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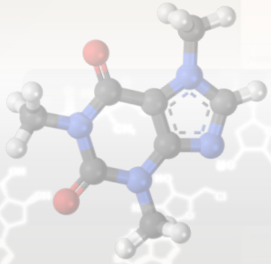
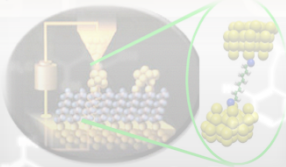
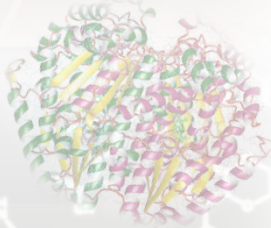
Graduate Student Class of 2016

Yale

Chemistry Symposium







Friday, August 25, 2017

Sterling Chemistry Laboratory

Schedule of Events

9:00 am – 9:30 am	SCL Upper Foyer	Breakfast
9:30 am – 9:45 am	SCL 110	New Faces at Yale
9:45 am – 10:45 am	SCL 110	Presentations, Session I
10:45 am – 11:00 am	SCL Upper Foyer	Coffee Break
11:00 am – 11:45 am	SCL 110	Presentations, Session II
11:45 am – 12:00 pm	SCL 110	TA Awards
12:00 pm – 1:00 pm	SCL Upper Foyer	Lunch
1:00 pm – 2:00 pm	SCL 110	Keynote Lecture
2:00 pm – 2:45 pm	SCL 111	First Year Meeting with DGS
2:45 pm – 3:15 pm	SCL 18, 19 21, 23, 111	Sub-discipline Meetings
3:30 pm – 4:30 pm	SCL 110	Presentations, Session III
4:30 pm – 4:45 pm	SCL Upper Foyer	Coffee Break
4:45 pm – 5:30 pm	SCL 110	Presentations, Session IV
5:30 pm – 6:30 pm	SCL 2nd Floor Lounge Outside of teaching labs	Poster Session
6:30 pm – End	CRB Courtyard	BBQ Dinner

Presentation Schedule

Session I

Session II

Keynote Lecture

Presentation Schedule

Session III

3:30 pm – 3:50 pm ◆ Chris Shugrue (Organic) 10
Phosphothreonine as a Catalytic Residue in Peptide-Catalyzed Asymmetric Transfer Hydrogenations

3:50 pm – 4:10 pm ◆ Kelly Culhane (Biophysical) 11
Parathyroid Hormone Shows Novel Calcium Sensing Ability in Binding to Parathyroid Hormone 1 Receptor

4:10 pm – 4:30 pm ◆ Mike Pegis (Inorganic) 12
Efficient and Robust Hydrogen Peroxide Production from Dioxygen using Sensitized Nickel Oxide Photoelectrocatalysts

Session IV

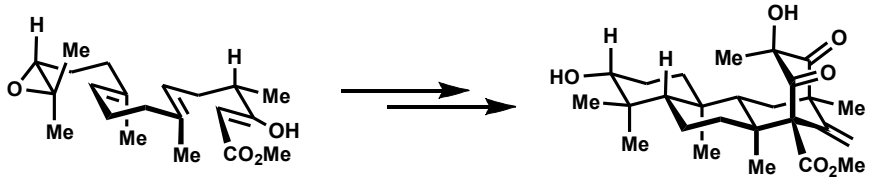
4:45 pm – 5:05 pm ◆ Jessica Yuan (Chemical Biology) 13
Proteogenomic Identification of Non-Annotated E. coli Stress Response Proteins

5:05 pm – 5:25 pm ◆ Patrick Kelleher (Physical) 14
Trapping and Structural Characterization of Exit Channel Complexes in the Water-Mediated $X^- + N_2O_5$ Reactions (X = Cl, Br, I) with Cryogenic Vibrational Spectroscopy

Total Synthesis of (±)-Berkeleyone A

Masha Elkin ◆ Newhouse Group

In our ongoing efforts toward the synthesis of complex and biologically relevant natural products, we report a 13-step total synthesis of the cytotoxic meroterpenoid berkeleyone A.



2 steps from commercial materials

berkeleyone A (1) (caspase-1 inhibitor)

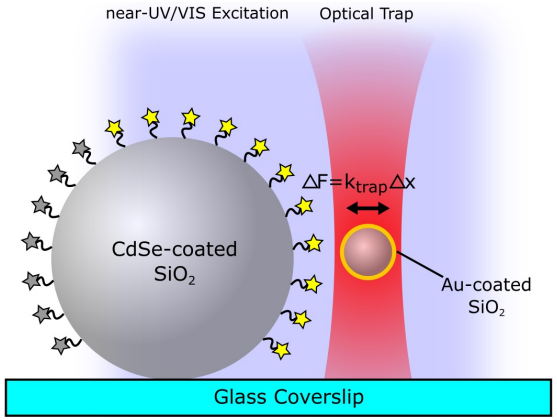
The molecular skeleton is formed using the first examples of two critical construction reactions: (1) an epoxide-initiated, β-ketoester-terminated polycyclization, and (2) an isomerization–cyclization cascade to generate the remaining bicyclo [3.3.1]nonane framework. The resulting 6-step synthesis of the carbocyclic core of the berkeleyone natural products has been used to access protoaustinoid A and berkeleyone A, and will aid future biosynthetic investigations into the origin of related natural products.

Developing Solution-Phase Absorption Spectroscopy at Nanoscale & Single Molecule Level Through an Optical Trapping Scheme

Alex Parobek ◆ Ganim Group

We describe a new method for acquiring nanoscale (~10 molecules) near-UV/VIS absorption spectra in water at room temperature. In this method, the femtoNewton forces arising from molecular absorption are measured using an optically trapped gold nanoshell probe. The technique is demonstrated by resolving the nanoscale absorption spectra of cadmium selenide quantum dots and sulforhodamine dye. This design can be scaled down to the single molecule limit and used to study kinetics by watching the absorption spectrum of a molecule change during a chemical reaction.

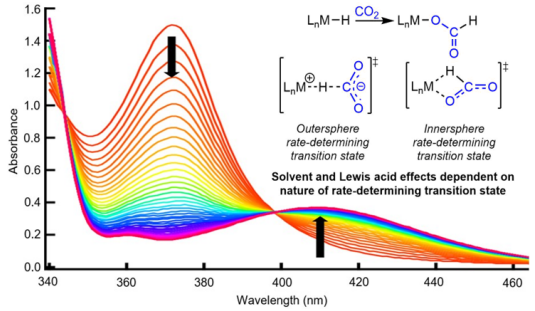
To perform single molecule infrared spectroscopy probing a wide range of molecular vibrations, a broadband plasma generated IR source (<1000 – 2800 cm^{-1}) has been developed and coupled into a microscope. In conjunction with the force-detected absorption method described above, this source will be used for time-domain spectroscopy that resolves the free induction decay of a single molecule, and provides its IR absorption spectrum via Fourier transformation.



Mechanism-Dependent Lewis Acid and Solvent Effects on the Insertion of Carbon Dioxide into Metal Hydrides

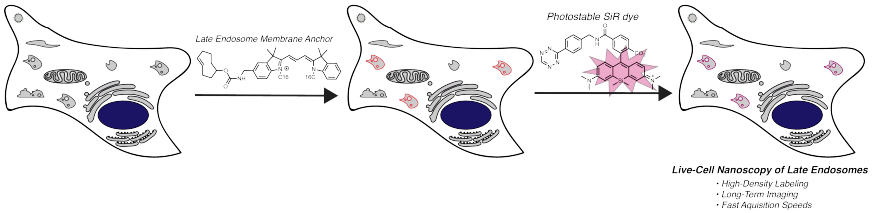
Jessica Heimann ◆ Hazari Group

The abundance, low cost, and nontoxicity of carbon dioxide make it an attractive feedstock for the sustainable syntheses of carbon-based commodity chemicals such as methanol and formic acid. Although the high thermodynamic and kinetic stability of CO_2 currently limits its use as a carbon source, the potential for greener industrial processes and the resulting environmental benefits provide powerful motivation to study carbon dioxide conversion chemistry. One promising approach for the functionalization of CO_2 is the utilization of homogeneous transition metal catalysts. In several catalytic processes, the insertion of CO_2 into a metal hydride or the microscopic reverse decarboxylation of a metal formate is proposed to be an important elementary step. Using a rapid mixing stopped-flow instrument to measure the rate of CO_2 insertion into metal hydrides under various conditions, we demonstrate that an innersphere CO_2 reaction, proposed to have a direct interaction between CO_2 and the metal in the rate-determining transition state (TS), shows no rate enhancement from Lewis acids (LA) and only a small solvent effect. In contrast, an outersphere CO_2 insertion reaction, proposed to proceed with no interaction between CO_2 and the metal in the rate-determining TS, exhibits a dramatic LA effect and a large solvent effect.



Development of Lipid-Based Probes for Live Cell Super-Resolution Imaging of Late Endosomes

Aarushi Gupta ◆ Schepartz Group

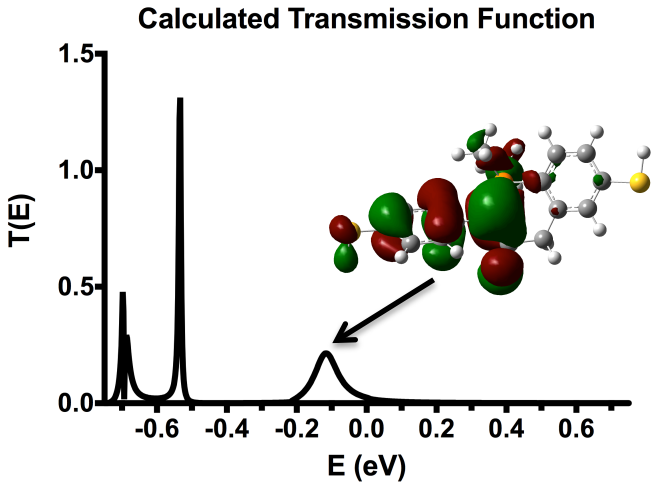


Fluorescence imaging has been crucial to understanding organelle structure and function, and the advent of super resolution microscopy has enhanced the understanding of organelle dynamics with remarkable resolution of subcellular structures. In vivo imaging techniques in biology have traditionally taken advantage of large fusion proteins such as GFP, but their reduced photostability and increased size renders them inferior compared to organic fluorophores. The Schepartz group at Yale was the first to introduce a novel two-component labeling strategy based on a modified ceramide lipid to selectively label the Golgi apparatus in live HeLa cells using silicon rhodamine dye compatible with live cell STED microscopy. This approach has been recently expanded to long-term STORM imaging of the plasma membrane, ER, and mitochondria in live HeLa cells and live neurons. This work focuses on the development and utilization of functionalized lipid analogs that traffic to late endosomes, an essential component of the endocytic pathway. With this novel high-density labeling approach, we have captured the first long-term STED videos of late endosomes and their membrane components in live HeLa cells.

Design and Theoretical Characterization of Novel Molecular Rectifier Candidates

Adam Matula ◆ Batista Group

Unimolecular rectifiers—single organic molecules that act as one-way conductors of electric current—remain highly sought after for their potential in applications ranging from molecular electronics to solar energy-driven systems. Here we present a novel class of molecular rectifier candidates based on a functionalized phosphonium-ylide core. These species show great promise for directional charge transfer without the significant loss of overall conductance. We implement a non-equilibrium Green's function technique using density functional theory to calculate the current flowing through our candidate molecules under forward and reverse biases as well as to identify the orbital(s) responsible for conduction and the mechanism by which directional charge transport is permitted. By carefully tuning the energetics of the frontier orbitals via functionalization, we design a species with a predicted intrinsic rectification ratio nearly five times higher than anything previously reported as well as a system with two non-degenerate highly transmitting states at low bias.



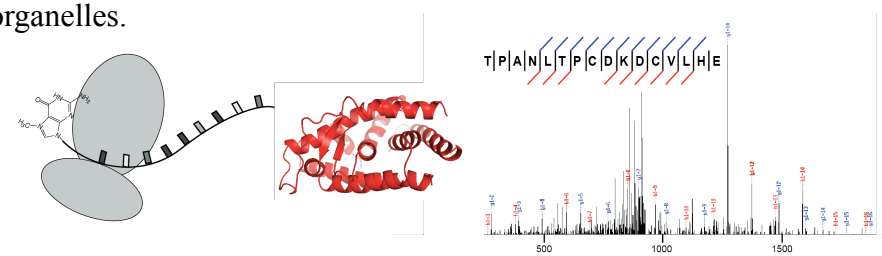
KEYNOTE SPEAKER

Sarah Slavoff

Sarah Slavoff, Ph.D. is an assistant professor of Chemistry and Molecular Biophysics and Biochemistry at Yale University.

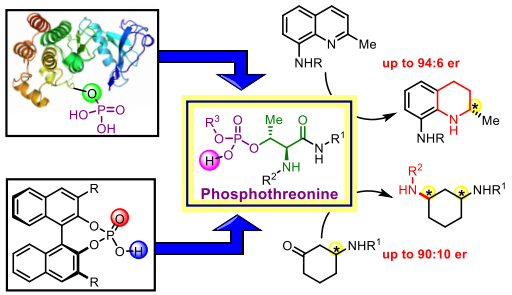
Sarah was born on June 25, 1983 in small-town Elmer, NJ. She received her B. S. in biochemistry at the University of Maryland, College Park in 2005, then carried out her graduate studies in chemical biology at MIT with Alice Ting. Sarah then moved up the road to Harvard to work with Alan Saghatelian as an NIH postdoctoral fellow. In 2014, Sarah joined the faculty of the Chemistry Department at Yale University. She was named a Searle Scholar in 2016.

Professor Slavoff's research group applies chemical tools to gain new insights into how genomes work. Her research has helped to reveal entirely new classes of genes – in genomes from bacteria to human – that were previously refractory to detection and annotation, and shown that these newly discovered genes have important biological functions. The Slavoff research group is also reshaping our understanding of how mRNA decay – the process that turns off gene expression – is regulated in human cells, by characterizing the function of a newly discovered peptide that perturbs the formation of decay-associated membrane-less organelles.



Phosphothreonine as a Catalytic Residue in Peptide-Catalyzed Asymmetric Transfer Hydrogenations

Christopher Shugrue ◆ Miller Group

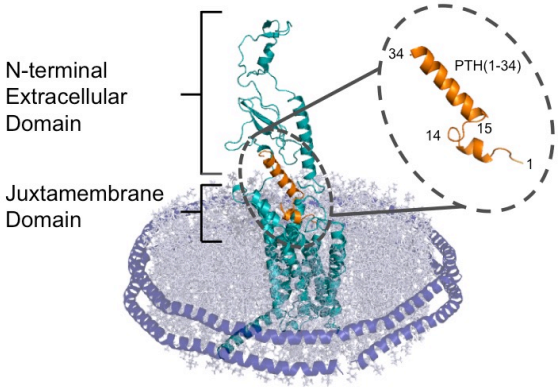


The capacity of catalysts to functionalize complex molecules with high levels of selectivity is of immense importance. The many challenges facing synthetic chemists today underscores the need for new and powerful catalysts. One such class of catalysts, chiral phosphoric acids (CPAs), has proven to be particularly effective in asymmetric catalysis. Apparently unrelated is the regulation of cellular function through the phosphorylation of proteins. Sitting at the interface of these two areas is phosphothreonine (pThr), which is well known in nature as a post-translational modification product. However, while the effects of Thr-phosphorylation on the structure and function of enzymes are well known, they have yet to be reported as Brønsted acid catalysts. It could be envisioned that incorporating pThr into minimal peptide sequences could produce a complementary class of CPAs. Indeed, a pThr-embedded peptide was recently discovered that catalyzes the asymmetric transfer hydrogenation of 8-aminoquinolines with NADH-mimic, Hantzsch ester, with up to 94:6 er. This system has been further applied to the reductive amination of 3-amidocyclohexanones with up to 90:10 er. We hope that this will not only spur interest in the scope of reactivity of pThr-embedded peptides, but also raise questions about new roles that pThr could play in nature.

Parathyroid Hormone Shows Novel Calcium Sensing Ability in Binding to Parathyroid Hormone 1 Receptor

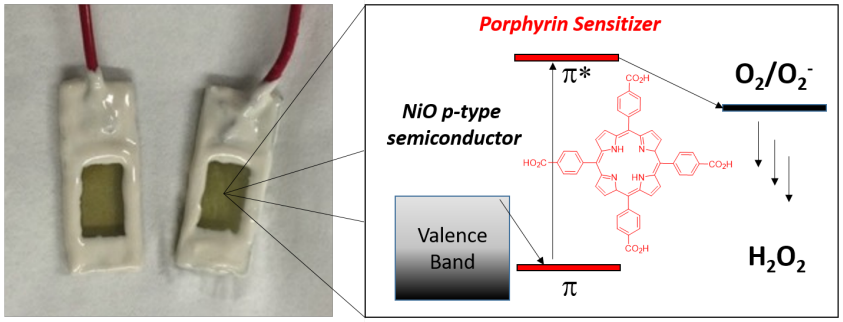
Kelly Culhane ◆ Yan Group

Parathyroid hormone (PTH) binds to a family B GPCR, parathyroid hormone 1 receptor (PTH1R). One of its functions is to regulate Ca^{2+} homeostasis in bone remodeling, during which Ca^{2+} can reach concentrations up to 40 mM. A truncated version of PTH, PTH(1-34) can fully activate PTH1R and has been clinically used for osteoporosis treatments. In this study, we used fluorescence anisotropy to examine the binding of PTH(1-34) to PTH1R purified in nanodiscs (PTH1R-ND) and found that the affinity increases 5-fold in the presence of 15 mM Ca^{2+}. However, PTHrP(1-36), another truncated endogenous agonist for PTH1R, does not show this Ca^{2+} effect. Mutations of Glu19 and Glu22 in PTH(1-34) that are not conserved in PTHrP(1-36) largely abolished the Ca^{2+} effect. We conclude that PTH(1-34) can uniquely sense Ca^{2+} while activating PTH1R. This dual function of a peptide hormone is a novel observation in endocrine signaling. Understanding it can potentially reveal the complex role of PTH signaling in bone remodeling and improving the PTH(1-34) treatment for osteoporosis.



Highly Efficient and Robust Hydrogen Peroxide Production from Dioxygen using Sensitized Nickel Oxide Photoelectrocatalysts

Michael Pegis ◆ Mayer Group

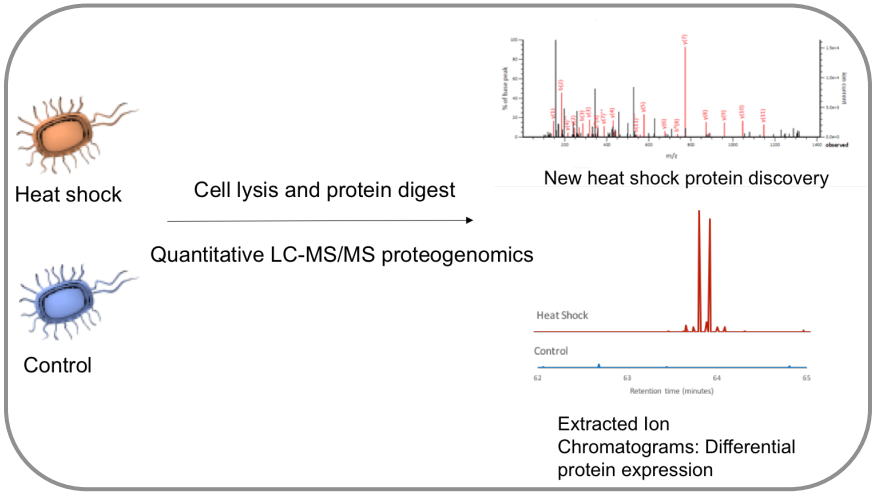


Hydrogen peroxide is an important commodity chemical produced annually at a large scale. Current industrial technology relies on indirect hydrogenation of dioxygen from dihydrogen via the anthraquinone process. In many cases, on-site production is desired due to the cost or danger of transporting large quantities of H_2O_2. Herein, we report a new method to produce hydrogen peroxide directly from air using p-type photoelectrocatalysts and a mild electrochemical bias. The sensitization of nickel (II) oxide (NiO) with *meso*-tetra(4-carboxyphenyl)porphyrin produces a highly active material capable of producing H_2O_2 directly from air or dioxygen with high Faradaic efficiency and low overpotential in pH 6 aqueous solutions. The electrodes are highly stable, exceeding 8000 turnovers and producing millimolar concentrations of hydrogen peroxide over 24 hours. This new approach for H_2O_2 production may enable new technologies useful for the production of commodity chemicals and the developing world.

Proteogenomic Identification of Non-Annotated E. coli Stress Response Proteins

Jessica Yuan ◆ Slavoff Group

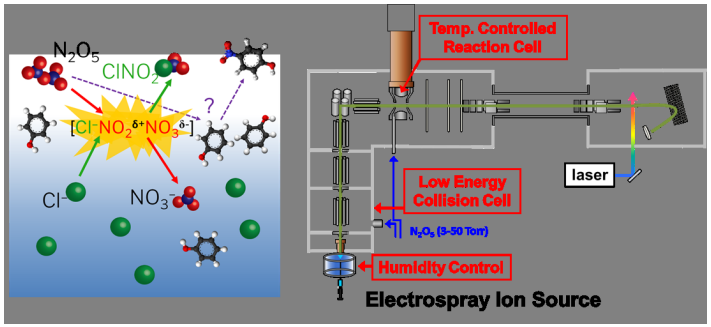
Small proteins (50 amino acids or less), while playing important roles in diverse biological processes, have traditionally been overlooked in genome annotation efforts due to challenges in their detection and functional characterization. Furthermore, after their discovery, determining the functions of small proteins is challenging, especially if they exhibit low sequence similarity to known proteins. We have recently developed a quantitative proteogenomic pipeline for the mass spectrometry-based identification of non-annotated small proteins in *E. coli* that are specifically expressed under stress conditions, suggesting that they may be functional. We have applied this method to the discovery of novel *E. coli* cold shock proteins that are translated from non-canonical start codons, and more recently to the discovery of a small, membrane-associated heat shock protein.



Trapping and Structural Characterization of Exit Channel Complexes in the Water-Mediated $X^- + N_2O_5$ Reactions (X = Cl, Br, I) with Cryogenic Vibrational Spectroscopy

Patrick Kelleher ◆ Johnson Group

The heterogeneous reaction of N_2O_5 with sea spray aerosols yields the $ClNO_2$ molecule, which is postulated to occur through water-mediated charge separation into NO_3^- and NO_2^+ followed by association with Cl^- to release the gas phase $ClNO_2$ product. Here we address an alternative mechanism where the attack by a halide ion can yield XNO_2 by direct insertion in the presence of water. This is accomplished by reacting $X^-(D_2O)_n$, (X=Cl, Br, I) cluster ions in an octopole ion guide with N_2O_5 to produce ions with stoichiometry $[XN_2O_5]^-$. These species were cooled in a 40 K ion trap and structurally characterized by vibrational spectroscopy obtained using the D_2 messenger tagging technique. Analyses of the resulting band patterns with anharmonic theory indicates that they all correspond to exit channel ion-molecule complexes based on the association of NO_3^- with XNO_2, with the NO_3^- constituent increasingly perturbed in the order I>Br>Cl. These results establish that XNO_2 can be generated even when more exoergic reaction pathways are available involving chemical transformation of the water molecule into nitric acid.



Speaker Biographies

Masha Elkin (Newhouse Group) ◆ Masha was born in Moscow, Russia and grew up in the greater Boston area. As an undergraduate at Washington University in St. Louis she worked for Vladimir Birman on the design and synthesis of chiral ligands for asymmetric transition metal catalysis. As a fourth-year graduate student in the Newhouse group, she is pursing the total synthesis of fungal meroterpenoids and the development of novel synthetic methods. Outside of the lab, Masha enjoys reading, cooking, and playing with her dog.

Alex Parobek (Ganim Group) ◆ Alex grew up in the small town of Munster located in the urbanized plains of Northwest Indiana, commonly referred to as "The Region." In his home state, Alex began his scientific journey by enrolling as a chemistry undergraduate at Purdue University. There he performed gas-phase UV/UV and UV/IR spectroscopic research with Professor Timothy Zwier on monomer subunits of lignin and photoproducts of Titan's atmosphere. After graduating from Purdue in 2014, Alex enrolled into the chemistry graduate program at Yale where he joined the lab of Professor Ziad Ganim. Alex is currently a fourth year graduate student and has worked to develop a plasma generated IR source in pursuit of performing single molecule IR absorption spectroscopy in solution. In his free time, Alex enjoys cycling, gaming, writing, and teaching people about chemistry and physics.

Jessica Heimann (Hazari Group) ◆ Jessica grew up just south of Atlanta in Peachtree City, Georgia. She attained her Bachelor of Science in Chemistry from Rice University in Houston, Texas, where she explored the use of carbon nanomaterials as potential heavy metal adsorbents in aqueous environments. Currently a third year graduate student in the Hazari lab, Jessica now studies the insertion of carbon dioxide into transition metal hydrides in order to guide the development of improved hydrogenative and dehydrogenative catalysts. When she is not sitting in a dark corner running stopped-flow experiments, Jessica enjoys playing IM softball, winning Mario Tennis tournaments with the Hazari group, paddle boarding, and taking long walks on the shores of Azeroth.

Speaker Biographies

Aarushi Gupta (Schepartz Group) ◆ Aarushi Gupta grew up in the vibrant Silicon Valley and moved south to UC San Diego for her undergraduate studies. While there, she realized she liked organic chemistry as much as she liked burritos, and pursued undergraduate research with Prof. Michael Burkart. Her projects focused on developing various probes to understand the protein-protein interactions of bacterial Fatty Acid Synthase systems. She decided that it was then time to experience winter, and came to Yale to pursue her graduate degree in Chemical Biology. As a third year in the Schepartz lab, she has been developing probes to image the endocytic system with STED and STORM nanoscopy. While she's not on Science Hill, she's usually running around East Rock, eating in one of New Haven's fine restaurants with her friends, or trying to make cupcakes.

Adam Matula (Batista Group) ◆ Adam graduated from the University of Minnesota – Twin Cities with a B.S. in Chemistry and a B.A. in Political Science. His undergraduate research focused on the design and synthesis of novel stationary phases for high performance liquid chromatography (HPLC) as well as the development and method testing of HPLC protocols for detailed compositional analysis. Now a fourth year graduate student in the Batista Lab, Adam uses theory to study electron transfer processes in energy materials. In his free time he enjoys playing recreational soccer, hiking, and eating his way through New Haven's unique food scene.

Christopher Shugrue (Miller Group) ◆ Chris was raised in Rocky Hill, Connecticut, which is a suburb of the fine city of Hartford. He attended the College of the Holy Cross as an undergraduate, receiving a B.A. in Chemistry. After pursing an NSF-REU at the University of Texas at Austin under the tutelage of Prof. Stephen Martin, Chris began his studies at Yale in 2013 and is now a fifth-year graduate student in the Miller group. His research has involved the development of phosphothreonine-embedded peptides as a new class of chiral phosphoric acid catalyst. He is particularly interested in the exploration of structurally dynamic catalysts and their applications towards systems with "hairy" site- and stereoselectivity concerns. In addition to being notorious for his memorable (and truly hilarious) puns, you might also find Chris in deep collaboration with our Science Hill neighbors, playing IM softball for "Balco's Finest".

Speaker Biographies

Kelly Culhane (Yan Group) ◆ Kelly Culhane is a fifth year student in Elsa Yan's group. She grew up in Hartland, WI and graduated from St. Olaf College in 2012 with a Bachelor's degree in Chemistry and minors in neuroscience and biomolecular sciences. Her undergraduate research focused on protein structure and function. In the Yan group, Kelly studies the signaling of Parathyroid Hormone 1 receptor using fluorescence anisotropy and other biophysical techniques.

Michael Pegis (Mayer Group) ◆ 5th year graduate student. Seattle, Wa. Undergraduate institution: Western Washington University, Bellingham, Wa. Undergraduate research focused on the synthesis and characterization of dendrimer encapsulated nanoparticles for the conversion of biomass to biofuels. Current research is focused on the improvement of electro- and photoelectrocatalysts for the oxygen reduction reaction. Outside of lab, Mike enjoys ultimate frisbee, ping pong, and hiking.

Jessica Yuan (Slavoff Group) ◆ Peijia (Jessica) Yuan was born in China and (mostly) grew up in Sunnyvale, CA. She attended UC Berkeley as an undergraduate, where she worked in the labs of Prof. Richard Harland and Prof. John Hartwig. During undergrad, she also spent a semester in Belgium, learning fluorophore synthesis at the KU Leuven under Prof. Wim Dehaen. Before arriving at Yale, she did a summer internship in the Crop Protection division at BASF in Ludwigshafen, Germany. Her current research in the group of Prof. Sarah Slavoff focuses on the mass spectrometric discovery of small stress-response proteins in E. coli. Outside of lab, she is on the Executive Board of the student-run Yale Journal of Biology and Medicine, and in her spare time enjoys attending concerts whenever possible.

Patrick Kelleher (Johnson Group) ◆ Patrick is a 5th year graduate student in the Johnson Lab. He grew up on the south shore of Long Island in Baldwin, New York. He received my undergraduate degree from Stonehill College in Massachusetts. While a student at Stonehill, Patrick did research in Arthur Utz's lab at Tufts University on mode-selective reactivity of methane gas on catalytic metal surfaces. His current research in the Johnson lab is focused on exploring the microscopic origins of macroscopic behavior displayed by atmospheric particles using mass spectrometry and vibrational spectroscopy. When not in lab, Patrick enjoys running, skiing, and playing ultimate frisbee. He also plays on the Chemistry department intramural teams for volleyball, soccer, and softball.

Acknowledgements

The second year chemistry graduate students would like to thank all those who made this symposium possible, including Yale University's Chemistry Department for their support and generosity, and today's outstanding presenters for highlighting the diversity of research in the department. We would especially like to express our gratitude to Professor Sarah Slavoff for graciously agreeing to deliver this year's keynote lecture.

We hope that the combined efforts of everyone involved in the symposium have provided a warm welcome to Yale Chemistry's newest graduate student class!