Dear Prospective Graduate Student:

Thank you for your interest in our Graduate Program in Chemistry at Michigan State University. A graduate education in chemistry is focused on an original research project that you will perform under the direction of our faculty. This brochure is meant to introduce you to our Department and the research opportunities that will be available to you should you continue your education at MSU. Chemistry is an enabling science that is central to many fields. As a result, you will find many of our faculty engaged in research that addresses global problems, including those of energy, sustainability, health, and the environment. There is a table on pages 12-13 showing how our faculty classify their research programs with respect to the actual focus of their work and with respect to the classical “areas” of Chemistry (analytical, inorganic, organic and physical). Our goal is to educate the next generation of scientists and to do everything possible to support students as they work toward their degrees and to prepare students for their independent careers in industry or academics. I am very happy that you are considering Graduate Study in Chemistry as the next step in your education, and sincerely hope that our program becomes your top choice!

Best Wishes,

Robert E. Maleczka, Jr.
Professor of Chemistry and Chair
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Chemistry Graduate Office
320 Chemistry Building
Michigan State University
East Lansing, MI 48824
(517) 353-1092
fax: (517) 353-1793
graduateoffice@chemistry.msu.edu
http://www.chemistry.msu.edu
Welcome
to our Graduate Program brochure! We appreciate you considering the pursuit of a graduate degree in Chemistry at MSU, and we'd like to introduce you to our faculty, give you an overview of some of the broad-based cutting-edge scientific research that they and their graduate students are performing here at Michigan State University every day, and provide a brief description of our graduate program. We'll also give you a glimpse of MSU's beautiful 5,200+ acre campus, and describe a little of mid-Michigan life in the greater Lansing area.

As our understanding of the workings of nature expands with the advancement of scientific knowledge and technology, the science of Chemistry, which lies at the center of many of the universe's mysteries, today is growing and changing at an unprecedented rate. MSU's Department of Chemistry has nonetheless consistently managed to stay at the forefront in chemistry research and teaching. We have done this by evolving and transforming as the science changes: through established faculty members developing and expanding their research interests to encompass the new challenges presented by the expanding frontier of knowledge; by hiring new faculty to broaden and enhance the capabilities of the department; and by changing course curricula, developing new teaching methods and techniques, and creating new courses to cover the ever-increasing knowledge base, while at the same time maintaining an academic program rooted in the basics of the discipline. Achieving these tasks is both challenging and exciting, and we invite you to join us in our ever-changing exploration at the forefront of chemistry research.

In the pages that follow, we can only give you only the broadest overview of the Chemistry Department, its faculty and their research interests, and what it's like to be a graduate student in Chemistry at MSU. You may have questions and concerns which are not met by the information found herein, and we encourage you to access our website or contact the Chemistry Graduate Office staff who will be happy to answer your questions directly. The contact information can be found on the Table of Contents page at the front of this brochure. We also encourage you to contact faculty members directly if you have questions or interest in their particular research. Their contact information may be found on the pages in the Research Interest section beginning on page 12.

We hope you will choose the MSU Department of Chemistry for pursuing your graduate education. It can be your stepping-stone to a successful career in Chemistry, as it has been for many others!
THE DEPARTMENT

of Chemistry occupies an air-conditioned building with 280,000 ft² of floor space distributed over five main floors, two basements, a penthouse complex, an office annex and a lecture-hall wing. Approximately 60% is devoted to research laboratories, instrument facilities, and supporting shops. All graduate students have 24-hour access to the building, their research laboratories and offices, and the computer rooms.

The Chemistry Department moved into its current building when its construction was completed in 1964. At that time it was a state-of-the-art chemistry teaching and research facility. In the late 1990s the building underwent a large scale $11 million renovation, and was later further improved in another $12 million renovation to preserve that status. In April 2005, the State of Michigan agreed to fund a $17.1 million addition to the Chemistry Building to accommodate our expansion and enhance our efforts in both graduate and undergraduate education. Construction of this annex was completed in Fall 2007, along with the expansion and renovation of all the chemistry teaching laboratories. These updates provide for current state-of-the-art research and teaching facilities that allow the continued pursuit of our world-class research and teaching programs. Such costly investments by the University in the infrastructure of our Department reflect the high level of support and respect that the Chemistry Program commands from MSU’s administration.

The ability to carry out interdisciplinary Chemistry-related research at MSU has been enhanced by the Biomedical and Physical Sciences (BPS) Building, which abuts and connects to both the Chemistry and Biochemistry Buildings. This recent structure houses the Physics-Astronomy and Microbiology Departments among others, fostering new and enhancing existing collaborations of our Chemistry faculty with faculty from other departments having interests in areas such as materials science, biochemistry and biophysics research.

Research Facilities

Individual research laboratories typically have a substantial collection of supplies and equipment, including spectroscopic and structural analysis tools. Increasingly, however, modern research in Chemistry requires access to expensive state-of-the-art equipment, making it necessary to purchase such items on a shared basis and to provide staff for operation and maintenance. Facilities to pursue research in emerging areas of Chemistry are present in the Chemistry Building and are accessible to all graduate students:

Located in the Chemistry building, the Max T. Rogers NMR Facility provides twelve high-field Varian/Agilent NMR spectrometers with proton resonance frequencies ranging from 300 – 600 MHz. This includes four 300 MHz instruments for routine studies, three 400 MHz NMR spectrometers for solid-state experiments, two 500 MHz spectrometers for routine and advanced experiments, two fully automated 500 MHz spectrometers equipped each with 96 sample robotic autosamplers, and a 600 MHz instrument for biomolecular and advanced small molecule work.

In addition to the equipment housed in the chemistry building, the Max T. Rogers NMR Facility also operates the only ultrahigh field 900 MHz NMR (21.14 tesla) system in Michigan, located in a nearby building. This Bruker Avance system is equipped with a TCI triple-resonance inverse detection CryoProbe, which provides unparalleled sensitivity for 1H as well as 13C detection. The instrument is also equipped to run solid-state NMR experiments using a variety of different probes.

Since mass spectrometry is an indispensable tool in many research areas, Department researchers have easy access to twelve mass spectrometers at the MSU Mass Spectrometry and Metabolomics Core (http://rtsf.msu.edu/massspec.html), located in the adjacent Biochemistry Building. The Core offers a variety of GC/MS, LC/MS/MS, and MALDI mass spectrometers with an assortment of inlets and ionization methods, and functions as an open access laboratory. Students are encouraged to become trained instrument users; training includes discussions of theory and operation of Core instruments; following
The Chemistry Department X-ray collect routine PXRDs. Graduate students and perform sample analyses upon analysis via x-ray fluorescence, AA, and Raman spectrometers. and gas chromatographic equipment, and expertise in x-ray technology. In addition, we have a new powder diffraction instrument that is used to collect routine PXRDs. Graduate students may request hands-on training in the use of these instruments, which allows for them to gain valuable experience and expertise in x-ray technology.

In addition to these major instrument facilities in the Department, conveniently-located instrument rooms house liquid and gas chromatographic equipment, UV-VIS, FTIR, FT-MS, and fluorescence and Raman spectrometers. Elemental analysis via x-ray fluorescence, AA, and ICP are also available in the Chemistry Building.

The Chemistry Department operates exceptionally well-equipped shops for the design and fabrication of unique and custom instrumentation and apparatus, and the repair of existing equipment required for research and teaching. The Machine Shop and the Glassblowing Facility are staffed by experienced professionals who are a vital component of the research performed at MSU. If you need something but can’t buy it anywhere, it can likely be constructed with facilities in our Department.

### Computational Facilities

Our well-equipped computational facilities are continuously being upgraded. All students at MSU are granted free access to the Internet, including free dial-up service for local off-campus connectivity, a free e-mail address, and file space and assistance in constructing personal pages on the World Wide Web. Accommodation for 100 Mb/s twisted-pair wired Internet connectivity for laptops is provided across campus, including the libraries, many of the lecture halls, and throughout the Chemistry building. Wireless connectivity (a/g/n) is also freely available throughout the campus, including the entire Chemistry building.

The University provides access to supercomputers in the MSU High Performance Computer Center, and has 50 microcomputer and PC workstation laboratories around Campus, including a PC laboratory here in the Chemistry Building.

In addition to well over 500 PC, Macintosh and unix-based workstations in the individual faculty research laboratories, the Chemistry Department’s Computational Chemistry Facility operates a Linux cluster with 24 processors in 12 compute nodes (48 cores) and 4 GB of memory per node. We also have a 2.2 GHz, 32-core compute server with 256 GB of RAM and 3 TB of disk space in an 8-stripe RAID array of 10k-rpm SAS drives. These systems complement the 12 Linux workstations used in our Computational Chemistry classroom, and there are support staff to aid in computation and visualization of theoretical calculations and simulations. Graduate courses in computational chemistry and visualization are regularly offered by the Chemistry Department. These computing facilities are routinely utilized by many Chemistry graduate students, including those carrying out research that is primarily experimental in nature.

A 10 Gb/s fiber-optic network connects nearly all the buildings on campus; the Chemistry Building is internally networked by a twisted-pair wired LAN operating at 100 Mb/s which connects to the rest of campus through the 10 Gb/s fiber-optic backbone. The building also has WiFi a/g/n connectivity throughout the entire building. MSU’s campus is connected to the Internet through two dedicated 10 Gb/s links.

### Academic and Technical Staff

The Chemistry Department’s technical staff assist in the execution of research and teaching by faculty and graduate students, and they do so extremely well. During their stay, most graduate students find that many of these people become integral parts of their education and research programs. In addition to the administrative and secretarial staff, we owe much to the dedication and outstanding work of the following academic and technical support staff:

#### Academic Specialists/Lecturers:
- Dr. Ardeshr Azadnia, Organic Labs Coordinator
- Dr. Virginia Cangelosi, Dr. Thomas Carter
- Dr. Amy Pollock, Director of General Chemistry
- Dr. Kathryn Severin, Analytical/Physical Labs Coordinator
- Dr. Chrysoula Vasileiou
- Dr. Joseph Ward, General Chemistry Labs Coordinator

#### Computing and Information Technology:
- Dr. Thomas Carter
- Mr. Chris Pfeffer
- Mr. Paul Reed

#### Max T. Rogers NMR Facility:
- Dr. Daniel Holmes
- Dr. Li Xie

#### X-ray Crystallography Facility:
- Dr. Richard J. Staples

#### Scientific Glassblowing Facility:
- Mr. Scott Bankroff, Master Glassblower

#### Machine Shop:
- Mr. Glen Wesley

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*The Department is home to master scientific glassblower Scott Bankroff’s well-equipped workshop.*
THE GRADUATE PROGRAM

Chemistry is summarized below. Complete requirements for specific programs are available from the Chemistry Graduate Office, or in our online graduate student handbook “Chemistry Graduate Program Guide”, available at [https://www.chemistry.msu.edu/graduate-program/current-students/graduate-program-guide/](https://www.chemistry.msu.edu/graduate-program/current-students/graduate-program-guide/).

**Financial Support**

Essentially every Chemistry graduate student is provided financial support while pursuing their graduate degree. There are two types of support typically available: Teaching Assistantships (TAs), and Research Assistantships (RAs). Because the Chemistry Department provides chemistry courses to service a large number of students in many other disciplines (e.g., Engineering, Biology or Physics majors), our need for TAs is always great.

First-year graduate student TAs typically serve as instructors in recitations or lab sections in the lower undergraduate courses, while TAs who are further along in their graduate education typically serve in upper-level undergraduate courses and even graduate-level courses. However, the Chemistry Faculty are very aggressive in pursuing research grant support, so quite often their students are paid from these grants and serve as RAs instead, and are paid to perform research.

RA’s are not required to teach.

In the Fall of 2016, incoming first-year graduate students received annual stipends of $24,428. Furthermore, Graduate Assistants (both TAs and RAs) are provided with health insurance, a tuition waiver of up to nine credits for each of the Fall and Spring semesters and up to five credits for the Summer semester (the normal full course load for Chemistry Graduate Students is six credits per semester), and a waiver of the matriculation fees each semester. These fringe benefits are substantial, totaling over $15,000 per year for an out-of-state student. These assistantship stipends are automatically increased in the second year, and for 2016-17, the increase for second year students was to $25,619 annually. (The Chemistry Department has historically supported Ph.D. candidates in good standing for a period of up to 5 years to allow for successful completion of their degree requirements.) We expect these values to be increased 1.5-3% for the coming 2017-18 academic year.

Most students are appointed as TAs when they first arrive, and are assigned a faculty member as their initial advisor until they formally join a research group. This occurs in their first year, and thereafter the remainder of their graduate career typically consists of a combination of TA and RA appointments, where the distribution of time spent as TA or RA depends on the student’s ability, the individual research group, and availability of research funds.

In addition to TA and RA support, several types of Graduate Fellowships are also available. Historically, the high quality of Chemistry Graduate Students has allowed them to compete successfully for first-year Fellowships from the College of Natural Science and the University. The Graduate School at MSU is dedicated to a diverse educational community through Fellowship programs as well. Students and faculty routinely work together to secure National Fellowships from organizations such as the American Chemical Society, the National Science Foundation, the National Institutes of Health, and the Department of Homeland Security.

**Research Advisor Selection**

Our Ph.D. program is designed to encourage students to get involved in their research quickly. New graduate students are expected to interview faculty and select a Research Advisor in their first semester, so they can begin their dissertation research project by the beginning of the second semester. By the end of their second semester, each student, in consultation with their Research Advisor, suggests three additional Faculty to serve with their Research Advisor as a Guidance Committee for their Ph.D. degree.

**Language Requirement**

While we believe that mastery of a second language is an important aspect of any education, and we strongly encourage all students to give serious consideration to the study of an additional language, there is no formal language requirement in the Graduate Program in Chemistry.

**Seminar**

Each Ph.D. candidate is required to give two seminars—one in their second year, and another before graduating. Each week throughout the year, public seminars in each of the four areas are presented by graduate students. These seminars are a vital component of our Ph.D. program, and provide essential educational opportunities to both the speakers and their audiences.

**Course Requirements**

As part of their education, graduate students are required to take at least six graduate-level courses. Depending on the student’s research interests and prior training, some of these courses may be in other departments such as...
Biochemistry, Chemical Engineering, Physics, or Environmental Toxicology. There are no core-course requirements. Each student works in consultation with their Advisor and Guidance Committee to establish personalized course work requirements. In this way, each student can tailor the appropriate balance between focused course work in a single area and the breadth of their overall graduate education.

**Research**

Performing research at the forefront of science and developing the ability to think critically about complex problems are the essence of the Ph.D. in Chemistry. Examinations, seminars, and course work are all designed to prepare the student for research.

Descriptive titles of our Faculty's research interests (research which is carried out mainly by graduate students) are listed on pages 12 and 13, and more detailed descriptions of their research are given on subsequent pages. Selection of a Research Advisor normally includes selection of a research topic at the same time.

In addition to the research carried out in the Chemistry Department, there are a number of centers and programs on campus that provide research opportunities and financial support to graduate students in Chemistry. Groups of faculty on campus have created a number of programs to bring together researchers from different departments who share common interests. Frequently, the grants they secure provide for student support. In some cases, student participation in such programs is rather informal; while in other cases, students become a part of both the department and the program, satisfying course work and research requirements in each. Some examples of such entities which are currently active on campus include the Biotechnology Training Program, the Center for Integrative Toxicology, the Center for Biological Modeling, the Center for Microbial Ecology, and the Center for Structural Biology. Such programs allow students in the Chemistry Department to pursue a variety of interdisciplinary research projects that involve scientists in other departments. In addition to these formal programs, faculty in Chemistry collaborate on research projects with many other departments and colleges, and some Chemistry Faculty hold joint appointments in other departments.

**Dissertation and Final Defense**

The independent research and creative components of each student's research program are described in a written dissertation. This original contribution to the body of knowledge in the Chemical Sciences is defended by the candidate before the student’s Guidance Committee. A portion of this examination is open to the public.

**Graduate Courses**

We believe that our graduate course offerings are unique, and afford our students the opportunity of obtaining an outstanding education. Included in our catalog are several graduate laboratory courses such as **Chem 834—Advanced Analytical Chemistry**. Another important aspect of our program are Special Topics Courses. One way that students can learn about a research area is by joining a professor’s research program; a second way is by taking an advanced Special Topics course given by a faculty member on their research area. By having the faculty offer in-depth courses in their areas of expertise, students can master several new and exciting areas of chemical research as represented in our Department.

Chemistry graduate student Benjamin Klar in Prof. Hamann's group measures the photoelectrochemical efficiency of a thin-film electrode their group has designed.
The following graduate-level courses are currently offered by the Chemistry Department:

811 Advanced Inorganic Chemistry I
Fall. 3 credits.
Principles of chemical bonding, electronic structure, and reaction mechanisms of main group and transition metal compounds. Concepts of group theory.

812 Advanced Inorganic Chemistry II
Spring. 3 credits.
Descriptive chemistry of inorganic compounds. Emphasis on synthesis, structure, and reactivity patterns of coordination, organometallic, and solid state compounds of transition metals and main group elements.

820 Organometallic Chemistry
Spring. 3 credits.
Organometallic functional groups. Principles of electronic structure, and bonding in organometallic species will be related to reactivity patterns in common systems. Preparation of complexes with applications to catalytic and stoichiometric organic syntheses.

832 Mass Spectrometry
Spring. 3 credits.
Instrumentation of mass spectrometry. Interpreting mass spectra of organic and inorganic molecules. Applications to analysis of large molecules and chromatography.

834 Advanced Analytical Chemistry I
Fall. 3 credits.
Basic electronics and data acquisition/analysis, electrochemistry, and statistics for chemists.

835 Advanced Analytical Chemistry II
Spring. 3 credits.
Separations, molecular spectroscopy, and mass spectrometry.

836 Separation Science
Spring of odd-numbered years. 3 credits.
Physical and chemical principles of separations, column technology, and instrumentation for gas, liquid, and supercritical fluid chromatography.

837 Electroanalytical Chemistry
Spring of even-numbered years. 3 credits.
Modern electroanalytical chemistry. Theory and applications to chemical and biological problems. Coulometry, voltammetry, ion-selective potentiometry and other electrochemical techniques.

838 Computer-Based Scientific Instrumentation
Fall of odd-numbered years. 3 credits.
Electronic and computer-aided measurement and control in scientific instrumentation and experimentation. Principles and applications of digital computers, operational amplifiers, digital logic devices, analog-to-digital converters, and other electronic instruments.

845 Structure and Spectroscopy of Organic Compounds
Fall. 3 credits.
Structural and stereochemical principles in organic chemistry. Applications of spectroscopic methods, especially nuclear magnetic resonance, static and dynamic aspects of stereochemistry. Spectroscopy in structure determination.

850 Intermediate Organic Chemistry
Fall. 3 credits.
Traditional and modern basic reaction mechanisms and principles and their synthetic applications.

851 Advanced Organic Chemistry
Spring. 3 credits.
Structure, reactivity, and methods. Acid-base reactions, substitution, addition, elimination, and pericyclic processes. Major organic intermediates related to simple bonding theory, kinetics, and thermodynamics.

852 Methods of Organic Synthesis
Spring. 3 credits.

881 Atomic and Molecular Structure
Fall. 3 credits.
Postulates of quantum mechanics, analytical solutions of the Schrödinger equation, theoretical descriptions of chemical bonding, spectroscopy, statistical mechanics, and statistical thermodynamics.

882 Kinetics and Spectroscopic Methods
Spring. 3 credits.
Rate equations and mechanisms of chemical reactions: reaction rate theory, kinetic theory of gases, photochemistry. Spectroscopic methods, and applications of spectroscopy in reaction kinetics.

883 Computational Quantum Chemistry
Fall. 3 credits.
Computational methods in determining electronic energy levels, equilibrium nuclear configurations, and other molecular properties.

888 Computational Chemistry
Spring. 3 credits.
Computational approaches to molecular problems. Use of ab initio and semi-empirical electronic structure. Molecular mechanics and molecular dynamics software.

890 Chemical Problems and Reports
Fall, Spring, Summer. 1 to 6 credits.
Investigation and report of a nonthesis problem in chemistry.
Sec. 001 – Faculty Seminar Series
Sec. 002 – Second Year Oral
Sec. 003 – Graded Research
Sec. 004 – Summer Area Seminars/Special Topics

913 Selected Topics in Inorganic Chemistry
Fall, Spring. 1 to 3 credits.
Chemistry of metal-metal bonds and clusters, organometallic chemistry, layered oxides, and complex layered oxides. Photochemistry. Solid state chemistry and applications of quantum mechanics.

918 Inorganic Chemistry Seminar
Fall, Spring. 1 credit.
Advances in inorganic chemistry reported by graduate students.

924 Selected Topics in Analytical Chemistry
Fall, Spring. 2 to 3 credits.
Advanced computer techniques, surface chemistry, analytical chemistry of polymers, or statistics for chemists.

938 Analytical Chemistry Seminar
Fall, Spring. 1 credit.
Advances in analytical chemistry reported by graduate students, faculty and guest lecturers.

956 Selected Topics in Organic Chemistry
Fall, Spring. 1 to 3 credits.
Heterocyclic and organometallic chemistry, natural products, photochemistry, free radicals, or reaction mechanisms.

958 Organic Chemistry Seminar
Fall, Spring. 1 credit.
Advances in organic chemistry reported by graduate students.

971 Emerging Topics in Chemistry
Fall, Spring. 1 to 3 credits.
Discussion of a research topic of emerging interest in chemistry. Preparation of a proposal for funding of research.

987 Selected Topics in Physical Chemistry I
Fall. 1 to 3 credits.
Topics such as kinetics and photochemistry, macromolecular and surface chemistry, molecular spectroscopy, electric and magnetic properties of matter, or applications of statistical mechanics to chemical problems.

988 Selected Topics in Physical Chemistry II
Spring. 1 to 3 credits.
Topics such as analysis and interpretation of molecular spectra, advanced molecular structure theory, magnetic resonance, X-rays and crystal structure, scientific analysis of vacuum systems, or problems in statistical mechanics.
991 Quantum Chemistry & Statistical Thermodynamics I
Fall. 3 credits.
Principles and applications of quantum chemistry. Partition functions, spectroscopic measurements, and thermodynamic applications.

992 Quantum Chemistry & Statistical Thermodynamics II
Spring. 3 credits.
Analytical and numerical methods for solving quantum chemical problems. Statistical mechanics of solids and liquids.

993 Advanced Topics in Quantum Chemistry
Spring of odd-numbered years. 3 credits.
Spectroscopic theory, properties of atoms and molecules in electric and magnetic fields, intermolecular forces. Many-body theory, molecular electronic structure, solid state chemistry, or molecular reaction dynamics.

994 Advanced Topics in Statistical Mechanics
Spring of even-numbered years. 3 credits.
Nonequilibrium statistical mechanics and thermodynamics. Correlation functions and spectroscopy, light scattering, magnetic relaxation, transport properties of fluids and gases, or statistical mechanics of chemical reactions.

995 Nuclear Chemistry Seminar
Fall, Spring. 1 credit.
Advances in nuclear chemistry reported by graduate students, faculty, and guest lecturers.

998 Physical Chemistry Seminar
Fall, Spring. 1 credit.
Advances in physical chemistry reported by graduate students.

999 Doctoral Dissertation Research
Fall, Spring, Summer. 1 to 20 credits.

MSU’s Campus is spectacularly beautiful in autumn. (Can you find the heart?)
GRADUATE STUDENT LIFE

In a typical year, approximately 40 new graduate students begin the Graduate Program in Chemistry. When they arrive, they are each assigned to a faculty advisor in their chosen area of interest, and provided with desk space in a research lab. In this way, first year graduate students quickly get to know the faculty and other more established graduate students, accelerating their integration into the Department. By the end of their first semester, the new students are expected to choose their permanent research advisors who then provide office space in their own research laboratories. With ~200 graduate students currently distributed among our approximately 40 faculty members, the average research group’s size is around 5 students. Since multiple research projects are usually underway in every faculty member’s group, students do not typically encounter situations where a large number of researchers are working on small aspects of a single large project. In many cases, the graduate students and their advisors are the sole researchers working on a particular project. Our Department’s high faculty-to-graduate student ratio allows for individual interactions between advisor and student on a very frequent if not daily basis.

As discussed previously, graduate students are supported as teaching assistants (TAs) or research assistants (RAs). When students are assigned a teaching assistantship, there are often many TA positions available, and students have the opportunity to state the teaching assignment that they prefer — such as laboratory instructor or recitation instructor. During the summer semester a smaller number of courses are offered, and fewer TA positions are available. Most students are supported in the summer either as a Graduate Research Assistant or as a Student Research Assistant, allowing them to concentrate full-time on their research. Support during Summer is normally provided by research grants. Our Department is committed to providing uninterrupted support for all students in good standing for a period of up to five years, and we expect to do so in the future, as long as current financial conditions continue.

The graduate student experience in Chemistry begins with graduate class work, and an introduction to chemical research through interactions with the faculty, senior graduate students and postdoctoral fellows. As a new student’s research skills mature, they develop into fully contributing members of the scientific community and help advance the forefront of knowledge in the Chemical Sciences.

In addition to these roles, graduate students are also vital participants in the Department and the University. Graduate students elect members to serve on Departmental decision-making committees such as the Educational Policies Committee, the Advisory Committee, and the Undergraduate Chemistry and Lab Committee. Graduate students may also serve on University-wide Committees. The Council of Graduate Students (COGS) has
traditionally played a strong leadership role on campus. It has worked with the University to negotiate tuition waivers, health insurance and other benefits for graduate students.

A new student’s first interaction with the Department is the Orientation Program, which has been organized and run by the Chemistry Graduate Office and Graduate Students since 1976. Some graduate students in Chemistry elect to participate in Science Theatre, an award-winning campus-wide group of volunteers who, through public demonstrations and presentations, stimulate public interest in science. Science Theatre reaches over 20,000 students, parents, and teachers each year. It has received the 1993 American Association for the Advancement of Science Award for Public Understanding of Science and Technology, and has been featured on CNN’s “Headline News” and “Science and Technology Week.”

There are also several professional organizations that many in the Department participate in. These include the American Chemical Society, ACS Women in Chemistry, and The National Organization for the Professional Advancement of Black Chemists and Chemical Engineers (NOBCChE). These organizations have all recently won awards for their very active and inventive outreach efforts.

The daily activities within the Department for graduate students are rich and varied. Their typical day may include attending classes, presenting a recitation as a TA, taking in seminars or departmental colloquia, stealing a little time out at one of the University’s three fitness gymnasiums or three pool facilities, and of course, research. Many students ask about the time “required” in the lab, after hearing horror stories of long hours required slaving over test tubes. While it’s true that being in graduate school is not the same as having a 9-to-5 job, the time involved in research should be viewed as a learning opportunity, not a chore. Students naturally become excited and enthusiastic about their research, and about being involved in pursuits that yield never-before-obtained results and information, which is a unique and truly exciting experience. Graduate students come back to lab after dinner and on weekends not because they are required to, but because they are eager to find what they will learn next. Research is an exhilarating experience, and this is what motivates the best students. The work that they perform here as graduate students has an impact on Science and a profound effect on what they achieve later on in their professional careers.
after graduation

Upon the successful completion of our Ph.D. program, our students have amply demonstrated their ability to conduct vital, independent research. The Chemistry Department and the University are committed to assisting our students in the pursuit of their career goals. Information about academic, governmental and industrial positions and postdoctoral fellowships is updated daily and made available to all graduate students. Assistance in résumé writing is available, and résumés are collected from students and made available to employers upon request. Each year a number of industrial recruiters, frequently MSU Chemistry alumni themselves, visit the Chemistry Department and the University for on-campus interviews of prospective employees.

The University operates an outstanding service for graduating students at all levels through the MSU Career Services Network, which can be reached at (517) 355-9510, ext. 174 or on the web at [http://careernetwork.msu.edu/](http://careernetwork.msu.edu/). This facility is the focal point for on-campus interviewing, and offers an extensive assortment of resources designed to assist students in the selection and pursuit of career options. Individual advising is available, as well as workshops on job-seeking strategies, résumé writing and interviewing. They stock a wealth of career assessment material, employer literature and information on recent hiring trends, salary levels, and employment opportunities.

Obviously, a comprehensive list of the thousands of MSU Chemistry Department alumni and their current positions cannot be listed here. However, the following list of employers is representative:

### Selected Corporations with MSU Chemistry Ph.D. Alumni

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### Selected Universities with MSU Chemistry Ph.D. Alumni

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### National Research Laboratories with Chemistry Ph.D. Alumni (permanent staff and post-doctoral positions)

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THE DIVERSE RESEARCH INTERESTS of the Chemistry Faculty do not permit their easy classification into the traditional areas of Chemistry: Analytical, Physical, Organic and Inorganic. However, they are listed here in a matrix of different aspects of chemistry research and with a broad, descriptive title for their research interests, with their principal interest indicated by a red star (★). More information about the research activities of the Faculty, including their interdisciplinary interests, is provided in the individual descriptions of their research on the pages which follow.

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Spintronics and photonics are new branches of material science that aim at the storage, manipulation, and transmission of information using electronic spin and photons as the basic unit of information, paralleling in many ways the traditional approaches that are based on conventional electronics: that is, the use of the electronic charge degree of freedom to process information. These approaches, in theory at least, hold enormous potential for the development of advanced data encryption, information computing, and energy transfer processes. In parallel to these advances, many interesting effects based on the reduced dimensionality of materials have been discovered over the last two decades or so, leading to the emergence of the new fields of nanotechnology and nanoscience.

Our group is interested in the study of new nanoscaled inorganic materials that are relevant to energy and information storage and transfer applications. Our strategy is fundamentally interdisciplinary, and involves the development of materials synthesis and characterization methods, the use of a wide array of magneto-optical and electrochemical tools to understand the underlying physics that govern these novel materials, and the design of simple working devices to manipulate and optimize energy and information processes at the nanoscale.

In particular, we are interested in the study of magnetic semiconductors such as magnetite (Fe₃O₄), Ga₃MnAs, and rare-earth-based semiconductors (i.e., EuTe). In the bulk, these materials are known to exhibit many interesting effects such as giant Faraday rotation, optical second harmonic generation, spin-photogalvanism, and light-induced magnetization, that are all connected to the ability to store and extract information and/or energy based on the electronic spin degree of freedom. One very compelling objective that illustrates the over-arching theme of our lab is the realization of a spin-light emitting diode (spin-LED) using chemically processed colloidal materials, as it epitomizes some of the different challenges we are interested in taking up:

- Synthesis of ferromagnetic nanomaterials for spin polarization;
- Coupling of these materials into conductive heterostructured films;
- Efficient transport of charge carrier through interfaces;
- Long-range spin-polarization of electrical current;
- High efficiency conversion of spin-polarized current into circularly-polarized emitted light.

Ultimately, our goal is to push forward the limits of our understanding of the physics of novel complex nanomaterials through careful chemical manipulation and detailed spectroscopic and magnetic investigations, which will open up new avenues for addressing current issues relevant with energy/information storage/transfer.

A schematic spin-LED: negative charge carriers’ spins are polarized following transport through a spin-polarized layer; these spin-polarized electrons then recombine with positive charge carriers, leading to the emission of circularly-polarized light.
The Beck group uses femtosecond nonlinear spectroscopy to study photophysical and photochemical processes in photosynthetic light-harvesting proteins. The current focus is on how carotenoids function in energy transfer and photoprotection mechanisms in light-harvesting proteins. The long-range goal is to learn the principles that can be used to design and optimize materials for light capture and excitation energy conversion to fuels. Two-dimensional electronic spectroscopy (2DES) allows us to characterize the formation and decay of electronic coherences and intermediate states or to discern the motion of the surrounding protein or solvent medium. We conduct this work with a structural biological perspective; a goal of the research is to understand how the structure of a chromophore and the electrostatic environment derived from the binding site in a protein results in optimal function in energy transfer or photoprotection.

In one project, we are studying the peridinin–chlorophyll a protein (PCP, Figure 1), a light-harvesting protein from marine dinoflagellates that incorporates a carbonyl-substituted carotenoid, peridinin, as its main light-absorbing chromophore. Energy absorbed from the mid-visible part of the solar spectrum by peridinin is transferred efficiently to chlorophyll a on the < 3 ps timescale. PCP represents an important system in which the energy transfer function is optimized by the protein environment and by chemical modification of the active chromophore. An intramolecular charge-transfer (ICT) character is produced in peridinin by the electron-withdrawing character of the carotenoid substituent and the distorted conformation of the conjugated polyene backbone derived from its binding site. The result is a very long lifetime for the $S_2 (1\text{Bu}^\circ)$ excited state and improved yields of excitation energy transfer to the chlorophyll a acceptors via quantum coherent and Förster mechanisms.

In a new collaboration with Professor Cheryl Kerfeld (MSU–DOE PRL and LBNL), we are studying the photochemistry and structural dynamics associated with the photoactivation of the orange carotenoid protein (OCP, Figure 2) from cyanobacteria. OCP uses another carbonyl-substituted carotenoid, 3′-hydroxyechinenone, as a light sensor and as a quencher of excited states in the cyanobacterial phycobilisome. We are also interested in the mechanism with which OCP serves as a quencher of singlet oxygen, a reactive oxygen species that is produced as a byproduct in photosynthesis by recombination of charge-separated states in the photosystem II reaction center. Here the ability of OCP to stabilize low-lying triplet states of 3′-hydroxyechinenone is likely to be very important.

Figure 1. Peridinin–chlorophyll a protein from Amphidinium carterae (IPPR.pdb).

Figure 2. Orange carotenoid protein from Synechocystis PCC 6803 (3MG1.pdb).
Controlling interfacial fluidity. Covalently bound interfacial adlayers are not fluid, and fluid adlayers are not physically or chemically robust. These limiting cases have frustrated advances in fields such as molecular-scale lubrication, chemical separations and cellular adhesion. We are developing a novel family of interfaces that can be bound to an interface and at the same time retain the properties of a fluid. Both the thermodynamic driving force for complexation and the kinetics of surface diffusion can be controlled through metal ion complexation, system pH, the surface complexing moieties, and the amphiphile head groups.

Characterizing interfacial heterogeneity. We quantitate molecular motion on molecular length scales and over micron to millimeter length scales, using two complementary microscopy techniques. Using these techniques, we can evaluate the fluidity of a wide range of interfaces and, significantly, we can now characterize transient structural non-uniformities in mono- and bilayer films. This latter capability offers a new way to explore the presence of previously invisible spatial variations in chemical composition, with applications ranging from sensor interface design to in situ plasma membrane characterization.

Using Catalysis to Convert Biofeedstock to Hydrocarbons. It is clear that we need to diversify our range of sources for energy, ideally taking full advantage of solar, wind and other renewable resources. Despite the transformation that is currently underway, there will be, for the foreseeable future, the need for hydrocarbon for some applications. We are developing a versatile multi-step flow-through catalytic process designed to convert input derived from waste biomass (e.g. corn stalks) to hydrocarbons in a way that can be readily adjusted for the biomass feedstock. Work in this area is focused on heterogeneous catalysis based on metal nanoparticles immobilized on micro- and nano-porous structures.

Long Range Order in Ionic Liquids. Ionic liquids are a class of materials that can be described as salts that are liquids at room temperature. These materials are typically visous fluids and they have found use in areas ranging from organic synthesis to chemical sensing and energy storage. The organization that exists within ionic liquids is not well understood and has until recently been thought to be on the orders of nanometers in length. Our recent work has shown that when ionic liquids are placed in proximity to a charged surface, the charge induces order that persists on the sub-millimeter length-scale — five orders of magnitude greater than expected. These new findings not only provide insight into the structure of these systems, but also opens the door to novel applications in energy storage and electronically-controlled optics.


Role of Acid Sphingomyelinase in Shifting the Balance Between Proinflammatory and Reparative Bone Marrow Cells in Diabetic Retinopathy, Harshini Chakravarthy, Svetlana Navitskaya, Sandra O’Reilly, Jacob Gallimore, Hannah Mize, Qi Wang, Nemin Kady, Chao Huang, G. J. Blanchard, Maria B. Grant and Julia V. Busik, Stem Cells 2016, 34, 972-983.

Using Catalysis to Convert Biofeedstock to Hydrocarbons. It is clear that we need to diversify our range of sources for energy, ideally taking full advantage of solar, wind and other renewable resources. Despite the transformation that is currently underway, there will be, for the foreseeable future, the need for hydrocarbon for some applications. We are developing a versatile multi-step flow-through catalytic process designed to convert input derived from waste biomass (e.g. corn stalks) to hydrocarbons in a way that can be readily adjusted for the biomass feedstock. Work in this area is focused on heterogeneous catalysis based on metal nanoparticles immobilized on micro- and nano-porous structures.

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The research interests of our lab can be subdivided into the three main areas of **Bioorganic Chemistry**, **Synthetic Chemistry**, and **Organic Spectroscopy**.

**Bioorganic Chemistry** efforts are geared towards elucidation of the interaction of bioactive compounds with receptors and proteins. We rely heavily on de novo protein design and mimicry of natural systems to better understand how certain biological processes occur. As an example, we have initiated research into designing protein mimics of rhodopsin, the protein responsible for vision, which can bind retinal as a protonated Schiff base ([PSB]) (same binding mode as in rhodopsin). These protein mimics are used to investigate the wavelength regulation mechanism that enables color vision. Currently we are exploring the potential to use our engineered proteins as colorimetric and fluorescent proteins for cellular tagging and intracellular pH sensors.

**Synthetic Chemistry** program is generally focused on the development of new reactions that utilize simple organic molecules and through designed manipulations lead to more complex systems. In most cases, our methodologies lead to the production of heterocycles with regio- and stereocontrol. These transformations are then highlighted in total syntheses of natural products that exhibit interesting biological activities. Recently we have reported the catalytic asymmetric chlorolactonization of alkenoic acids and unsaturated amides to furnish chiral heterocycles. These reactions are catalyzed by (DHQD)_2PHAL in combination with various N-chlorinated hydantoins as the terminal chlorenium sources. Halofunctionalization of different compounds, understanding the mechanism of these transformations and the details of enantioselections are currently under investigation.

In the area of **Organic Spectroscopy**, we are interested in developing host/guest systems that can be used in the absolute stereomolecular determination of chiral compounds. We accomplish this through the design and synthesis of chimeric receptors, which upon binding with the chiral compound function as reporters of chirality. We rely heavily on Circular Dichroism (CD) as the tool for observing the host/guest interactions between the chiral compounds and the receptors. In particular, we will take advantage of the excitonic coupling between independently conjugated chromophores that make up the receptors to establish non-empirical guidelines for the absolute stereomolecular determination of asymmetric centers.

**Selected Publications**


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**Babak Borhan**

**Synthetic and Bioorganic Chemistry and Organic Spectroscopy**

**Professor**

(b. 1966)

B.S., 1988, Univ. of California, Davis; Ph.D., 1995, Univ. of California, Davis; Postdoctoral Fellow, 1995-98, Columbia Univ.

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The focus of our research is to develop evidence-based approaches to teaching, learning, and assessment. Our work involves a wide range of activities and methods including designing ways to assess both what students know and how they use their knowledge, developing curriculum materials, and evaluating the effects of transformation efforts both within and across disciplines.

To design effective curricula we need to know what students bring to the table both in their prior knowledge and what they are able to do with that knowledge. We also must understand how and why students develop ideas that are not scientifically sound. For example we have shown that for many students, when they consider how the molecular level structure of a substance can be used to predict macroscopic properties, their ideas are often a loosely woven tapestry of concepts, facts and skills, rather than a useful framework of ideas.

Our approach to curriculum transformation uses a design based research cycle in which we identify what students should know and be able to do, design and implement a curriculum that would meet these goals, assess student achievement and use the results of the assessments to revise the curriculum and accompanying assessment materials. These assessments require students to construct (free form) structures, diagrams, and models, and to develop explanations for phenomena. Our formative assessment system, beSocratic (http://besocratic.chemistry.msu.edu), is designed to recognize and respond to student input.

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Using this system we have evaluated how students in both traditional and CLUE curricula understand a range of chemical ideas and phenomena. For example we have shown that CLUE students are more likely to understand that intermolecular forces are interactions between small molecules (not within) as shown in the Sankey diagram below. We have also shown improvements in understanding structure property relationships, and understanding of acid base reactions.

Sankey diagram showing how CLUE and traditional students represent intermolecular forces as within or between molecules.
Statistical Mechanics and Quantum Mechanics are the methods we use to create theories and computational algorithms for the simulation of protein structure-function relations. A major effort is devoted to accelerating MD to reach realistic time scales. Another area of interest is ab initio molecular dynamics of electron localization in a variety of liquids. Ongoing studies include simulations and analysis of large-scale protein domain movements, proton translocation, and excess electron localization.

New methods are under development that can enhance the sampling of protein configurations to be able to explore the free energy cost for large domain motions. In the five residue opioid peptide met-enkephalin we have used long simulations along with a clustering and transition path analysis to obtain the major pathways of dihedral states visited for transitions between open and closed configurations and their correlation with committors (small values mean intermediate states return to initial state before visiting final state and vice versa).

Protein stability is based on a delicate balance between energetic and entropic factors. Intrinsically disordered proteins (IDPs) interacting with a folded partner protein in the act of binding can order the IDP to form the correct functional interface by decrease in the overall free energy. We develop methods evaluate the part of the entropic cost of ordering an IDP arising from their dihedral states. As shown in the plot below, the conformations based on the dihedral sampling is very dependent among all the dihedrals. This leads to a reduction of the entropic cost of binding relative to independent dihedral conformations.

Plot of committor versus end-to-end (EtoE) distance for the DIHED angle pathways. The first four strongest (highest overall flux) pathways are indicated: P1 solid line, P2 double line, P3 dashed line, and P4 dotted line. The sizes of the circles indicate the state populations. Also displayed are ensembles of backbone structures for the various states indicating the broad yet distinct conformations sampled.

Population fractions of the first 100 states sorted by decreasing size along with the assumed independent state populations for those states. There are $3^6 = 531,441$ possible states for the 6 phi and 6 psi three-conformation dihedrals. The strong dependence among the dihedral conformers sampled is evident in this data representation.

**Selected Publications**


Ultrafast lasers, with pulse durations shorter than $10^{-15}$ s—less time than it takes for atoms to move—have already led to Nobel Prizes in Chemistry and Physics. These lasers are ideal for probing and controlling chemical reactions. Our group has three well-funded thrust areas of scientific leadership: (a) Understanding and controlling chemistry under intense laser field radiation: Exploring molecular dynamics at energies ranging from $10^{15}$ to $10^{20}$ W/cm². (b) Biomedical imaging and sensing: Label-free biomedical imaging and explosives detection. (c) Development of novel spectroscopic approaches: New laser sources, pulse shapers, and computers will revolutionize how we study chemical reactions. Progress in or research programs requires fundamental advances in science, often questioning established dogmas and accomplishing what others have determined to be impossible.

Understanding and controlling chemistry under intense laser field radiation — High intensity laser light has provided notable advances across a broad range of disciplines including physics, chemistry, medicine, and defense. Our common understanding of light-matter interactions fails at extreme intensities, especially when the field strength of the incident radiation is strong enough to deform the Coulomb potential of the atom and liberate electrons. At intense enough fields those electrons become relativistic, opening up an abundance of novel atomic and molecular processes to investigate. In our lab, we take advantage of laser sources and pulse shaping methods we have developed to understand and to control the dynamics of exotic chemical reactions in gas, liquids, and solids induced by strong laser fields. Our recent projects include study of exotic chemical reactions, such as the formation of H3+, to explore unlikely chemical processes involving dissociation and formation of multiple chemical bonds, occurring under the influence of strong laser fields.

Mechanism for H3+ formation involving a roaming neutral H2 molecule.

In addition, we explore relativistic pulse compression to achieve high efficiency conversion of femtosecond pulses into attosecond pulses.

Biomedical Imaging and Sensing — Whether the goal is to diagnose and treat retinal diseases or detect oral cancer, the challenge is perfecting chemically resolved imaging. Our group has been pioneering laser technology for unstained biomedical imaging. In both areas, developments from our group are a combination of fundamental scientific advances with source development. We routinely collaborate with a number of medical centers nationally as well as other research groups on MSU’s campus.

Selected Publications


The Draths research group creates microbial organisms for use in chemical synthesis. Our research encompasses creation of new metabolic pathways that do not exist in nature, construction of the microbial chassis needed to express these pathways, and subsequent microbial synthesis of targeted chemicals under controlled culture conditions in batch reactors. An iterative approach to catalyst design and evaluation allows us to evaluate the feasibility of newly created, microbe-catalyzed syntheses in both pharmaceutical and large-scale commodity chemical applications.

We have two significant areas of interest:

- Enabling microbes to synthesize commodity chemicals from methane.
- Microbial synthesis of highly functionalized molecules.

Researchers in the lab will receive training in a variety of disciplines that may include organic synthesis, analytical methodology, molecular biological techniques, protein expression and purification, execution of enzyme assays, and operation of batch fermentation reactors. We welcome researchers who seek a multidisciplinary education. If you are interested in changing the landscape of chemical synthesis and building a research effort from the ground up, check us out! ☝️

Selected Publications
Green chemistry is being elaborated that enables CO₂ fixed by plants to be converted into chemicals currently derived from the BTX (benzene toluene xylene) fraction of petroleum refining. Nonrenewable fossil fuel feedstocks, carcinogenic starting materials and toxic intermediates are avoided. In addition, an array of new monomers is being synthesized to identify structures that are: (a) free of endocrine disruption activity, and (b) lead to polymers and plasticizers characterized by novel materials properties.

Current commercial synthesis of \( p \)-hydroxybenzoic acid begins with BTX-derived benzene and proceeds through cumene and phenol as intermediates. Carboxylation of potassium phenolate affords \( p \)-hydroxybenzoic acid monomer, which typically constitutes 50% of the mass of liquid crystalline polymers. A green synthetic alternative has been elaborated whereby \( p \)-hydroxybenzoic acid is synthesized in a single step in high conversion and good selectivity from nontoxic shikimic acid. Shikimic acid, in turn, is microbially synthesized from plant-derived glucose or isolated directly from plants such as *Ginkgo biloba*. Shikimic acid’s solubility in \( n \)-butanol and propensity to crystallize from \( n \)-butanol facilitate its isolation from fermentation broth or plant tissue. Green synthesis of \( p \)-hydroxybenzoic acid eliminates the need for using carcinogenic benzene as a starting material and toxic phenol as an intermediate.

BTX-derived xylene is industrially oxidized to terephthalic acid, which is polymerized with ethylene glycol to produce poly(ethylene terephthalate) PET. Over 50 × 10⁹ kg of terephthalic acid are globally produced each year. Two green synthetic alternative routes have been developed. Isoprene and acrylic acid microbially synthesized from glucose undergo a cycloaddition to form 4-methylcyclohex-3-ene-1-carboxylic acid. Dehydrogenation affords terephthalic acid. Alternatively, \( cis, cis \)-muconic acid microbially synthesized from glucose is isomerized and the resulting \( trans, trans \)-muconic acid reacted in a cycloaddition with bioethanol-derived ethene to yield cyclohex-2-ene-1,4-dicarboxylic acid. Dehydrogenation affords terephthalic acid. In addition to use of renewable feedstocks, the new routes enable the first practical synthesis of substituted terephthalates when substituted acrylic acids and substituted ethenes are employed. Furthermore, a parallel world of 1,4-cyclohexane and 1,4-cyclohexene 1,4-dicarboxylic acids has been created, which affords unique opportunities to avoid aromatic-associated, endocrine disruption activity while enabling the fabrication of novel materials.

**Selected Publications**

The major focus of our research is to elucidate the structures of biologically important proteins, enzymes, enzyme/substrate, protein/ligand and protein/nucleic acid complexes. These high-resolution structural “snap shots” reveal a wealth of information regarding the biology, mechanism and chemistry of these biological molecules and assemblies. We then take these insights and verify them by mutagenesis and various assays. We are also involved in applying our structural insights in protein design applications.

**Eucharyotic Transcription.** SNAPc is a five protein complex required for the initiation of all snRNA genes by both RNA Pol II and Pol III. It is one of the few factors that is involved in both Pol II and Pol III initiation and is therefore a key target for understanding the similarities and differences between these two systems. We have developed a co-expression strategy that allows us to co-express and purify this complex to high levels in an active form. We are in the process of crystallizing and determining the structure of this complex. This will be one of the largest protein complexes involved in transcription to be structurally characterized at atomic resolution. We have also determined the structure of the Oct-1/DNA/SNAP-190 peptide complex, the first structure of a transcriptional activator interacting with a partner in the basal transcriptional machinery.

**Structure and Mechanism of Enzymes.** We have determined the structures of all three of the enzymes in the starch biosynthetic pathway, ADP-glucose pyrophosphorylase, Branching enzyme and glycogen/starch synthase. ADP-glucose pyrophosphorylase is an allosteric enzyme that regulates the entire pathway. From this structure we obtained a detailed, molecular understanding of how this enzyme is regulated by activators and inhibitors. Our eventual goal is to use this information to redesign the enzyme to be more active, potentially increasing the starch content in cash crops. Our structure of glycogen synthase showed for the first time that several glycogen binding sites exist outside the enzyme’s active site. Though the function of these sites is not clear, they are important for the enzyme’s activity and understanding their role is a focus of our future work. We have also identified seven glycan binding sites external to the active site of Branching enzyme. Our mutational work has demonstrated that several of these sites are also critical for the enzyme function and we are in the process of determining their role. In general, it appears that these enzymes that act on polymeric substrates often have external binding sites to orient and localize the enzymes to the polymers. In collaboration with the Walker lab, we have also investigated the structure, mechanism and specificity of some of the enzymes involved in Taxol biosynthesis, including phenylalanine aminomutase (PAM) and benzoic acid CoA ligase. The structures of 2 PAMs have been determined, and a variety of benzoic acid CoA ligase substrate structures have been determined for use in rationally extending the substrate specificity of these enzymes.

**A Rhodopsin Protein Mimic.** In collaboration with the Borhan lab, we have been involved in redesigning small cytosolic proteins to be rhodopsin mimics. We have redesigned cellular retinoic acid binding protein II and cellular retinoic acid binding protein II to bind and form a protonated Schiff base with the retinal chromophore. Further, we have constructed a spectrum of protein pigments that bind the same chromophore retinal, but alter the absorbance of this chromophore over 219 nm. We have also developed new fluorescent proteins that can be used as fluorescent protein fusion tags, extending the range of fluorescent proteins and adding pH sensing to their repertoire.

**Plasmin and Pathogen Infection.** The blood coagulation pathway is a central target for pharmaceuticals aimed at clot prevention, stroke, heart disease etc. We have focused our attention on plasminogen, the enzyme responsible for the dissolution of blood clots by cleavage of fibrinogen. Plasminogen is also involved in the infectivity of a number of bacterial pathogens including streptococcus, staphylococcus, bubonic plague, impetigo and others. These pathogens have cell surface plasminogen receptors and activators, allowing them to co-opt plasminogen’s ability to degrade the body’s extracellular matrix, allowing infection to spread. We determined the first structure of one of these receptors, Plasminogen-activating group A streptococcus M-like protein bound to a plasminogen fragment. Our goal is to use this and further structural information to develop novel antibiotics against these pathogens.

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*Potato tuber ADP-glucose pyrophosphorylase.*
Hamann Group Research: There is a LOT of energy from sunlight striking the Earth’s surface: approximately $10^{27}$ Joules/second. For comparison, the averaged worldwide energy demand is approximately $10^{18}$ Joules/second. The Hamann group is engaged in interdisciplinary research to address basic science issues related to new methods and materials for utilizing this incredible resource to produce electricity and chemical fuels. Of specific interest are regenerative and non-regenerative photoelectrochemical cells, including dye-sensitized solar cells and thin-film absorber photocatalytic systems. In addition, we are interested in the use of ammonia as an energy (hydrogen) carrier and are investigating the electrocatalytic synthesis and electrolysis of ammonia.

Dye Sensitized Solar Cells: We are investigating the fundamental role of the relevant dye-sensitized solar cell, DSSC, components (redox shuttle, photoanode and sensitizer) involved in key efficiency-determining processes. Ultra-fast electron injection from a photoexcited sensitizer into a photoanode produces a charge separated state with typically high quantum efficiency. We are primarily interested in the subsequent processes of dye regeneration and recombination which control the efficiency of charge collection. We systematically vary the components involved in each reaction and interrogate them with a series of photoelectrochemical measurements. The general lessons learned will ultimately be used to develop design rules for next generation DSSCs comprised of molecules and materials which are capable of overcoming the kinetic and energetic constraints of current generation cells.

Thin Film Absorber Solar Cells: We are interested in exploring the use of thin films to overcome the problems associated with short collection length materials. One absorbing material of current interest is $\alpha$-Fe$_2$O$_3$ (hematite). Hematite is an attractive material for solar energy conversion due to the abundance of iron in the earth’s crust, the extremely low cost, chemical stability and environmental harmlessness. In addition, hematite has been shown to be a promising water oxidation photocatalyst in a fuel-forming (non-regenerative) photoelectrochemical cells. We are currently elucidating the rate limiting steps as well as water oxidation mechanism on the electrode surface. Additional topics of recent interest include understanding the effect of substrate and underlayer materials, incorporation of dopants, and surface layers (e.g. catalysts) on the water oxidation efficiency. Additional oxide, nitride and oxynitride semiconductor materials are also under current investigation.

Ammonia Electrocatalysis: Nitrogen is the most abundant gas in Earth’s atmosphere and water is the most abundant liquid on Earth’s surface; combining the catalytic reduction of $\text{N}_2$ with the oxidation of $\text{H}_2\text{O}$ to produce $\text{NH}_3$ offers a route to scalable renewable energy storage. Liquid ammonia has an energy density comparable to methanol, and the stored chemical energy can in principle be used to generate electricity or $\text{H}_2$ on demand. The electrolysis of liquid $\text{NH}_3$ has received limited attention to date, however. We are therefore exploring the electrocatalytic conversion of liquid $\text{NH}_3$ to $\text{H}_2$. We are also engaged on a broader collaborative effort to develop and investigate new electro-catalysts based on earth-abundant materials for $\text{NH}_3$ synthesis and electrolysis.
Protein folding is an amazing molecular process that occurs by sorting out an astronomical number of possible conformations down the free energy landscape. In a crowded cellular environment, however, environmental stresses or mutations can mislead polypeptide chains to misfolded or catastrophic aggregate states (Fig. 1). Therefore, these unnecessary proteins have to be selectively cleared from cells for quality control and regulatory purposes. For the past decades, there have been remarkable advances in understanding these phenomena and related diseases. However, efforts have been largely limited to water-soluble proteins excluding the other major class of proteins that reside in cell membranes.

Our research focuses on a fundamental biological question, how membrane proteins are made and destroyed in cells (Fig. 2). Membrane proteins comprise approximately 30% of all proteins encoded in genes and carry out numerous critical cellular functions. Approximately 60% of all drug developments are targeted at membrane proteins. The folding problem of membrane proteins is directly connected to human health. Indeed, accumulation of misfolded or misprocessed membrane proteins causes serious diseases such as Alzheimer’s disease, cystic fibrosis, and cancer. To answer our cardinal question, we investigate two conceptually connected areas by multi-disciplinary approaches including biochemical, biophysical, and chemical methods.

Chaperone-assisted membrane protein folding: YidC/Oxa1/Alb3 is a membrane protein family that plays a critical role in folding and assembly of membrane proteins in the inner membranes of bacteria, mitochondria, and chloroplasts. In *E. coli*, YidC forms a membrane insertion pore independent of SecYEG complex, major protein translocation machinery. YidC also has a chaperone activity: it facilitates the folding of a variety of SecYEG-dependent proteins. To understand how YidC acts as chaperone, we will tackle three specific problems:

• What are the driving forces in YidC-substrate interaction?
• What mechanism does YidC use to facilitate folding of membrane proteins?
• How are the structure and dynamics of YidC related to the function?

Controlled degradation of membrane proteins: Rapid protein degradation is a crucial cellular process that enables the clearance of misfolded proteins and regulatory proteins that are no longer needed. In all cells, this process is mediated by AAA+-protease superfamily. FtsH is the only membrane-localized AAA+-protease, which degrades both membrane and cytosolic proteins. To understand the principles of the quality control mechanism of membrane proteins, we focus on three specific questions using FtsH from *E. coli* as model.

• What sequence or structural features of substrates are subject to degradation?
• What is the role of the FtsH transmembrane domain in recognition and translocation of substrates?
• How is the proteolytic activity modulated by other membrane-bound cofactors?

Graduate students will gain a training opportunity in DNA manipulation, expression and purification of membrane proteins, biophysics of lipid bilayers, protein labeling, and various biophysical tools such as fluorescence, EPR, and X-ray crystallography.

**Fig. 1. Ruggedness of free-energy landscape in protein folding (modified from Hartl et al., Nature 2011, 475, 324-332.)**

**Fig. 2. From the cradle to the grave: overall scheme of membrane protein research in the Hong lab.**


H. laboratory has broad interest in structural biology of membrane proteins and biomolecules involved in metal homeostasis. By applying multidisciplinary approaches, including X-ray crystallography, NMR and other biochemical/biophysical/cell biological methods, we are aiming to clarify the detailed molecular mechanism of how the complicated biological system works at atomic level. Currently, we have two major projects and several collaborative projects ongoing.

**Zinc Transporter - ZIP family.** Zrt-Irt like protein (ZIP) family consists of a group of integral membrane proteins playing crucial roles in zinc and iron transport across cell membrane. In human genome, the fourteen members are involved in a variety of biological processes and associated with human diseases. Our current research is focused on ZIP4, a representative member in the mammalian ZIP family. ZIP4 is exclusively responsible for zinc uptake from intestine under normal conditions and ZIP4 mutations lead to a lethal genetic disorder, Acrodermatitis enteropathica (AE). ZIP4 is also upregulated on pancreatic cancer cells and essential for the growth of these extremely aggressive cells. In this project, our aims include: (1) Solve the crystal structure of ZIP4; (2) Elucidate zinc transport mechanism; and (3) Clarify the molecular mechanism of zinc-induced ZIP4 endocytosis. This work will also provide a structural framework for rational drug design against pancreatic cancer and other relevant diseases. (**Figure 1**)

**Lipid Kinase – PIPK family.** Phosphatidylinositol phosphate kinase (PIPK) family is a central player in the metabolism of phosphoinositides (e.g., PIP2), which are crucial signaling molecules in numerous biological processes. It has also been proposed that PIPKs are potential drug targets for human diseases, including a variety of cancers, diabetes, inflammations and chronic pain. The aim of our research is to establish the catalytic mechanism of the interfacial reaction, the molecular mechanism of substrate specificity, and particularly, the regulation mechanism by their binding partners and lipid molecules. We are also interested in structure-based drug design. (**Figure 2**)

**Collaborative projects: Lar proteins.** LarA is a nickel-dependent racemase which catalyzes the inversion of the stereochemistry of lactic acid. The activity of LarA absolutely depends on a newly-discovered cofactor which is biosynthesized by LarB, LarC and LarE. We are working with Dr. Robert Hausinger at the Skaggs Institute for Chemical Biology at Scripps and Dr. Edward Brown (Harvard University), we are conducting structural biology studies on CaSR, particularly on the extracellular domain (ECD) where metals/ligands bind and many disease-causing mutations occur. Our goal is to establish a structural framework for better understanding the activation mechanism by their binding partners and lipid molecules, which is crucial for the design of agonist and antagonist of CaSR against severe human diseases. (**Figure 3**)

**Calcium Sensing Receptor.** Calcium sensing receptor (CaSR) is a G protein-coupled receptor (GPCR) and a central player in calcium homeostasis in our body. Through collaboration with Dr. Jenny Yang (Georgia State University) and Dr. Edward Brown (Harvard University), we are conducting structural biology studies on CaSR, particularly on the extracellular domain (ECD) where metals/ligands bind and many disease-causing mutations occur. Our goal is to establish a structural framework for better understanding the activation mechanism by their binding partners and lipid molecules, which is crucial for the design of agonist and antagonist of CaSR against severe human diseases. (**Figure 4**)

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**Figure 1. Topology of ZIP4.** The extracellular domain of ZIP4 is shown in cartoon mode. (PDB: 4X82)

**Figure 2. Function and regulation of PIPS5K.**

**Figure 3. Crystal structure of LarA (left) and the Ni(II)-containing catalytic center (right).** The Ni(II) pincer complex, composed of the organic compound PTTMN and a bound Ni(II), is a novel cofactor discovered recently. (PDB: SHUQ)

**Figure 4. Crystal structure of the extracellular domain of human Calcium Sensing Receptor.** (PDB: 5FBK and 5FBH)
The chemistry of carbohydrates and their biology is the major emphasis of our research. Carbohydrates play important roles in many biological processes such as inflammation, tumor metastasis, bacterial and viral infections. Detailed understanding of many of these processes is still lacking. Building on our strength in synthetic chemistry, we take a multi-disciplinary approach to study this important class of molecules. Our research encompasses several areas including synthetic organic chemistry, nanoscience and chemical immunology.

In the synthetic chemistry area, we are developing novel methodologies for assembling biologically active oligosaccharides and glycoconjugates. Traditional carbohydrate synthesis is very tedious and time-consuming. In order to expedite the synthetic process, we have developed novel one-pot glycosylation methodologies, where multiple sequential glycosylation reactions are carried out in a single reaction flask to yield desired oligosaccharides without time-consuming intermediate purifications. One of the methods we developed, the pre-activation based iterative one-pot method, has achieved higher synthetic efficiencies in several syntheses compared to the automated solid phase based method. We are applying the methods we developed to total synthesis of a wide range of highly complex oligosaccharides and glycoconjugates. A representative example of the molecules we have synthesized is shown in Fig 1. We are continuing to synthesize biologically important carbohydrates.

In our nanoscience program, we combine the multifaceted properties of carbohydrates with the unique functions of nanoparticles by immobilizing carbohydrates onto the external surface of magnetic nanoparticles. The magnetic glyco-nanoparticles (MGNPs) produced retain the biological recognition of carbohydrates and at the same time enhance the avidity of carbohydrate-receptor interactions by thousands of times. The magnetic nature of the nanoparticles enables us to use magnetic resonance imaging (MRI) as a non-invasive method for disease detection. An example of this is shown in Fig. 2, where the presence of atherosclerotic plaques (the major cause of heart attack and stroke) in rabbits can be easily detected by MRI after injection of the MGNPs. Besides detection and imaging applications, we are exploring the utility of MGNPs for targeted drug delivery. We found that by incorporating drugs onto MGNPs, the cytotoxicity of the drugs towards cancer cells can be significantly enhanced. We are continuing to develop magnetic glyco-nanoparticles for non-invasive detection and treatment of diseases such as cancer, atherosclerosis and Alzheimer’s disease.

In the immunology area, harnessing the awesome power of body’s immune system to fight cancer is an attractive strategy to cancer treatment. It is well known that many tumor cells have unique carbohydrate structures over-expressed on the cell surface. However, the low immunogenecities of these tumor-associated carbohydrate antigens present a formidable challenge for the development of carbohydrate based anti-cancer vaccines. To overcome this obstacle, we are developing novel carrier systems such as cowpea mosaic virus capsid (CPMV) and bacteriophage Qβ to deliver tumor associated carbohydrate antigens to the immune system and to boost the immune responses against carbohydrates as diagrammed in Fig. 3. We discovered that antigens displayed in a highly organized manner can elicit much stronger immune responses. Vaccination with our constructs successfully protected the immunized mice from tumor development in several tumor models. This is an excitingly new direction for the development of anti-cancer vaccines.

![FIG. 3](image3.png)

**Selected Publications**


**Reference:**

Quantum systems in time-dependent fields – We are deriving new results for quantum systems that are perturbed by time-dependent electromagnetic fields, in cases where the adiabatic theorem does not hold. In their text *Quantum Mechanics*, Landau and Lifshitz showed that the excited-state coefficients in the wave function can be separated into adiabatic and non-adiabatic terms. Ordinarily, one would expect to find cross-terms between the adiabatic and non-adiabatic coefficients, when the expectation value of the Hamiltonian is computed. However, Anirban Mandal and I proved that the cross-terms vanish identically. The energy separates completely into adiabatic and non-adiabatic terms. The adiabatic term accounts for the adjustment of the ground state to the perturbation—without transitions—while the non-adiabatic term gives the energy change due to transitions to excited states. Subsequently, we proved that the power absorbed by a molecule from an applied field is equal to the time-derivative of the non-adiabatic term in the energy.

The standard Hamiltonian for a molecule in an electromagnetic field includes an arbitrary gauge potential, which arises when the vector and scalar potentials of the applied field are altered by a gauge transformation, leaving the electric and magnetic fields themselves unchanged. Physically meaningful quantities must be gauge-invariant, so the expectation value of the standard molecular Hamiltonian cannot be interpreted as the energy of a molecule in an applied field—a problem recognized in the mid-1950’s by Kramers. Anirban Mandal and I analyzed the full Hamiltonian for the molecule and the electromagnetic field, and showed that the standard Hamiltonian for the field contains a gauge-dependent term that exactly cancels with the gauge-dependent term in the molecular Hamiltonian. This opens a route to determine the energy of a molecule in a field, in a gauge-invariant way.

Currently, we are investigating the differences between our results for the probability of transitions to excited states for systems in laser fields vs. transition probabilities obtained from Fermi’s “golden rule.” We are looking at donor/acceptor complexes and three-state model systems, where there is rapid decay from the initially excited state.

Collision-induced spectroscopic processes – Spectroscopic processes that are forbidden for single molecules may be observed in dense gases and liquids, due to electronic charge redistribution that occurs during molecular collisions. Our recent work has focused on collision-induced absorption of infrared radiation by samples containing H₂ or H₂/He mixtures in stellar atmospheres, and on collision-induced absorption by oxygen and nitrogen in Earth's atmosphere. We evaluate the total dipole moments as functions of the bond lengths, intermolecular distances, and orientation angles, and then express the results in the spherical-tensor form needed for spectroscopic line shape calculations. Line-shape calculations based on our results have been carried out by our collaborators, Lothar Frommhold and Martin Abel (University of Texas, Austin) and Tijs Karman, Gerrit Groenenboom, and Ad van der Avoird (Radboud University, Nijmegen, Netherlands).

Manipulation of labeled biomolecules with light – We are also working on a theoretical analysis of the dynamics of fluorescently labeled protein molecules in laser fields. The theory of optical manipulation of molecules is well established for small molecules where the induced dipole forces predominate, and for very large molecules where the net forces associated with Mie scattering predominate. Fluorescently labeled proteins fall into an intermediate size range, where neither of the limiting cases applies and new theory is needed. This project involves collaboration with members of Bob Cukier’s research group, who provide expertise in molecular dynamics simulations. Our current work focuses on leucine zipper proteins interacting with fluorescently labeled DNA strands.

Collision-induced binary absorption spectrum of N₂ gas at 78 K, calculated with our ab initio dipole moments. Contributions to the spectrum are separated based on the angular momentum of each N₂ molecule, the vector sum of their angular momenta, and the angular momentum of relative rotation of the molecules [from T. Karman, E. Miliordos, K. L. C. Hunt, G. C. Groenenboom, and A. van der Avoird, *J. Chem. Phys.* 2015, 142, 084306].
Probing mechanisms and theory, from molecular interactions to process design, Jackson group efforts range from fundamental:

- Novel aspects of hydrogen bonding, including hydridic-to-protonic
- Computational modeling to design and interpret reaction mechanisms and structures

...to eminently practical chemistry:
- “Green” catalysts and pathways from renewables to useful “petro-” chemicals
- Alkali metal reductants “tamed” by dispersion in silica or alumina

More information can be found at www2.chemistry.msu.edu/faculty/jackson/ two active areas are outlined below, where the common thread is mechanistic. By understanding molecular interactions and reactions we seek rules to design materials and processes with targeted characteristics. From the post-doc to the high-school level, scientists trained in the group have gone on to excellent positions in academics, industry, or governmental research.

Hydridic-to-protonic hydrogen bonding: Our discovery and studies of this interaction, AKA dihydrogen bonding, began with a high school student studying NaBH4•2H2O (Fig. 1). Besides the novelty of hydrogen’s serving as the nucleophile in a hydrogen bond, this work has uncovered reactions governed by the material’s phase and local stoichiometry as well as a bona fide crystal-to-crystal solid state transformation.

Dihydrogen bonding projects have focused on crystal engineering; design of bond-selective infrared activated reactions; and searches for possible biological and synthesis significance.

**Green Chemistry:** We seek to replace fossil petroleum with renewables as the basis for chemicals and fuels via catalytic paths starting from biomass-derived feedstocks. Target products are commodity and specialty chemicals and fuels. Reaction optimization is guided by mechanistic explorations of rates, substituent effects, isotopic labeling, and variations in media and conditions. Meanwhile, new nanocatalysts and reagents are also under development.

**Synergy:** Our catalytic and electrocatalytic reductions of bio-derived feedstocks in water (practical) now intersect with the dihydrogen bond (fundamental) work; interfacial dihydrogen bonding of metal-bound hydride sites under water seems to strongly affect their reactivity. In turn, the quest for “biomass refinery operations” via electrocatalytic reduction of bio-based feedstocks unexpectedly found ary1 ether cleavage over a simple Nickel electrode (Figure 2). Such serendipities and synergies between practical and fundamental; synthesis, structure and mechanism; and experiment and theory pull us back to the lab each day.
Research in our laboratory aims to understand the molecular underpinnings of biological systems and pathways at multiple levels. We take a multidisciplinary approach combining structural biology (x-ray crystallography, electron microscopy), biochemistry, biophysics (analytical ultracentrifugation, isothermal titration calorimetry, surface plasmon resonance, etc.), chemical biology, cell biology, and computational methods to investigate the mechanisms that underlie fundamental biological processes at atomic, molecular, cellular, and systems levels. Our current research efforts are mainly directed towards the following areas:

**Molecular basis of cell-cell communication in development.** Formation of multicellular structures with specific biological functions, such as tissues that manifest planar polarity, entails intricate communication networks whereby cells ‘talk’ to each other through specific molecular interactions to coordinate their activities and collectively form elaborate multicellular structures. Planar polarity is a property required for diverse developmental processes that polarizes orientation and behavior of cells across a tissue plane. Defects in planar polarity are associated with a variety of diseases, including cancer, polycystic kidney disease, and neural tube defects. The core components of planar polarity signaling include Celsr adhesion GPCRs, which establish polarized cell-cell junctions across proximal-distal cell boundaries by recruiting distinct molecular complexes to the membrane. Ongoing work in our laboratory aims at gaining structural insights into activation mechanisms of the Celsr adhesion GPCRs with respect to their ectodomain interactions, propagation of conformational changes in the receptor domains across the membrane, and interaction of the receptors with their downstream effectors.

**Structural basis for molecular interactions regulating autophagy.** Autophagy is an evolutionarily conserved process through which cells degrade and recycle unnecessary components to produce new molecular building blocks. As such, it is essential for cellular and tissue homeostasis as well as cell adaptation or survival under stress conditions. Dysregulation of autophagy is implicated in many pathological situations such as cancer, diabetes, and neurodegenerative diseases. The long-term goal of this line of research is to gain an in-depth understanding of the specific molecular interactions that drive distinct steps in the process of autophagy. Our current efforts focus on the autophagy factors essential for autophagosome biogenesis and autophagosome-lysosome fusion processes in fission yeast, which will allow us to tease apart species-specific as well as evolutionarily conserved molecular interaction principles that govern autophagy.

**Structural basis for molecular interactions regulating necrotic cell death.** Cell death is a crucial process during development, homeostasis, and (patho)physiology of multicellular organisms. An imbalance in cell death is linked to many diseases: too much or too sensitive cell death is associated with inflammatory and degenerative diseases, whereas too little or too insensitive cell death can promote cancer and autoimmune diseases. Necrotic cell death is morphologically characterized by cytoplasmic granulation and organelle swelling followed by the loss of cell membrane integrity and release of the cellular contents into the surrounding extracellular space. During regulated necrosis, stimulation of death receptors induces formation of a supramolecular signaling complex termed necosome, which translocates from cytosol to the plasma and intracellular membranes and forms membrane disrupting pores, thereby executing cell death. Ongoing work in our laboratory aims at elucidating the structural basis for the molecular interactions that underlie membrane disruption in necrosis. By combining biochemical and structural approaches, we seek to characterize the protein-protein and protein-lipid interactions required for necrotic membrane disruption; obtain structural models for the membrane disruptive molecular machineries; and validate our models using quantitative liposome- and cell-based functional assays.

**Selected Publications**


Global profiling of metabolites, the small molecules produced by living things, provides one of the most powerful strategies for learning about gene and protein functions. This approach, known as metabolomics, is generating information that will serve as the foundation for engineering of plants and microbes to produce renewable feedstocks for high-value bioactive chemicals and biofuels. Metabolite profiles also are important indicators of health and disease, and many metabolites serve important signaling functions that regulate physiological states ranging from inflammation to resolution of tissue damage.

Research in the Jones laboratory is driven by a desire to understand how genetics and environment combine to influence biological chemistry by: (1) developing analytical and biochemical tools for deep profiling and spatial localization of specialized metabolites, (2) developing experimental and data mining approaches to accelerate discoveries of natural products in plants and the genes involved in their accumulation, (3) deployment of mass spectrometry measurements of human exposures to nutrients, toxins, and endogenous metabolites that drive epigenetic regulation of factors that influence disease (and may be inheritable traits), and (4) measurements of small molecule biomarkers whose levels reflect the effectiveness of disease treatments.

Many plants accumulate large quantities of bioactive phytochemicals and are prolific biochemical factories. Our laboratory has pioneered rapid metabolite profiling protocols based on ultrahigh performance liquid chromatography (UHPLC) coupled to high-resolution time-of-flight mass spectrometry (MS). By employing rapid gradients and by multiplexing collision potentials across a lens between the mass spectrometer ion source and mass analyzer, ~500 metabolites are measured in a 5-minute analysis. This allows for large-scale screening of genetic variants to guide gene function discoveries. Ongoing research involves labeling metabolites using $^{13}$C to investigate metabolic dynamics coupled with elucidation of metabolite structures using MS and NMR.

We also investigate whether inflammatory, anti-inflammatory, and analgesic metabolite biomarkers in the blood and urine of human patients indicate mechanisms underlying the effectiveness of various treatments of traumatic brain injury. In addition, since more diseases are associated with environment and lifestyle than specific genetic factors, our lab is adapting our analytical methods to investigate the exposome, which is the entire range of molecules (e.g., from foods, environment, gut microbes) to which individuals are exposed.

Selected Publications

- Comparative structural profiling of trichome specialized metabolites in tomato (Solanum lycopersicum) and S. habrochaites: acylsugar profiles revealed by UHPLC/MS and NMR. B. Ghosh, T. C. Westbrook, and A. D. Jones, Metabolomics 2014, 10, 496-507.
Modeling advanced materials with applications in solar energy conversion, chemical sensing, photocatalysis, and other fields is the focus of research in the Levine group. We apply the methods of computational chemistry to develop an understanding of the microscopic motions of nuclei and electrons in materials, and demonstrate how these motions determine the materials’ macroscopic properties. Students in my group will carefully apply a combination of quantum chemical and molecular dynamics techniques, developing and extending theoretical methods as dictated by the problem.

One goal of our research is to understand how the properties of thin film and nanoscale semiconductor materials, which compose next generation solar cells and chemical sensors, are affected by the characters of their surfaces. These materials have desirable and tunable properties, and offer an inexpensive alternative to more traditional materials for solar energy conversion. Unfortunately, the non-radiative decay of electronic excitations at surface sites results in the conversion of electronic energy to useless heat, thus decreasing the efficiency of energy conversion. By constructing computer models of small clusters designed to mimic semiconductor surfaces, we inform the design of future materials by identifying the microscopic dynamics of such non-radiative decay.

In order to produce knowledge which most significantly impacts the development of next generation optoelectronic devices, we wish to extend the length- and timescales accessible via simulation. To this end, we take advantage of the similarity between the physical simulations and computer games by employing processors designed for gaming to accelerate our scientific computations. Through the development of algorithms and software, we work to take accurate first principles methods typically limited to the simulation of small molecules and extend them to the nanoscale.

The simulation of photodynamics requires the determination of ground and excited electronic wavefunctions at thousands of nuclear geometries. It is therefore necessary to use methods which are capable of quickly and stably calculating the electronic wavefunction of states of various characters (e.g., localized trap states vs. delocalized exciton states vs. charge transfer states). Multireference (MR) electronic structure methods provide such flexibility. With the above goals in mind, we are developing MR methods with lower computational cost, greater numerical stability, and greater accuracy than more widely used approaches for application in the study of semiconductor photochemistry.

In addition to modeling physical behaviors which cannot be directly observed, recent advances in computation and high performance computers allow researchers to approximate the results of experiments, thus saving time and effort. For example, much effort is spent experimentally screening molecules for various optoelectronic applications. Taking advantage of developments which allow the fast prediction of the photophysical properties of molecules in conjunction with genetic algorithms, we computationally evolve molecules with a desirable set of properties. By building trial molecules from a “primordial soup” of molecular fragments, testing their “fitness” for a given application using electronic structure methods, and automatically “mutating” and “crossing” them to produce fitter and fitter generations, we can search a massive molecular space for promising candidates before a single wet experiment is run. We hope this strategy will accelerate the development of materials for energy conversion, light emission, and other applications.

Selected Publications


Benjamin G. Levine
Theoretical Chemistry of Materials

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The ease of transitions between different states of the atomic nucleus carry a wealth of information and can be used in a variety of applications from describing the basic configuration of the nucleus’ constituent protons and neutrons to constraining the synthesis of heavy elements in the energetic astrophysical events. Nuclear properties are expected to vary significantly as a function of proton or neutron number. Radioactive nuclei are produced and isolated at the National Superconducting Cyclotron Laboratory at Michigan State University. The nuclei of interest are deposited into a solid-state detector and their subsequent decay radiations are monitored. Decay spectroscopy provides a sensitive and selective means to populate and study low-energy excited states of daughter nuclei and a variety of different decay modes can be exploited depending on the nucleus of interest.

One branch of the groups recent experimental work has focused on $^{68}$Ni. It has been predicted that multiple spin-zero states exist with significantly different intrinsic deformations in $^{68}$Ni. The energies, and decay transition rates of the excited states, can provide information on the coexisting structures. The first excited state spin-zero state of $^{68}$Ni decays through the emission of a conversion electron (photon emission is forbidden) which is delayed with respect to the populating beta-decay electron resulting in a characteristic signal shape from the solid-state detector. The energy of the conversion electron provides the energy of the excited state in $^{68}$Ni. Combined with the decay rate of the state, the strength of the transition can be determined and compared with expectations. The results confirm the theoretical picture of both single-particle and collective configurations coexisting at similar excitation energies.

The other focus of the group lies in inferring the photon strength functions (related to the photon transition rates) of highly-excited states populated in the beta-decay of a short-lived nucleus. The photon strength function combined with a knowledge of the number of nuclear states as a function of energy enables the calculation of various reactions that are expected to occur through statistical processes. One such reaction is the capture of a neutron onto the atomic nucleus increasing its mass by one unit. Neutron capture rates are a necessary ingredient to predict elemental abundances produced in energy astrophysical events, such as supernovae and neutron star mergers, which are expected to lead to the synthesis of a significant amount of the elements heavier than iron. Abundance predictions require neutron capture rate uncertainties of roughly a factor of two while current constraints can reach over two orders of magnitude. The resulting impact on abundance predictions is shown in the figure. Recent work from my group has investigated the neutron capture of $^{68,69}$Ni and the resulting impact on elemental synthesis.

**Selected Publications**

Our group is interested in a) the total synthesis of biologically important natural products, b) the invention of new reactions and strategies in organic synthesis, and c) green chemistry.

**Green Chemistry:** Central to our research is the development of efficient and environmentally benign reactions and strategies. The Pharmaceutical Roundtable of the American Chemical Society’s Green Chemistry Institute deemed cross-couplings that avoid halorneristics as their top aspirational reaction. In collaboration with Professor Mitch Smith, we are inventing such reactions. Specifically, we are using catalytic C–H activation/borylation, often combined with subsequent chemical events, to generate pharmaceutically relevant building blocks for organic synthesis and the late stage functionalization of drugs and drug candidates.

Another of our green chemistry ventures aims to minimize the need for tin in various processes. For example, we have developed an allylation/hydrostannation sequence where the tin waste from the allylation is recycled in situ so as to allow its use in the hydrostannation. This chemistry employs polymethylhydroxiloxane (PMHS), which is an oligomeric non-toxic waste product of the silicon industry, as the stoichiometric reductant.

Another of our green chemistry ventures is to double-decker silsesquioxanes (DDSQ’s) for polymer applications. As part of a collaboration with Dow Chemical, we have also used PMHS in conjunction with our borylation chemistry to regioselectively generate building blocks of interest to the agrochemical industry. Here the combination of Pd(OAc)2 and PMHS generates siloxane encapsulated Pd(0) nanoclusters.

**Total Synthesis:** The unifying thesis behind all of our methodological and mechanistic studies is that the chemistry to emerge from such studies should be applicable to real synthetic problems. We view target synthesis as the best proof of this concept. For example, as part of our green chemistry program, we look to make TMC-95A and autolymycin by the strategic application of our own synthetic methods.
The low-energy properties of atomic nuclei are predicted to show dramatic changes when the ratio of neutrons-to-protons in the nucleus becomes extremely unbalanced. My research group is working to deduce the electromagnetic properties of nuclei which have extreme neutron-to-proton ratios. The desired nuclei, which exist for only fractions of a second, are produced in very small quantities using intermediate-energy reactions at the National Superconducting Cyclotron Laboratory (NSCL) at Michigan State University.

Two electromagnetic properties of interest are the nuclear magnetic dipole moment and nuclear electric quadrupole moment. The dipole moment is sensitive to the orbital component of the angular momentum of any unpaired protons and/or neutrons in the nucleus. The dipole moment provides information on the nuclear quantum structure and the occupied single-particle states. The quadrupole moment is a measure of the deviation of the average charge distribution of the nucleus away from spherical symmetry. The shape of the collection of protons and neutrons in the nucleus, e.g. the nuclear collectivity or “deformation”, can be inferred from the quadrupole moment.

One way to deduce the electromagnetic moments of nuclei is via Collinear Laser Spectroscopy (CLS). The CLS method involves the co-propagation of a low-energy beam (~ 60 keV) of atoms/ions with laser light. Fixed-frequency laser light is Doppler tuned into resonance by varying the energy of the beam, with the subsequent fluorescence detected by a photomultiplier tube. The resulting hyperfine spectrum, a product of the interaction of atomic electrons with the nucleus, is analyzed to extract the nuclear magnetic dipole and electric quadrupole moments.

We have installed and commissioned a CLS beam line in the low-energy experimental area at NSCL as part of the Beam Cooling and Laser Spectroscopy (BECOLA) facility. The BECOLA facility also includes a cooler and buncher, which accepts the rare isotope beams from the NSCL beam thermalization area and converts them into a low-emittance, pulsed beam to improve the sensitivity of the CLS measurement. Stable beams of Ca, K, Sc, Mn, Fe, and Ni have been produced from off-line ion sources, and the hyperfine spectra have been collected and analyzed. We have also measured the hyperfine spectra for the short-lived radioisotopes $^{36,37}$K (depicted below) and $^{52,53}$Fe, produced at rates of order $10^3$ per second, with the goal of understanding the trends in charge radii in the vicinity of neutron shell closures. We plan to extend the reach of such studies with the implementation of a new pulsed laser system, whereby optical pumping will be used to preferentially populate and electronic state favorable for collinear laser spectroscopy.

Charge radii for potassium isotopes. The values for the radioactive isotopes $^{36}$K ($N=17$) and $^{37}$K ($N=18$) were measured at the BECOLA facility at NSCL.
Electron Paramagnetic Resonance (EPR) spectroscopy provides an ideal tool for the determination of the structures of paramagnetic centers in chemical systems. The origin of this structural information is the spin-spin coupling between the magnetic moments of the paramagnetic center and nuclei that lie less than 6 Å away. Unfortunately, these spin-spin couplings are often weak and as such, they are buried by the inhomogeneous broadening of the EPR absorption lineshape. In the McCracken lab, we are applying the advanced EPR methods of Electron Spin Echo Envelope Modulation (ESEEM) and Electron-Nuclear Double Resonance (ENDOR) to determine the structures about paramagnetic centers in metalloenzymes. Our studies are aimed at using the information we gain from these experiments to understand the chemistry that occurs at metal centers and answer questions concerning structure-function relationships that cannot be addressed using other structural tools like NMR or X-ray crystallography in isolation.

The figure shown below details two different applications of ESEEM spectroscopy to characterize the ligation structure of an Fe(II) ion located at the heart of the catalytic site of the enzyme Tyrosine Hydroxylase. This enzyme is present in the central nervous system of mammals and catalyzes the rate-limiting step in the biosynthesis of the catecholamine neurotransmitters, dopamine, epinephrine and norepinephrine. Our gateway into the structure is the EPR spectrum of an FeNO$_7$ derivative of the enzyme and is shown in figure (a). This spectrum is about 200 mT wide and provides no features that can be attributed to ligands bound to Fe(II), or substrates and cofactors that may bind to the enzyme in Fe(II)’s second coordination sphere. Figure (b) shows $^2$H-ESEEM spectra, obtained at seven different magnetic field positions across the EPR spectrum, that arise from hyperfine coupling between a deuterium atom of 3,5 $^2$H - tyrosine bound to the enzyme and the paramagnetic Fe-NO center. The amplitudes and lineshapes of these spectra can be fit to a spin Hamiltonian model to provide the location of the coupled deuterium with respect to the axis of the Fe-NO bond, and the direction of the C-$^2$H bond associated with the labeled substrate. Figure (d) summarizes these results showing that substrate tyrosine binds so that a coupled deuteron (red ball in figure d) is positioned 4.1 Å from the Fe(II) and that the vector connecting the metal ion with this coupled deuteron makes an angle of 25° with the Fe-NO bond axis. These data represent the first structural information gained on the binding of the amino acid substrate at the catalytic site of this family of enzymes. By repeating these measurements on substrates deuterated at other positions, our crude magnetic structure can be built into an atomic level structure. The second type of experiment is a 2-dimensional ESEEM measurement that has proved useful for viewing the stronger hyperfine couplings that arise from the Fe(II) ligands. The spectrum shown in figure (c) was collected at 260 mT (aqua arrow in figure(a)) and shows off-diagonal cross-peaks, circled in red, that are diagnostic for bound water and/or hydroxide ligands.
Ultrafast Spectroscopy of Transition Metal Complexes. Our research efforts in this area concern the short time scale photoinduced dynamics of transition metal complexes. By “short time scale”, we refer to processes occurring between the time a photon is absorbed by a molecule and the point at which that molecule is fully relaxed in its lowest-lying excited state. Some of the questions we are addressing with this research include the following: (1) what is the general time scale for excited-state evolution in transition metal complexes? (2) what is the mechanism of this process? (3) how do the geometric and electronic structures of the compounds, the surrounding medium, and other factors couple to and/or influence this process? and (4) to what extent can we use this information to control excited-state dynamics? Certain of these questions are very fundamental in nature, whereas others are geared toward work on solar energy conversion. What distinguishes the group, we believe, is our ability to carry out both the synthesis and spectroscopic characterization of a wide range of inorganic molecules. This enables us to systematically examine chemical perturbations to excited-state electronic and geometric structure, and in so doing develop a comprehensive picture of how transition metal chromophores absorb and dissipate energy.

Spin and Spin Polarization Effects on Excited-State Dynamics. Electron spin is a fundamental property of Nature. Although many of the more common physical observables linked to spin are well documented (e.g., magnetism), the degree to which spin and spin polarization influences the chemistry of molecular systems is not as clear. We are pursuing the design and development of chemical systems that will allow us to determine whether there exists a cause-and-effect relationship between the physical and photophysical properties of molecules and their innate spin properties, and if so, to what extent can we exploit this connection in order to manipulate the chemistry of molecular systems. Much of this work centers on the study of so-called donor-acceptor assemblies wherein energy and electron transfer processes are being examined in systems containing spin-coupled paramagnetic fragments. Through careful synthetic manipulation of these compounds, correlations between the observed excited-state reactivity and the involvement of spin-polarized electronic states of the donor and/or acceptor can be realized. Coupled to this experimental work are theoretical studies that exploit recent advances in density functional theory. We believe that these combined efforts will forge an important link between magnetism and electron/energy transfer processes, thereby allowing us to establish a new paradigm in the emerging field of molecular spintronics.
Research at the interface between the computational sciences and biology is our group focus. We work on a number of problems and collaborate with experimentalists at every opportunity. Research areas of most interest include computer-aided drug design (CADD), the role potential function error plays in drug design and protein folding, metalloenzymes and metal ion homeostasis, development and application of linear-scaling quantum mechanical methods to biological problems and NMR and X-ray structure refinement using quantum mechanical methods. For further details go to the group web page at http://merzgroup.org.

In the structure-based drug design area we are interested in developing novel tools to predict the binding affinity of ligands for a given receptor. Along these lines we developed a novel knowledge-based protein-ligand scoring function that employs a new definition for the reference state (see the Figure), allowing us to relate a statistical potential to a Lennard-Jones (LJ) potential. In this way, the LJ potential parameters were generated from protein-ligand complex structural data contained in the PDB. Forty-nine types of atomic pairwise interactions were derived using this method, which we call the knowledge-based and empirical combined scoring algorithm (KECSA). Validation results illustrate that KECSA shows improved performance in all test sets when compared with other scoring methods especially in its ability to minimize the RMSE.

Metalloenzymes carry out a myriad of biological functions and we have a long-term interest in modeling the structure and function of proteins involving metal ion catalysis or homeostasis. A recent publication illustrates an example of the study of transition metal homeostasis. A metal-mediated interprotomer hydrogen bond has been implicated in the allostatic mechanism of DNA operator binding in several metal-sensing proteins. Using computational methods, we investigated the energetics of such zinc-mediated interactions in members of the ArsR/SmtB family of proteins (CzrA, SmtB, CadC and NmtR) and the MarR family zinc-uptake repressor AdcR, each of which feature similar interactions, but in sites that differ widely in their allostatic responsiveness. We provided novel structural insight into previously uncharacterized allosteric forms of these proteins using computational methodologies. We find this metal-mediated interaction to be significantly stronger (~8 kcal/mol) at functional allosteric metal binding sites compared to a non-responsive site (CadC) and the apo-proteins. Simulations of the apo-proteins further revealed that the high interaction energy works to overcome the considerable disorder at these hydrogen-bonding sites and functions as a “switch” to lock in a weak DNA-binding conformation once metal is bound. These findings suggested a globally conserved functional role of metal-mediated second-coordination shell hydrogen bonds at allosterically responsive sites in zinc-sensing transcription regulators.
Research in nuclear chemistry that is centered on the production and use of the most exotic, short-lived nuclei provides the ability to produce beams of very exotic radioactive ions. These short-lived nuclei are interesting in their own right, some of which have not been observed before. My graduate students work on unraveling the mechanisms of nuclear reactions, on studying the decay properties of the most exotic nuclei, or on developing new techniques to separate, capture and deliver exotic nuclei. The National Superconducting Cyclotron Laboratory (NSCL) is a unique facility that brings together a strong group of nuclear scientists and provides an exceptional setting for studying the properties of nuclei right on the MSU campus. The very high energy beams react with a target nuclei to produce new nuclear fragments with a distribution of sizes, some of which are very unstable and quite unusual. The probability distributions of the products and the momenta, or velocities, of the fragments are distributed around that of the beam and we have shown that they can be predicted by models of the nuclear reaction. The fast-moving fragments are passed through an isotope separator to produce beams of individual radioactive ions. We help to design and develop these fragment separators, which have become the central instruments for research at the NSCL and the Facility for Rare Ion Beams (FRIB) under construction at MSU. The NSCL currently relies on its second-generation fragment separator completed in 2001 while a revolutionary new fragment separator is being constructed for the FRIB facility that will replace the NSCL.

Along with using the new fragment separator for production and decay studies, our group has developed a series of auxiliary devices to slow down the exotic reaction products to thermal energies. The initial devices used a helium filled chamber tailored to stop and collect the exotic isotopes produced by the A1900 fragment separator. The gas is removed using a differential pumping system in a process related to atmospheric-sampling mass spectrometry. The so-called gas-catcher system was used in many successful and extremely precise mass measurements at the NSCL carried out by the group headed by Prof. Bollen (MSU Physics). More recently the thermalized ions were used in collinear laser spectroscopy experiments, precision decay studies, and nuclear reaction studies. We are currently completing construction of a next-generation device based on the concept of a reverse cyclotron. The reaction products spiral inward towards the center of a helium-filled chamber in a strong magnetic field. The so-called cyclotron-stopper uses a four-meter diameter superconducting magnet that weighs approximately 200 tons (see below).

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Nuclear Chemistry

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Ph.D., 1978, Univ. of California, Berkeley;
Postdoctoral Fellow, 1978-81, Lawrence Berkeley Laboratory;
Visiting Scientist, 1987-88, GSI, Darmstadt, BRD;
Associate Director, 1995-99 & 2009-11, National Superconducting Cyclotron Laboratory;
Chairman, 2004, ACS Division of Nuclear Chemistry & Technology;
ACS Glenn T. Seaborg Award for Nuclear Chemistry, 2011;
Associate Director for Operations, 2015- , National Superconducting Cyclotron Laboratory.

Selected Publications

Photograph of the gas-filled reverse-cyclotron during testing in 2014. The device relies on an inner 2 meter diameter beam chamber contained inside a 200 ton superconducting magnet. The particles will enter parallel to the floor from the right and be bent onto spiral paths by the magnetic field. They will slow down by collisions with helium gas and the thermalized ions will be extracted along the central axis.
Developing sustainable and environmentally friendly approaches to products is one of the major challenges facing chemists. Some important developing methodologies for producing target compounds in fewer steps with less waste are catalyzed multicomponent coupling reactions, which allow access to structurally complex compounds in a single step.

In one project, our group is developing titanium-catalyzed multicomponent coupling procedures to make nitrogen-based heterocycles either in a single pot or in a single step. Titanium catalysis is advantageous in that the metal is both abundant and nontoxic.

In the exploding diagram at right are some of the procedures developed for heterocyclic synthesis. These new protocols are applied to natural product synthesis and investigated for their biological activity. For example, with the Tepe group, we have discovered a new class of proteasome inhibitors based on the quinoline core structure with potential applications in inflammatory disease and cancers like multiple myeloma.

To evaluate ligands for early transition metal catalysis, like in the project above, we have developed a chromium(VI), d⁰-system that is very synthetically versatile, NCr(NPr_i₂)₂X, where X is the ligand under scrutiny. Using this system, we parameterize ligands based on their sterics and electronics. The experimental results for a large selection of anionic ligands have been published and are shown below. Ligands are evaluated sterically using either %V₈₄₄₄ or Solid G. An illustration from the %V₈₄₄₄ analysis for the X = Cl compound is shown below, where the ligand’s effect on the primary coordination sphere is estimated.

These new parameters, dubbed Ligand Donor Parameters (LDP), have been correlated with spectroscopic and reactivity data from a variety of systems and will hopefully be a useful tool for chemists when optimizing and designing high valent catalysts.

In these projects, and others, we are attempting to widen and optimize the applications of transition metals, and we are investigating new possibilities for applications in human health and other areas.

**Selected Publications**


My research program focuses on (i) ab initio quantum theory of molecular electronic structure and other many-body systems, (ii) molecular properties, spectroscopy, and photochemistry, (iii) reaction mechanisms and dynamics, and (iv) theory of intermolecular forces. We design and apply quantum-mechanical methods that enable precise determination of potential energy surfaces and property functions for both existing and hypothetical molecular species in their ground and excited states. We are also interested in accurate quantum calculations for strongly correlated systems, weakly interacting molecular clusters, and atomic nuclei.

Quantum theory of molecular electronic structure. The key to understanding molecular electronic structure and dynamical behavior of molecules is an accurate assessment of the many-electron correlation effects. Our group focuses on the development and applications of new quantum-mechanical methods that include correlation, particularly on the coupled-cluster theory and its renormalized, active-space, extended, multi-reference, and response variants that allow us to study bond breaking, electronically excited states, electron-transfer processes, molecular properties in vibrationally and electronically excited states, and transition probability coefficients for various types of spectroscopy. We also develop approximated coupled-pair approaches for strongly correlated systems and local correlation coupled-cluster methods characterized by the linear scaling of the CPU time with the system size and natural parallelism, and their multi-level extensions that can be applied to high accuracy ab initio calculations for systems with hundreds of atoms. Our primary interest is in high-accuracy methods that allow us to be predictive. We write computer codes for the standard and new coupled-cluster methods which are distributed world-wide through a popular electronic structure package GAMESS. Some of our methods are also available in NWChem and, in the original or modified form, Q-Chem and MRCC packages.

Many-body methods of quantum mechanics and nuclear physics. Our new ab initio methods for many-electron systems can be applied to other many-fermion systems, including atomic nuclei. We performed several highly successful ab initio coupled-cluster calculations for 4He, 16O, and valence systems around 16O using modern nucleon-nucleon interactions. We also carried out unprecedented coupled-cluster calculations for 56Ni and its isotopes. We are looking for the alternative approaches to accurate calculations for many-fermion systems with pair-wise interactions, including the use of two-body cluster expansions to represent the virtually exact many-fermion states.

Molecular properties, spectroscopy, and photochemistry. We use linear-response coupled-cluster methods, along with other ab initio approaches, to calculate molecular multipole moments and (hyper)polarizabilities and the effect of nuclear motion on these properties. We use first-principles theories to obtain vibro-rotational and electronic spectra, including van der Waals precursors of photo-induced charge-transfer reactions. We have demonstrated that the lowest excited state of methylcobalamin should be interpreted as metal-to-ligand charge-transfer excitation and that azulene possesses the doubly excited state below the ionization threshold, which can drive multi-phonon ionization experiments related to Rydberg fingerprint spectroscopy. We have provided definitive information about structural and spectroscopic properties of several organic biradicals and small metal nanoparticles, including, for example, geometries of low-energy isomers of Au5 and the photoelectron spectra of Ag2+ and Au4+.

Reaction mechanisms and dynamics. We performed successful computational studies for several important organic chemistry reactions, including the Cope rearrangement of 1,5-hexadiene, cycloaddition of cyclopentene to ethylene, thermal stereomutations of cyclopropane, and isomerization of bicyclo[1.1.0]butane to buta-1,3-diene. We carried out unprecedented coupled-cluster calculations for CuO2 and Cu2O2 systems, relevant to oxygen activation by metalloenzymes, for photoinitiated charge-transfer reactions. We have demonstrated that the lowest excited state of methylcobalamin should be interpreted as metal-to-ligand charge-transfer excitation and that azulene possesses the doubly excited state below the ionization threshold, which can drive multi-phonon ionization experiments related to Rydberg fingerprint spectroscopy. We have provided definitive information about structural and spectroscopic properties of several organic biradicals and small metal nanoparticles, including, for example, geometries of low-energy isomers of Au5 and the photoelectron spectra of Ag2+ and Au4+.

Intermolecular interactions. Intermolecular potentials are a necessary ingredient for the determination of the structure, stability, and dynamics of weakly bound clusters and condensed phases. We are interested in pair-wise non-additive interactions, which are important when three or more atoms or molecules interact, and study interactions in dimers. •
Knowledge of molecular-scale interactions is central to understanding reactivity, energy, and dynamics in chemical systems for both novices and experts. Exploration of molecular-scale interactions is a theme that is common to Dr. Posey’s research in chemistry education and experimental physical chemistry.

Building Chemistry and Mathematics Understanding at the Introductory Level

In 2012, the President’s Council of Advisors on Science and Technology (PCAST) reported that one million additional college graduates with STEM degrees would be needed over the next 10 years to meet the anticipated demand for technically skilled workers. Unfortunately, many students interested in pursuing STEM careers enter college without the background and skills required to succeed in general chemistry, often the first required science course. In fact, fewer than 40% of the students who enter college as STEM majors graduate with a STEM degree.

Developmental chemistry courses to support underprepared students have typically focused on drilling in algorithmic problem-solving rather than on helping students to construct an understanding of core ideas in chemistry and make meaning of the supporting mathematics. We are studying a new approach built around two core ideas in chemistry: 1) bonding and electrostatic interactions and 2) structure and properties of matter. Since learning is a developmental process, we aim to help students build increasingly complex and scientifically correct understanding of these core ideas, which is both transferable and robust, by carefully scaffolding their learning on existing knowledge. We blend scientific practices (using models, constructing scientific explanations, and applying mathematical thinking) with content in instruction to further support students in building and using their knowledge. We are studying the impact of this novel approach to developmental chemistry on student motivation, self-efficacy, science identity, and success in general chemistry.

Early work has shown that even when scientific practices largely replace traditional chemistry calculations, student success in our developmental chemistry course strongly correlates with mathematics background. Students in our course often struggle with the same mathematics that students in non-credit-bearing-remedial (NCBR) algebra courses find most challenging. These topics include: (1) proportional reasoning; (2) linear rates of change and interpreting the rate of change from a graph; (3) modeling of covarying relationships with functions; and (4) translating between multiple representations. In collaboration with mathematics education researchers, we are developing and studying the impact of interventions that target mathematics understanding for the developmental chemistry course and interventions that contextualize mathematics using chemistry and other science applications for an enrichment workshop associated with a NCBR algebra course.

Slow Protein Dynamics

Proteins exhibit richly textured energy landscapes near the native fold with barriers that can be surmounted by structural fluctuations at physiological temperatures. Numerous low-energy barriers near the native fold result in an ensemble of conformational states with equilibrium fluctuations poised to play a significant role in both biological function and creation of the misfolded states implicated in diseases including Alzheimer’s, Parkinson’s, Creutzfeldt-Jakob, and bovine spongiform encephalopathy.

Many of the dynamic processes in proteins that are relevant to biological function and misfolding involve collective, large-amplitude motions occurring on timescales of μs and longer. Long-lived triplet states responsible for phosphorescence emission permit us to extend the time window for electronic emission spectroscopy to this physiologically relevant time regime. We have shown that time-resolved phosphorescence spectroscopy and the phosphorescence dynamic Stokes shift can be used to characterize timescales for large-amplitude motions near the native fold in proteins. This approach can be used to measure barrier heights near the native fold and to study the influence of the hydration layer on protein dynamics.

Selected Publications


Time-resolved phosphorescence spectra from ZnII-substituted cytochrome c exhibit a dynamic Stokes shift response arising from protein dynamics on the μs timescale.

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Molecular oxygen, O₂, is a powerful oxidant, which is kinetically sluggish under ambient conditions. The ability of living cells to overcome this barrier using transition metal enzymes lead to the explosion of aerobic life. We are interested in understanding mechanisms of O₂ activation in biology and their applications from fundamental and industrial chemistry to climate control and biomedical solutions. Working with metalloenzymes, their synthetic analogs, and subcellular organelles, we use a range of spectroscopic, electrochemical, and engineering approaches to resolve structures and mechanisms of highly reactive bio-inorganic complexes and associated electron transfer steps.

Enzymes use transition metals to overcome spin restrictions of triplet O₂, which oxidizes the metal/protein complex in a concerted, multi-e⁻ step. The resulting highly oxidized species, in turn, initiate chemical reactions with specific substrates. Protein moiety tunes reactivity of the metal through coordination environment and accessibility.

Methane Monoxygenase, an enzyme in methanotropic bacteria, uses a pair of FeIV ions to accomplish an unrivaled conversion of methane to methanol. This reaction is of major interest for liquid fuels production from natural gas and as an initial step in the industrial synthesis. Using time-resolved laser spectroscopy, we observed this reaction in real time and resolved the mechanism that puzzled the field for the last two decades. Many more analogous enzymes with unresolved mechanisms are awaiting their turn.

Enzymatic O₂ activation always starts with reduction, followed by metal oxidation yielding formal Fe≡O state (top path), which activates the substrate SH to transient S• radical. By reversing the reaction under large positive electrode potential we can generate FeV=O directly from water, circumventing the need for O₂ (bottom path) and opening intriguing possibilities for applied catalysis and new analytical methods.

Mitochondria are power plants of the cell: semi-autonomous organelles, which capture the energy of e⁻ current from food to O₂ to make ATP. A choreographed chain of enzymatic redox reactions takes place in the impermeable inner mitochondrial membrane, which isolates mitochondria from the cytosol. It makes detection of functional changes in whole mitochondria in such metabolic disorders as diabetes, Alzheimer’s disease, etc., difficult. We are developing a fundamentally new method to study intact mitochondria. It is based on dynamic redox equilibrium of natural metabolites, membrane transport, and electrochemistry on specifically modified electrodes. We establish chemically-mediated e⁻ current from fiber electrodes into mitochondrial enzymes and further to oxygen, mimicking natural metabolic pathways as an artificial “respiration in a tube”.

SELECTED PUBLICATIONS


Radionuclides are important tools for tracing biological, chemical, and physical processes. The National Superconducting Cyclotron Laboratory (NSCL) and the upcoming Facility for Rare Isotope Beams (FRIB) have the potential to supply unique radioisotopes that are otherwise difficult to produce. The challenge of obtaining these rare isotopes from NSCL and FRIB is in the need for rigorous chemical or physical purification of sub-nanogram quantities of individual elements from a complex mixture of spallation and fragmentation products. The purpose of my research is to parse and purify the stock of co-produced radionuclides to obtain both high radionuclidic purity and high specific activity for application in basic science, medical, chemical and biological research. Of particular interest are transition and rare earth radiometals for use in the development of new diagnostics and therapeutics against invasive disease.

Radiometals in Medicine – Research into the molecular identity of cancerous and other malignant cells has identified biological vectors that can seek out disease sites in vivo. In order to trace the biodistributions and pharmacokinetics of these new vectors, preclinical Positron Emission Tomography (PET) has expanded beyond the organic and pseudo-organic radionuclides (11C, 13N, 14,15O, 18F) to include a host of longer-lived and unconventional radiometals (e.g. 44Sc, 45Ti, 52Mn, 64Cu, 89Zr, and 140Nd). Beyond receptor- and epitope-based PET, radiometals also facilitate development of metal-based drugs, allow tracing of the native and mimetic nature of metals in the body, can be used to track nanoparticle drug delivery vehicles, and in some cases have unique exploitable decay properties (e.g. 140Nd in Figure 1 below). Further, the diagnostic metals are often isotopically matched to therapeutic nuclides, motivating a rapid transition from diagnostic imaging to targeted radionuclide therapy.

A new water-cooled beamstop at NSCL will provide access to a selection of radiometals including 47Sc, a therapeutic analog to the positron emitter 44Sc. 47Sc forms following 47Ca decay (Figure 2), which is co-produced in high yield during 48Ca irradiations at NSCL. Isolation of 47Ca allows production of a 47Sc generator that extends the usable lifetime of 47Sc in addition to providing it in high purity and with high specific activity.

**Figure 1:** (left) Pre- and (right) post-mortem PET/CT scan of a mouse 16h after injection with a somatostatin receptor 2 (sst2) targeting peptide, DOTA-LM3, labeled with 140Nd. The white circle is drawn over the pancreas (sst2 +) where the difference in the pre- and post-mortem pancreatic signal is due to rapid diffusion of 140Nd’s short-lived daughter nuclide, 140Pr, from the highly perfused pancreas into the blood stream. With further development, similar techniques with 140Nd may be used to determine the in vivo internalization status of labeled therapeutics.

**Figure 2:** A simplified decay scheme for 47Ca and 47Sc. The low energy beta particles from 47Ca and 47Sc are therapeutic, and the 159 keV gamma ray has an appropriate energy for imaging with single photon computed tomography (SPECT).

**Table 1**

<table>
<thead>
<tr>
<th>Radioisotope</th>
<th>Half-Life (d)</th>
<th>Decay Mode</th>
<th>Emission Energy (keV)</th>
<th>Decay Fraction</th>
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</thead>
<tbody>
<tr>
<td>47Ca</td>
<td>4.5</td>
<td>β⁻</td>
<td>1297 keV</td>
<td>67%</td>
</tr>
<tr>
<td>47Sc</td>
<td>3.3</td>
<td>γ</td>
<td>159 keV</td>
<td>68%</td>
</tr>
<tr>
<td>47Ti</td>
<td>67%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Gregory W. Severin

**Radiochemistry**

**Assistant Professor**

(b. 1981)


517-353-1087

**Selected Publications**


*Novel Preparation Methods of 52Mn for ImmunoPET Imaging, Graves, SA et al., Bioconjug. Chem. 2015, 26(10), 2118-2124.*

*Bringing radiotracing to titanium-based antineoplastics: solid phase radiosynthesis, PET and ex-vivo evaluation of antitumor agent [45Ti(salan)Ti(dipic)], Severin, GW et al., J. Med. Chem. 2015, 58(18), 7591-7595.*

Our research ranges from developing metal-catalyzed reactions that act on organic and inorganic substrates, to designing polymers that interact in interesting ways with enzymes and drugs. The connecting theme is developing new chemistry and mentoring the next generation of scientists to tackle the challenge of sustainably meeting the needs of our species, which is predicted to number 9.5-13 billion people by the year 2100. We have several ongoing projects and frequently collaborate with scientists in academia and industry.

We have had long-standing interest in reactions of metal boryl complexes (M–BZ₂, where Z is an anionic substituent such as alkoxide) with organic molecules. Organoboron compounds are used extensively in pharmaceutical, agrochemical, and advanced materials industries. Consequently, new chemistry within this molecular class can eliminate steps and reduce waste streams associated with synthesis of these valuable intermediates. In this regard, we have developed new catalytic reactions, such as additions of B–B bonds to olefins and synthesis of B–C bonds from hydrocarbons and boranes, etc. The first thermal example of the latter catalytic reaction, now commonly referred to as C–H borylation, was discovered in our group. More recently, we have found that by incorporating combinations of hydrophilic and hydrophobic groups along the backbone, polymers that behave as nanomicelles can be prepared. Since the length of the initial polymer, and the sizes of hydrophilic and hydrophobic groups that are subsequently introduced, determine the sizes of the nanomicelles, we are exploring host-guest chemistry of these materials. For example, we have found that the nanomicelles can interact with enzymes to make them soluble in organic solvents with retention of enzymatic activity.

The newest project in our group explores the synthesis of ammonia and related nitrogen compounds using renewable energy. Ammonia synthesis via the Haber-Bosch process currently consumes approximately 2% of the energy we produce. The H₂ that is required in the Haber-Bosch synthesis is produced by reacting methane or coal with water, which also generates large quantities of CO₂. Our goal is to develop new approaches for NH₃ synthesis that can be coupled effectively to renewable energy sources like solar and wind, whose availability is intermittent.

The flip side of this project is that ammonia and other nitrogen compounds like hydrazine and hydrazine have been used as fuels. In fact, the X-15 aircraft that still holds speed and altitude records was fueled by NH₃. An example of a renewable nitrogen-based fuel cycle is shown below.

![A cycle where nitrogen, water, and renewable energy could produce fuels with no CO₂ emissions.](image)

**The catalytic cycle for Iridium C–H borylation.**

Our early polymer work focused on synthesis of biodegradable polymers with controllable properties. This evolved into the design of monomers with functional groups, which gave polymers that could readily modified through chemical reactions. Recently, we have found that by incorporating combinations of hydrophobic and hydrophilic groups along the backbone, polymers that behave as nanomicelles can be prepared. Since the length of the initial polymer, and the sizes of the nanomicelles, we are exploring host-guest chemistry of these materials. For example, we have found that the nanomicelles can interact with enzymes to make them soluble in organic solvents with retention of enzymatic activity.

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The flip side of this project is that ammonia and other nitrogen compounds like hydrazine have been used as fuels. In fact, the X-15 aircraft that still holds speed and altitude records was fueled by NH₃. An example of a renewable nitrogen-based fuel cycle is shown below.
Solving biological problems at the molecular level with the help of novel biotechnology method development is the primary goal in the Spence group. To accomplish this goal, our group blends a variety of methods found not only in the chemical sciences, but also bioengineering, pharmacology, and physiology. Our publication record is exemplary of this broad approach to solving problems; specifically, in the past 3 years, our group has published papers in journals whose primary focus is analytical chemistry, diabetes, pharmacology, and microfluidic devices, to name a few. We employ any measurement scheme necessary to find answers and make new discoveries. Therefore, it is not uncommon for students in the Spence group to be experts in cell culture and cell preparation, but also understand the basics behind laser-induced flow cytometry, chemiluminescence technique, or how to prepare microfluidic devices from 3D-printing technology. During the past year or so, we have also used NMR, circular dichroism spectroscopy, absorbance spectroscopy, atomic absorption spectroscopy, gel electrophoresis, HPLC, amperometry, cyclic voltammetry, and scintillation counting in our efforts.

All of the work performed in the Spence group is problem-based and hypothesis-driven. Moreover, most of our work is centered around the bloodstream and complications that arise in, or from, the bloodstream during disease onset. For example, since 2006, our group has been interested in studying C-peptide, a 31 amino acid peptide secreted from the pancreatic beta cells with insulin. Recently, our group has discovered that C-peptide demonstrates activity on red blood cells (something insulin does not do), but only when bound to zinc. We are also in the process of determining how this zinc binds to C-peptide, and if it induces structure in the peptide that subsequently leads to its binding to the red cell. Our ultimate objective with this project is to prepare a correct formulation of Zn-bound C-peptide that can be re-administered to people with Type 1 diabetes, who no longer produce C-peptide in their bodies due to beta cell destruction.

In addition to our work in diabetes, we also have recently reported findings concerning hydroxyurea, the only proven therapy for people with Sickle Cell Disease. We also dedicate resources and time to studies involving platelets for Cardiovascular Disease and Stroke. Finally, a new branch of our laboratory efforts focus on improving stored red blood cells for Transfusion Medicine. Here we are formulating new, yet simple, storage solutions for the blood cells. Preliminary evidence suggests that some of the properties of our stored red cells are as fresh on day 35 of storage as they are on day 1! We hope to continue these efforts in the next few years to improve human health.

A new technique in our group involves 3D-printing. Nearing 30 years since its introduction, 3D printing technology is set to revolutionize research and teaching laboratories. With regard to research settings, 3D printing has been limited to biomedical applications and engineering, although it shows tremendous potential in the chemical sciences. The Spence group aims to utilize 3D printing technology to help us solve the problems listed above, especially those related to cell-cell communication, blood flow, and tissue-on-chip applications.

Research currently underway in the Spence group is focused on (a) platelets, (b) sickle cell disease, and (c) stored blood, in addition to our long-standing investigations involving diabetes.
Proteomics aims to comprehensively identify and quantify proteins in a biological system, including protein expression, localization, interaction, post-translational modifications (PTMs) and turn over. It routinely employs reversed-phase liquid chromatography (RPLC)-electrospray ionization (ESI)-tandem mass spectrometry (MS/MS) for protein identification. Capillary zone electrophoresis (CZE)-MS/MS has also attracted great attentions for proteomics due to its advantageous features. First, CZE-MS and RPLC-MS can produce complementary identifications and the combination of these two techniques can improve proteomic scale, and especially enhance protein isoform identifications. Second, CZE can produce much better intact protein separation than RPLC. Third, CZE-MS can yield higher sensitivity than RPLC-MS. Fourth, CZE can separate proteins in their native conditions (close to pH 7), and CZE-native MS is invaluable for native proteomics.

Our research focuses on development of new techniques for exploring CZE-MS for high-resolution, ultra-sensitive and native proteomics, and also applications of the new techniques for answering important questions in developmental biology and cancer.

**I** Couple multi-dimensional LC and/or electrophoresis-based protein pre-fractionation with CZE-MS/MS to improve the resolution of protein isoform separation and identification. The long-term goal is to generate a complete protein isoform database for human cells. We also collaborate with biologists to apply our proteomic techniques for understanding embryo early development using Zebrafish and fruit fly as model systems.

**II** Couple magnetic beads and monolithic materials-based immobilized enzymes with CZE-MS for highly efficient digestion and ultrasensitive detection of proteins from single cells. Single cell proteomics is invaluable for native proteomics. We will couple the interface with CZE-MS for online native protein cleanup, separation and native mass spectrometry detection. The long-term goal is to apply this system for native proteomics, which aims to achieve large-scale analysis of protein complexes in native conditions.

**III** Develop a microdialysis interface using a hollow fiber membrane for highly efficient and rapid removal of detergents and salts from native proteins. We will couple the interface with CZE-MS for online native protein cleanup, separation and native mass spectrometry detection. The long-term goal is to apply this system for native proteomics, which aims to achieve large-scale analysis of protein complexes in native conditions.

Selected Publications


Research in our group is interdisciplinary and spans several fields: physical and analytical electrochemistry, carbon materials, corrosion science and neuroscience. We conduct fundamental research with advanced carbon materials to address key problems and technological needs in energy, health and the environment. Our core science lies in the preparation, processing and application of diamond and diamond-like carbons. We seek to considerably improve the ability to prepare and control the material properties of single and polycrystalline diamond, and nitrogen-incorporated tetrahedral amorphous carbon, and to explore frontier applications where the unique material properties are essential for performance.

**Electrochemical Detection and Sensing** – Boron-doped diamond and nitrogen-incorporated tetrahedral amorphous carbon thin-film electrodes are being used in electrochemical detectors coupled with flow injection analysis, liquid chromatography and capillary electrophoresis. We are developing new electrochemical assays for different classes of analytes important in health and the environment. Optically transparent diamond electrodes are also being developed for use in spectroelectrochemical sensing.

**Neuroanalytical** – In vitro electrochemical, immunohistochemical and neuropharmacological methods are being used to study how neurogenic signaling in the vasculature (ATP and norepinephrine) and the gastrointestinal tract (5-HT and NO) is altered in obesity. These measurements make use of diamond and carbon fiber microelectrodes, and tissues from animal models and humans. The dysfunction in neurogenic signaling is linked to inflammation. Therefore, we are also working on in vitro electrochemical measurements of peroxynitrite (PON); a biomarker of inflammation. The work has important implications for understanding the underlying mechanisms of obesity-linked hypertension and motility disorders.

**Corrosion Protective Coatings and Surface Pretreatments** – Research is being conducted to understand how advanced inorganic coatings and surface pretreatments inhibit corrosion on aluminum and magnesium aerospace alloys. We are particularly interested in the formation, structure and corrosion protection afforded by trivalent chromium process coatings on various aluminum alloys (AA2xxx, 6xxx and 7xxx). Electrochemical measurements are utilized to assess the corrosion status of specimens in the laboratory and during different accelerated degradation tests.

**Nanostructured Carbon Powders for Separations and Chemical Sensing** – We are preparing high surface area and electrically conducting diamond or diamond/nanocarbon composite powders for use in separations and chemical sensing. The diamond powders are produced by overcoating a substrate powder (diamond, sp2 carbon or metal oxide) with a thin layer of boron-doped ultrananocrystalline diamond. These nanoscale powders offer superb microstructural stability, corrosion resistance and stability over a wide pH range. The conducting and functionalized powders are being developed for use in electrochemically-modulated and reversed-phase liquid chromatography.
Our research program provides an interdisciplinary blend of synthetic and medicinal chemistry that includes the total synthesis of natural products, the discovery of new reactions, as well as the evaluation for their cellular mechanism and medicinal properties. Natural products are still the primary source for medicines, and marine sponge metabolites represent a highly diverse and complex class of natural products with remarkable biological activities. Our laboratory is focused on the total synthesis of marine sponge alkaloids, to examine their potent anti-cancer and anti-neurodegenerative properties.

**The Oroidins:** The oroidin family of alkaloids is a highly diverse and complex class of biologically active secondary marine sponge metabolites containing characteristic pyrrole-2-carboxamide and 2-aminoimidazoline (or derivatives thereof) moieties. Members of this group include the highly publicized palau’amine as well as the structurally related phakellins and phakellstatins. Our group recently developed a novel NBS mediated addition of guanidines to olefins, which was used in the total synthesis of dibromophakellin and many of its analogues. Cellular studies in our lab subsequently identified the human proteasome as a target responsible for the exiting biological properties these compounds elicit.

**Natural Product Inspired Scaffold Design:** Our scaffold design program aims at the development of small molecular weight scaffolds containing a high degree of diversity. The skeletal diversity of our scaffolds is inspired by natural products, but unlike their natural counterparts these scaffolds are readily optimized for their pharmacokinetic and pharmacodynamic properties. For example, our imidazolone-based Chk2 inhibitors (left below), can protect normal cells from ionizing radiation (IR) without interfering with IR-induced killing of tumor cells. Another example includes the imidazoline-based proteasome modulators, which elicit remarkable in vivo anti-cancer efficacy (right below). More recently, we are modifying our natural product scaffolds to prevent the aggregation of proteins such as alpha-synuclein and tau, which are involved in the pathogenesis of Parkinson’s and Alzheimer’s disease, respectively. ☑

**Selected Publications**


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Jetze J. Tepe

**Synthetic and Medicinal Chemistry**

**ASSOCIATE PROFESSOR**

(b. 1968)

B.S., 1992, Jacksonville Univ.;
Ph.D., 1997, Univ. of Virginia;

517-353-0497

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Selected Publications

- Substituted quinolines as noncovalent proteasome inhibitors, McDaniel, Tanner J.; Lansdell, Thereasa A.; Dissanayake, Amila A.; Azvedo, Lauren M.; Claes, Jacob; Odom, Aaron, and Tepe, Jetze J., Bioorganic and Medicinal Chemistry 2016, http://dx.doi.org/10.1016/j.bmc.2016.04.005
- Indolo-phakellins as β5-specific noncovalent proteasome inhibitors, Beck, Philipp; Lansdell, Theresa A.; Hewlett, Nicole M.; Tepe, Jetze J. and Groll, Michael, Angewandte Chemie Int. Ed. 2015, 54, 2830-2833.
We use interdisciplinary methods to evaluate enzyme catalysts from various sources, such as bacteria, plants, and yeast, with non-natural substrates. Our vision is to transform natural compounds or synthetically derived chemicals to novel products. Transfer of the genes encoding these enzymes into a chassis organism can potentially make various bioactive molecules in vivo or in vitro.

**Paclitaxel (Taxol) Pathway Aminomutase.** A Taxus phenylalanine aminomutase (TPAM) converts (2S)-α-phenylalanine (2S)-α-Phe to (3R)-β-Phe and lies on the paclitaxel (Taxol) biosynthetic pathway in Taxus plants. The aminomutase forms a transient MIO-NH₂ adduct with a finite lifetime. The lifetime of adduct was unknown for TPAM or any of the several enzymes in this family until we used stopped-flow monitoring of product release to measure the exponential burst phase at pre-steady state.

**Andrimid Pathway Aminomutase.** Hammett correlations show how electron-withdrawing and electron-donating substituents on the aryl ring changed the rate-determining step of an aminomutase (PaPAM)-catalyzed reaction. Studies on this family of enzymes (class-I lase) that includes PaPAM began in 1967. Our group, for the first time, showed that the rate-determining step of a class-I lase aminomutase is sensitive to the electronics of the substituents and changes from the elimination to the amination step. Our goal is to repurpose these aminomutases to produce value-added phenylpropionanoids.

**Taxus Aeryltransferases (AT) and Bacterial CoA Ligases.** Access to paclitaxel analogs (docetaxel, cabazitaxel, paclitaxel C, and tesetaxel) used 1) for breast, ovarian, and prostate cancers, 2) to stem complications from stent implants in heart surgery, and 3) to work potentially as neuroprotectants against stroke still needs an 11-12 step semi-synthesis. Semi-synthesis involves protecting group manipulations that compromise yields. We propose to use regioselective biocatalysts to bypass protecting group chemistry to make these paclitaxel analogs. Coupling acyltransferases with CoA ligases (below) provides a Green source for precursor of drug analogs.

A new graduate student can embark on studies involving organic synthesis of novel surrogate substrates. Other areas of training include molecular cloning techniques, expression of various enzymes in *E. coli*, and assay development. Included are basic biochemical applications and molecular engineering approaches related to enzyme kinetics, enzyme purification and characterization, and various analytical techniques (such as NMR, GC/MS, LC-MS(/MS), and X-ray crystallography).
Nuclear magnetic resonance (NMR) spectroscopy in the solid state is a powerful approach to determine atomic-resolution structure and motion in systems for which the molecules do not rapidly tumble. Our research focuses on application of solid-state NMR to problems in membrane fusion, bacterial inclusion bodies, and inorganic materials.

**Membrane Fusion:** Fusion between cells and cellular components has an essential role in living organisms for such significant physiological processes as egg fertilization and synaptic transmission in the nervous system. Membrane fusion is also an important step in HIV and influenza viral infection of human cells and is mediated by proteins in the viral membrane that bind to the target cell membrane during infection. We are using solid-state NMR to determine the conformations, membrane locations, and oligomerization states of the membrane-bound HIV and influenza viral fusion proteins and using these data to develop an atomic-resolution structural model of fusion protein-induced membrane fusion.

**Bacterial Inclusion Bodies:** Proteins for fundamental research or therapeutic purposes are usually produced by putting the DNA which codes for the protein into *E. coli* bacteria, culturing the bacteria to high densities, and then inducing production of the “recombinant” protein. Most of the recombinant protein is usually sequestered in non-crystalline solids in the bacterial cytoplasm that are termed “inclusion bodies” and which are viewed negatively by researchers because typical solubilization protocols for inclusion bodies are denaturing with the subsequent requirement of refolding whose success is variable and dependent on the specific protein. Because there is little molecular-level structural information on inclusion body protein, we are carrying out solid-state NMR studies with inclusion body protein in whole bacterial cells. One overall goal is development of non-denaturing solubilization protocols for inclusion body protein.

While doing this research, students learn a variety of skills which could include peptide synthesis, protein expression and purification, design and repair of NMR equipment, NMR theory and pulse sequence development, and computer simulation. Our research is benefiting from the enhanced sensitivity and resolution of the 900 MHz NMR spectrometer at MSU.
The research in our group focuses upon the development and understanding of computational methodologies, and studies in heavy element chemistry, catalysis, protein modeling, drug design/understanding of disease, metal organic frameworks, green chemistry, and many other areas. One of the great features of theoretical and computational chemistry is that they can be utilized to investigate a broad array of challenges, and our group often finds ourselves engaged in areas as diverse as method development and studies of diatomic molecules to protein modeling and studies of the mechanical properties of materials of importance in areas such as aircraft design.

Development and understanding of methodologies. Much of our group’s efforts are focused upon the development of ab initio approaches that aim for accurate prediction of thermochemical properties across the periodic table. Included in our efforts has been the development of successful and versatile ab initio composite schemes, called correlation consistent Composite Approaches (ccCA), that provide reduced computational cost (in terms of computer time, memory, and disk space) means to achieve energetic predictions. The approaches are useful for ground-state, excited-state, and transition-state energies, and can be applied to situations where single-reference wavefunctions or where multireference wavefunctions (i.e., bond-breaking, diradicals) are necessary. Included in our work is the development of Gaussian basis sets, providing new additions to the correlation consistent basis set family, and rigorous evaluation of existing and new basis sets. Another area of interest is in gauging the performance of methodologies, such as density functional theory, particularly for situations where there may be few, if any, needed experiments for comparison. Significant efforts have focused upon transition metals.

We have interest in approaches for non-dynamic electronic correlation needed to describe bond-breaking and excited states, particularly approaches that could circumvent or reduce the most computationally demanding multireference wavefunction-basis-based approaches. We are identifying diagnostic criteria to assess the need for such approaches for transition metal species, and are developing DFT correction terms to account for non-dynamic electron correlation.

Heavy element chemistry. The complexity of the heavy elements results in their great utility in applications from cell phones to stealth technology. We are developing a better understanding of the fundamental properties of lanthanide species, as well as the methodologies needed to describe their energetic and spectroscopic properties, and utilizing this knowledge in areas such as separation science and the development of new methodologies for heavy elements.

Catalysis. Homogeneous and heterogeneous catalysis are of interest, and we investigate a broad range of catalytic reactions, including water-gas shift reactions and reactions of importance in the breakdown of lignin. We also have interest in modeling and trying to improve upon Mother Nature, considering the effectiveness of plant proteins such as RuBisCO, the CO2-fixing enzyme in the Calvin cycle.

A comparison of homogeneous and heterogeneous catalysis. In partnership with a pharmaceutical company, we are considering small molecule binding cavities, utilizing docking techniques and other approaches for the design and understanding at the molecular level of potential pharmaceuticals that could be important in anti-inflammatory disease. We also are investigating how changes in structure impact activity, and the role of signal transduction cascades in disease.
Wulff Group Research is concentrated in the area of organic synthesis and catalysis. We are motivated by the pursuit of novel approaches in synthetic organic chemistry involving design and development of new asymmetric organocatalysis, organometallic chemistry, mechanistic studies and total synthesis of natural products.

Research Field Highlights

1) New Enantioselective Organocatalysis

Boroxinate Catalysis

R1 R2
+ 2 HO-R3
1. toluene
100°C
2. imine

S-VAN/PAOL
Heteroatom Diels-Alder reaction
cis-Aziridination
trans-Aziridination
Aminoaallylation

Fischer Carbene Chemistry

Fischer Carbene Complex

(CO)Cr = R1 R2

Representative Transformations

Benzannulation Reaction
Cyclohexadienone Annulation
Tautomer Arrested Annulation
Biaryl Synthesis
Macrocycles

3) Mechanistic Investigations on Organocatalysis

Chiral Counterion H-Bonding Catalysis

(S)-VANOL-B3 Anion

H-Bonding Sites

4) Total Synthesis of Natural Products

Phomactin B2
Sphingamine
Phytosphingosine
Sedrine
α-Tocopherol

Selected Publications


to graduate study begins when the Chemistry Department extends an offer of acceptance, which we routinely do to applicants from all around the world. Applying to our Graduate Program can easily be accomplished online at:

http://www.chemistry.msu.edu/apply

Incoming graduate students are expected to have the equivalent of a Bachelor’s Degree in Chemistry, including at least one year of organic chemistry, one year of physical chemistry, at least one course in inorganic chemistry and at least one course in analytical chemistry/instrumental analysis — all at the undergraduate level. Minor deficiencies in these requirements may be remediated during the first year of the student’s graduate program.

Each application for admission to the graduate program is considered individually by the faculty members on the Graduate Admissions Committee. Transcripts, three letters of recommendation, GRE scores, TOEFL or TSE scores for international students, and a statement of purpose are required of each applicant. Admission decisions are based on the apparent training, skills, experiences, and attitude of the applicant, and the likelihood of a successful graduate career at MSU. Offers of acceptance are made to only a small fraction of the many applicants each year.

To begin the application process, please follow the Application Procedures which are listed on the Chemistry Department’s website:

http://www.chemistry.msu.edu/apply

Submit the Applicant Datasheet and the University Application electronically, and arrange to have your three letters of recommendation, transcripts, official test scores, and statement of purpose mailed directly to the Chemistry Department Graduate Office.

After submitting your Applicant Datasheet, you may check your application status through our website under Graduate Program, Check Application Status. Your Status Page will indicate what items have been received and what items are still missing, and will also give a short note at the end of the page concerning your general application status. Most applicants will receive a final decision on their application sometime between January and March, although some decisions are made before and after that time period. As soon as we have made a decision on your application, the decision will appear on your Status Page, and we will contact you through e-mail.

We hope that you will seriously consider choosing the Graduate Program in Chemistry at Michigan State University. Successful careers in Chemistry begin at MSU!
Michigan State University was the country’s first land-grant institution and was founded in 1855. The University was created with an initial focus on agriculture and farm science. When it was created, it established a new approach to education, research and public service. MSU is now the largest institution of higher learning in the state, with more than 200 programs of undergraduate and graduate studies in 19 colleges.

A Brief History of MSU

In 1855, the Michigan State Legislature passed Act 130 which provided for the establishment of the “Agricultural College of the State of Michigan,” which came to be known as the Michigan Agricultural College or “MAC.” They also appropriated “twenty-two sections of Salt Spring Lands for its support and maintenance...”, as well as $40,000 to carry the college through its first 2 years of operation. The MAC was formally opened and dedicated on May 13, 1857, in what is now East Lansing. MAC was the first agricultural college in the nation, and served as the prototype for the 72 land-grant institutions which were later established under the Federal Land Grant Act of 1862, officially known as the “Morrill Act” after its chief sponsor, Senator Justin Morrill of Vermont. The MAC’s original tract of land in East Lansing consisted of 677 acres, but additional lands were purchased over the years as the MAC grew to become Michigan State University. Presently MSU’s campus and farms cover about 5,198 acres, of which about 2,100 acres are in existing or planned campus development.

The Campus

The East Lansing campus of MSU is one of the most beautiful in the nation. Early campus architects designed it as a natural arboretum—a living laboratory—with 7,000 different species of trees, shrubs and vines represented. There are about 200 major buildings, 100 miles of walkways, and 12 miles of bicycle paths on campus. The campus is a unique blend of the traditional and the innovative. The Red Cedar River bisects the campus; north of the river’s tree-lined banks and grassy slopes is the older, traditional heart of the campus. Some of the existing ivy-covered red-brick buildings found in this part of campus were built just after the Civil War. On the south side of the river are the more recent additions to campus—the medical complex, the veterinary medical center, and most of the science and engineering buildings, including Chemistry. The National Superconducting Cyclotron Laboratory (NCSL) is also south of the river next to Chemistry and has recently completed a multimillion dollar upgrade to operate two cyclotrons in tandem, providing a wide range of heavy-ion beams, and includes a new office wing. This facility has received international recognition both for its active programs of basic research and for its pioneering innovations in cyclotron design. In addition, in 2010 MSU won a hotly-contested national competition to host the US-DOE Facility for Rare Isotope Beams (FRIB), a $600M national user facility scheduled to begin construction in 2013 as an important extension to the NCSL.

Beyond the East Lansing campus of Michigan State University—about an hour’s drive away—are our two natural
science research facilities: the Kellogg Biological Station at Gull Lake, and Hidden Lake Gardens near Tipton. The 2,200 acre Kellogg Biological Station is a bird sanctuary, experimental farm and research forest, and a national center for lake-and-land ecological research. Hidden Lake Gardens is a 670 acre landscape arboretum which serves as an outdoor classroom. Located in the Michigan Irish Hills, Hidden Lake features a conservatory complex containing collections of tropical, arid, and temperate plants from around the world. Both facilities are open to visitors all year.

The Arts

The arts have flourished at MSU, especially in the past two decades after our impressive performing arts facility, the Wharton Center for Performing Arts, opened in the Fall of 1982. From the very beginning it has been the showcase for an extraordinarily broad array of performances in music, theater, and dance and popular shows. The Wharton Center’s two large concert halls are regularly used for recitals, concerts and theater productions by faculty, student groups, and visiting and touring performing artists. The Center brings to our campus dozens of professional musical and theatrical productions each year, such as 2017-18 upcoming events like Finding Neverland, Something Rotten, and Disney’s The Lion King, and performers such as Squirrel Nut Zippers, and Emanuel Ax, Leonidas Kavakos, and Yo-Yo Ma.

In 1992, the Wharton Center was the site of one of the debates between U.S. Presidential hopefuls Bill Clinton, George H. Bush and H. Ross Perot. It’s a short one-block walk from the Chemistry Building to the Wharton Center.

MSU is also home to the Jack Breslin Student Events Center, a 15,000+ seat arena which is home to the MSU Spartan basketball team, and also periodically plays host to world-class concerts and attractions.

A facility that offer both educational and recreational opportunities is the MSU Museum. The Museum houses documented research collections in Anthropology, Paleontology, Zoology and Folklife as well as regularly hosting traveling exhibits.

In addition, the new $26M Eli and Edythe Broad Art Museum is now a premier venue for international contemporary art in the Lansing area. The old Kresge Art Center’s art collection has been combined with the Broad Museum; it was strongest in examples of 19th and 20th century art, but it also contains a wide variety of other artworks such as Egyptian sculpture of the Coptic Period, etchings by Rembrandt, and works by Salvador Dali, Ansel Adams, and Auguste Rodin.

Recreational Opportunities

Many recreational activities are available on campus and in the Lansing area. Walking and running trails, available extensively throughout the campus, take you through protected natural areas along the Red Cedar River. MSU has two 18-hole golf courses available to students, faculty and staff. There are three fitness centers that provide basketball, handball and squash courts, exercise machine rooms, and aerobic workouts. Two indoor ice skating rinks, an indoor tennis facility, more than thirty outdoor tennis courts, and five swimming pools are accessible as well. In both summer and winter, nearby state parks such as Rose Lake and Sleepy Hollow offer many activities. In Michigan, snow is not a problem, but rather an activity, so bring your skis!

MSU, which was admitted to the Big Ten in 1948, has a rich tradition in athletics. MSU first competed in conference football in 1953, sharing the title that year with Illinois. Since that time, MSU has enjoyed considerable success in Division I athletics, including NCAA titles in basketball and hockey, among other sports. Graduate students, faculty, and staff in the Chemistry Department are strong supporters of the athletic programs, which offer ample opportunities for social interactions outside of the laboratory.
Academics

There are over 50,500 students on campus—from all 83 counties in Michigan, all 50 U.S. states, and 138 foreign nations. Of these, approximately 11,400 are in graduate and professional programs. By gender, MSU is 51.5% women and 48.4% men. Michigan State leads all public universities in attracting National Merit Scholars, and is also a leader in the number of students who win National Science Foundation Fellowships. MSU was the first university to sponsor National Merit Scholarships.

The extensive MSU library system includes the main library and 5 branches. A total of over four million volumes are housed in these facilities. Across the street from Chemistry is the Abrams Planetarium, one of the most active planetariums in the world. It is used for teaching, and offers shows and exhibits to the general public.

If students are the lifeblood of a campus, then the faculty is the heart of a great university. The more than 5,000 MSU faculty and academic staff continue to distinguish themselves, and include 9 current members in the National Academy of Sciences, and honorees of prestigious fellowships such as the Fullbright, Guggenheim and Danforth.

The Chemistry Department and MSU continue to evolve, crossing traditional research boundaries to offer teaching and research opportunities that will have an impact on the future of science. MSU is well known for its interdisciplinary research centers, which have an outstanding record for solving not only scientific problems, but social problems as well. These include the Department of Energy Plant Research Lab, The Center of Research Excellence in Complex Materials, the Institute for Environmental Toxicology, the A. H. Case Center for Computer-Aided Engineering and Manufacturing, the Mass Spectrometry Facility, the Center for Advanced Microscopy, the Institute of Water Research, the National Food and Safety Toxicology Center, the Center for Ethics and Humanities in the Life Sciences, and the Institute for Children, Youth and Families. The federal government has selected MSU’s campus as the site for a number of facilities such as the National Superconducting Cyclotron Laboratory, the Plant Research Laboratory (a U.S. Department of Energy facility) and the USDA Avian Disease and Oncology Laboratory.

University-wide research has led to important developments throughout MSU’s history. Early research led to agriculturally important vegetable hybrids, and the process for homogenization of milk. More recently, the world’s widest-selling and most effective type of anti-cancer drugs (cisplatin and carboplatin) were discovered in the Chemistry Department at MSU, and crop cultivars have been developed at MSU that can be used to produce biodegradable plastics.

Housing

A variety of living accommodations is available to graduate students. One option is the Owen Graduate Center, which offers traditional furnished rooms, private telephones, and free broadband computer networking, with two rooms sharing an adjoining bathroom and shower. Housekeeping services are provided for all. The hall has recreational and laundry facilities and a cafeteria. Many incoming graduate students find Owen Graduate Center a good place to begin, and after a short period of time they get to know the surrounding area and then move off-campus. The Owen facility is only two blocks from the Chemistry Building.

A second on-campus option is the University apartment system. About 2,000 furnished one- and two-bedroom apartments are available on-campus, primarily intended for married students and their families. Also available now are beautiful four bedroom on-campus University apartments for students.

The third option is, of course, off-campus housing. Many apartment complexes are available within a two-mile radius of campus, some within a few blocks of the Chemistry Building. In the past, graduate students in Chemistry have also rented condominiums and houses — either

Cobb Great Hall at the Wharton Center for Performing Arts at MSU seats over 2,400 guests, and is home to many Broadway plays, concerts, and comedy and dance performances each year. The Center also houses the Pasant Theatre (600 seats), the Fairchild Theatre (600 seats) and the MSU Concert Auditorium (3,600 seats). It opened in 1982, and was expanded and renovated in 2008.
alone or in small groups. The cost of living is very reasonable in the Lansing area, and houses can still be purchased with monthly mortgage payments that are competitive with apartment costs. This is why, each year, some students decide to buy a home in the area while they are in the graduate program. The surrounding communities are varied, and offer rural and small-town settings as well as “big city” alternatives, without the usual congestion or pollution of a larger metropolis. MSU provides information on current off-campus housing listings to prospective students upon request.

For further information on MSU housing options for graduate students, you may call toll free 1-877-954-8366, or visit the University Housing web site at:

http://liveon.msu.edu/

Michigan State University was founded in 1855 by an Act of the Michigan State Legislature; this Act was subsequently used as the template for the federal “Morrill Act” which has provided for the funding of 72 land-grant institutions in other States across the U.S. As a result, this sign proudly proclaims our status as “The Pioneer Land Grant College”.

The Breslin Student Events Center, home of the Spartans basketball team, has the capacity to accommodate over 16,000 fans. It also plays host to many MSU Commencements, large concerts, monster truck rallies and the occasional circus.

For more information about life at MSU and in the greater Lansing area, please visit the MSU Graduate School home page at:

http://grad.msu.edu/prospective/
LANSING, MICHIGAN’S CAPITAL, 
is centrally located in Michigan’s lower peninsula. The greater metropolitan area has a population of approximately 460,000, and is home to several large industries. The city offers a variety of restaurants, the Lansing Symphony Orchestra, a number of theater companies, and the Lansing Lugnuts. The Impression 5 Science Museum, the R. E. Olds Transportation Museum, and the Michigan Historical Museum attract visitors from throughout the region. Major local employers include MSU, the Michigan state government, and General Motors. Several high-tech companies are located in the area, including the Michigan Biotechnology Institute, Emergent Biosolutions and Neogen Corporation.

There is a large scientific community in the Lansing area which, along with MSU, is owing in part to the presence of a number of the State of Michigan research laboratories in the area, including the Department of Agriculture, the Department of Natural Resources and Environment, the Department of Public Health Laboratories, and the Michigan State Police Crime Laboratories. In addition to MSU, Lansing Community College, the Thomas M. Cooley Law School, and Davenport College are all located in the capital city area, and the MSU College of Law is housed on the MSU campus.

It’s only a short distance to a number of other Michigan cities that are scientific, educational and cultural centers as well. For example, Kalamazoo, which lies about 80 miles to the southwest, is the home of Western Michigan University and Kalamazoo College (a premiere liberal arts institution). Chemists at MSU also interact with scientists at the University of Michigan and Pfizer (formerly both Warner-Lambert and Pharmacia & Upjohn) in Ann Arbor, and a number of other research laboratories in the state, including Dow Chemical (Midland, MI) and Dow Corning (Midland, MI), General Motors (Detroit), Ford (Dearborn, MI), and BASF (Wyandotte, MI).

Situated in the heart of the Great Lakes region of the U.S., MSU’s East Lansing Campus is centrally located not only to metropolitan areas such as Chicago and Detroit, but to outstanding natural resources and to northern Michigan’s world-class summer and winter resorts. Michigan’s Upper Peninsula is a relatively undeveloped and unspoiled area of immense natural beauty with a population density of less than twenty persons per square mile. It offers many unique “get-away” opportunities for all seasons. The Lansing area itself provides a variety of recreational opportunities including many golf courses, boating and beach life at Lake Lansing in the summer, and cross-country skiing in the winter. Hunting and fishing opportunities are also found widely throughout the state.

The Lansing area has outstanding transportation facilities. Lansing has an award-winning bus system (CATA) which operates both dedicated campus-only bus routes and routes that connect campus with metropolitan Lansing. Bicycles are a common mode of transportation in the area. Several miles of special bike paths are provided on campus which stretch into outlying towns. Transportation to other cities is also available by air, rail and bus. The Capital City Airport in Lansing and the Amtrak railroad station in East Lansing are both readily accessible from MSU. East Lansing is a stop on the train line that links Chicago to Toronto, Canada.

Complementing campus life is the city of East Lansing, which surrounds the northern edge of the MSU campus. East Lansing is noted for its congenial atmosphere and tree-lined avenues. Shops, restaurants, bookstores, cafes, malls and places of worship serve the student’s needs. East Lansing provides students with a relaxing and stimulating environment for their graduate school experience.
The State of Michigan, Michigan State University, and the MSU Chemistry Department have a common component to their histories — they have played important roles in defining a vision for the future. At the state level, the automobile industry established a new model for industries around the country. As the pioneer land grant university, MSU was dedicated to the discovery and application of knowledge. From the very beginning, the faculty were expected to engage in research that resulted in the acquisition of new knowledge, and to use this new knowledge to improve the quality of life for the citizens of the state and the world. This tradition of scientific research at MSU is frequently traced back to 1877, when MSU botanist William J. Beal became the first person to cross-fertilize corn, leading to today’s vastly improved cultivars and hybrids which produce greatly increased yields.

When MSU was founded as Michigan Agricultural College in 1855, it dared to develop a chemistry curriculum. At the time, major U.S. universities emphasized the study of Greek, Latin, rhetoric, and philosophy. Not only did MSU develop a program in chemistry, it did so in an innovative way — approaching the discipline not as a static science to be taught in classrooms, but as an experimental discipline in which concepts are discovered and tested through creative thought and research. Today in the USA, many universities compete for grants from federal and private sources to support academic research. MSU competes very effectively in this endeavor. Each year, the number of proposals submitted by MSU faculty increases, leading to corresponding increases in federal research money on campus. The university faculty have made a permanent commitment to maintain a strong graduate program at MSU, and funding agencies have come to recognize MSU’s research programs as good investments. The State, the University, and the Chemistry Department continue to be dynamic forces which are defining aspects of the country and the role of Universities for the foreseeable future. We hope that you share our excitement, and will consider becoming a part of it!
Visit our website:

www.chemistry.msu.edu