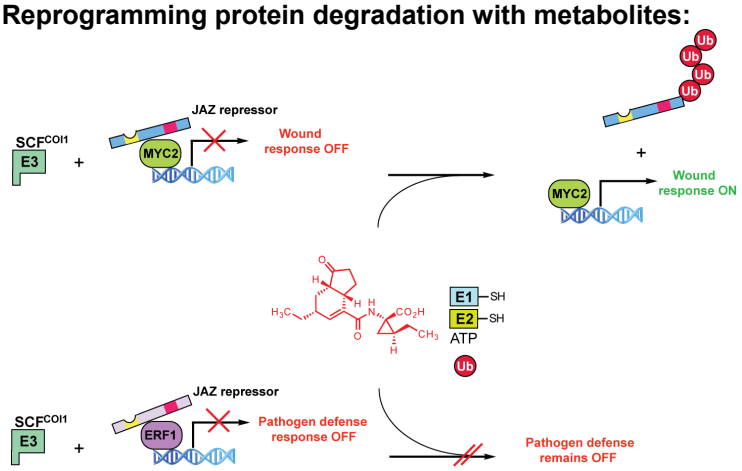
The human genome encodes roughly forty E2 and an estimated 1000 E3 enzymes; the various interactions between ubiquitin-conjugating (E2) and ubiquitin ligase (E3) enzymes are substrate-specific and can produce linkages through any of the seven available lysines, although the basis for this precise catalysis is largely unknown. Interestingly, production of endogenous metabolites can reprogram the activity of ubiquitin ligases, the 26S proteasome – or both – allowing for adaptive responses to a variety of environmental stimuli, including pathogens. Meanwhile, pathogens have evolved clever mechanisms to produce molecular mimics of these hormones for the purpose of crippling the host. Our hypothesis is that small molecules reprogram components of the ubiquitin-proteasome system and can aid in virulence and bacterial proliferation. Our research program is dedicated to understanding 1) the construction of ubiquitin chains and 2) the role secondary metabolites play in reprogramming protein ubiquitylation.

1) Mechanistic Studies on the Formation of Polymeric Ubiquitin Chains

The breast and ovarian cancer type 1 susceptibility protein (BRCA1) is involved in multiple genomic surveillance and repair complexes – mutations in BRCA1 account for ~50% of patients with inherited breast cancer. BRCA1 is a hormone-sensitive ubiquitin ligase that constructs chains of variable linkage, dependent upon the interacting E2. We seek to establish the reactivity of physiologically relevant E2 enzymes and quantify the kinetics of polyubiquitin chain formation in two facets: in the event of DNA damage and in the presence of estrogen. In response to DNA damage, BRCA1 catalyzes lysine-6 linked ubiquitin chains, although the scope of E2s responsible for this activity and the functional significance of this topology have not been explored. Moreover, interactions with transcriptional activator estrogen receptor-alpha modulate the activity and substrate scope of BRCA1 in the presence of endogenous

hormones such as estrogens. We hypothesize that the critical ubiquitin ligase activity of BRCA1 and its sensitivity to hormones bridges the connection between tissue-specific cancers and the ubiquitin-proteasome system. Our work will contribute to defining the temporal framework of DNA repair and will ultimately help to unravel the oncogenesis of hormone-responsive cells.

2) Reprogramming protein degradation with metabolites:



We believe that specific metabolites mediate distinct pathogenic effects against the innate immune response of the host cell, resulting in a compromised immune system and deviation from normal cellular activity. However, these cryptic metabolites and the mechanisms by which they enhance virulence are poorly understood. The model organism, *Arabadopsis thaliana*, deploys small molecules such as (+)-7-jasmonate-isoleucine and indole-3-acetic acid to regulate the attachment of ubiquitin to proteins and defend itself from harmful invaders. In retaliation, the plant pathogen, *Pseudomonas syringae*, has.developed the biosynthetic machinery to produce (+)-coronatine and the indole-3-acetic acid lysyl conjugate for the purpose of commandeering and reprogramming ubiquitin ligase activity. The mechanism of this molecular subversion is unknown and we seek to understand the chemical basis for these events and extend this work to other host-pathogen interactions. We have begun to synthetically characterize these small molecules and classify their biological consequences in pathogenesis; ultimately, our aim is to extrapolate the information gleaned from these natural systems to develop small molecules that target specific protein degradation machinery

Selected Publications

- Strieter, E. R.; Koglin, A.; Aron, Z. D.; Walsh, C. T. "Cascade reactions during coronafacic acid biosynthesis: elongation, cyclization, and functionalization during Cfa7-catalyzed condensation." *J. Am. Chem. Soc.* **2009**, *131*, 2113
- Strieter, E. R.; Bhayana, B.; Buchwald, S. L. "Mechanistic studies on the copper-catalyzed *N*-arylation of amides." *J. Am. Chem. Soc.* **2009**, *131*, 78.
- Koglin, A.; Löhr, F.; Bernhard, F.; Rogov, V. R.; Frueh, D. P.; Strieter, E. R.; Mofid, M. R.; Güntert, P.; Wagner, G.; Walsh, C. T.; Marahiel, M. A.; Dötsch, V. "Structural basis for the selectivity of the external thioesterase of the surfactin synthetase." *Nature*, **2008**, *454*, 907.
- Strieter, E. R.; Vaillancourt, F. H.; Walsh, C. T. "CmaE: A Transferase Shuttling Aminoacyl Groups between Carrier Protein Domains in the Coronamic Acid Biosynthetic Pathway." *Biochemistry* **2007**, *46*, 7549.
- Strieter, E. R.; Buchwald, S. L. "Evidence for the Formation and Structure of Palladacycles During the Pd-Catalyzed C-N Bond-Forming Reaction with Catalysts Derived From Bulky Monophosphinobiaryl Ligands." *Angew. Chem. Int. Ed.* **2006**, *45*, 925.
- Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. "The Role of Chelating Diamine Ligands in the Goldberg Reaction: A Kinetic Study on the Cu-Catalyzed Amidation of Aryl Iodides." *J. Am. Chem. Soc.* **2005**, *127*, 4120.
- Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. "Insights into the Origin of High Activity and Stability of Catalysts Derived from Bulky, Electron-Rich Monophosphinobiaryl Ligands in the Pd-Catalyzed C-N Bond Formation." *J. Am. Chem. Soc.* **2003**,*125*, 13978

Awards

- American Cancer Society Post-doctoral Fellowship, 2005-2008
- ACS Division of Organic Chemistry Graduate Fellowship, 2003-2004
- UW-Madison Hilldale Fellowship for Undergraduate Research

JAMES C. WEISSHAAR

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Research

We participate in the revolution in fluorescence microscopy of biological systems. It is now possible to measure the spatial distribution of proteins and DNA loci with 30-nm precision in live cells and to track their motion in real time. The result is an unprecedented, high resolution view of biological structure and activity. Areas of current interest include: (1) The motion and spatial distribution of GFP-labeled species in live *E. coli* cells. Species of interest include RNA polymerase, ribosomes, architectural proteins, and specific DNA loci. The transcription/translation machinery (ribosomes, the nucleoid, and RNAP) all exhibit a remarkable level of *spatial organization*. (2) The time-resolved attack of antimicrobial agents on single bacterial cell membranes. Examples include LL-37, a human antimicrobial peptide, and synthetic random copolymers designed by the Gellman group. Simultaneous two-color imaging of the antimicrobial and cytoplasmic or periplasmic GFP yields unprecedented insight into the mechanism of attack. (3) The spatial distribution and function of proteins in the tomasyn family, mutations in which are believed to be important factors in Type-2 diabetes. (4) The interaction of actin fibers with secretory vesicles, before and after exocytosis.

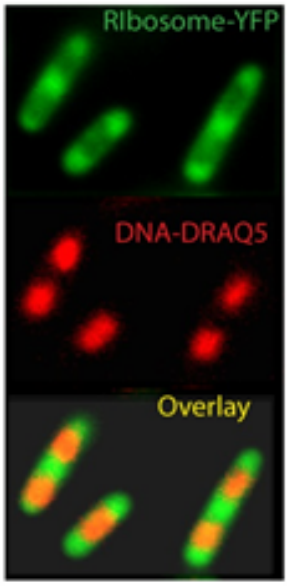

Fig. 1. Widefield image of ribosomes and DNA in live *E. coli* showing strong ribosome-DNA segregation.

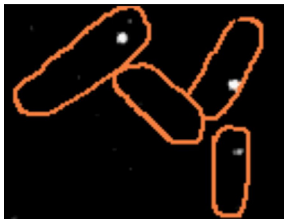

Fig. 2. Live-cell 2-D PALM images of three photoactivated Kaede molecules. Outline of four *E. coli* cells sketched by hand.

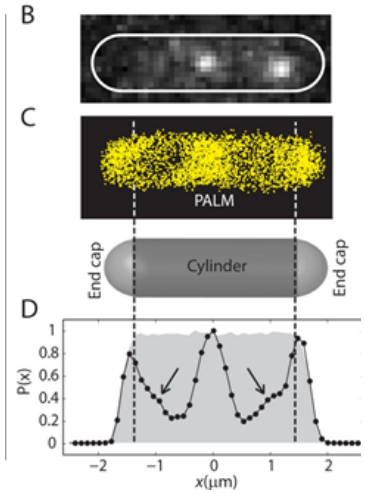

Fig. 3. Superresolution imaging of ribosomes in live *E. coli*. Axial distribution shows strong segregation.

Selected Recent Publications

- M.C. Konopka, K.A. Sochacki, B.P. Bratton, I.A. Shkel, M. T. Record, and J.C. Weisshaar, Cytoplasmic Protein Mobility in Osmotically Stressed *Escherichia coli*, J. Bacteriology **191**, 231-237 (2009).
- T. Wang, E. Smith, E. R. Chapman, and J. C. Weisshaar, Lipid Mixing and Content Release in Single-Vesicle, SNARE-driven Fusion Assay with 1–5 ms Resolution, Biophys. J. **96**, 4122-31 (2009).
- T. Wang, C. Ingram, and J.C. Weisshaar, Model Lipid Bilayer with Facile Diffusion of Lipids and Integral Membrane Proteins, Langmuir **26**, 11157-64 (2010).
- J. Mondal, B. Bratton, Y. Li, A. Yethiraj, and J.C. Weisshaar, Entropy-based Mechanism of Ribosome-Nucleoid Segregation in *E. coli* cells, Biophys. J. **100**, 2605-13 (2011).
- K. Sochacki, I. Shkel, M. Thomas Record, and J. C. Weisshaar, Diffusion of GFP in the periplasm of *E. coli* under conditions of osmotic stress, Biophys. J. **100**, 22-31 (2011).
- E. Smith and J.C. Weisshaar, Docking, not fusion, as the rate-limiting step in a SNARE-driven vesicle fusion assays, Biophys. J., **100**, 2141-50 (2011).
- K. Sochacki, K. Barns, R. Bucki, and J.C. Weisshaar, Real-time attack on single *Escherichia coli* cells by the human antimicrobial peptide LL-37, PNAS **108**, *E*77-81 (2011).
- B. Bratton, R.A. Mooney, and J.C. Weisshaar, Spatial Distribution and Diffusive Motion of RNA polymerase in live *E. coli*, J. Bacteriology **193**, 5138-5146 (2011).
- S. Bakshi, B. Bratton, and J.C. Weisshaar, Subdiffraction-Limit Study of Kaede Diffusion and Spatial Distribution in Live *Escherichia coli*., Biophys. J. **101**, 2535-2544 (2011).

Awards

- American Association for the Advancement of Science Fellow, 2009
- Fellow, American Physical Society, 2001
- Wisconsin Alumni Research Foundation Kellett Mid-Career Research Award, 1998-2003
- Vilas Associate Award, UW-Chemistry, 1997-1998
- Evan P. Helfaer Professor of Chemistry, 1996-2001
- Upjohn Award for Teaching Excellence in Chemistry, 1995
- Hilldale Undergraduate Research Awards, 1993, 1995, 1999, 2001, 2002 (with undergraduates K. Haug , W.-K. Woo, V. Chen, T. Huppert, L. Klein)
- Romnes Faculty Research Fellowship, UW-Madison, 1991-1996
- Dreyfus Research Grant for Newly Appointed Faculty in Chemistry, 1981

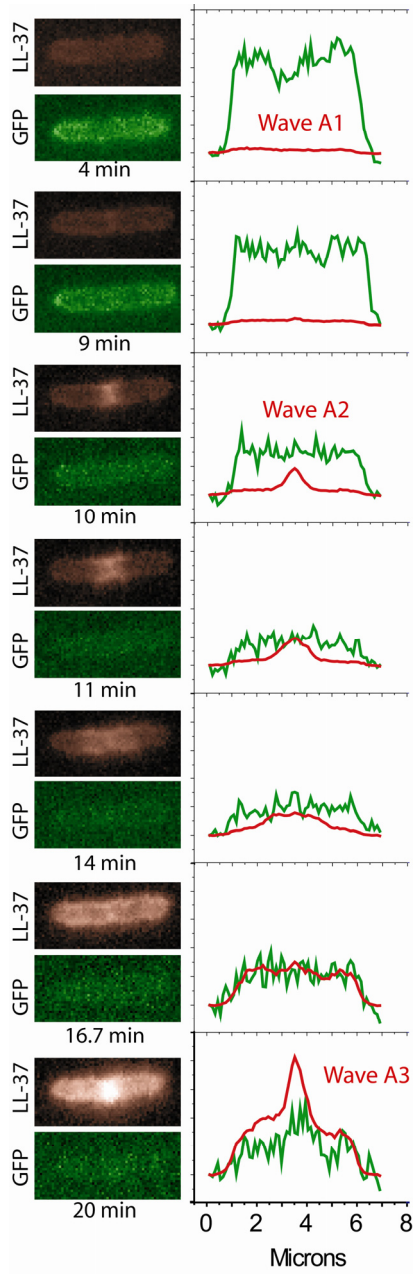

Fig. 4. Periplasmic GFP and rhodamine-LL-37 images vs time. Axial intensity plots at right. The attack comes as three waves, the second of which spreads outward from mid-cell and lyses the outer membrane, releasing GFP.

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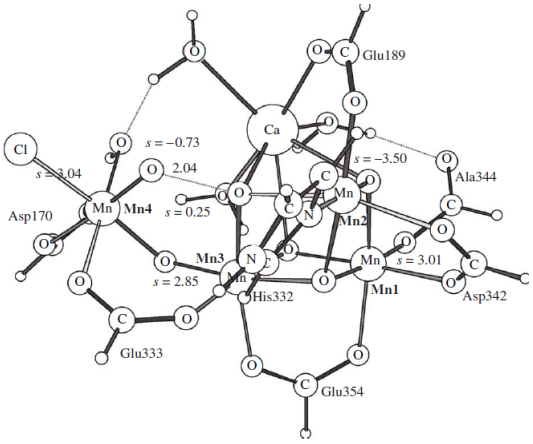
Research

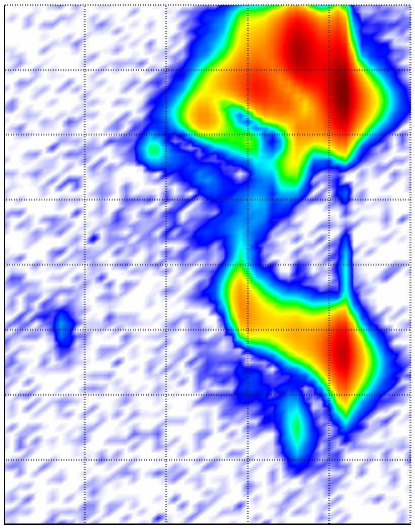
Our group has developed the field of multiply resonant coherent multidimensional spectroscopy (CMDS). It uses multiple, tunable laser beams to excite multiple vibrational and electronic states so rapidly that they create multiple quantum coherences (MQCs). MQCs are quantum mechanically entangled superposition states where each pair of states in the MQC reemit light beams at the frequency difference of the states. New beams are created by nonlinear processes. Monitoring the intensity of the beams as a function of their frequencies creates multidimensional spectra. The spectra contain cross-peaks between quantum states that are coupled by intra- or inter-molecular interactions. The coupling requirement makes the method highly selective for interactions. Changing the time delays between excitation pulses provides the complete dynamics of the coherences and populations present in the superposition state.

Our laboratory uses both picosecond and femtosecond systems to access a wide variety of quantum states. We use these methods to measure the electronic and vibrational states of molecules and the properties of materials. Our research program has four current directions- method development and instrument design, quantum confined nanostructures, photocatalytic materials, and oxygen evolution in photosystem II,. We use our methods to measure the coherent and incoherent dynamics of charge transfer in complex nanostructures including the oxygen evolving complex (OEC) and donor and acceptor materials developed by the Jin and Hamers' groups. By forming MQCs from the electronic states and vibrational states, we hope to measure the dynamics and interstate coupling with quantum state resolution. Our goal is developing a fundamental understanding of dynamics that controls the efficiency the charge transfer in photovoltaic and photocatalytic,systems.

We are also applying our methods to understanding the oxygen evolving center (OEC) of photosystem II (PSII). The OEC contains a cubane-like structure of four Mn ions, a Ca, and four O ions. It is supported by a number of amino acid ligands. The successive absorption of four light photons results in the sequential accumulation of oxidizing equivalents on the OEC's Mn and O ions. By exciting MQCs containing the Mn electronic states and vibrational states of the amino acid ligands and the O-Mn-O modes of the cubane core, we hope to identify the specific couplings and valences of the different parts of the OEC and how they change during the successive accumulation of charge. We also hope to measure the kinetics of changes so we can provide a detailed mechanism for oxygen evolution.

The left hand figure shows the OEC in PSII. The right hand figure shows the CMDS spectra from a 12 quantum coherence of the symmetric and asymmetric stretch modes of a Rh dicarbonyl chelate. The spectrum probes the molecule's potential energy surface through ladder climbing transitions up to the 6th overtone.





Selected Publications

- L. A. Yurs, S. B. Block, A. V. Pakoulev, R. S. Selinsky, S. Jin, and J. C. Wright; Journal of Physical Chemistry C, 115, 22833-22844 (2011). "Multiresonant Coherent Multidimensional Electronic Spectroscopy of Colloidal PbSe Quantum Dots."
- J. C. Wright, Annual Review of Physical Chemistry, 62; 62; 209-230 (2011). "Multiresonant Coherent Multidimensional Spectroscopy."
- S. B.Penwell and J. C. Wright; Journal of Physical Chemistry B, 115, 5564 (2011). "Multiresonant Coherent Multidimensional Spectroscopy of the Vibrationally Induced Decarboxylation of AOT: Deuterium Oxide Reverse Micelles."
- Kornau, K. M.; Rickard, M. A.; Mathew, N. A.; Pakoulev, A. V.; Wright, J. C. Journal of Physical Chemistry A, 115, 4054 (2011). "Multiresonant Coherent Multidimensional Vibrational Spectroscopy of Aromatic Systems: Pyridine, a Model System."
- A. V. Pakoulev, S. B. Block, L. A. Yurs, N. A. Mathew, K. M. Kornau and J. C. Wright; Journal of Physical Chemistry Letters 1, 822-828 (2010). "Multiply Resonant Coherent Multidimensional Spectroscopy- Applications in Materials Science."
- A. V. Pakoulev, M. A. Rickard, K. M. Kornau, N. A. Mathew, L. A. Yurs, S. B. Block and J. C. Wright; Accounts of Chemical Research 42, 1310-1321 (2009). "Mixed Frequency-/Time-Domain Coherent Multidimensional Spectroscopy: Research Tool or Potential Analytical Method?"
- N. A. Mathew, L. A. Yurs, S. B. Block, A. V. Pakoulev, K. M. Kornau and J. C. Wright; J Phys Chem A 114, 817-832 (2009). "Fully Coherent and Partially Coherent Pathways in Multiply Enhanced Odd-Order Wave-Mixing Spectroscopy."
- N. A. Mathew, L. A. Yurs, S. B. Block, A. V. Pakoulev, K. M. Kornau and J. C. Wright; J Phys Chem A 113, 9261-9265 (2009). "Multiple Quantum Coherence Spectroscopy."
- N. A. Mathew, S. B. Block, L. A. Yurs, K. M. Kornau, A. V. Pakoulev and J. C. Wright; J Phys Chem A 113, 13562–13569 (2009). "Multiply Enhanced Odd-order Wave Mixing Spectroscopy."
- J. C. Wright In Lasers in Chemistry; 1 ed.; Lackner, M., Ed.; Wiley-VCH Verlag: Weinheim, 2008; Vol. 1, p 173-227.
- V. Pakoulev, M. A. Rickard, N. A. Mathew, K. M. Kornau and J. C. Wright; *J Phys Chem A 111*, 6999-7005 (**2007**). "Spectral quantum beating in mixed frequency/time-domain coherent multidimensional spectroscopy."
- Mark A. Rickard, Andrei V. Pakoulev, Nathan A. Mathew, Kathryn M. Kornau, and John C. Wright; *J. Phys. Chem. A 111*, 1163 – 1166 (**2007**). "Frequency- and Time-Resolved Coherence Transfer Spectroscopy."
- M. A. Rickard, A. V. Pakoulev, K. Kornau, N. A. Mathew and J. C. Wright; *J. Phys. Chem. A 110*, 11384-11387 (**2006**). "Interferometric Coherence Transfer Modulations in Triply Vibrationally Enhanced Four-Wave Mixing."
- Andrei V. Pakoulev, Mark A. Rickard, Kent A. Meyer, Kathryn Kornau, Nathan A. Mathew, David E. Thompson, and John C. Wright, *J. Phys. Chem. A*, *110*, 3352-3355 (**2006**). "Mixed frequency/time domain optical analogues of heteronuclear multidimensional NMR"
- Kent A. Meyer, David E. Thompson, and John C. Wright, *J. Phys. Chem. A 108*, 11485-11493 (**2004**). "Frequency and Time-Resolved Triply Vibrationally Enhanced Four-Wave Mixing Spectroscopy."
- Kent A. Meyer and John C. Wright, *J. Phys. Chem. A 107***,** 8388-8395 (**2003**). "Interference, Dephasing, And Coherent Control In Time-Resolved Frequency Domain Two Dimensional Vibrational Spectra."

Selected Awards

- Graduate Student-Faculty Liaison Committee Outstanding Mentor Award, 2008
- NSF Creativity Grant Extension, 2005-2007
- Fellow of the American Association for the Advancement of Science, 2005
- Fellow of the American Physical Society, 2003
- Benjamin Smith Reynolds Award for Teaching Excellence in Engineering, 2002
- Andreas C. Albrecht Chair of Chemistry, 2001-present
- Dow Lecturer at University of British Columbia, 3/26/02
- Kellett Mid-Career Faculty Researcher Award, 1997-present
- Chancellor's Excellence in Teaching Award, 1994
- Upjohn Award for Excellence in Teaching, 1992
- Evan Helfaer Chair of Chemistry, 1991-1996
- American Chemical Society Award in Spectrochemical Analysis, 1991
- I. Romnes Faculty Fellow, 1984
- Applied Spectroscopy Society William F. Meggars Award, 1981
- Phi Beta Kappa

ARUN YETHIRAJ

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Research

Our research focuses on theoretical studies of soft condensed matter. While it is clear that the short-range structure of complex fluids plays an important role in determining the physical and chemical properties, the complexity of these systems precludes modeling them on an atomistic level. A judicious choice of coarse-grained models that hopefully capture the essential features without incorporating much of the detail is therefore a crucial step in the theoretical study of these systems. We are interested in constructing such models, and then employing theory and computer simulation to investigate their properties, with the final aim of predicting experimental observables. Our research has two components: the development of methods, and the application of these methods to understand the structure and dynamics of condensed phases. Some areas of current interest are:

Polymers in ionic liquids. Ionic liquids, which are usually composed of a large organic cation and a small anion, have generated considerable excitement for their varied potential applications and interesting physical properties. We are interested in the properties of *polymers* in ionic liquids. The viability of ionic liquids in materials applications is limited by their lack of mechanical integrity, which may be provided by mixing them with a polymeric material. The phase behavior of polymers in ionic liquids is fascinating and very different from that in water or organic solvents. We are developing coarse-grained and realistic molecular models for the computer simulation of polymers in ionic liquids. The emphasis is on developing systematically coarse-grained models that take into account the local *chemical detail* (bond angle and torsional angle distributions, etc.), as well as the effect of the ionic liquid *solvent*. The methods we develop and the knowledge we obtain should be useful in the study of other complex fluids including surfactants, biological macromolecules, and gels.

Self-assembly. We are studying the self-assembly of molecules into nano-structured materials using theory and computation. An interesting goal is the directed self-assembly of molecules where the chemical nature of the molecules is altered to drive the assembly into specific nanostructures. Some of the fascination arises because small differences in the intermolecular interactions can result in very different mesoscopic structures. We are interested in two classes of soft matter: surfactants and lipid/peptide mixtures. In both cases, the molecules assemble into a variety of lyotropic liquid crystal phases such as cylinders, gyroid, and lamellae. We are using simulations of atomistic models, and models with different degrees of coarse-graining to study the effect of intramolecular and intermolecular interactions on the self-assembly of these systems. The surfactant system has possible applications in fuel cell membranes. The lipid/peptide mixtures should shed light on the effect of peptides on the intrinsic curvature of lipid bilayers. In addition to providing insight on these systems, this work should also provide benchmark results for the development of coarse-grained force fields for surfactants, lipids, and peptides.

Membrane biophysics. The cell membrane is a very heterogeneous environment with several types of lipids and peripheral and integral membrane proteins. We are using simple models to study three different aspects of membrane biophysics: the diffusion of membrane components, the self-assembly of lipids (rafts), and the self-assembly of proteins. The lateral diffusion of proteins and lipid molecules in cell membranes is essential to many physiological processes including diffusion-controlled reactions, such as in the electron transfer reactions involving cytochromes in the mitochondria, and the binding of hormones. We are using a combination of computer simulation, geometric analyses, and percolation theory to elucidate the effect of obstacles (integral membrane proteins) on the diffusion of lipids and GPI anchored proteins.

Selected Publications

- J. Mondal, B. J. Sung, and A. Yethiraj, "Sequence dependent self-assembly of -peptides: Insight from a coarse-grained model", *J. Chem. Phys.* **132**, 065103 (2010).
- G. Reddy and A. Yethiraj, "Solvent effects in polyelectrolyte adsorption: Computer simulations with explicit and implicit solvent", *J. Chem. Phys.* **132**, 074903 (2010).
- B. J. Sung and A. Yethiraj, "Structure of Void Space in Polymer Solutions", *Phys. Rev. E* **81**, 031801 (2010).
- J. S. Kim and A. Yethiraj, "Crowding effects on association reactions at membranes", *Biophysical J.* **98**, 951-958 (2010).
- X. Zhu, P. Koenig, M. Hoffman, A. Yethiraj, and Q. Cui, "Establishing effective simulation protocols for β- and α/β-peptides. III. Molecular Mechanical (MM) model for Acyclic β-amino acids", *J. Comput. Chem.* **31**, 2063-2077 (2010).
- Z. Wu, Q. Cui, and A. Yethiraj, "A new coarse-grained model for water: The importance of electrostatic interactions", *J. Phys. Chem. B* **114**, 10524-10529 (2010).
- J. Mondal, X. Zhu, Q. Cui, and A. Yethiraj, "Self-assembly of β-peptides: Insight from the pair and many-body free energy of association", *J. Phys. Chem. C* **114**, 13551-13556 (2010).
- J. Mondal, X. Zhu, Q. Cui, and A. Yethiraj, "Sequence dependent interaction of β-peptides with membranes", *J. Phys. Chem. B* **114**, 13585-13592 (2010).
- J. S. Kim and A. Yethiraj, "Crowding effects on protein association: The effect of interactions between crowding agents", *J. Phys. Chem. B* **115**, 347-353 (2011).
- H. T. Jung, B. J. Sung, and A. Yethiraj, "The effect of the chain stiffness on tracer diffusion in polymeric matrices", *J. Polym. Sci. B: Polymer Physics* **49**, 818-825 (2011)
- L. Frischknecht and A. Yethiraj, "Two- and Three-Body interactions among nanoparticles in a polymer melt", *J. Chem. Phys.* **134**, 174901 (2011).
- J. Mondal, B. Bratton, Y. Li, A. Yethiraj, and J. C. Weisshaar, "Entropy-based Mechanism of Ribosome-Nucleoid Segregation in E. coli Cells", *Biophysical J* **100**, 2605-2613 (2011).
- Z. Wu, Q. Cui, and A. Yethiraj, "The driving force for the association of hydrophobic peptides: The importance of electrostatic interactions in coarse-grained water models", *J. Phys. Chem. Lett.* **2**, 1794-1798 (2011).
- J. Mondal and A. Yethiraj, "Driving force for the association of amphiphilic molecules", *J. Phys. Chem. Lett.* **2**, 2391-2395 (2011).

Awards

- Senior Editor, *The Journal of Physical Chemistry*, 2007 to present
- Vilas Associate Award, 2006
- Fellow, American Physical Society, 2001
- Alexander von Humboldt Research Fellowship, 1999
- Samuel C. Johnson Distinguished Fellowship, 1998
- Alfred P. Sloan Fellow, 1997-1999
- National Science Foundation, CAREER award (formerly the NYI), 1995
- National Science Foundation, Research Initiation Award, 1994
- Edward M. Schoenborn Award for Outstanding Ph.D. Candidate in Chemical Engineering, North Carolina State University, 1991
- Specialist Editor, Computer Physics Communications

TEHSHIK P. YOON

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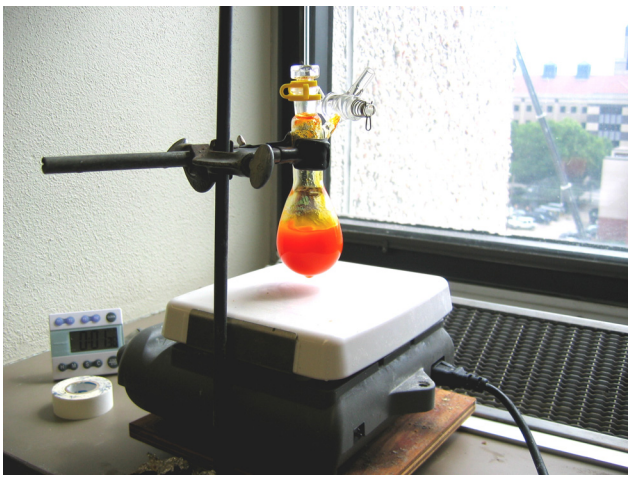
Research

The central theme of research in the Yoon group is the development of new catalytic methods for organic synthesis. We are most interested in reactions with the following features:

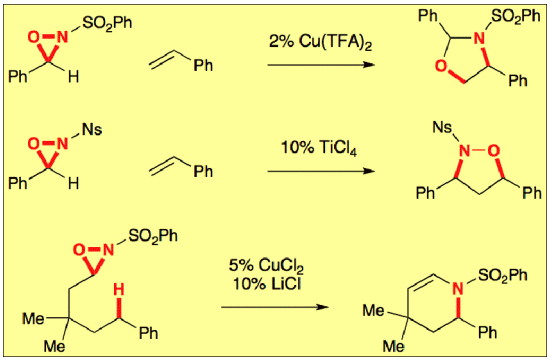
1. *Synthetic utility.* The most important consideration we use in choosing new research problems is the potential to improve upon current state-of-the-art approaches to constructing complex molecular structures.
2. *Mechanistic novelty.* We focus on reactions with unusual mechanistic features or that involve novel modes of catalysis.
3. *Stereoselectivity*. A particular focus of our lab is the development of enantioselective catalysts that can efficiently control the stereochemistry of newly formed bonds.
4. *Sustainability*. We are interested in minimizing the environmental impact and maximizing the long-term sustainability of methods developed in our labs.

Visible Light Photocatalysis in Organic Synthesis



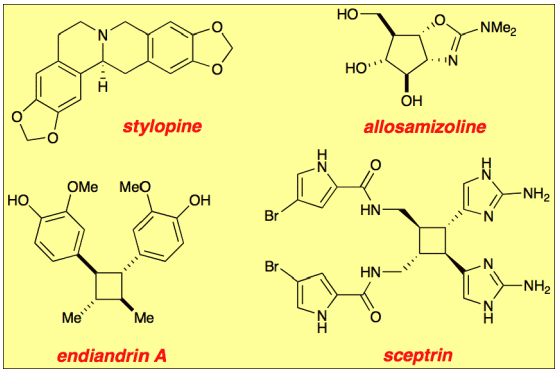
Sunlight is a safe, inexpensive, and endlessly renewable reagent. Most organic compounds, however, absorb light only at short wavelengths of ultraviolet light that are relatively poorly emitted in the solar spectrum. Conventional high-pressure UV photochemical reactions are thus rarely utilized on industrial scales, as they are energy-intensive, hard to scale, and relatively expensive. We are developing strategies to use transition metal photocatalysts in interesting new photochemical reactions that use visible wavelengths of light. By enabling the use of direct sunlight in synthetically useful reactions, we hope to pioneer a new, environmentally responsible approach to synthetic organic photochemistry.

New Reactions of Oxaziridines



A fundamental challenge in synthetic organic chemistry is the ability to add of oxygen- and nitrogen-containing functional groups to otherwise unfunctionalized hydrocarbon feedstocks (alkanes, alkenes, arenes) in a regioselective and stereoselective fashion. We are investigating the ability of three-membered heterocycles called oxaziridines to perform a wide variety of such oxidative functionalization reactions. We have developed methods to synthesize a range of structures, including 1,2-aminoalcohols, 1,3-aminoalcohols, isoxazolidines, piperidines, pyrrolidines, tetrahydroisoquinolines, and other structures that are commonly found in biologically active natural products and pharmaceutical agents.

Total Synthesis of Natural Products



The long-term goal of research in our group is the development of new methods for organic synthesis that can find broad applicability in the synthesis of complex molecular structures. The total synthesis of biologically active and architecturally interesting natural products represents the ultimate demonstration of the utility of new reactions and consequently constitutes a vital aspect of our research program. In addition, the challenges encountered in the course of a long multistep synthesis help to inform our approach to new reaction development.

Selected Publications

- "Radical Cation Diels-Alder Cycloadditions by Visible Light Photocatalysis," Lin, S.; Ischay, M. A.; Fry, C. G.; Yoon, T. P. *J. Am. Chem. Soc.* **2011**, *133*, 19350–19353.
- "Photocatalytic Reductive Cyclizations of Enones: Divergent Reactivity of Photogenerated Radical and Radical Anion Intermediates," Du, J.; Ruiz Espelt, L.; Guzei, I. A.; Yoon, T. P. *Chem. Sci.* **2011**, *2*, 2115-2119.
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- Williamson, K. S.; Yoon, T. P. "Iron-Catalyzed Aminohydroxylation of Olefins" *J. Am. Chem. Soc.* **2010**, *132*, 4570-4571.
- Partridge, K. M.; Guzei, I. A.; Yoon, T. P. "Carbonyl Imines from Oxaziridines: Generation and Cycloaddition of N-O=C Dipoles" *Angew. Chem. Int. Ed*. **2010**, *49*, 930-934.
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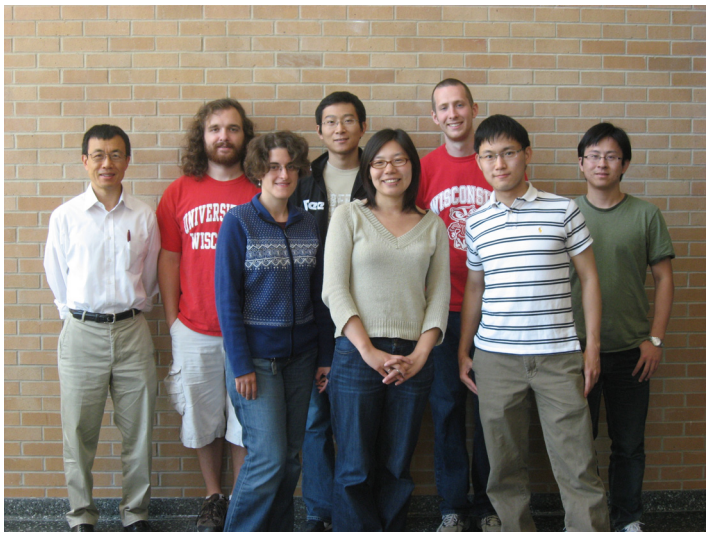
- Du, J.; Yoon, T. P. "Crossed Intermolecular [2+2] Cycloadditions of Acyclic Enones: Synthesis of Unsymmetrical Cyclobutanes by Visible Light Photocatalysis" *J. Am. Chem. Soc*. *131*, 14604-14605.
- Ischay, M. A.; Anzovino, M. E.; Du, J.; Yoon, T. P. "Efficient Visible Light Photocatalysis of [2+2] Enone Cycloadditions." *J. Am. Chem. Soc*. **2008**, *130*, 12886–12887.
- Michaelis, D. J.; Ischay, M. A.; Yoon, T. P. "Activation of N-Sulfonyl Oxaziridines Using Copper(II) Catalysts: Aminohydroxylations of Styrenes and 1,3-Dienes." *J. Am. Chem. Soc*. **2008**, *130*, 6610-6615.
- Partridge, K. K.; Anzovino, M. E.; Yoon, T. P. "Cycloadditions of N-Sulfonyl Nitrones Generated by Lewis Acid-Catalyzed Rearrangement of Oxaziridines." *J. Am. Chem. Soc*. **2008**, *130*, 2920-2921.
- Michaelis, D. J.; Shaffer, C. J.; Yoon, T. P. "Copper(II)-Catalyzed Aminohydroxylation of Olefins." *J. Am. Chem. Soc*. **2007**, *129*, 1866-1867.

Awards

- Eli Lilly Grantee, 2011
- Camille Dreyfus Teacher-Scholar Award, 2010
- Alfred P. Sloan Research Fellowship, 2009
- Amgen Young Investigator Award, 2009
- Beckman Young Investigator Award, 2008
- Research Corporation Cottrell Scholar award, 2008
- National Science Foundation CAREER Award. 2007

LIAN YU



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Research

Soft materials, molecular solids, crystallization, polymorphism, amorphous solids, molecular motions in solids

Solids of organic molecules are being explored for applications in pharmaceutical and electronic technologies. These soft materials exhibit properties and physical phenomena unknown for hard materials. In this laboratory, physical measurements and crystallization experiments are performed to understand the formation, properties, and transformation of molecular solids. Our major techniques are crystallography, calorimetry, spectroscopy, and microscopy.

(1) Polymorphism of Organic Materials. Polymorphism, the ability of the same molecule to crystallize in different structures, is important in the manufacture of drugs and specialty chemicals because polymorphs have different properties. Our work aims to discover polymorphs and control crystallization in polymorphic systems. A polymorphic system discovered in this laboratory (ROY) has the largest number of coexisting polymorphs of solved structures. Such a system helps elucidate the origin of polymorphism and study structure-property relations. Some questions being investigated include: Why do some molecules have many polymorphs and others seemingly none? Why do polymorphs grow from the same liquid at rates orders of magnitude different? What determines the probability of one polymorph nucleating on another during crystallization?

(2) Crystallization of Organic Glasses. For many applications, amorphous solids (glasses) are preferred over crystalline solids. Organic glasses are materials for organic electronics, bio-preservation, and delivery of poorly soluble drugs. Any amorphous material must be stable against crystallization because crystallization negates its advantages. We study how organic glasses crystallize. Despite their solidity, glasses can crystallize, sometimes surprisingly fast. We are investigating fast modes of crystal growth that emerge in organic liquids as they are cooled to become glasses. The phenomenon is unknown or uncommon for hard materials. Some questions being investigated include: Is crystal growth from glasses controlled by crystal/liquid structural similarity? How does crystal growth from glasses differ from diffusion-controlled growth in low-viscosity liquids? Is fast surface crystal growth caused by high surface molecular mobility? Can surface crystallization be suppressed with a coating? How does surface-enhanced crystallization differ from bulk crystallization?

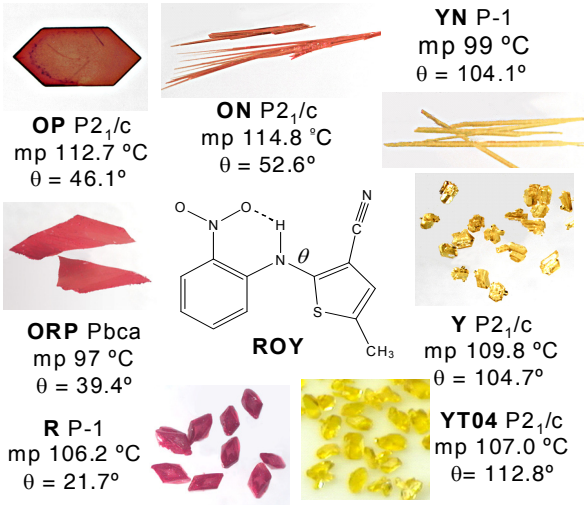

Figure 1. The simple molecule ROY forms at least ten polymorphs with different colors and molecular conformations; the structures of seven polymorphs (shown) have been solved, the current record for organic molecules.

(3) Molecular Motions in Organic Solids. Molecular motions in a solid control how fast physicochemical changes can occur. We are studying two types of molecular mobility in organic solids: surface diffusion and moisture diffusion. The method of surface grating decay is used to measure surface molecular mobility. This property is of interest because crystal growth can occur much faster at the surface than in the bulk of organic glasses. Raman microscopy is used to measure moisture diffusion. This property is important because the interaction with water is a major mechanism for the degradation of pharmaceutical and food products.

Selected Publications

- Zhu, L.; Brian, C.; Swallen, S. F.; Straus, P. T.; Ediger, M. D.; Yu, L. Surface Diffusion of an Organic Glass. *Phys. Rev. Lett.*, *106*, 256103-1 to 256103-4 (**2011**).
- Cai, T.; Zhu, L.; Yu, L. Crystallization of Organic Glasses: Effects of Polymer Additives on Bulk and Surface Crystal Growth in Amorphous Nifedipine. *Pharm. Res.*, *28*, 2458–2466 (**2011**).
- Sun, Y.; Zhu, L.; Kearns, K. L.; Ediger, M. D.; Yu, L. Glasses Crystallize Rapidly at Surfaces by Growing Crystals Upward. *Proc. Natl. Acad. Sci. U. S. A.*, *108*, 5990-5995 (**2011**).
- Zhu, L.; Cai, T.; Huang, J.; Stringfellow, T. C.; Wall, M.; Yu, L. Water Self Diffusion in Glassy and Liquid Maltose Measured by Raman Microscopy and NMR. *J. Phys. Chem. B*, *115*, 5849-5855 (**2011**).
- Gunn, E.; Ilia Guzei, I. A.; Yu, L. Does Crystal Density Control Fast Surface Crystal Growth in Glasses? A Study with Polymorphs. *Crystal Growth & Design*, *11*, 3979-3984 (**2011**).
- Yu, L. Polymorphism in Molecular Solids: An Extraordinary System of Red, Orange, and Yellow Crystals. *Acc. Chem. Res.*, *43*, 1257-1266 (**2010**).
- Sun, Y.; Xi, H.; Ediger, M.D.; Richert, R.; Yu, L. Diffusion-Controlled and "Diffusionless" Crystal Growth near the Glass Transition Temperature: Relation Between Liquid Dynamics and Growth Kinetics of Seven ROY Polymorphs. *J. Chem. Phys., 131*, 0745061/1-074506/9, (**2009**).
- Dawson, K.J.; Kearns, K.L.; Yu, L., Steffen, W.; Ediger, M.D. Physical Vapor Deposition as a Route to Hidden Amorphous States. *Proc. Nat'l. Acad. Sci., 106*, 15165-15170 (**2009**).
- Kearns, K.L., Sun, Y.; Yu, L.; Ediger, M.D. Calorimetric Evidence of Two Distinct Molecular Packings in Stable Glasses of Indomethacin. *J. Phys. Chem. B, 113,* 1579-1586 (**2009**).
- Xi, H.; Sun,; Yu, L. Diffusion-Controlled and Diffusionless Crystal Growth in Liquid o-Terphenyl Near its Glass Transition Temperature. *J. Chem. Phys., 130*, 094508/1-094508/9 (**2009**).
- Tao, J.; Sun, Y.; Zhang, G.G.D.; Yu, L. Solubility of Small-Molecule Crystals in Polymers: D-Mannitol in PVP, Indomethacin in PVP/VA and Nifedipine in PVP/VA. *Pharm. Res., 26*, 855-864 (**2009**).
- Huang, J.; Stringfellow, T.C.; Yu, L. Glycine Exists Mainly as Monomers, Not Dimers, in Supersaturated Aqueous Solutions: Implications for Understanding its Crystallization and Polymorphism. *J. Am. Chem. Soc., 130*, 13973-13980 (**2008**).
- Chen, S.; Xi, H.; Yu, L. Cross Nucleation between ROY Polymorphs. *J. Am. Chem. Soc.*, *127*, 17439-17444 (**2008**).
- Swallen, S.; Kearns, K.; Mapes, M.; McMahon, R.; Kim, S.; Ediger, M.; Yu, L.; Wu, T.; Satija, S. Extraordinarily Stable Glassy Materials Prepared by Vapor Deposition. *Science*, 315, 353 – 356 (**2008**).
- Sun, Y.; Xi, H.; Ediger, M. D.; Yu, L. Diffusionless Crystal Growth from Glass Has Precursor in Equilibrium Liquid. *J. Phys. Chem. B* **2008**, *112*, 661-664.
- Sun, Y.; Xi, H.; Chen, S.; Ediger, M. D.; Yu, L. Crystallization near Glass Transition: Transition from Diffusion-Controlled to Diffusionless Crystal Growth Studied with Seven Polymorphs. *J. Phys. Chem. B* **2008**, *112*, 5594-5601.
- Yu, L. Survival of the fittest polymorph: how fast nucleater can lose to fast grower. *CrystEngComm*, **2007**, *9*, 847 – 851.
- Wu, T.; Sun, Y.; Li, N.; de Villiers, M.; Yu, L. Inhibiting Surface Crystallization of Amorphous Indomethacin by Nanocoating. *Langmuir* **2007**, *23*, 5148-5153.

Awards

- David Grant Research Achievement Award in Physical Pharmacy, American Assoc. of Pharmaceutical Scientists, 2011
- AstraZeneca Visiting Professor, University of Manchester, UK, 2009.
- Fellow, American Association of Pharmaceutical Scientists, 2006.
- Lilly Research Laboratories President's Award, 2003.

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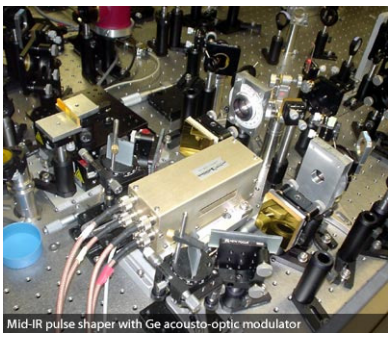
Research

The Zanni group studies topics in biophysics and the energy sciences using 2D IR spectroscopy. We have research projects underway on carbon nanotube energy transfer, solar cell charge transfer, and the mechanism of protein aggregation in type 2 diabetes, to name only a few topics. We specialize in scientific problems in which structural dynamics and/or interfacial phenomena are important. Systems that have these characteristics are very difficult to study with more traditional structural methods, and so our techniques often provide some of the best available structural and dynamical information.

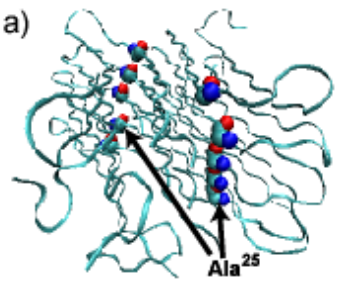
We are also very active in developing the technology behind multidimensional spectroscopies. These multidimensional spectroscopies include 2D IR spectroscopy, 2D sum-frequency generation (SFG) spectroscopy, and (soon) 2D Vis spectroscopy. We develop new pulse sequences and new experimental methods for more easily and accurately collecting these spectra.

In tandem to our technological efforts, we also focus on adapting (bio)chemical techniques to 2D IR spectroscopy, including protein expression, protein ligation and inorganic chemistry. For example, we have used expressed protein ligation to isotope label one of two domains in a lens protein, and we have synthesized inorganic probes of protein environment in analogy to EPR spin labels.

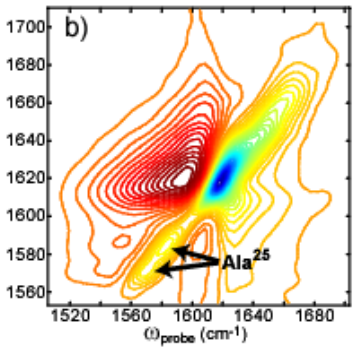
As a result of our wide ranging interests, students and postdoctoral researchers in our group obtain a range of experiences from technique development to synthesis or biosynthesis to topical applications. We also collaborate extensively with theorists, organic chemists and material scientists who are interested in simulating or using 2D IR spectroscopy for their research.



Our mid-IR pulse shaper – the first of its kind!



The amyloid peptide we are studying that is implicated in type 2 diabetes.



2D IR spectrum of amylin that recently appeared on the cover of C&E News.

Selected Publications

- Middleton CT, Marek P, Cao P, Chiu CC, Singh S, Woys AM, de Pablo JJ, Raleigh DP, Zanni MT, "Two-dimensional infrared spectroscopy reveals the complex behavior of an amyloid fibril inhibitor," Nature Chemistry, In Press.

- Moran SD, Woys AM, Buchanan LE, Bixby E, Decatur SM, Zanni, MT, "Two-dimensional IR spectroscopy and segmental 13C labeling reveals the domain structure of human gD-crystallin amyloid fibrils," PNAS, In Press.

- Xiong, W, Laaser JE, Mehlenbacher RD, Zanni MT. "Adding a dimension to the infrared spectra of interfaces using heterodyne detected 2D sum-frequency generation (HD 2D SFG) spectroscopy," PNAS, 108, 20902 (2011).

- Middleton, C.T., Buchanen, L.E., Dunkelberger, E., Zanni, M.T., "Utilizing lifetimes to suppress random coil features in 2D IR spectra of peptides," JPC Letters, 2, 2357, 2011. PMCID**:** PMC3182477**.**

- Wang, L., Middleton, C.T, Singh, S., Reddy, A., Woys, A.M., Strasfeld, D.B., Marek, P., Raleigh, D.P.; de Pablo, J.J., Zanni, M.T., Skinner, J.L., "2DIR Spectroscopy of Human Amylin Fibrils Reflects Stable β-sheet Structure," JACS, *133*, 16062 (2011). PMCID: PMC3196637

- Laaser, J. E., W. Xiong, and Zanni, M.T. "Time-domain SFG spectroscopy using mid-IR pulse shaping: Practical and intrinsic advantages," J. Phys. Chem. B, 115, 2536-2546 (2011).

- M. Woys, Y.-S. Lin, A.S. Reddy, W. Xiong, J. J. de Pablo, J. L. Skinner, M. T. Zanni, "2D IR line shapes probe ovispirin peptide conformation and depth in lipid bilayers", J. Amer. Chem. Soc., *132*, 2832 (2010).

- W. Xiong, J. E. Laaser, P. Paoprasert, R. Franking, R. J. Hamers, P. Gopalan, and M. T. Zanni, "Transient 2D IR spectroscopy of charge injection in dye-sensitized nanocrystalline thin films," J. Amer. Chem. Soc., 131, 18040 (2009).

Awards

- NAS Award for Initiatives in Research, 2011
- H.I. Romnes Faculty Fellowship, UW-Madison, 2011
- Raymond & Beverly Sackler Prize in the Physical Sciences, 2011
- National Academy of Sciences Research Initiatives Award, 2010
- Fellow of the American Physical Society, 2010
- ACS Nobel Laureate Signature Award for Graduate Education in Chemistry, 2010
- Presidential Early Career Award in Science and Engineering (PECASE), 2009
- Coblentz Award, 2006
- Alfred P. Sloan Research Fellow, 2006
- Benjamin Smith Reynolds Award for Excellence in Teaching Engineers, 2005
- Packard Foundation Science and Engineering Fellowship, 2005
- Beckman Young Investigators Award, 2004
- National Science Foundation CAREER Award, 2003
- Research Corporation Innovation Award, 2002
- Camille and Henry Dreyfus New Faculty Award, 2002
- American Chemical Society Nobel Laureate Signature Award for Graduate Education in Chemistry, 2001
- National Institute of Health Postdoctoral Fellow (NRSA), 2000
- American Chemical Society Regional Award, Rochester, NY, 1994
- Bausch and Lomb Scholar, University of Rochester, 1990

Facilties, Equipment and Resources in the Chemistry Department

Facilities

The Chemistry Department occupies a modern, air-conditioned building. All of the graduate course activities are in the same building, as is the extensive chemistry library. Graduate students receive a key to the library for access at all hours. Research facilities are among the best in the country. The machine shop can produce anything from microware to a huge vacuum chamber, and the glassblowing shop and the electronics shop are equally impressive. Many research instruments have been built there, and students have a special area for their own shop work and electronics projects. Access to shop service and specialized equipment makes the most sophisticated construction projects possible.

Chemistry Instrument Center

The UW–Madison Chemistry Department maintains a comprehensive research instrumentation facility that is open and accessible to students. The Paul Bender Chemical Instrumentation Center (CIC) provides Chemistry Department researchers with state-of-the-art instrumentation in the areas of magnetic resonance (NMR and ESR), mass spectrometry, and x-ray crystallography. Each area is headed by a Facility Director. These individuals, all Ph.D. chemists, advise and work with students on the experiments and on the science. Two highly skilled electronics engineers attend to instrument maintenance and upgrades. Interested students will get hands-on access to most departmental instrumentation, an experience that is intended to be an integral part of a Wisconsin education. Practical training in NMR is provided in formal courses, taught by the NMR staff, while individual instruction is provided for more complex techniques. Qualified student operators have key privileges and around-the-clock access to instruments.

Nuclear Magnetic Resonance Spectroscopy

Seven research spectrometers constitute the state-of-the-art nuclear magnetic resonance facility in our Department. Routine proton, carbon, fluorine and phosphorus spectra are obtained on two Bruker 300 MHz NMR instruments. A Varian Mercury 300 MHz spectrometer has modern automation capabilities, that is particularly useful for screening studies. This spectrometer enables undergraduates to easily participate in research projects. Much of the NMR research investigating organometallic compounds is performed on Varian UNITY-500 and Bruker AVANCE 360 MHz instruments. A very wide range of temperatures and multinuclear capabilities are provided on these instruments. Varian INOVA–500 and 600 MHz spectrometers provide the highest field strengths for the most complex and demanding experiments. We have recently been funded for new NMR instrumentation that will further expand these capabilities by fall 2011. All of this equipment is available for student use, and extensive training in the theoretical and experimental aspects of modern NMR spectroscopy is provided both through formal courses (Chemistry 636 and 637) and when appropriate by individual tutorial. Drs. Charles Fry and Monika Ivancic, NMR Facility Ph.D. chemists, are available to help in the interpretation of spectra, and to assist in the design and implementation of more sophisticated experiments such as those involving pulsed-field gradients, selective excitation, and multiple dimensional NMR.

Also available in the facility is a new Bruker EleXsys E500 ESR Spectrometer. This equipment can be used for solution, powder, and single crystal X-band studies. The spectrometer is connected to the department ethernet and includes a PC based off-line data station for ESR data reduction and plotting. Several irradiation sources are available, as are variable temperature capabilities to run spectra between 4 K and 325 K.

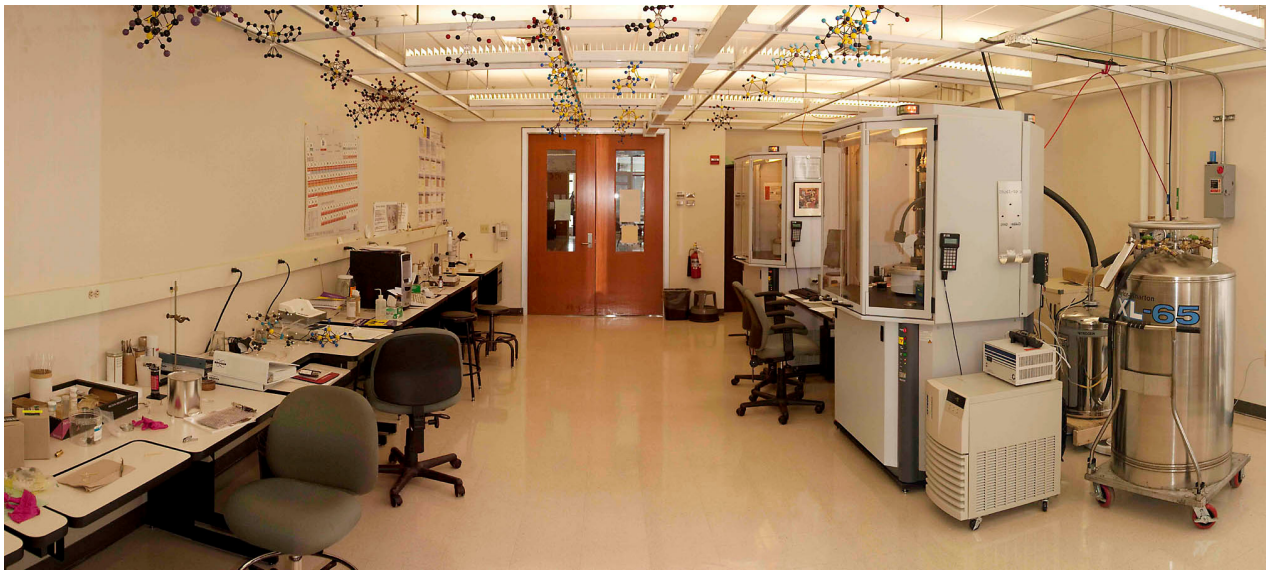
Mass Spectrometry

Five mass spectrometers are located in the Mass Spectrometry Laboratory in the new wing of building. Three different ionization techniques are available on the different instruments. Three of the instruments are normally in electrospray ionization mode, one in matrix-assisted laser desorption/ionization mode (MALDI), and one in electron impact mode. This allows a wide range of samples to be characterized. The 2002 Nobel Prize in Chemistry (Fenn and Tanaka) recognized the importance of having electrospray ionization and laser desporption/ionization in a modern laboratory. The prize also points up the necessity of continuously upgrading analytical instrumentation to give Wisconsin students opportunities to make state-of-the-art measurements.

As of this writing, the mass spectrometers in the lab are a Micromass LCT (orthogonal electrospray ionization, reflectron time-of-flight analyzer), a Bruker Reflex II (MALDI, reflectron, time-of-flight analyzer, delayed extraction, 337 nm nitrogen lazer), a Shimadzu LCMS-2010 (electrospray ionization, single quadrupole analyzer, autosampler, photoarray detector, fraction collector), a Micromass AutoSpec (electron impact ionization, magnetic sector analyzer), and a Finnegan TSQ700 (electrospray ionization, triple quadrupole analyzer). Both the Bruker Reflex II and the Shimadzu LCMS-2010 are operated by graduate students who have been trained by the Laboratory Directory, Dr. Martha M. Vestling. To get experience in the operation of all the instruments, graduate stduents are urged to consider becoming a mass spectrometry TA.

Chemistry 638, Introduction to Mass Spectrometry, is a one-credit course team taught by Dr. Vestling and Dr. Amy Harms, biotechnology Center Mass Spectrometry Laboratory, to promote the design of good experiments for our instruments. It provides information on the various mass spectrometers, on how to prepare samples, and how to analyze the data. Dr. Vestling and assistants work closely with individual students and faculty in the Department on specific research projects.

A GCMS is available in the Advanced Analytical Chemistry teaching Laboratory. See the Department Facilities website for pictures and details.



Molecular Structure Laboratory

The Molecular Structure Laboratory, located on the second floor of the new building, is supervised by its Director, Dr. Ilia Guzei. The lab has a full array of single crystal diffraction equipment for structural characterization of crystalline materials. The results provided by an X-ray single crystal experiment include coordinates of atoms in the unit cell in the lattice, atomic connectivity, and interatomic distances and angles. Structural data allow three-dimensional analysis of the molecular geometry which can enable a researcher to understand or explain properties of the compound. Data are collected on two state-of-the-art Bruker diffractometers with CCD area detectors and a Siemens P4 diffractometer with a point detector, using either Mo or Cu sealed-tube generators. The diffractometers are independently controlled by PC computers and fitted with nitrogen-streaming low temperature devices. Data collections are routinely conducted at 173(2) K which allows handling of air- and moisture-sensitive samples in addition to air-stable crystals. The data are analyzed on one of seven PC computers situated in the X-ray computer laboratory. The Bruker SHELXTL program package is most often used for structure solution and refinement. The Cambridge Structural Database containing the results of nearly all published structures of organic and organometallic compounds is also available and can be searched with program ConQuest. Dr. Guzei works closely with students and faculty in the preparation of manuscripts reporting structural experiments.

Library

The Chemistry Library, located in the Daniels wing of the Chemistry Building, is available to you 24 hours per day. The Chemistry Library's collection is part of an integrated UW-Madison campus library system that includes over 20,000 electronic journals, 650 indexing databases (including SciFinder Scholar, Reaxys, Inorganic Crystal Structure Database, and Web Cambridge Structure Database) and 7.3 million printed volumes. Two librarians and several part-time employees staff the library. Instruction in the use of Library resources is available. See the Chemistry Library website for more information: *chemistry.library.wisc.edu.*