

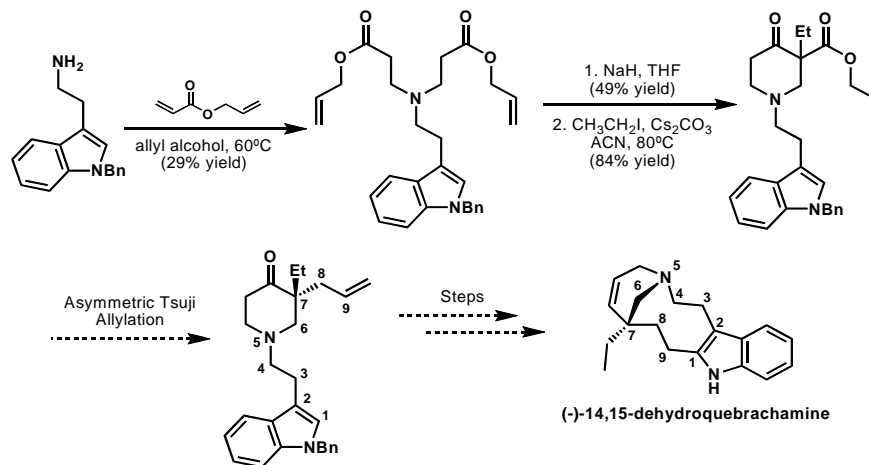
## Session G – Chemistry (Alphabetical)

### Toward the Asymmetric Total Synthesis of (-)-14,15-Dehydroquebrachamine

Anguel T Alexiev

Mentors: Brian M. Stoltz and Hosea M. Nelson

An intermediate toward the synthesis of indole alkaloid (-)-14,15-dehydroquebrachamine is prepared from the known N1-benzyltryptamine via a Michael addition of allyl acrylate, a Dieckmann cyclization, and subsequent alkylation. The remaining steps of the total synthesis are proposed, with a key step being an asymmetric Tsuji allylation which would complete the carbon framework and set the stereocenter of the molecule.



### Ring Closing Metathesis of Substituted Azobenzenes for Polymer Synthesis

Garrett Blake

Mentors: Robert Grubbs and AJ Boydston

Azobenzenes have shown the ability to switch between cis and trans isomers via irradiation with UV light. Incorporation of these systems into polymers would allow dynamic, photoinduced changes in polymer size. Synthesis of the azobenzenes requires attachment of terminal alkene 'tethers' to the benzene ring followed by metathesis of the tethers to form a closed-ring system. The azobenzenes were synthesized from commercial nitrophenol starting materials and the ring-closing metathesis was conducted via ruthenium metathesis catalysts (Grubbs 2nd Generation). Few azobenzene systems were able to be ring-closed primarily due to conformational complications. One system has formed a closed ring via dimerization. Further work on this project would involve continued synthesis of single-unit azobenzene rings and incorporation of the ring-closed systems into polymers via ring-opening or ring-expansion metathesis.

### Study on the Self-Assembly of Brush Copolymers

Edward H Bramston-Cook

Mentors: Robert H. Grubbs and Yan Xia

The solid state self-assembly brush copolymers containing polylactide and poly(n-butyl acrylate) as the side chains was investigated using atomic force microscopy (AFM) and small angle X-ray scattering (SAXS). Symmetric block and symmetric random copolymers both self-assemble into highly ordered lamellar morphologies with domain spacings characteristic of block length and side chain length respectively, indicating highly extended backbone conformation of the brush copolymers even in their solid-state assemblies. Symmetric PL-*r*-PBA exhibits domain spacing and order-disorder transition temperatures independent of brush polymer molecular weight.

### Simulation on Temperature Dependence of Solvated Electron Diffusion in H2O

Xi (Sherry) Chen

Mentor: Thomas Francis Miller

Molecular dynamics (MD) simulations involving electron transfer processes are vital to modern engineering applications such as solar energy conversion, bio-energetic processes, and semiconductor-water interface physics. Unfortunately, electron transfer processes are difficult to simulate via conventional MD methods

because these systems span vastly different length and time scales. Ring polymer molecular dynamics (RPMD) is a novel method for approximating nuclear and electronic dynamics in complex molecular system. Here we present novel extensions of RPMD method to dynamic calculations (simulations). We studied the dynamics of an excess electron in a SPC water box at temperatures ranging from 0oC to 100oC. The dependence of the electron's diffusion constant on temperature is inferred from the data and compared to both experimental results and results from conventional MD simulations.

### **Visualization of an Early Intermediate Preceding the Formation of a Stable Complex During Protein-Protein Interaction**

Jaeyoon Chung

*Mentor: Shu-ou Shan*

The signal recognition particle (SRP) and its receptor (SR) together form a universally conserved molecular machinery in delivering newly synthesized proteins to their correct destinations, including the eukaryotic endoplasmic reticulum (ER) and the bacterial plasma membrane. The interaction mechanism between these two components (SRP and SR) of this machinery is of particular importance in this project. Previous experiments have discovered the presence of an early intermediate, which forms independently of GTP and seems to adopt a multitude of conformations, on the SRP-SR pathway towards the stable, closed complex, which can only be formed in the presence of GTP. To further probe the structural properties of the early complex as well as its role in transitioning into the stable, closed complex, single cysteine mutants for both SRP and SR were generated, labeled with donor and acceptor dyes, respectively, and FRET experiments carried out both in the presence and absence of GTP, from which a distance distribution between the donor and acceptor probes could be calculated. FRET results indicate that the distance distribution between the donor and acceptor probes for the early intermediate tend to be spread out across a bell curve, indicating an ensemble of conformations, while distance distribution for the closed complex is largely fixed to a single distance.

### **Design and Synthesis of Polymers Modified With Cyclic Peptides**

Laura J Decker

*Mentors: Robert H. Grubbs and Rosemary Conrad*

Peptides naturally fold in patterns dependant on chemical properties of the amino acids within the chain. If small peptide segments are synthesized into a ring to create a cyclic peptide, the natural folding features of proteins, such as  $\beta$ -turns, will be mimicked. This idea can be applied to peptides used in polymers for vascular grafts because the grafts need to last in human body conditions. The goal of this project was to synthesize a cyclic peptide that could be used to modify a polymer. Such a polymer would be elastic like blood vessels by mimicking the aggregation of natural proteins. Solid-phase peptide synthesis (SPPS) was used to create the elastin-based linear Lys-Val-Pro-Gly-Val-Gly (KVPGVG). This linear chain was subsequently be cyclized in a dilute solution using triethylamine and diphenylphosphoryl azide. Once cKVPGVG is synthesized, it can be coupled to a norbornene monomer through an amide bond formation with the lysine's amine side chain and the carboxylic acid of the monomer. The polymer will be formed through ring-opening metathesis polymerization (ROMP). Other cyclic peptides can be synthesized for similar purposes, such as cyclic Arg-Gly-Asp (RGD) and cyclic Arg-Glu-Asp-Val (REDV), both of which promote functions such as cell adhesion.

### **Modeling G Protein Coupled Receptor Loop Conformations Using the Direct Monte Carlo Method**

Garrett K. Drayna

*Mentor: William A. Goddard III and Ravinder Abrol*

Proteins embedded in the cell membrane allow a cell to communicate with its outside environment. One important class of membrane proteins are G Protein Coupled Receptors (GPCRs). It has been extremely challenging to get crystal or NMR structures of GPCRs due to experimental difficulties. The primary alternative to experimental structure prediction is an *ab initio* computational approach. While accurate *ab initio* methods exist for the prediction of the transmembrane regions of GPCRs, existing loop prediction algorithms are inconsistent and lack the accuracy necessary for correctly predicting the ligand binding sites. The prediction of loop structures is complicated by the extremely large configurational space of the loops. In this project, we plan to develop a new and efficient algorithm for GCPR loop prediction based on the Direct Monte Carlo method. It is a hierarchical method which uses novel sampling techniques to reduce the number of structures that need to be created and evaluated. Additionally, it uses a more accurate energy function in the form of the DREIDING Force Field. This algorithm will be optimized by comparison of known GPCR loops structures with the predictions.

## **Ligand Exploration for the Asymmetric Tsuji-Trost Reaction**

Diane Plummer

*Mentors: Brian Stoltz and Nathan Bennett*

Catalytic methods for converting racemic substrates to enantiomerically enriched products are highly useful in synthetic organic chemistry. In particular, processes that produce enantiopure quaternary carbon centers are valuable due to the synthetic challenge of this moiety. One reaction capable of creating such centers on six-membered carbocycles with excellent yields and enantiomeric excess is the palladium catalyzed Tsuji (or the Tsuji-Trost) reaction. However, this reaction loses effectiveness in yield and selectivity for five and seven-membered ring substrates. To improve efficacy for such substrates, we plan to alter the oxazoline ligand bound to palladium. Specifically, we have changed the electronics and sterics on the bidentate oxazoline ligand to test the effects on the yield and enantiomeric excess of several different sized ring substrates.

## **Binding of Chloride to Polypropyleneimine and Polyamidoamine Dendrimers in Aqueous Solutions**

Neha Samdaria

*Mentors: Professor William A. Goddard III and Mamadou Diallo*

Water purification is essential for various medical, chemical and industrial applications. However, current water treatment systems make use of high pressure driven membrane processes such as reverse osmosis (RO), which makes them expensive. Dendrimer Enhanced Filtration (DEF) provides a promising alternative to RO. This process makes use of globular macromolecules known as dendrimers, which contain pH dependent reactive functional sites that are able to bind and release anions such as chloride. Additionally, their large size allows them to be effectively filtered out from aqueous solutions without the need for high pressures. The properties of these dendrimers are essential to their function, as their charge and composition affects the strength of their electrostatic and hydrophobic interactions with anions. In this study, we used a combination of acid-base titrations, ultrafiltration experiments and ion chromatography to measure the binding of chloride to a G5-NH<sub>2</sub> Polypropyleneimine (G5-NH<sub>2</sub> PPI) dendrimer and a G4-NH<sub>2</sub> Polyamidoamine (G4-NH<sub>2</sub> PAMAM) dendrimer in aqueous solutions. From these measurements, we extracted the extent of binding and fractional binding of chloride to the dendrimers. These results were then combined with dendrimer protonation data to provide greater insight into the chloride binding mechanism of both dendrimers and to highlight some of the chemical differences between the two which allow the G4-NH<sub>2</sub> PAMAM dendrimer to bind more chloride than the G5-NH<sub>2</sub> PPI dendrimer. The findings will be used to expand current molecular dynamic simulation models to incorporate previously discounted functional sites and to further the understanding of chloride binding to dendrimers.

## **Extending the Scope of eFF, a Method to Compute Excited Electron Dynamics**

Dahye Song

*Mentors: William A. Goddard, III, Julius T. Su, and Andres Jaramillo-Botero*

The electron force field (eFF) is a method to compute the dynamics of large scale highly excited electronic systems; it has been parameterized for the elements H, He, Li, Be, B, and C. However, the electrons of atoms of higher nuclear charge have a more complex structure, making it a challenge to extend eFF to the rest of the periodic table. Here, we simplify the interactions in the eFF model by replacing the combined potential of the core electrons with a single pseudopotential. We discuss the procedure used to derive the pseudopotential, and the accuracy of using the pseudopotential to compute the geometries and energies of molecules and periodic solids containing silicon. The development of a core pseudopotential for eFF should enable the computation of the dynamics of solid-state materials containing higher row elements with high accuracy and low computational cost.

## **Effects of Mutations of Finger-Loop on the Function of Signal Recognition Particle**

Ziying Wang

*Mentor: Shu-ou Shan*

Membrane and secretory proteins contain signal sequences that specify the cellular destination of the protein for secretion or for integration into cell membranes. As proteins are being synthesized from the ribosome, signal sequences are recognized by a protein targeting machinery named the Signal Recognition Particle (SRP), which subsequently binds with its receptor (SR). The Signal Recognition Particle is comprised of three domains: N, G, and M. The M domain intrigues prime interest because it contains the signal-sequence-binding site and provides primary contact with 4.5S RNA, which also contacts the ribosome. The M-domain is connected to the N and G domains by means of a flexible linker. Despite this, binding of ribosome and signal sequence in the M-domain trigger changes in the structure of SRP that allows it to efficiently bind the SR with the help of the SRP RNA. The signal-sequence-binding site contains a Finger-Loop, which is proposed to be the key to these changes in the structure and function of the SRP

in response to cargo binding. Mutations of the Finger-Loop region will enable us to understand better the protein translocation process that is of great importance in a functional eukaryotic cell.