Welcome to the Undergraduate Research Program at Trinity University’s Department of Chemistry! The Chemistry and Biochemistry faculty takes great pride in being one of the top undergraduate programs in the country. This informational packet serves as a brief introduction to the undergraduate research opportunities available in our department. The general information is directed towards current Trinity students, high school students looking at potential colleges, and local high school students interested in research opportunities. Any faculty member would be glad to discuss the program and individual research topics. Please do not hesitate to contact us by email; contact information can be found at:

http://new.trinity.edu/academics/departments/chemistry/faculty-staff

**Program Scope**
The chemistry department has seven research-active faculty members representing all of the major disciplines of chemistry (Analytical, Biochemistry, Inorganic, Organic and Physical). These professors run externally funded research programs that provide undergraduate chemistry and biochemistry students opportunities to work closely with professors on cutting-edge projects using state-of-the-art research equipment, publish their research in the top journals in our fields, and present their research at major conferences. Faculty members have laboratory space in the Center for the Sciences and Engineering, and many faculty members collaborate with groups at major research institutions and national laboratories. Departmental instructional facilities (see list of major equipment on our website) are also utilized by faculty research groups, particularly during the summer research program. Increasingly, chemistry and biochemistry projects are at the interface of traditional research disciplines, particularly with biology, applied physics, and engineering. We have developed a number of collaborations between various research groups at Trinity, and there are numerous non-chemistry majors in our research program.

The strength of our program is evidenced by the external funding that the faculty has successfully attracted. Over the period 2007-2016, the chemistry faculty managed an average of $1.2 Million per year in active, externally funded grants from the Beckman Foundation, the National Science Foundation, the National Institutes of Health, the Robert A. Welch Foundation, the Camille and Henry Dreyfus Foundation, Research Corporation for Science Advancement, the Keck Foundation, the American Chemical Society, and the San Antonio Area Foundation. These funds help to support summer stipends for undergraduate and high school students, major research equipment, research supplies, instructional equipment, and salaries for technicians and postdoctoral research associates. The Department also participates in several inter-departmental initiatives, which have provided substantial funding for equipment and student stipends over the last several years. Our research generates scientific publications with student co-authors, far more per faculty member than the national average for undergraduate institutions.

Summer Research Program

Instead of teaching courses during the summer term, the Chemistry department is focused entirely on research with students using all laboratories, facilities, and equipment. In 2018, faculty and departmental grants supported 37 undergraduate students for the 10-week summer program. This makes our program one of the largest chemistry summer undergraduate research programs in the country. All summer research students receive a summer stipend (approx. $4000); Trinity University also covers the dormitory costs for summer research students.

One of the hallmarks of our program is its accessibility to students early on in college. In 2018, more than half of the students had just completed their first or second years of college. Faculty have extensive experience in developing projects that are appropriate for students in their first year of college. The application process starts in January, and the program runs from mid-May to the end of July.

Research During the Semester

Research opportunities are also available for course credit or on a volunteer basis during the semester. Professors generally expect about 6 hours of work in and out of the lab per week for one hour of credit. Students are asked to talk with at least 3 faculty members to discuss research opportunities before being admitted into a research group.

Research Areas

The following pages give brief summaries of the areas of research under active investigation by our faculty. If you have questions about the opportunities in specific research groups, please do not hesitate to contact any of our faculty. We would enjoy the opportunity to share with you more information about our programs and our department. For questions about the summer research program, please contact our Summer Research Program Coordinators, Drs. Corina Maeder (cmaeder@trinity.edu) and Jason Shearer (Jason.shearer@trinity.edu).
Fundamental Laboratory Studies of Microenvironments

The Davis Research Group utilizes elements of chemistry, physics, engineering, and computer science to develop advanced analytical techniques to study the unique properties of microenvironments and address science questions relevant to atmospheric chemistry, sustainability, climate, human health and indoor air quality. Microenvironments are ubiquitous in nature and science. Examples include biological cells and atmospheric aerosols. Understanding the chemistry and physics occurring in these small, isolated compartments is essential to understanding human health and global climate, among other things. From the sea to the atmosphere to our bodies, these microscopic environments influence our daily lives in ways yet to be understood. Our research aims to increase our understanding of micro-environmental properties to increase our understanding of the world and how we can improve it. In the Davis Research Group, there will be ample opportunities for students to develop instrumental techniques (such as that shown at right), design and build control electronics, write and develop software, perform experiments, process data, and present their work through presentations and publications.

Currently, there are several ongoing research directions.

1. **Marine polymer self-assembly in the atmosphere:** Marine polysaccharides are known to self-assemble into ordered aggregates, such as polymer gels, at the ocean surface. Recently, marine polymer gels have also been observed in cloud/fog droplets. Due to their dense, compact nature, self-assembled gels in atmospheric particles are speculated to change the microstructural properties and chemical reactivity of that particle. However, these points remain largely unexplored. One initial project within my research group will study self-assembly of polymer material under the complex conditions relevant to the atmosphere, thus advancing fundamental physical chemistry knowledge and constraining important properties relevant to atmospheric science in terms of understanding air quality and climate.

2. **Going beyond the beaker: production of ROS in microdroplets:** To date, bridging the gap between atmospheric models and atmospheric observations has proven difficult. This difficulty is largely due to the extreme chemical complexity of atmospheric particles and the unique but poorly understood properties of microenvironments. In the Davis Research Group, there are opportunities to study how these unique microdroplet properties lead to unique chemistry that cannot be replicated through “beaker synthesis”. One example includes studying the production of reactive oxygen species (ROS), including hydroxyl radical production under atmospheric conditions, as shown in image to the right.

3. **Indoor air quality:** We spend the majority of our time inside a building. However, less is known about indoor air chemistry than the chemistry occurring in the outdoor environment. A recent research push has led to an explosion of information about indoor air quality, but there is much research to be done. In the Davis Research Group, there will be opportunities to pursue research related to indoor air quality in the workspace, studying the types of particulate generated under “blue-collar” labor conditions.

More details on the Davis Research Group can be found at https://sites.trinity.edu/davis-lab.
Research in the Hunsicker-Wang laboratory will focus on studying enzymes that utilize or bind metal ions, called metalloproteins. There are two major areas of interest: iron-sulfur cluster enzymes and cytochrome oxidase proteins.

Iron-sulfur proteins make up ~30% of all metalloproteins. These proteins utilize iron and sulfur atoms that are organized into clusters. These proteins are often involved in electron transfer reactions. Specifically, the Rieske protein, which is part of Complex III in the respiratory chain, contains a [2Fe-2S] cluster, which is ligated to the protein via 2 cysteine and 2 histidine residues. The reduction potential of this protein depends on the organism and the type of system that it was derived from. Previous studies have shown that the number of hydrogen bonds to the cluster, the solvent accessibility, and the type of charge residues near the cluster all affect the reduction potential. Research on this protein involves making site-specific mutations, purifying, crystallizing and solving the structure of the mutant enzymes. The reduction potentials of these mutants are also evaluated. This protein is also be chemically modified with reagents that alter the properties of specific amino acids. This approach allows a greater variety of chemical properties to explore. Chemical modification also allows study of how individual amino acids contribute to the electron transport function within the protein.

Reactive oxygen species (ROS) are destructive and form from the reduction of molecular oxygen. One hypothesis is that a mismatch in the potential of the Rieske protein with its partners within Complex III leads to the production of ROS and may lead to neurodegenerative diseases. This hypothesis is starting to be explored in the Hunsicker-Wang lab.

Cytochrome oxidase is complex IV in the respiratory system. Within this protein, there are 4 metal sites, 2 heme-iron sites and 2 copper binding sites. One of the copper sites is the CuA center, found in subunit II of cytochrome oxidase. This center may also be involved in H+ translocation within cytochrome oxidase. Subunit II can be expressed as an isolated protein. The Hunsicker-Wang lab is exploring how the histidines in this protein may function to pump H+ using chemical modification and site-directed mutagenesis. Additionally, the lab is also studying how the copper ions are incorporated into CuA when cytochrome oxidase is assembled. The protein, Sco, is thought to be involved in the process but its exact role is not well-defined. Thus, studies are aimed at understanding what role(s) that Sco plays in the assembly of the CuA site.
Research in the Maeder Lab centers on understanding the mechanisms involved in gene expression, specifically that of pre-messenger RNA splicing. In eukaryotes, initially, RNA transcribed from DNA may have intervening non-protein coding sequences, or introns. These sequences must be removed for accurate protein translation. The removal of these introns must be precisely coordinated to avoid inaccuracies that can result in many diseases, including cancer and retinitis pigmentosa. This process is known as pre-messenger RNA splicing.

A large macromolecular complex of RNA and proteins called the spliceosome facilitates splicing. The mechanism of pre-mRNA splicing involves large-scale rearrangements of protein-RNA complexes, which must be regulated to ensure both splicing timing and accuracy. Our research focuses on understanding these large-scale rearrangements within the spliceosome. The spliceosome is composed of five small nuclear ribonucleoprotein complexes (snRNPs). Dynamic rearrangements occur both within and between the snRNPs during the splicing cycle. These rearrangements are indicators that splicing is proceeding accurately. Our research aims to dissect the molecular interactions that stimulate spliceosome assembly and activation. Specifically, we are currently focused on the role of the Dib1 protein and its interactions in regulating these rearrangements. Dib1 is essential for cell viability and splicing and is conserved from yeast to humans. Dib1 (Figure 1) is a small protein with a thioredoxin-like fold and little is known about its function. Using site-directed mutagenesis and yeast growth assays, we have identified amino acids that are important for splicing. We are now trying to characterize the protein using biochemical and molecular biology techniques in order to understand the importance of these amino acids in splicing. For example, a change to an amino acid in the core of protein may cause the protein to be less stable overall, while a change to a amino acid in an external loop may be important for interactions with binding partners. Our works aims to determine the function of Dib1 through this characterization and whether it might be involved in the regulation of spliceosome assembly directly or indirectly.

Our studies on the spliceosome are quite interdisciplinary. In our lab, we use a variety of biochemical, molecular biological, and genetics techniques to dissect the importance of protein-nucleic acid and protein-protein interactions in the spliceosome. Students have opportunity to perform: 1) biochemistry assays, including gel based kinetic unwinding assays, binding assays for protein-RNA and protein-protein interactions, and structural studies using circular dichroism, 2) molecular biology, including protein purifications, DNA cloning, and RNA transcription and purification and 3) genetic assays using *Saccharomyces cerevisiae* (Baker’s yeast) including gene deletion, tetrad analysis and growth assays. In addition, we have a collaborative project with Dr. Kelvin Cheng in Physics in which students perform computational modeling studies on the spliceosome. These theoretical studies inform and parallel our experimental studies.
You probably know that a catalyst speeds up a reaction but is not consumed like a reactant is. Heterogeneous catalysts are solid materials that perform chemical reactions – essentially, the molecules stick to the catalyst surface from the liquid or gas phase. The surface then allows them to react via pathways (i.e. mechanisms) that aren’t available in solution (or in the gas phase). Heterogeneous catalysts are by far the most important industrial catalysts (petroleum refining, emissions control, fine chemicals production). They are also key components to many developing technologies, such as solar energy conversion and fuel cells. This makes catalysis one of the most important technologies in industrial chemistry, and means that future catalytic chemistries will be important parts of solutions to our most urgent societal and environmental needs for decades to come.

The Chandler group studies the art and science of supported nanoparticle catalysts, which are one of the most common classes of heterogeneous catalysts. These materials typically consist of a high surface area oxide (the support) that has metal nanoparticles (NPs) spread across the surface. The NPs are typically 1-10 nm in diameter, or roughly 100 to 100,000 atoms. We are currently focused on Au catalysts, especially understanding reaction mechanisms over Au particles and learning to tune the unique chemistry of Au by incorporating other metals.

Some of the art comes in learning to prepare metal NPs in solution. We try to control how metal atoms assemble in solution so that we can control the structure and properties of the catalyst. In the picture above, we would like to control the number and types of atoms (pink vs. gray balls) on the surface of the metal particle. These particles can then be deposited onto a metal oxide support and the stabilizing molecules (which are added to control the synthesis) can be removed.

For the science, we are interested in studying what factors influence the reactivity of metal nanoparticles, how we can control them, and how we can use that knowledge to develop new reactions. We spend a lot of time trying to understand reaction mechanisms on catalysts and developing tools for using kinetics (especially biochemical kinetic tools) to probe catalyst properties. Mechanistic studies require kinetics studies, so there are always projects for students who are interested in learning about how molecules react and how we figure that out. We investigate many different types of reactions, including hydrogenations and oxidations, and are especially interested in the role that water can play as a co-catalyst. It turns out that, just like in organic chemistry, in heterogeneous catalysis, proton transfers can play important roles in reaction mechanisms – we are currently working to better understand the role of protons in heterogeneous catalysis and are using our findings to think about new reactions.
Research in the Shearer Group is broadly centered on understanding how the electronic structure of biologically and industrially relevant transition metal species contribute to their reactivity and physical properties. Central to our work is the synergistic use of synthetic, spectroscopic and computational chemistry. Although we perform some work with naturally occurring biological systems or industrial catalysts, we primarily study synthetic mimics of these systems to probe a specific aspect of their chemistry. Briefly outlined below are two projects currently being undertaken by the Shearer Group.

1. **Probing Nickel Containing Superoxide Dismutase.** Nickel containing superoxide dismutase (NiSOD) catalyzes the conversion of highly toxic superoxide (O$_2^-$) into dioxygen and hydrogen peroxide by making use of a Ni$^{II}$/Ni$^{III}$ redox couple. In the reduced Ni$^{II}$ oxidation state the nickel-site is contained in a distorted square planar NiN$_2$S$_2$ coordination environment with ligands derived from Cys2, Cys6, the N-terminal amine nitrogen and an amide nitrogen from Cys2. An unusual feature of the NiSOD active site that we have been probing is the fact that one of the coordinated Cys sulfur ligands is protonated, forming a Ni-S(H$^+$)-Cys moiety. A number of roles for this moiety can be envisioned; our hypothesis is that protonation of the Cys sulfur ligand poises the nickel site for reactivity. We postulate that protonation raises the energy of orbitals that are predominantly nickel in character allowing for electron transfer from Ni$^{II}$ to O$_2^-$, thus generating O$_2^{2-}$ (peroxide) and Ni$^{III}$. To test this hypothesis, we are preparing a number of metallopeptide based mimics of NiSOD along with small transition metal complexes that can support reversible Ni-S(H$^+$)-Cys formation. By spectroscopically examining the influence of sulfur protonation in such mimics, we seek to understand the role(s) of the Ni-S(H$^+$)-Cys moiety in NiSOD reactivity, and Ni-S-R containing compounds in general.

2. **Metalloprotein Redesign.** The repurposing of proteins and enzymes by organisms is a key evolutionary mechanism; through random changes to existing biological scaffolds an organism can generate new proteins with new functions. Biological chemists apply this strategy to the redesign of proteins with new and novel functions wherein a large library of random mutants is generated, screened, and refined over multiple generations. One can also apply a rational redesign strategy, wherein knowledge concerning protein folding and structure is applied towards creating specific protein scaffolds with desirable functions. We are currently redesigning small metalloproteins that are synthetically accessible. Use of synthetic methods allows us to screen proteins in a reasonably rapid manner. Also, we can incorporate unnatural amino-acids into the protein scaffold, which can impart unique attributes to the resulting system. For example, initial calculations suggest we can alter a zinc finger protein, which contains a structural zinc center, into a blue-copper like protein, which transfers electrons. To ligate Cu within this scaffold unnatural and $d$-amino acids need to be incorporated into the protein sequence. Substitution of Cu with Ni is predicted to generate a metalloenzyme that can perform organometallic transformations under biologically relevant conditions.
Chemical Synthesis, Bioorganic Chemistry and Chemical Biology

Research in the Cooley lab spans the interface of chemistry and biology. I believe strongly in the power of synthetic organic chemistry to access new approaches to solve problems. Students in my lab will have the opportunity to design and synthesize new molecules and assess their ability to detect and treat human disease under the following two major project areas.

The first project describes a new strategy to amplify molecular signals as a way to detect biomolecular interactions and potentially, disease. We have developed fluorogenic monomers that are not fluorescent in monomer form, but glow when incorporated into a polymer by atom transfer radical polymerization (ATRP, see figure). The fluorescence is quantifiable by fluorescence readers or visible to the naked eye. We are designing new monomers to improve their water solubility, optimizing our fluorogenic polymerization for detection applications, and working on the direct detection of proteins and biomolecular interactions. Students in this sub-group synthesize molecules, run polymerization reactions, and analyze the polymers formed by NMR and other polymer and fluorescence analysis techniques.

The second project is generally in the field of drug delivery and prodrug synthesis and evaluation. A prodrug is a “caged” version of a drug that is inactive until release to the free drug is achieved under specific biological conditions. We are developing prodrugs for AA 147, a molecule that activates a stress-responsive signaling pathway that could be particularly helpful for treatment after reperfusion injury, where blood flow is lost and then restored, such as occurs during heart attacks and strokes. We are synthesizing prodrug versions of AA 147 that are selectively uncaged by the presence of reactive oxygen species (ROS), which occur at high levels during reperfusion events. We are also exploring other types of releaseable AA 147 prodrugs to improve pharmacodynamics properties for in vivo animal studies. Students on this project design and synthesize prodrug conjugates, examine their stability and release kinetics to free drug in the presence of ROS such as hydrogen peroxide, and work with collaborators to evaluate their biological potential for disease treatment.
Amber is the fossilized end product of resinous materials exuded by plants millions of years ago (Figure 1). It is found on every continent except Antarctica. There are at least five chemically distinct types of amber, depending on the botanical material from which the original exudate came from. Nuclear magnetic resonance (NMR) spectroscopy can distinguish these different botanical sources and provide a means of determining authenticity of amber and learning about its geographical sources.

More generally, exudates are complex mixtures of organic compounds produced by plants, usually as the result of injury or disease. Secreted as liquids, exudates may harden to solids in hours to months (Figure 2) on the surface of the plant. These materials have found numerous practical applications throughout human history, and they provide a molecular window to the classification of plants (taxonomy). We have found that exudates are remarkably robust and consistent in their molecular constitution within a single plant and from plant to plant within a given species. There are several, distinct chemical constitutions of exudates. Resins, which can form amber through fossilization, are composed of terpenoid compounds. Gums are made of polysaccharides. Gum resins like frankincense and myrrh contain both materials. Kinos contain phenols. Although these four chemical groups are the largest, there are several other smaller but distinct chemical groups,

We are carrying out a worldwide survey of plant exudates from all plant families, and of amber, necessitating field acquisition of materials and analysis by NMR in the lab. We also are examining the effect of heat on the molecular structure of amber and its slightly younger colleague, copal. Heat has been used to alter the properties of amber prior to carving. Spectroscopic examination of artificially heated samples may clarify how structure change with heating.
Dr. Adam R. Urbach  
Bio-Organic and Supramolecular Chemistry

The chemistry of pharmaceuticals and medical diagnostics requires the ability to find a specific protein in a complex mixture, such as blood, and stick to it. Pharmaceuticals block the normal function of that protein. Medical diagnostics measure the quantity of that protein. The Urbach group develops new approaches to the “recognition” of specific proteins that are predictable from their sequences of amino acids (which are often known), and we develop applications of this science. Students are involved in every aspect of the work, including experimental design and implementation, problem solving, data analysis, and communication of the work through presentations and publications.

Students in the Urbach research group learn a range of techniques, which can include: 1) organic synthesis to make peptides and other small molecules; 2) material synthesis; 2) protein expression and purification using molecular biology techniques; 3) protein semi-synthesis; 3) NMR spectroscopy, mass spectrometry, and X-ray crystallography to characterize molecular structure; 3) microcalorimetry, stopped-flow spectroscopy, and gel electrophoresis to measure the thermodynamics and kinetics of interaction; and 4) UV-visible, fluorescence, and circular dichroism spectroscopy to study electronic and structural properties. This combination of methods and approaches offers students a breadth of technique and depth of study that is an excellent foundation for further study in organic chemistry, biophysical chemistry, medicinal chemistry, biochemistry, bioengineering, and biotechnology.

Current projects are focused in several areas: 1) Continuing to improve our ability to recognize proteins and proteins on the basis of their amino acid sequences. Our discoveries have established new rules for predictive protein recognition (Figure below), and we are currently working to expand the range of proteins that are accessible by our compounds, to target proteins in complex mixtures, and to increase the strength and selectivity of interaction. 2) Developing new approaches to recognizing biological molecules at very low concentrations. In living systems, many molecules of interest are present at vanishingly small concentrations. These targets are only accessible using receptors that can bind to them very strongly, and we are developing fundamentally new methods to ultra-strong binding. 3) Developing new approaches to drug formulation. We are currently exploring an approach to formulating small molecule and protein drugs and controlling their release over long time scales (long-acting drugs).

The image at left shows an experimentally determined, high-resolution structure of our receptor, Q7 (the cyclic molecule that looks like a cage), binding to human insulin (the ribbon molecule). This is the first synthetic receptor for insulin, and it is extraordinarily selective for insulin versus other proteins, even in human serum. This structure confirms our hypothesis that binding occurs at a specific amino acid residue, the terminal phenylalanine ($\text{Phe}^{\text{B1}}$, which fits inside the cage). A Trinity student in his first year of college grew the crystal of the complex shown at left, which was crucial for determining its structure. (*Journal of the American Chemical Society*, **2011**, *133*, 8810-8813).
Physical and Chemical Properties of Nanoparticle Metal Catalysts

Fundamental studies of the unique physical and chemical properties of metal nanoparticle catalysts are an important area of scientific research. An important aspect of these catalysts concerns the interaction of the metal nanoparticles with the underlying support. This is especially true for reducible metal oxide supports. The literature contains a number of examples that demonstrate how electronic metal – support interactions (EMSI) between metal nanoparticles and the support material are very important as they control electronic transfer and catalytic transformations that occur at the catalytic active site.

Understanding the mechanisms that control charge transfer and the activation of reactive species at specific sites can therefore aid in the design of more efficient and selective catalysts. Research in our laboratory therefore concerns fundamental EMSI studies examining adsorbate-induced charge transfer: from adsorbate to metal nanoparticle to the support.

Previously students in our laboratory discovered that chemisorption of carbon monoxide on the gold nanoparticles causes electronic transfer from the gold to the titania support, leading to the reduction of the titania. This caused the transmission of infrared light through the catalyst to decrease (due to light scattering) as the surface of the titania roughened.

More recently students discovered the same phenomena with the adsorption of hydrogen on gold catalysts. Through systematic laboratory experimentation utilizing infrared spectroscopy, we will be conducting a thorough investigation of this interesting metal-to-support electronic interaction. This work will provide a greater understanding of catalytic reactions involving hydrogen, along with a better understanding of the importance of metal – support electronic interactions in gold catalysts.

Our research goals are: (1) to provide a deeper understanding of electronic metal – support interactions for these catalysts; and (2) to develop greater knowledge of the mechanism associated with hydrogen adsorption and dissociation, including hydrogen spillover. The ultimate outcome of these studies will be the further development of our understanding of metal nanoparticle catalysts.