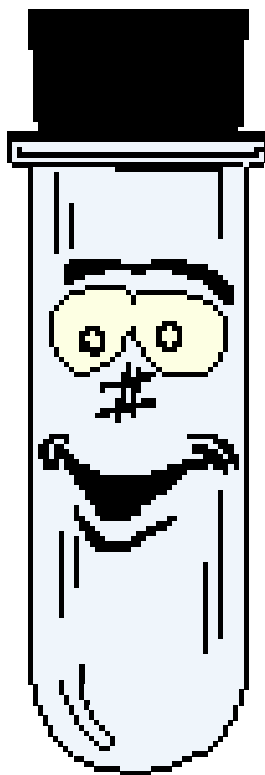


RESEARCH IN CHEMISTRY AT BOISE STATE UNIVERSITY:

OPPORTUNITIES FOR UNDERGRADUATE STUDENTS



Updated 7/2007

WHY DO CHEMISTRY RESEARCH AS AN UNDERGRADUATE?

The best way to get a real sense of how scientists do their jobs is to apply the scientific background you've been developing in your classes to a research project. In research, there are no "right" answers. Often a great deal of time must be invested in order to obtain experimental results of high enough quality to be analyzed and interpreted. It can be sometimes be painstaking, tedious work.... However, it can also be fascinating and engaging (which is why people do it).

Regardless of your ultimate career goals, experience with a research project will help you. It is a crucial experience if you intend to study chemistry past the B.S. level. It can also be helpful as a resumé-builder for industrial positions or for application to other post-graduate professional schools (e.g., medical school).

Ultimately, though, the reason to do research is to learn how to ask questions that other people haven't asked before, how to design an experiment to address that question, and how to interpret the results of experiments and draw conclusions. These skills require critical and careful thinking and will serve you well in any future endeavor.

WHAT ARE THE RESEARCH OPPORTUNITIES FOR UNDERGRADUATES IN THE BSU CHEMISTRY DEPARTMENT?

Research for Credit

There are three courses in which students can enroll to receive credit for research work:

CHEM-296, CHEM-396, and CHEM-495.

Each course requires instructor permission for enrollment. While there are no official prerequisites for CHEM-296 or CHEM-396, some faculty have placed restrictions on the academic background of students. This guarantees that the student has the appropriate background both to understand the project and to execute it safely and reliably.

CHEM-495, which is required of all chemistry majors for graduation, requires a written report of the work completed in the course. (See below for more information about CHEM-495).

There is no limit to the number of times one can enroll in these courses or the number of credits for which one enrolls. (The exception to this is that the department will not allow any student to enroll in CHEM-495 for more than 1 credit at a time).

One credit obligates a student to do 3-4 hours of research work per week. The course number & number of credits for which one enrolls is determined through discussion between the student and the faculty mentor with whom the research will be conducted. The faculty mentor specifies details of the commitment (e.g., time expectations, how the laboratory notebook should be kept, how files should be backed up, basic laboratory rules, etc.). The faculty mentor will also provide each student with appropriate safety training.

Research for Profit

Occasionally, individual faculty members have grant funding which allows him or her to pay a student to participate in research activities beyond what the student is doing for credit. Most of these positions are filled on a first-come first-served basis and are often filled by students who have already demonstrated their commitment and ability by doing research for credit. (Thus, if you eventually want to be paid to do research, it makes sense to talk with faculty about it early in your academic career; be prepared to enroll for credit before getting paid).

HOW MANY CREDITS SHOULD I TAKE?

The minimum research requirement described below is just that... anyone who has done research can tell you that 3-4 hours per week is not enough time to see real results of your research efforts. If you enroll for only one credit, you should expect that at least some of the time, you will put in more than 3-4 hours per week. However, like most things, you get out what you put in. If you put a lot of effort and energy into your research, you are more likely to really gain something substantial from the experience. *It is, therefore, our recommendation that you enroll for as many credits as your schedule allows.*

It is interesting to note that exit interviews with graduating chemistry students indicate that students who have done more than the minimum requirement tend to feel they got more out of the experience than those who have simply completed the minimum requirement for graduation.

WHAT IS THE MINIMUM RESEARCH REQUIREMENT FOR GRADUATION?

All chemistry majors are required to complete a minimum of 2 credits of research (CHEM-495) in order to graduate. These credits must be taken in two different semesters (minimum of 1 credit each semester). The enrolled student is obligated to complete 3-4 hours of research work per week for each credit.

HOW DO I GET INVOLVED IN RESEARCH?

1. Read this handout.

Many of the chemistry faculty have ongoing research projects and are interested in involving undergraduate students. This handout will give you a sense of the type of research each faculty member is doing, as well as some of the requirements that each faculty member has for students working in his or her lab.

2. Contact individual faculty members you think you might be interested in working with.

Set up an appointment with each one. Ask about what projects are going on and if you might be able to become involved. If other issues are important to you (e.g., whether or not there is funding available to pay you), now is the time to ask.

3. Plan ahead.

Bear in mind that many students are interested in doing research, so faculty are often “booked” about a year in advance for space in his or her lab.

4. Iron out a commitment.

This simply involves making a verbal commitment to work with an individual faculty member. Make sure both you and the faculty member are in agreement about the terms of your working in the lab (when you will start working, how many credits, how many hours per week, when those hours will be, what the expectations for receiving an “A” are, how many semesters are you expected to work? Etc.).

5. Take care of paperwork/logistics.

For most research courses, special permission and signatures are required for registration. When you are ready to enroll, go to the faculty member for the appropriate form and signature required. You’ll need to specify CHEM-296/396 or CHEM-495. You will be provided with further instructions about how to file the appropriate form.

Faculty Research Interests

The following is a summary list of faculty interested in involving undergraduate students in research projects. For more details on each person's research interests, see the following pages.

Name/specialty area	Research Interests		
Brown, Eric Inorganic Chemistry	Bioinorganic chemistry; synthetic modeling of metalloprotein active sites	SN 314 426-1186	ebrown@chem.boisestate.edu
Charlier, Henry Biochemistry	Enzymology of carbonyl, lipid, and alcohol metabolism	SN 311 426-3474	hcharlier@chem.boisestate.edu
Cornell, Ken Biochemistry	Biochemistry of methionine salvage and microbial quorum sensing pathways.	SN 320 426-5429	kcornell@chem.boisestate.edu
Organic Chemistry		SN 310 426-2393	
LeMaster, Cliff Physical Chemistry	Internal vibrational redistribution, chaotic systems, gas phase NMR, and computational chemistry	SN 340 426-4491	clemast@chem.boisestate.edu
McCormick, Mike Organic Chemistry	Natural product synthesis, heterocycles, chemical education.	SN 312 426-3026	mmccormick@chem.boisestate.edu
McDougal, Owen Bio/Organic Chemistry	Biomedical research of neurotoxins; biomass fuel briquettes; chemical education through spectroscopy and green chemistry	SN 323 426-3964	omcdougal@chem.boisestate.edu
Oxford, Julie* Biochemistry	Biochemical and biophysical studies of extracellular matrix proteins	SN 211 426-2395	joxford@boisestate.edu
Peloquin, Jeff Physical Chemistry	Spectroscopic studies of the photosynthetic Mn oxygen-evolving center and Mn catalysts	SN 313 426-1423	jpeloquin@chem.boisestate.edu
Russell, Dale Analytical Chemistry	Analytical electrochemistry; electrokinetic methods and environmental analysis	SN 316 426-3975	drussell@chem.boisestate.edu
Warner, Don Organic Chemistry	Organic synthetic methodology; synthesis of biologically active natural products	SN 315 426-3030	dwarner@chem.boisestate.edu

* Prof. Oxford is a faculty member in the Biology department. She is interested in involving chemistry students in her research.

Faculty Mentor: **Eric Brown**

Area: Synthetic Bioinorganic and Coordination Chemistry

Office: SN-314

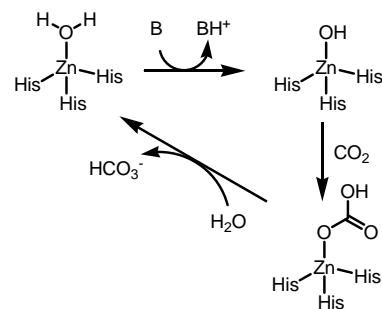
Phone: 426-1186

e-mail: ebrown@chem.boisestate.edu

Overview of Research Interests:

Proteins containing transition metal ions carry out a variety of important functions in biological systems. Consequently, understanding how these chemical transformations occur and what factors regulate their reactivity is an important research area. One important area that has provided invaluable insight into the structure and function of numerous metalloenzymes is the synthetic modeling approach. In principle, the synthetic modeling approach involves the synthesis of low molecular weight complexes that model the structural and functional units of the enzymes. By studying the synthetic model complexes, useful information such as spectroscopic and structural data and identification of possible intermediates or pathways in the enzymatic cycle can be obtained.

An example of a system that we are currently developing model complexes for is carbonic anhydrase. Carbonic anhydrase is an enzyme that catalyzes the reversible hydration of carbon dioxide to form bicarbonate. The enzyme has numerous physiological roles such as transporting carbon dioxide from metabolizing tissues to the lungs, carbon dioxide storage in plants and fluid balance within our body. Much of the interest in the enzyme stems from the latter role where inhibitors are being developed to control intra-ocular pressure. The active site of carbonic anhydrase contains a mononuclear zinc center coordinated by three histidine residues and a highly acidic water molecule. An important hydrogen-bonding interaction between the zinc-bound water molecule and a neighboring threonine residue is proposed to stabilize and control the binding mode of the unstable bicarbonate intermediate. We hope to understand how secondary interactions, i.e. hydrogen-bonding, influence the reactivity of the enzyme through the synthesis, characterization and examination of reactivity of model complexes supported by ligand systems that contain hydrogen bond donors.



Mechanism of carbonic anhydrase

Students will obtain multidisciplinary training in the synthesis and characterization of organic and inorganic compounds. For example, students will develop their synthetic organic and inorganic skills by synthesizing new ligands and exploring their metal complex chemistry. Since the research involves the synthesis and characterization of reactive, air-sensitive transition metal complexes, students will learn to work in an inert-atmosphere glove box and develop Schlenk techniques. They will also be exposed to a variety of characterization methods that will be used to characterize the compounds and to examine their reactivity. These include NMR, infrared, UV-Vis, EPR, resonance Raman and X-ray crystallography. Finally, students will develop an understanding of mechanism by examining the reactivity of the model complexes with either natural or model substrates.

If you are interested in Dr. Brown's work, please make an appointment to speak with him.

Faculty Mentor: **Henry Charlier**
Area: Biochemistry
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e-mail: hcharlier@chem.boisestate.edu

Overview

My overall research interests involve the fields of enzymology and protein chemistry. Proteins are very interesting molecules that serve a variety of functions in living organisms. My current research involves studies in three areas as briefly described below:

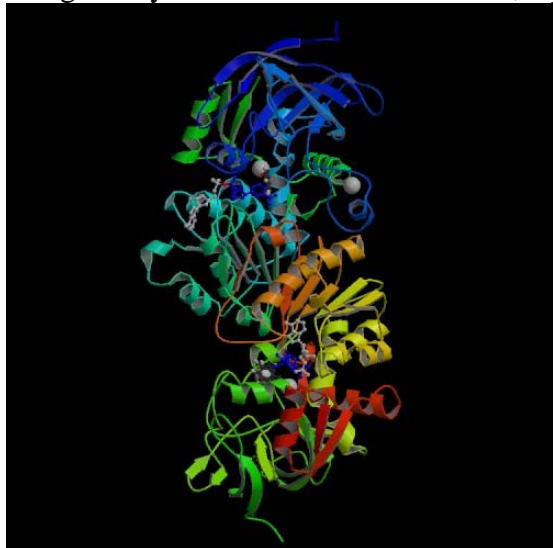
I Carbonyl Reductase - Carbonyl reductase (CR), E.C. 1.1.1.184, catalyzes the NADPH-dependent reduction of a wide range of carbonyls. CR has been connected to several important processes including but not limited to quinone detoxification, neuroprotection, prostaglandin metabolism, and, of clinical interest, anthracycline metabolism. CR reduction of anthracyclines significantly impacts their use in the treatment of cancer as it has been linked to both drug resistance and cardiotoxicity mechanisms. Therefore, inhibition of CR in conjunction with anthracycline therapy offers the potential both to increase the effectiveness of the drugs and to decrease the risk of the associated cardiotoxicity. The major emphasis of this work is to better understand how CR recognizes the molecules to which it binds, be they substrates or inhibitors. Equipped with this information, drugs may be designed to control CR with the intention of reducing the risk of cardiotoxicity during anthracycline cancer treatment. Also, as the role of CR in other pathways is better understood such drugs may be used to treat other diseases as well.



Structure of human carbonyl reductase. From <http://www.rcsb.org/pdb/explore/explore.do?structureId=1WMA>

II Alcohol Dehydrogenase - Alcohol dehydrogenase (ADH), E.C. 1.1.1.1, catalyzes the reversible oxidation of ethanol, using NAD as a cofactor. This reaction is a rate-limiting step in alcohol metabolism. ADH may be an important determinant in the development of alcoholism and fetal alcohol syndrome and is therefore widely studied. In addition, it is often studied to gain insight into how enzymes catalyze reactions. My research project with ADH focuses on evaluating the contribution of electrostatic interactions in coenzyme binding. In past studies, a lysine at position 228 (K228) has been implicated in controlling, at least in part, coenzyme (NAD⁺ and NADH)

binding. In particular, the positive charge at this position is hypothesized to interact with the negatively charged coenzymes. In order to evaluate the role of charge at position 228, we mutated the lysine at this position to alanine, glutamine, and glutamate, each of which changes the charge at this position. In a past study this lysine was also mutated to arginine, which conserves the positive charge at 228. Currently, all of these mutants are being analyzed for effects on coenzyme binding using steady state and transient kinetics, equilibrium binding studies, and computational chemistry.



Structure of horse liver alcohol dehydrogenase. From <http://www.rcsb.org/pdb/explore.do?structureId=1HLD>

III Phosphotriesterase – Phosphotriesterase (PTE), E.C. 3.1.8.1, catalyzes the hydrolysis of synthetic organophosphate triesters and phosphorofluoridates. Compounds in this family include several pesticides and nerve agents. This enzyme has potential use in nerve agent and pesticide decontamination. Work in my lab involves using protein chemistry and genetic engineering techniques to modify this enzyme to enhance its utility in organophosphate compound degradation.



Structure of bacterial phosphotriesterase. From <http://www.rcsb.org/pdb/explore/explore.do?structureId=1P6C>

If you are interested in Dr. Charlier's work, please make an appointment to speak with him.

Faculty Mentor: **Ken Cornell**

Area: Biochemistry

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Phone: 426-5429

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Overview

Infectious diseases still account for a large proportion of the morbidity and mortality in this country and abroad. The rise in multiply drug resistant organisms and the advent of new emerging pathogens necessitates the continued development of new drugs with novel mechanisms of action. This drug development is aided by the identification of metabolic differences that exist between the pathogen and the human host. Several exploitable differences in the manner in which the byproducts of methylation reactions and polyamine biosynthesis are salvaged back to the essential amino acid methionine, appear to exist between microbes and man. Two enzymes in the salvage pathway are of particular note: methylthioadenosine / S-adenosylhomocysteine nucleosidase (MTA/SAH nucleosidase) and methylthioribose kinase (MTR kinase), which are present in microbes but absent from mammalian cells. Drugs that target these enzyme activities should have a high degree of specificity for microbes and a correspondingly low toxicity to mammalian hosts.

In order to exploit these pathway differences for drug development, one focus of my lab is to identify, clone and express the target gene sequences for MTA/SAH nucleosidase and MTR kinase from a variety of pathogenic microbes, and purify the corresponding recombinant proteins. Analogs of methylthioadenosine and methylthioribose are then tested against these recombinant enzymes to ascertain their activity and predict further modifications to the drugs that may generate better inhibitors. In addition, my lab has worked closely with protein x-ray crystallographers to solve and examine the three dimensional structures of MTA/SAH nucleosidase and MTR kinase, and use this information to identify potential alterations to substrate analogs that would provide even greater inhibitory activity.

In recent years, an intimate connection has been found between the methionine salvage pathway and the production of signaling molecules in microbes (autoinducer 2) and plants (ethylene). In microbes, autoinducer 2 (AI-2) governs a variety of processes including the elucidation of virulence factors, biofilm formation, and bioluminescence. Inhibition of AI-2 production, either by chemical or genetic interruption of salvage pathway enzymes could be used to create microbes that are attenuated in their virulence and biofilm formation. These microbes should then be more susceptible to standard antimicrobials, or alternatively serve as live vaccines to stimulate host innate and adaptive immunity. In plants, chemical or genetic interruption of the methionine pathway should result in reduced levels of the hormone ethylene. As a consequence, a variety of ethylene dependent processes such as root growth and fruit ripening could be modulated. This could lead to the production of highly specific herbicides and fruit with increased market shelf life. The metabolic effects of the interruption of methionine salvage on microbial and plant signaling processes will continue to be a focus of the research in my lab.

A broad array of techniques are employed in my lab to accomplish the above studies, including: polymerase chain reaction, gene cloning, site-directed mutagenesis, protein chromatography, TLC, enzyme kinetics, UV- Vis- and Fluorescence spectroscopy, mammalian- microbial- and plant tissue culture, monoclonal antibody production, protein engineering, and many others. The following table lists organisms that are the focus of our research efforts:

Bacteria	Parasites	Plants
<i>E. coli</i> <i>Salmonella typhimurium</i> <i>Shigella flexneri</i> <i>Staphylococcus aureus</i> (MRSA) <i>Enterococcus</i> (VRE) <i>Borrelia burgdorferi</i> (Lyme disease)	<i>Giardia intestinalis</i> <i>Entamoeba histolytica</i> <i>Plasmodium falciparum</i>	<i>Arabidopsis thaliana</i> <i>Lycopersicon</i> (tomato) <i>Oryza sativa</i> (rice)

Students involved in research in my lab have opportunities to present their findings at local, regional, and national scientific meetings. Many have won awards for their research, and been supported by fellowships from Merck, INBRE, MSTMRI, Premedical, and the Dept. of Chemistry. A number of students have gone on to be co-authors on scientific publications arising from their research.

If you are interested in Dr. Cornell's work, please make an appointment to speak with him.

Faculty Mentor: **Cliff LeMaster**
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Undergraduate Research Opportunities in Computational and Experimental Chemistry

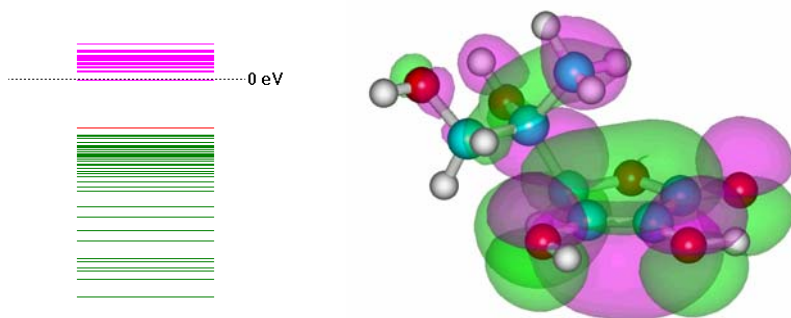
Computational chemistry is now one of the most important techniques that compliments all areas of traditional chemical research. From synthesis to spectroscopy, modern computational techniques, ranging from molecular mechanics to *ab initio* calculations, provide insights into the properties or reaction mechanisms of systems under investigation. For example, results from these computations can be compared with experimentally determined kinetic parameters using techniques such as gas-phase NMR.

The goal of this project is to introduce undergraduate students to the theory, techniques, and uses of computational chemistry. This serves three sub-purposes. First, students will have the opportunity to actually visualize chemical processes such as reaction mechanisms and conformational processes. Second, in doing so, they will acquire the ability to use an important modern tool, making them better prepared for graduate school or careers in industries where these sophisticated technologies are in use. Finally, students working in the experimental area will gain hands-on experience in gas-phase techniques and real-world NMR experience.

Methods

The goals outlined above will be achieved by (1) teaching students the theory and uses of computational methods in chemistry, including the differences between molecular mechanics and semi-empirical and *ab initio* quantum mechanical methods and the differences between the various force fields used in molecular mechanics; (2) by allowing students to use these methods to visualize the conformations of molecules and their importance as well as the energetics of reaction processes, including the energetics of conformational exchange reactions and the construction of potential energy functions; (3) by showing students how to judge the relative accuracies of the different methods in terms of their particular needs and to choose methods based on their advantages and disadvantages to the task at hand, and (4) by showing students how to make gas phase samples and obtain NMR spectra.

Students will utilize Gaussian 98 running under the UNIX operating system to calculate a variety of properties and visualize the results in Gaussview. Students may work on their computational research at home and at a convenient time (requires home computer and Internet provider). For more information on the methods and systems that will be studied please contact me.

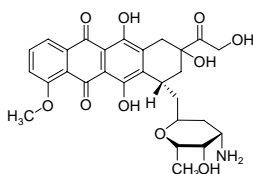


If you are interested in Dr. LeMaster's work, please make an appointment to speak with him.

Faculty Mentor: **Mike McCormick**
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Overview

The focus of the research in the McCormick Lab is twofold. First, is the synthesis of biologically active molecules containing heterocycles. Currently, we are in collaboration with Dr. Charlier synthesizing *carbonyl reductase* inhibitors and making analogues of anthracyclines. Anthracyclines, such as doxorubicin (figure 1) and daunorubicin are therapeutically used as anti-neoplastic agents. However, when carbonyl reductase acts upon doxorubicin, it can cause lethal acute cardiomyopathy in people who have been administered this drug. This is because the carbonyl reductase metabolite of doxorubicin is highly cardio-toxic. We are working on analogues of doxorubicin that would still act as anti-neoplastic agents that would not produce toxic metabolites. We are also synthesizing small molecules that could inhibit *carbonyl reductase* from acting upon doxorubicin.



Doxorubicin



Figure 2.

Figure 1.

Other biologically active compounds of interest include firefly luciferin. Modification of the heterocycles in luciferin has potential to become a valuable asset in the use of luciferase genes as reporter assays for *in vitro* and *in vivo* transcription. Drug companies can benefit greatly from live animal studies of their drug and find the targets of these drugs. The purpose of the alteration of the color of light emission is to allow for better tissue penetration of emitted light, which will enhance sensitivity of this assay. The main goal is to synthesize an analogue that can give a red-shifted light emission, but also can be administered into living systems. One analogue that was discovered was able to shift the wavelength effectively to red (Figure 2). Also of interest is to make analogues that help unlock the mechanism of why the wavelength is shifted.

A second area of research that I would like to explore is in chemical education. I like to take an active role in organic chemistry laboratory experiment development. Through a good lab curriculum, the teachings of lecture can be reinforced, making for more effective learning. Current topics for this include the development of organic labs as well as creating a chemistry art display.

If you are interested in Dr. McCormick's work, please make an appointment to speak with him.

Faculty Mentor: **Owen McDougal**
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Overview

My research interests include biomedical research of neurotoxins, properties of biomass fuel briquettes, and organic spectroscopy curriculum development. Students with as little as one year of general chemistry can begin work on the properties of biomass fuel briquettes, those with a full year of organic chemistry can begin work on organic spectroscopy curriculum development, and students with exceptional hands on involvement in instrumentation and a biochemistry background can be trained to work on the biomedical research of neurotoxins.

Biomass Fuel Briquettes

The biomass fuel briquettes that we study are composed of junk mail and yard waste. The ultimate goal of this project is to establish the viability of a household briquette maker that will allow individuals to produce a combustible material from substances that would otherwise go into landfills. We will attempt to prove that the fuel source is safe to use for cooking in a charcoal grill and heating in a conventional wood burning stove. The project uses calorimetry, gravimetric titration, and elemental analysis. The project will investigate emission safety concerns, quantity of particulates, composition of particulates, and the composition of the resultant ash. This endeavor is designed to offer environmentally conscientious students a research project that they can feel good about. Aspects of the project could involve and have in the past community training sessions focused on briquette production at local recycling centers. For further information on this topic please see: Seth Holstein, Richard Stanley, Owen McDougal, *Journal of Chemical Innovation*, "Fuel Briquettes Out of Junk Mail and Yard Wastes," **31**, No. 2, 22-28 (2001).

Organic Spectroscopy Curriculum Development

This project involves the generation of an online resource to facilitate the instruction of organic spectroscopy at undergraduate and graduate institutions. This project will require a computer savvy student that can acquire multidimensional NMR spectra of complex organic and biological molecules to be put into an existing database, interpret the spectra, and generate a web friendly presentation of these data. Additional knowledge in IR and MS are essential. Students pursuing this project will receive extensive hands on use of instrumentation. For more information please see the following two papers: Jonas Buser and Owen McDougal, *The Chemical Educator*, "A Pedagogical Approach to the Instruction of Organic Spectroscopy," Volume 9 Issue 1 (2004) pp 1-4. Aaron Hart and Owen McDougal, *The Chemical Educator*, "Spectroscopic Data Management for the Time-Strapped Educator," Volume 9 Issue 6 (2004) pp 374-377. For additional information, the web site <http://ospecweb.boisestate.edu> is currently active.

Biomedical Research of Neurotoxins

The neuronal nicotinic acetylcholine receptors (nAChRs) are highly sought after targets because of their role in regulating the release of neurotransmitters like dopamine, norepinephrine, glutamate, and acetylcholine. A drug that controls the flow of neurotransmitters through the nAChRs could serve as a treatment to diseases like Alzheimer's, Tourette's syndrome, and Parkinson's. This project focuses on a neurotoxin derived from a snail of the genus *Conus* known as a conotoxin that is subunit specific in its binding to neuronal nAChRs. The three dimensional structure of the

peptide will be determined by NMR derived constraints, pK_a values of key amino acid side chains will be determined by NMR techniques, and modifications will be made to the primary structure of the peptide to establish distance and charge requirements for ligand to receptor binding.

If you are interested in Dr. McDougal's work, please make an appointment to speak with him.

Faculty Mentor: **Julia Oxford**
Area: Biochemistry
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Overview

The research in my laboratory is focused on understanding molecular interactions within the immediate environment of the cell, the extracellular matrix (ECM). These interactions include protein-protein and protein-carbohydrate interactions. The major structural macromolecules of the ECM include collagens, hyaluronic acid and proteoglycans. These components are responsible for the biomechanical and material properties of the tissue. For example, the composition and organization of the ECM determines whether the tissue will be transparent (in the case of cornea) or will be suitable for mineralization (in the case of bone). The expression of components of the ECM is regulated at the DNA level, the mRNA processing level and at the posttranslational level, both temporally and spatially within an organism.

Projects in my laboratory are aimed at understanding molecular interactions that serve to regulate the organization of the molecules of the ECM. We use cartilage and bone as a model system for many of our studies, and the molecule Type XI collagen, which has been shown to play an essential role in the regulation of collagen fibril diameter and proteoglycan retention.

Currently, we are testing the hypothesis that the mechanism of collagen fibril growth involves molecular interactions between a globular amino propeptide domain (Npp) of type XI collagen and other ECM components. Another domain of interest is positioned adjacent to the Npp, and exists in six different forms, determined by alternative splicing of the mRNA. We express the proteins in bacteria and in human embryonic kidney cells and purify them chromatographically. Then, using a variety of biochemical and physical techniques, in collaboration with other researchers, we are working to address the following set of questions:

- Does type XI collagen Npp form a dimer? If so, what are the kinetics of binding?
- What is the structure of the Npp domain?
- Does alternative splicing of the mRNA for type XI collagen alter the function?
- Where are the isoforms of type XI collagen synthesized in an organism?
- Does the p6b isoform bind specifically to chondroitin sulfate?
- Does the p6b isoform play a direct role in the nucleation of calcium phosphate during bone mineralization and in arterial wall mineralization?
- What amino acid residues are important for interaction?
- How do changes in binding relate to normal developmental changes and to changes seen in diseases such as arthritis and in atherosclerosis?

If you are interested in Dr. Oxford's work, please make an appointment to speak with her.

Note that Dr. Oxford is a faculty member in Biology. She is interested in involving chemistry students in her work. Students working with Prof. Oxford may enroll in CHEM 495 and complete the research requirement for graduation in her laboratory.

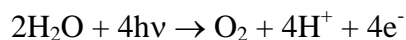
Faculty Mentor: **Jeff Peloquin**
Area: Physical Chemistry
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Phone: 426-1423
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Overview

The core of my research is the application of modern laser spectroscopy to the understanding of the mechanism of transition metal catalyzed reactions, with a specific emphasis on manganese. The lab is equipped with sufficient laser tools to allow the performance of time-resolved absorption, fluorescence and Raman spectroscopies.

Oxygenic Photosynthesis

In order to fix carbon, algae and plants require energy and electrons and they have developed a number of specialized protein complexes and metal active sites to acquire these nutrients. One protein complex, Photosystem II, contains a cluster of four manganese ions that catalyzes the following reaction



Students will use Resonance Raman spectroscopy to observe the various steps of this reaction and characterize the mechanism. Students will also learn the biochemical procedures for isolating the Photosystem II protein complex from spinach.

Green Chemistry

The chemical industry generates an enormous amount of hazardous waste that must be stored or disposed of. In order to lessen the waste's impact on the environment, either the chemical reactions need to be made more efficient or the waste converted to a less harmful form.

Many chemical reactions require strong oxidants or reductants and these reactants themselves are a source of waste. Since many molecules have altered redox chemistry when excited with UV or visible light, we will explore how light absorption can be used to allow the use of less hazardous oxidants or reductants in a number of manganese catalyzed reactions of interest to the chemical industry.

A corollary laser chemistry project will be to explore how excited state manganese complexes can be used to react with hazardous waste and convert the waste to a less harmful form. In addition to characterizing the mechanisms of the reactions, interested students will also have the opportunity to develop a reaction vessel to test if these experiments work on a large scale, outside of the test tube, and may be truly be a viable solution.

If you are interested in Dr. Peloquin's work, please make an appointment to speak with him.

Faculty Mentor: **Dale Russell**
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Overview

1. Electrochemical Sensors for heavy metals, organics and arsenic species.

There is urgent need for field portable analytical instrumentation for the detection and quantitation of chemical species in water. Applications include on site analysis of drinking water, waste and process waters, surface and ground waters. This is an on-going funded project focused on the development of electrochemical sensors for several target analytes including heavy metals such as mercury, uranium, and plutonium, organic contaminants, biologically important molecules such as catechols, and inorganic species such as arsenic ions. Highly selective binding sites are designed for the target analyte, and built into the surface of a semi conductive polymer. This polymer is then incorporated into a sensor suitable for hand held or autonomous operation. For some species, molecularly imprinted polymers (MIPs) are prepared for polyatomic analyte species. Sensors have been demonstrated for water-soluble species of mercury, uranium, thorium and plutonium. A sensor for benzene-like molecules and their metabolites has been demonstrated. Similar devices for detection of other selected VOCs and water soluble species of arsenic are being developed. Designs have been prepared for MIP-based sensors for chemical warfare agents. This multidisciplinary project combines efforts with electrical engineering and materials science departments to build field portable instrumentation for rapid detection of the target analytes.

2. Protein Characterization by Electrical Field Flow Fractionation (EFFF)

About 25 to 30% of the human genome encodes for membrane-bound proteins, yet they have proven difficult to isolate in functional form for study. The conventional methods such as electrophoresis were developed for hydrophilic proteins and do not readily apply to hydrophobic proteins. We have developed and demonstrated non-polar EFFF as a viable means of separating membrane proteins and of characterizing them with respect to size and surface charge. The hypothesis is that a non-polar environment during the separation would conserve the native conformation and enzyme activity. A student working on this project would extract proteins from biological membranes and use EFFF to isolate them. Based on the retention data obtained, charge, size, zeta potential and electrophoretic mobility can be determined for these molecules. A student would also demonstrate that enzyme activity was preserved, subsequent to isolation, by biochemical kinetic experiments.

Requirements for group membership:

C211 and C212 (Analytical Chemistry 1 and Analytical Lab); English Comp. requirement met.

If you are interested in Dr. Russell's work, please make an appointment to speak with her.

Faculty Mentor: **Don Warner**
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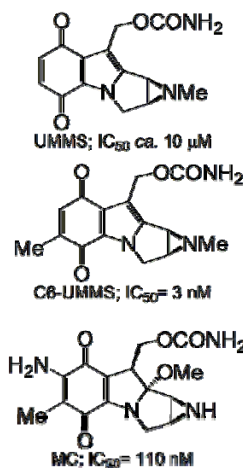
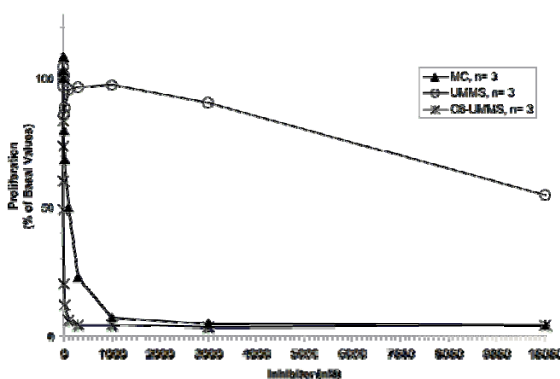
Overview: Students interested in working with me can either gain experience in sophisticated organic laboratory techniques through a bench-top research project, or in chemical education and curriculum development through a library and Internet research project. The experience gained will be relevant to future work in education, graduate school, medical school, chemical industry, or the pharmaceutical industry.

I. Ariziridinomitosenes Synthesis and DNA Binding Properties.

An aziridinomitosenes, a compound related to the clinically used anticancer agent mitomycin C, has recently been shown to form DNA interstrand cross-links under non-reductive conditions. The occurrence of the cross-link is significant for two reasons. First, mitomycin C prohibits cell proliferation via the formation of rare interstrand DNA cross-links. Second, aziridinomitosenes were previously thought to be

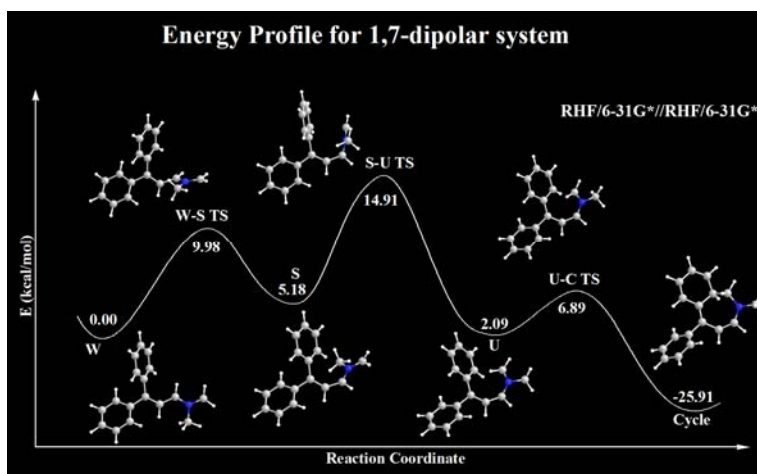
responsible solely for formation of less toxic DNA monoadducts. Several factors may facilitate this previously unobserved cytotoxic event, including the presence of additional electrophilic sites on the quinone ring at C-6 and C-7. Evidence suggests that the C-1 and C-10 electrophilic sites are key to cross-link formation, as is the case with mitomycin C, but the molecular structure of the cross-link is not known. The mechanism of DNA cross-linking by the synthetic aziridinomitosenes is hypothesized to involve monoalkylation of DNA at C-1 followed by nucleophilic attack at C-6 or C-7 of the quinone ring, which in turn activates C-10 for a second alkylation of DNA. Our current research efforts aim to identify the molecular structure of the DNA-aziridinomitosenes interstrand cross-link, determine the role of the four electrophilic sites, and investigate the physical properties required to induce cross-link formation. Specifically, we are currently preparing relevant mitosenes analogs, characterizing mitosenes with respect to physical properties, and are conducting in vitro assessments of DNA alkylation by mitosenes derivatives.

[³H]-Thymidine Uptake in HL-60 Cells



II. Synthetic and Computational Investigations of Electrocyclization and Cycloaddition Reactions of Azomethine Ylides.

Electrocyclization and cycloaddition of azomethine ylides and azaallyl anions offer potential for regio- and stereocontrolled formation of azacycles. Thus, these reactive



intermediates have been investigated computationally. Specifically, we have studied the properties of conjugated azomethine ylide and azaallyl anion systems that are theoretically capable of undergoing disrotatory electrocyclization due to their six pi electrons. As ring closure is dependent on the geometry of the intermediates, a computational study of conformer energies and interconversion energy barriers has been conducted. Initial studies suggest that intermediates substituted at the four position favor the U-geometry required for electrocyclization. Further calculations indicate that added steric hindrance at this position gives increased bias toward the U conformer while simultaneously lowering the activation energy required for electrocyclization. Related studies have examined the structural properties that facilitate spontaneous ring opening of 4-oxazolines to produce stabilized azomethine ylides.

If you are interested in Dr. Warner's work, please make an appointment to speak with him.