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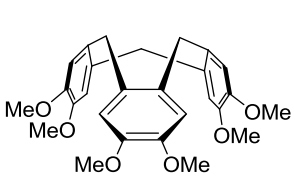
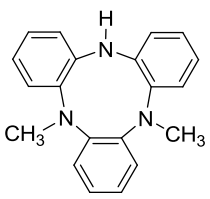
Loyola University Chicago -Research Experience for Undergraduates
Faculty Mentor List – Summer 2013

Miguel Ballicora: Regulation of Starch Synthesis - The ADP-glucose pyrophosphorylase (ADP-Glc PPase) is a regulatory enzyme that controls the synthesis of bacterial glycogen and starch in plants. Most of the bacterial forms are homotetramers, whereas the plant enzymes comprise two types of homologous but distinct subunits. The S subunit is generally catalytic; but some of the L subunits are not and play a regulatory role. L subunits in different plant tissues confer distinct allosteric properties. The wheat endosperm ADP-Glc PPase is active in absence of effectors, in contrast with all other ADP-Glc PPases. The REU student will study why it has these particular properties and what area of the protein is responsible. The S and L subunit genes will be synthesized for an optimized expression of the recombinant wheat enzyme in *E. coli*. Hybrid heterotetramers between the potato tuber S subunit and the wheat endosperm L subunit and vice versa will reveal whether the L subunit had the ability to confer the unique properties to the enzyme. Finally, chimeric constructs between the wheat endosperm and the potato tuber L subunits would reveal the areas responsible for these unique properties. A work with similar techniques in which an undergraduate student participated was already successful (Kuhn, et al., (2009) *J. Biol. Chem*. *in press*).

Daniel Becker: Supramolecular Synthesis - The goal of the research for the REU student is the study and further development of our newly-prepared supramolecular bowl-shaped molecule tribenzo-1,4,7-triazacyclononene (N3-CTV, see *J. Org. Chem.* **2010**, *75*, 7887-7892). This supramolecular scaffold can function as a host in host-guest interactions and also as a tridentate ligand for transition metals, and has applications in analytical detection, materials science, synthetic receptor design, catalysis, liquid crystals, and drug delivery. N3-CTV is prepared via sequential Pd-catalyzed couplings, and the primary goal for the REU student will be to elaborate this scaffold with substituents utilizing standard synthetic organic reactions including electrophilic aromatic substitution to "deepen" the pocket to enhance N3-CTV's ability to complex with other guest molecules. Research activities will include performing synthetic organic reactions, workups and chromatographic purifications, and analysis by NMR, IR and MS.



CTV



N3-CTV (dimethyl)

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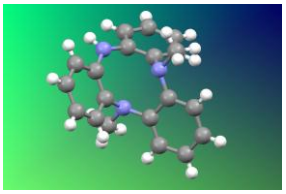
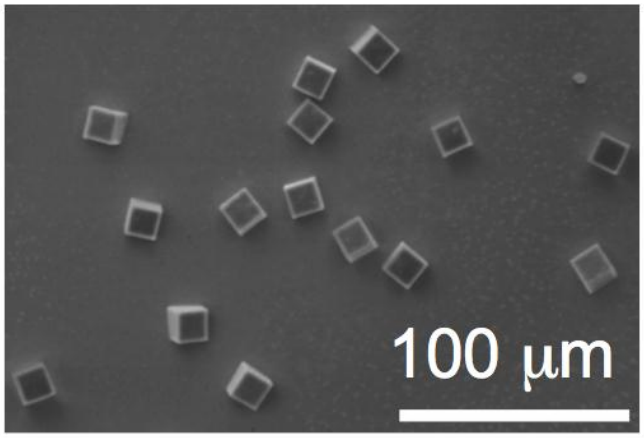

N3-CTV (dimethyl)
X-ray Crystal Structure

M. Paul Chiarelli: Identification of Unknown Pollutants using Tandem Mass Spectrometry – The lack of safe drinking water is believed to be leading cause of death and disease throughout the world. Recently there has been concern about the presence of a new class pollutants derived from personal care products, pharmaceuticals, and illicit drugs that may survive the water treatment process. Compounds such as these have the potential to exert adverse environmental and human health effects at low concentrations due to their pharmacological activity. We will analyze water samples taken from a variety of sources (e.g., Lake Michigan and the Chicago River) using tandem quadrupole spectrometry to identify new pollutants. Constant neutral loss and precursor ion scans are used to identify potential pollutants by detecting only those molecules with structural features that are suggestive of potential toxicity. Students who participate in this project will have an active role in water sampling, extraction, and analysis using LC/MS/MS methods.

Jacob W. Ciszek: Monolayer Based Control of MOF Nanoparticle Assembly onto Surfaces – Applications for metal organic framework requires interfacing this exciting material with surfaces. For some applications (solar cells, gas separation membranes) this must be done in a highly precise manner. We are studying how nanometer seeds of these materials can be attached to a surface with a high degree of control over density and orientation through the chemistry of a single molecule thick layer which coats the surface (monolayer). The REU student will be trained with a scanning electron microscope (right), monolayer preparation, and MOF synthesis and then quantify how subtle changes in the monolayer terminus impacts adhesion characteristics.



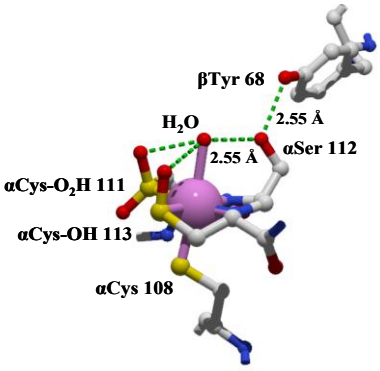
David Crumrine: New Dye-Complexes for Photodynamic Therapy
We have been attaching dyes to folate and other targeting molecules as potential improved photodynamic therapy (PDT) anticancer agents. Preliminary work was done on several neuropeptides from the FMRFamide series and was published. We have found that linking the dyes to cross-linked hemoglobins reduced the efficiency of singlet oxygen production, which means that the resultant molecules will be less active as PDT agents. We are analyzing this effect to improve the singlet oxygen production and to bring more oxygen into hypoxic tumors. We are also exploring new ways to modify the dyes to attach them directly to targeting agents such as folate. REU students working on this project will make new dye-folate complexes and test the mechanism of decreased singlet oxygen production in the presence of hemoglobin.

Patrick Daubenmire: POGIL General Chemistry and The Toulmin Model of Argumentation – Process Oriented Guided Inquiry Learning (POGIL) is a teaching and learning strategy used for general chemistry. It presents an initial model, information, or set of data. Students are then guided in building a conceptual understanding around this information through specific critical questions. The "invented" concepts are then applied to new problems as a way to revise or refine one's understanding. During class sessions students work in cooperative groups and build consensus in their analysis of the information and the subsequent "invented" concepts. Students' interactions during POGIL instruction have been observed and coded into into phases and bridges that characterize students' learning. Further research is necessary to assess to what degree these phases and bridges align with the Toulmin model of argumentation and what, if any, unique features of student interactions and learning might be explained by the phases and bridges model. The REU student would be involved in the analysis of videotape segments of student interactions in order to develop coding schemes and alignment measures between the phase and bridge and the Toulmin models.

Chad Eichman: A Biomimetic Approach to Chemical Synthesis - The biosynthesis of small organic molecules inspires chemists to create novel methodologies that mimic these natural processes. A biomimetic approach to create new bonds in organic molecules represents a challenging field in chemical synthesis because it is often very difficult to recreate enzymatic processes with high efficiency and selectivity. The goal of this REU project is to investigate new organocatalysts that promote the biomimetic construction of pharmaceutically important molecules. Hypervalent iodine catalysts are capable of dearomatizing phenols and allowing for nucleophilic attack onto the aromatic ring. This polarity reversal allows for the assembly of complex molecular architectures (see: *Angew. Chem. Int. Ed.* **2011**, *50*, 4068). Nature constructs a subset of bioactive molecules through two oxidative dearomatizations, however, performing these reactions in the laboratory setting has never been explored. The REU student will examine new hypervalent iodine catalysts for these biomimetic transformations. Through selected catalyst design, we can begin to uncover the required reaction conditions that mimic the enzymatic processes. The student will develop skills in organic synthesis, catalytic reactions, compound purification, and spectroscopic characterization.

Alanah Fitch: Electron Transfer in Clays – The REU students will use clay-modified electrodes to study transport and clay redox phenomena in thin clay films. Most of my recent work is in the area of $Ru(bpy)_3^{2+}$ impregnated clay films observed at electroactive planar wave guides. Results from that project indicate that the macroscopic structure of clay films can be controlled by a photoelectrochemical back side trigger. The REU students will be involved in microbial reduction of clays as investigated at planar waveguides; elucidation of the mechanism of the reaction of mediator anthraquinone 2-6 disulfonate with iron containing minerals; and the effect of clays on the kinetics of electron transfer coupled to proton transfer of quinone type species.

Richard Holz: Mechanistic Studies on Co- and Fe-type Nitrile Hydration Catalysts - Nitriles are used extensively to produce a broad number of specialty chemicals containing amines, amides, amidines, carboxylic acids, esters, aldehydes, ketones, and heterocyclic compounds. These compounds are used in a wide array of chemical reactions as feedstock for the production of solvents, extractants, pharmaceuticals, pesticides, and polymers. However, the harsh industrial conditions needed to hydrolyze nitriles to their corresponding amides, are often incompatible with the sensitive structures of many industrially and synthetically relevant compounds. Nitrile hydratases (NHase, EC 4.2.1.84) are enzymes in the nitrile degradation pathway that catalyze the hydration of nitriles to their corresponding amide under ambient pressures and temperatures at physiological pH. NHases have attracted substantial interest as biocatalysts in preparative organic chemistry and NHase containing bacteria have found some industrial applications in the large scale production of acrylamide and nicotinamide. However, little is understood about how NHases function. The goal of our research is to develop a fundamental understanding of the reaction mechanism of NHases. The REU student will use an interdisciplinary approach that incorporates kinetic, spectroscopic, biochemical, and X-ray crystallographic methods. The proposed project will benefit society by facilitating a more intelligent design and manufacture of nitrile based chiral pharmaceuticals and industrially important specialty chemicals such as acrylamide and nicotinamide. These studies will also provide insight into the development of more efficient and specific bioremediation methods for contaminated environments.



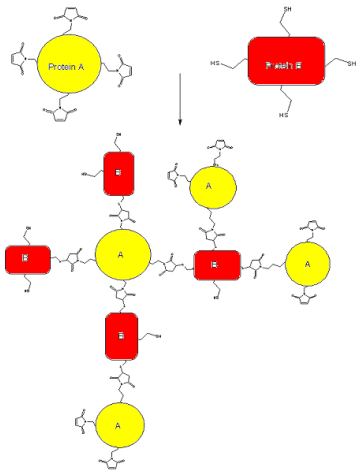
Active site of NHase from *P. thermophilia* (1IRE). Trivalent cobalt ion is six-coordinate with three cysteine sulfurs, two amide nitrogens and a water molecule.

Dan Killelea: STM studies of subsurface chemistry – Scanning tunneling microscopy (STM) provides the ultimate in spatial resolution, where images of individual atoms and molecules are obtained to follow each participant in a reaction as they occur. Reactions that are otherwise highly improbable in the gas-phase readily occur in the presence of a metal surface. Key questions remain as to the nature of the increased reactivity. The structure of the metal surface alone (i.e. defects) does not adequately describe observed reactivity. Atoms dissolved in the bulk of the metal, or subsurface atoms, are a source of non-equilibrium, energetic reagents. For example, alkenes are hydrogenated fully to alkanes over Pd surfaces with subsurface H, but when only surface H is available, the hydrogenation stops at the alkene. Current work in the Killelea lab focuses on using STM to determine the dynamics and kinetics of subsurface atomic species like H or O as they move to and from the surface of the metal. These studies will provide a foundation for developing methods to harness these powerful subsurface species in new synthetic approaches.

Dali Liu: Quorum Quenching Hydrolases - Through studying quorum-quenching *N*-acyl homoserine lactone hydrolases (AHL lactonases), we hope to discover new strategies to combat infectious diseases both in humans and plants. Quorum sensing

(QS) or "bacterial cell-to-cell communication based on population density" is widely employed to regulate the communal behaviors of bacteria including their pathogenesis. AHL lactonases are zinc dependent enzymes that can subvert the QS pathways (also known as quorum quenching) by degrading AHL-type QS signals. These enzymes have drawn considerable attention because of the potential applications in combating persistent infections. The REU student will employ methods in mechanistic enzymology, protein crystallography and microbiology to achieve a thorough understanding on these hydrolytic enzymes, including their catalytic mechanisms, protein dynamics and biological functions. In addition, based on the evolutionary connection between AHL lactonases and other metallohydrolases such as lactamases and phosphotriesterases, the student will conduct directed-evolution to generate other hydrolytic activity from lactonase.

Duarte Mota de Freitas: Biophysical Studies of Li^+ and Mg^{2+} Interactions with G-proteins: Implications for Bipolar Disorder. Lithium salts are used for the treatment of bipolar (manic-depressive) patients. The mechanism of the pharmacological action of Li^+ is not well understood at the molecular level. An attractive theory involving guanine nucleotide-binding (G-) proteins has been proposed based on the inhibition by Li^+ of G-proteins, with either stimulatory (G_s) or inhibitory (G_i) functions. Our hypothesis is that competition between Li^+ and Mg^{2+} bound to G-proteins may constitute the basis for the pharmacological action of Li^+. Current areas of interest in our group involve the application of fluorescence, and circular dichroism (CD) to the investigation of the protein interactions with Li^+ and Mg^{2+} and their effect on protein folding and stability. The REU student will conduct probe G-protein denaturation using fluorescence and CD. The goal of these studies is to understand the relative stabilities of wild-type and mutants of G_s and $G_{i\alpha1}$ in all conformations, i.e., the GDP-bound (inactive) form, the GTP-bound (active) conformation and the transition state analog conformation, GDP.AlF_4^- bound state. In addition to gaining experience on biological applications of fluorescence spectroscopy and CD, the REU student will learn several biochemical methods (cell culture, purification of proteins by nickel affinity chromatography and HPLC, site-directed mutagenesis, etc.).



Ken Olsen: Synthesis and Characterization of an Improved Hemoglobin Polymer - The search for a safer blood substitute has resulted in the identification of properties that are needed to minimize previously encountered side-effects with hemoglobin (Hb)-based blood substitutes. These properties include increased molecular weight to minimize vasoconstriction and incorporation of antioxidant enzymes, such as catalase and superoxide dismutase (SOD), to decrease reperfusion injury. The REU student will synthesize a Hb-based polymer (B in diagram) containing antioxidant enzymes (A in diagram), using complementary chemistry between maleimide and sulfhydryl groups. The REU student will measure the molecular weight range of the Hb-polymers and the polymers containing

antioxidant enzymes size-exclusion chromatography and SDS-electrophoresis and then determine their autoxidation rates, oxygen binding capacity, and thermal stability. Other potential projects for REU students include the synthesis of folate-targeted photodynamic therapy agents and molecular dynamics simulations of ligand-protein interactions.

Martina Schmeling: Chromium in the Environment and Humans -The proposed research will involve the separation and analysis of hexavalent chromium in environmental and biological samples. Chromium is present in nature mainly in two oxidation states: Tri-valent chromium, an essential element involved in regulating glucose in the human body, and hexavalent chromium, a highly toxic element responsible for neurological disorders. We have developed a method separating these two oxidation states and analyzing samples for the presence of hexavalent chromium in very low concentrations. We intend to apply our method to various kinds of sample, especially atmospheric aerosols and human body fluids. The REU student will help in acquiring samples and learn how to prepare these for chemical separation by ion chromatography and analysis by total reflection X-ray spectrometry as well as UV-VIS spectrometry. The results obtained can be used to trace pollution patterns and identify sources for hexavalent chromium in Chicago.