

WRM 74

Characterization of the composition and thermal decomposition profile of recycled carpet samples by TG-FTIR, TG-MS, and TG-GC-MS

Pamela J. Shapiro¹, *pamela.shapiro@netzsch.com*, **Carolyn Fischer**². (1) NETZSCH Instruments North America, Burlington, MA 01803, United States (2) NETZSCH Geraetebau GmbH, Selb, Germany

Billions of pounds of carpet are generated annually worldwide, a large percentage of which ends up in landfills, which is problematic because nylon is non-biodegradable. Limitations in landfill capacity and the environmental impact of disposing of carpet waste in this manner have made recovering nylon from carpet waste an increasingly important enterprise.

Since carpet compositions vary and can contain nylon-6 and/or nylon-6,6 along with variety of other materials, such as other polymer fibers, latex adhesive, dyes, and inorganic fillers, characterizing waste carpet composition and its thermal decomposition profile is essential for the recycling process. Thermogravimetric analysis (TGA) coupled with evolved gas analysis (EGA) by FTIR, MS, or GC-MS enables the simultaneous analysis of a material's thermal mass loss profile and identification of the gaseous species evolved during the decomposition.

In this study, material recovered from carpet waste was analyzed by TG-FTIR, TG-MS, and TG-GC-MS in order to compare the capabilities of the three combined thermal analysis/evolved gas analysis methods for identifying the composition of the recycled carpet. For this application, TG-GC-MS proved to be the most informative EGA method, identifying a variety of nylon decomposition products that have never before been reported.

WRM 75

Capillary IC – A New Platform for High Throughput or High Resolution Separations of Ionic Compounds

Peter Bodsky, *Peter.Bodsky@ThermoFisher.com*. Field Marketing, ThermoFisher Scientific, Sunnyvale, CA 94085, United States

There has been increasing interest in the development of capillary ion chromatography (IC) systems and methods for determination of ionic species. The practice of ion chromatography in capillary format offers a number of advantages.

Because the eluent consumption is very low, capillary IC systems can be operated continuously and thus are always on and always ready for analysis. Capillary IC systems offer improved compatibility with applications where amount of sample is limited. Capillary IC systems provide improved performance for determination of target analytes at trace levels. The use of capillary columns can improve separation efficiency and/or speed. The operation of capillary IC systems at low flow rates improves the system compatibility with a mass spectrometer. In addition, the use of capillary separation columns opens the door for the possibility of offering new selectivity for difficult applications using new columns packed with different stationary phases.

WRM 76

Analytical scheme for determining cytotoxicity and biomarkers of exposure for chlorpyrifos and 3,5,6-trichloro-2-pyridinol

Jeanette M. Van Emon, *VanEmon.Jeanette@epa.gov*, **Peipei Pan**. National Exposure Research Laboratory, U.S. Environmental Protection Agency, Las Vegas, Nevada 89193-3468, United States

External exposures to environmental contaminants may result in absorption leading to an internal dose, followed by distribution, metabolism, and excretion. Biomarkers have emerged as very powerful indicators of xenobiotic exposure to determine the presence and potential harmful effects of environmental contaminants for human exposure assessment and risk management. Biomarkers of exposure are metabolites or other constituents that can be measured in biological fluids or tissues. Ideally, these biomarkers can be directly linked with a pathological change. We determined cytotoxicity, apoptosis, cytokine expression, and the recovery of damaged cells induced by exposure to chlorpyrifos and 3,5,6-trichloro-2-pyridinol (TCP) on human embryonic

kidney cells. Apoptotic morphological changes in HEK293 cells were observed using an inverted microscope and showed reduction in cell volume, cell shrinkage, and wider intracellular spaces between the cells at the concentrations above 5 µg/ml and 10 µg/ml for chlorpyrifos and TCP. The IC₅₀ values at 24 hours of exposure, determined by a CCK8 assay, were 68.82 µg/ml and 146.87 µg/ml for chlorpyrifos and TCP, respectively. Annexin-V FITC/PI double stain assay was used to determine the apoptosis and the expression of interleukins 1-alpha and 6. The results showed the cytotoxic effect was in a dose and time dependent manner with the effect becoming more obvious with the increase of dosing concentrations and prolonged treatment time. Protein expression patterns before and after dosing are being determined using stable isotope labeling with amino acids in the cell cultures (SILAC) and LC/MS-MS. The SILAC technique is a simple and accurate approach that depends on the incorporation of amino acids containing substituted stable isotope nuclei (e.g., ²H, ¹³C, ¹⁵N) into proteins in living cells.

WRM 77

High-Resolution Structural Basis of G-protein Coupled Receptor Signaling Complexity

Rie Nygaard, *rnygaard@stanford.edu*. Chemistry, Stanford University, Stanford, CA 94305, United States

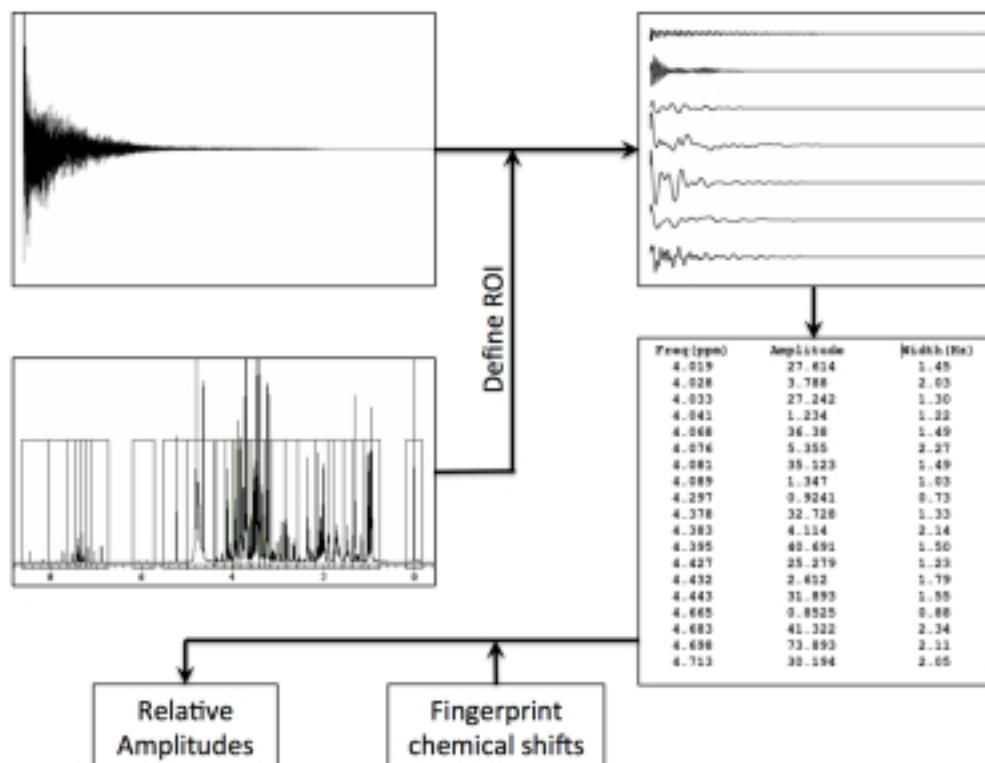
G-protein coupled receptors (GPCRs) are functionally versatile molecules that can modulate the activity of a number of different signaling pathways. This signaling complexity is achieved through structural plasticity where GPCRs can populate a multitude of conformations. X-ray crystallography allows us to understand a few low-energy conformational states. However, to fully understand the structural basis for the complex signaling behavior of GPCRs it is necessary to characterize the dynamic equilibrium of higher-energy conformations that are not readily crystallizable. The β_2 -adrenergic receptor (β_2 AR) is an ideal model system for probing GPCR structure and dynamics. It exhibits complex signaling behavior characteristic of many GPCRs activated by hormones and neurotransmitters, and available ligands have a broad range of affinities and efficacies. Moreover, the β_2 AR has been crystallized in both inactive and active states. We have incorporated ¹³CH₃ε-methionine into the β_2 AR to probe ligand-specific conformational states in four native transmembrane methionines. We obtained cHSQC spectra of β_2 AR unliganded and bound to an agonist, a neutral antagonist and an inverse agonist. The results demonstrate that these ligands stabilize distinct conformational states and provide evidence for conformational heterogeneity. The 2D spectrum of unliganded and neutral antagonist bound β_2 AR are nearly identical, while binding of the inverse agonist leads to a change in the resonances of Met82 near the ligand binding pocket. The largest spectral changes were observed in Met82 and Met215 (TM5) and Met279 (TM6) upon binding of a high affinity agonist B167107 used to obtain the active state structure of the β_2 AR. However, additional spectral changes were observed in agonist bound delta5- β_2 AR in the presence of a G protein mimetic camelid antibody (Nb80), demonstrating that a high affinity agonist alone cannot fully stabilize an active conformation. These NMR experiments provide new insights into conformational heterogeneity, and reveal conformational states not observed in current crystal structures.

WRM 78

Redefining high-throughput - CRAFT: A tool for automated deconvolution of NMR spectra"

Krish Krishnamurthy, *krish.krishnamurthy@agilent.com*. Agilent Technologies, Research Products Division, Santa Clara, CA 95051, United States

While used most often for structural analysis NMR is increasingly considered a critical quantitative tool and with advances in probe technologies NMR is very relevant for quantitation studies. Its intrinsic quantitative nature is being increasingly exploited in areas ranging from complex mixture analysis (as in metabolomics and reaction monitoring) to Quality Assurance/Control (QA/QC). However, complex NMR spectra are more common than not. So, extraction of quantitative information generally involves significant prior knowledge and/or operator interaction to deconvolute peaks of interest. We will discuss an algorithm



that achieves a Complete Reduction to Amplitude Frequency Table (CRAFT) in an automated and highly time-efficient fashion – thus converting the fid to a frequency-amplitude-linewidth table. The CRAFT tables can be used further for datamining of quantitative information using fingerprint chemical shifts of compounds of interest and/or statistical analysis of modulation of chemical quantity in a biological study (metabonomics) or process study (reaction monitoring) or QA/QC. The basic principle behind this approach as well as some example proof of concept results will be presented

WRM 79

Sum of the Parts: Composition and Architecture of the Bacterial Extracellular Matrix

Lynette Cegelski, cegelski@stanford.edu, Oscar McCrate, Xiaoxue Zhou, Courtney Reichhardt, Ji Youn Lim. Chemistry, Stanford University, Stanford, CA 94305, United States

Bacterial biofilms are complex multicellular assemblies that exhibit resistance to antibiotics and contribute to the pathogenesis of serious and chronic infectious diseases. New approaches and quantitative data are needed to define the molecular composition of bacterial biofilms. *E. coli* biofilms are known to contain polysaccharides and functional amyloid fibers termed curli, yet accurate determinations of biofilm composition at the molecular level have been elusive. The ability to define the composition of the extracellular matrix is crucial for the elucidation of structure–function relationships that will aid the development of chemical strategies to disrupt biofilms. We have developed an approach that integrates non-perturbative preparation of the extracellular matrix with electron microscopy, biochemistry and solid-state NMR spectroscopy to define the chemical composition of the intact and insoluble extracellular matrix of a clinically important pathogenic bacterium—uropathogenic *E. coli*. Remarkably, our data permitted a sum-of-all-the-parts analysis.

Electron microscopy revealed remarkable supramolecular shell-like structures that encapsulated single cells and enmeshed the bacterial community. Biochemical and simple solid-state NMR measurements of the matrix and constitutive parts established that the matrix is composed of two

major components, curli and cellulose, each in a quantifiable amount. This approach to quantifying the matrix composition is widely applicable to other organisms and to examining the influence of biofilm inhibitors. We have also discovered small-molecule biofilm inhibitors and examined their influence on biofilm composition and architecture. Collectively, our NMR spectra and the electron micrographs of the purified ECM inspire us to consider the biofilm matrix not as an undefined slime, but as an assembly of polymers with a defined composition and architecture.

WRM 80

NMR investigation of protein-protein interactions of the cataract-related variant G18V of human γ S-crystallin

Carolyn N. Kingsley¹, William D. Brubaker¹, Stefan Markovic², Anne Diehl², Hartmut Oschkinat², Rachel W. Martin¹, rwmartin@uci.edu. (1) Department of Chemistry, University of California, Irvine, Irvine, CA 92697, United States (2) Leibniz-Institut für Molekulare Pharmakologie, Berlin, Germany

The crystallin proteins of the eye lens are extraordinarily soluble and stable, remaining in solution for a lifetime despite concentrations in excess of 400 mg/mL in humans. Eye lens transparency is maintained via protein-protein interactions among the structural $\beta\gamma$ - and chaperone α -crystallins. Altered inter-crystallin interactions due to damage or mutation can lead to cataract, an opacification of the lens. The G18V variant of human γ S-crystallin is associated with juvenile-onset cataract and has increased aggregation propensity in vitro. Spot synthesis was used to construct libraries of tripeptides from both wild-type and G18V γ S-crystallin, and tripeptides binding more strongly to either the wild-type or the variant protein were selected for NMR analysis. Binding was measured for selected tripeptides, providing insight into the aggregation of this protein in the absence of molecular chaperones. Comparison of the solution NMR structures of wild-type and G18V γ S-crystallin, both presented here, reveal that the increased aggregation propensity of γ S-G18V involves substantial backbone rearrangement within the N-terminal domain, but not large-scale unfolding. The holdase chaperone protein α B-crystallin binds more strongly to the variant, via a well-defined interaction surface determined by solution-state NMR. In contrast, α B-crystallin binds wild-type γ S-crystallin only weakly and transiently. These structural studies suggest a potential mechanism for cataract formation via enhanced interactions between the γ S-crystallin molecules and the depletion of α B-crystallin in the lens.

WRM 81

Low Field Solid state NMR Investigations of Network Formation and Motional Dynamics in Well-Defined Model Poly(dimethylsiloxane) Elastomers

James P Lewicki, lewicki1@llnl.gov, Stephen J Harley, Robert S Maxwell. Chemical Sciences Division, Lawrence Livermore National Lab, Livermore, California 94550, United States

In this work a range of solid-state Nuclear Magnetic Resonance (NMR) methodologies have been applied to the study of dynamic network formation in end-linked poly(dimethylsiloxane) (PDMS) networks. The optimization of the structure of a series of model PDMS networks using ^1H Magic Angle Spinning (MAS), Magic Sandwich Echo (MSE) NMR and equilibrium solvent uptake analysis is reported. The influence of inter-crosslink molar mass, vinyl to silane ratio and Pt chelation effects on the dynamics of network formation have been studied using low field NMR methodologies in real time. It has been demonstrated that comparatively simple solid-state NMR methodologies can be utilized to study the dynamics of network formation and the relationship between the chemical identity of key structural components and the final network structure of a silicone elastomer.

WRM 82

Using NMR spectroscopy to identify how a slow conformational switch regulates the 24-hour circadian clock

Carrie L. Partch, cpartch@ucsc.edu, Patrick J. Sammons, Chelsea L. Gustafson. Department of Chemistry and Biochemistry, University of California Santa Cruz, Santa Cruz, CA 95064, United States

Cell-autonomous circadian clocks synchronize physiological processes into rhythms that coincide with the solar day, providing enhanced fitness by coordinating the timing of integrated processes

and optimizing energy utilization. Disruption of these molecular clocks leads to metabolic syndromes, cancer, and premature aging by eliminating the temporal coordination of physiology with the external environment. By developing a structural and mechanistic understanding of how the clock generates 24-hour timing, we hope to identify new strategies to treat a broad spectrum of human diseases. This project aims to identify the structural basis for transcriptional regulation by the primary circadian transcription factor, CLOCK:BMAL1, which drives dynamic transcriptional regulation of the genome on a daily basis. Our recent crystal structure of the DNA binding and tandem PAS (PER-ARNT-SIM) domains of the CLOCK:BMAL1 heterodimer illustrates how it assembles into a functional dimer, but lacks the partially structured regions downstream that dynamically regulate its activity. Using solution NMR spectroscopy, we identified a slow conformational switch in the BMAL1 C-terminal transactivation domain mediated by *cis/trans* isomerization of a conserved Trp-Pro backbone imide bond. Here we demonstrate how this slow timescale conformational switch contributes to regulation of the CLOCK:BMAL1 complex by controlling binding of activators and repressors. By studying the dynamics and interactions of this switch we hope to contribute to the molecular understanding of how the intrinsic 24-hour period of the mammalian circadian clock is generated.

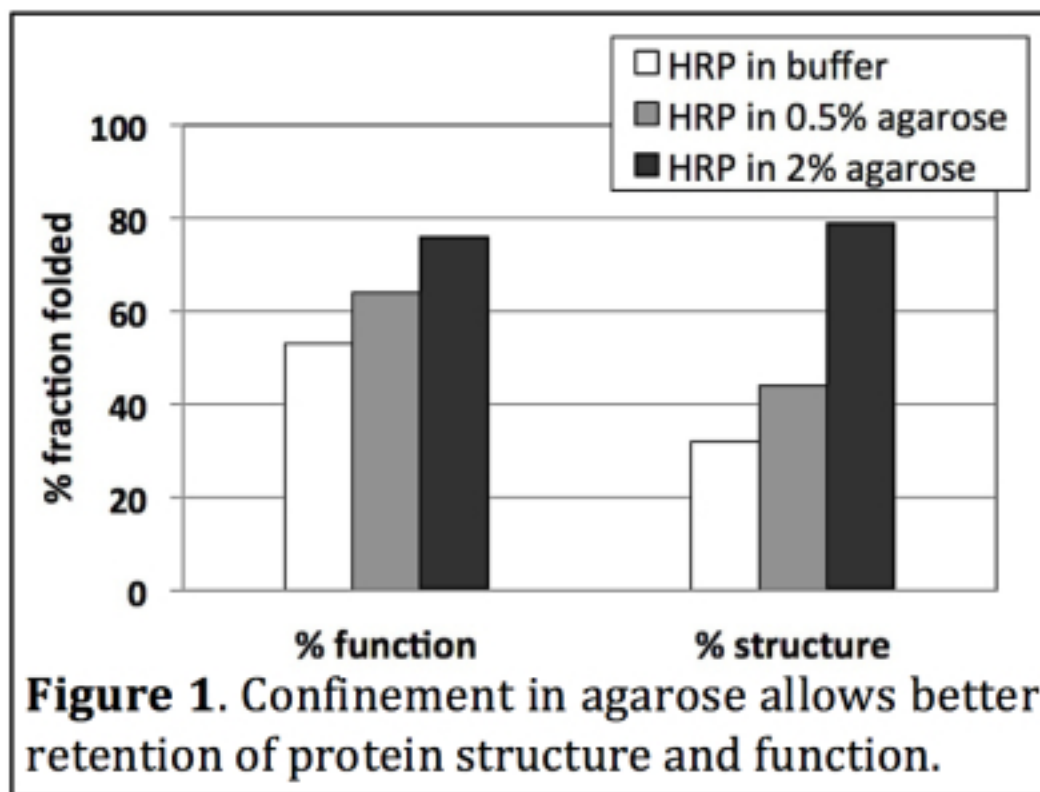
WRM 83

Function, structure, and stability of enzymes confined in hydrogels

Jeffrey Kunkel, Steven Long, Prashanth Asuri, asurip@scu.edu. Department of Bioengineering, Santa Clara University, Santa Clara, California 95053, United States

Research over the past few decades has attempted to answer how proteins behave in molecularly confined or crowded environments when compared to dilute buffer solutions. This information is vital to understanding in vivo protein behavior, as the average macromolecular space in the cell cytosol is much smaller than the macromolecules themselves.

In our study, we attempt to address this question using a model enzyme, horseradish peroxidase, encapsulated in agarose gels of different porosities. Under standard buffer conditions, we observe that the initial reaction rates of the agarose encapsulated HRP is lower than those of the solution phase enzyme. However, the encapsulated enzyme retains a higher percentage of its activity in the presence of denaturants. Moreover, the concentration of agarose used for encapsulation had a significant effect on the enzyme stability; HRP encapsulated in higher percentages of agarose were more stable than the enzyme encapsulated in lower percentages of agarose. Similar results were observed through structural measurements of HRP denaturation using an 8-anilino-1-naphthalene-sulfonic acid (ANS) fluorescence assay.



This work demonstrates the utility of hydrogels to study protein behavior in highly confined environments similar to those present in vivo; furthermore, the enhanced stability of gel-encapsulated enzymes may find use in the delivery of therapeutic proteins, as well as the design of novel strategies for biohybrid medical devices.

WRM 84

Automated Algorithm-Based Oxygen Transfer Rate Characterization in Production Bioreactors

Bernadette Dahlin, bernadette.dahlin@boehringer-ingelheim.com, Enrique Cervantes, Chung Chun. Boehringer Ingelheim Fremont, Inc., Fremont, CA, United States

Comprehensive hydrodynamic characterization of production bioreactors is necessary for the successful development, scale-up and tech-transfers of multiple drug substances from Process Development to Manufacturing. With bioreactors ranging from the 2 L and 5 L glass vessels in Process Sciences to the 12 kL stainless steel tank in the Manufacturing floor, a site-wide bioreactor characterization project would require extensive time and resources which may not be allocated due to other project commitments. An automated algorithm was developed to aid in the oxygen transfer rate (OTR) measurement, and the recipe required minimal user interaction once the cycle has been loaded. The automated recipe approach also helped in minimizing the experiment duration since it can run up to 12 conditions without any user input. To date, oxygen transfer rate data has been collected for the 2 L, 100 L stainless steel, and 100 L and 500 L single use bioreactors. At each scale, the OTR for 72 distinct conditions have been measured, and overlay has been modeled. These predictive OTR models expand the scale up/scale down toolkit available to process development engineers.

WRM 85

Expression of recombinant protein in *B. methanolicus*; a thermotolerant methylotroph

Claire Komives¹, claire.komives@sjsu.edu, Dewi Nilasari¹, Brian Wong². (1) Biomedical, Chemical and Materials Engineering, San Jose State University, San Jose, California 94027, United States (2) Boehringer Ingelheim, Fremont, CA, United States

B. methanolicus is an interesting organism for use as a production host due to the high growth temperature and ability to utilize methanol as a carbon and energy source. The work presented here is the first example of a recombinant protein expressed in the organism that is not native to the organism. *B. methanolicus* has been shown to be a good producer of amino acids. The talk will present some of the features of the host and the demonstration of expression of green fluorescent protein in fed batch and chemostat cultures.

WRM 86

Trans-acting acyltransferase domains: Tools for engineering polyketide biosynthesis

Briana Dunn¹, brianad@stanford.edu, Katharine Watts², Chaitan Khosla^{1,2}. (1) Department of Chemical Engineering, Stanford University, Stanford, CA 94305, United States (2) Department of Chemistry, Stanford University, Stanford, CA 94305, United States

Natural products have historically been an invaluable resource in the discovery and development of therapeutically active compounds. The polyketide class of natural products has seen huge success in the commercial drug arena, acting as a broad range of widely-used therapeutics. This biological diversity stems largely from the structural diversity of these small molecules, many of which are produced in an assembly-line fashion by large enzymatic complexes called modular polyketide synthases (PKSs). Each module of a PKS is comprised of several domains, and each domain plays a distinct role in extending and chemically modifying the growing polyketide chain. The acyltransferase domain (AT) is responsible for selection and incorporation of simple Coenzyme A- (CoA-) linked building blocks. Engineering of the AT domain for incorporation of novel substrates is an attractive approach in the production of new therapeutic polyketides. Some PKS modules lack integrated AT domains, and instead utilize stand-alone domains that act in *trans*. These domains are often responsible for catalyzing the transacylation of several different acyl carrier proteins (ACPs) in the assembly line. *Trans*-AT domains are potentially valuable tools for the engineering of building block selectivity, as they can be used to complement the activity of a selectively inactivated *cis*-AT domain. While most *trans*-AT domains characterized to date incorporate malonyl-CoA, several domains have been shown to accept substrates not naturally present in the host organism. Further, transacylation activity has been shown for several *trans*-AT domains with ACPs not from their native assembly lines.

Quantification of the acyl-CoA and ACP specificity of *trans*-AT domains is an important step in determining their utility. This work focuses on the kinetic characterization of *trans*-AT domains from the disorazole and kirromycin synthases, and examines their activity with several different CoA and ACP substrates. It also presents the *trans*-AT complementation of AT-null modules from the erythromycin synthase.

WRM 87

Non-invasive acoustical sensing and acoustic microfluidics: Applications in upstream bioprocessing

Sammy S Datwani, sdattwani@labcyte.com, R&D, Labcyte Inc., Sunnyvale, California 94089, United States

A newly developed method utilizing acoustic sensing (AS) in combination with acoustic droplet ejection (ADE) for precisely sensing fluid properties and for generating nanoliter volume droplets using focused acoustic energy will be presented with key applications for upstream bioprocessing. These technologies can be utilized to monitor the progress in the development of continuous upstream bioprocessing as well as for sample extraction for process analytical technologies.

Acoustic sensing and acoustic droplet ejection are truly non-invasive, tipless, touchless fluid monitoring and transfer technologies thereby making a unique platform for discovery and screening and for performing biological applications on the micro or nanoscale. Examples are presented which showcase the utility of these technologies for discovery/screening, monitoring reaction processes, enzyme engineering, and compound management, precise synthesis of drug-laden particles, biochemical assay assembly and protein crystallography.

WRM 88**Development of Enzyme Systems for the Production of Cellulosic Ethanol**

Thijs Kaper, Thijs.Kaper@dupont.com. Dupont Industrial Biosciences, Palo Alto, CA 94525, United States

To reduce dependence on fossil fuels and reduce carbon emissions into the atmosphere Dupont has developed an integrated process for cellulosic ethanol that covers the value chain from farm to fuel. An enzyme package has been developed through a combination of discovery and protein engineering that efficiently converts cellulose and arabinoxylan to monomeric sugars. Successful scale up of the technology has enabled the design of a commercial scale facility which is currently under construction in Iowa, USA. The facility will convert corn stover into ethanol and will come online next year.

WRM 89**GHS and what it means to laboratories**

Russell W Phifer, rphifer@wcenvironmental.com. WC Environmental, LLC, West Chester, PA 19380, United States

The implementation of the Globally Harmonized System for the Classification and Labeling of Chemicals impacts laboratories in two ways - employers must train employees on the GHS system, and make modifications to the facility Chemical Hygiene Plan to adopt the revised labeling requirements. This paper will help lab directors, EH&S personnel, and Principal Investigators provide a smooth transition.

WRM 90**Laboratory hazardous waste management: Best practices and the impact of the GHS**

David J. Keenan, davidkeen@sbcbglobal.net. Performance Safety Associates, Los Gatos, California 95032, United States

Each type of laboratory hazardous waste requires proper management from the moment the material is no longer needed until it is ultimately disposed. This presentation will help individuals to understand the requirements for proper waste identification and classification, along with the best management practices found in various types of laboratories. Considerations for the safe handling of hazardous waste as required by occupational safety and environmental protection agencies will be neatly summarized with the respect to current regulations and the forthcoming Global Harmonization System implementation.

WRM 91**Hazard assessment opportunities under the new Laboratory Standard**

Debbie M Decker, dmdecker@ucdavis.edu. Department of Chemistry, University of California, Davis, Davis, CA 95616, United States

Under the newly revised Laboratory Standard regulations, requirements for hazard assessment have become more important. This presentation will provide several techniques and options to accomplish hazard assessment, in the context of the new ACS Committee on Chemical Safety hazard assessment task force report.

WRM 92**Safety in the academic environment - a 30 year retrospective look forward**

John G Palmer, jpalmer@ucsd.edu. Retired - UC San Diego, San Diego, CA 92126, United States

Looking back over 30 years of working as a Health and Safety Director in a chemistry department where an advanced academic research and teaching environment was the norm can provide a useful perspective on how best to cope with new challenges and provide ideas on how to keep pace with expanding regulatory and managerial responsibilities.

WRM 93**University System-wide Actions to Improve Laboratory Safety Culture**

Ken Smith, ken.smith@ucop.edu. *Environmental Health and Safety, University of California, California, United States*

After the tragic death of one of its researchers, the University of California committed to a system-wide change in laboratory safety culture. With more than thousands of laboratories across 10 campuses and an estimated 50,000 researchers, this presented monumental challenges. In response the University of California developed a number of new policies, technological tools, and a PPE initiative designed to give UC researchers the tools they need to conduct safe research.

In establishing a unified system of policies, resources, and procedures throughout the UC system, UC has ensured that researchers arrive on campus educated in Laboratory Safety Procedures, equipped with the appropriate Personal Protective Equipment, and able to access tools to identify hazards and establish procedures for safe research.

WRM 94

UC and Cal-OSHA lab settlement agreement: One year later

Karen L Smith, ksmith23@ucmerced.edu. *Environmental Health and Safety, University of California, Merced, Merced, CA 95343, United States*

Sheri Sanji was fatally burned while working with t-butyllithium on December 28, 2008 in a UCLA research laboratory. Subsequently, charges were brought against the UC Regents and her professor, Dr. Haran. The Regents settled out of court while Dr. Haran continues to trial on three felony counts of willful violation of occupational safety and health standards. The settlement with the UC Regents applies to all chemistry and biochemistry departments of all ten UC campuses, not just UCLA.

Consequently, each campus must identify labs that fall under the agreement, train lab workers before beginning work, and write standard operating procedures. Each campus has approached the task in a different manner. UC Merced's approach will be discussed in detail, as well as lessons learned. Online tools developed by UC Davis IT will be presented, such as Radical for generating standard operating procedures, and the lab hazard assessment tool (LHAT) for PPE selection.

WRM 95

Quo Vadis: Laboratory safety after UCLA

Neal Langerman, neal@chemical-safety.com. *Advanced Chemical Safety, San Diego, California 92195-2329, United States*

Several high profile incidents in college and university laboratories across the country have result in death, serious injury, and major property damage. These incidents captured the attention of the press, the public, regulatory agencies and, for the first time, the US Chemical Safety Board (CSB). More detailed regulatory compliance may be on the horizon, without distinction as to laboratory type.

This presentation will discuss laboratory safety in the context of the academic and the industrial lab. This will include focus on the movement of academic lab scientists into the industrial lab, and related implications for specific training and performance standards associated with the industrial lab. He will also comment on contemporary changes in academic lab EHS now being driven by these high profile accidents which have occurred in recent years.

WRM 96

From The Control Room to the Courtroom

Carl Lippenberger, carl@lippenbergerlaw.com. *Law Offices of Carl Lippenberger, Mill Valley, CA 94941, United States*

From the control room to the courtroom: What's it been like? Was a technical background helpful? What do I know now that I didn't know then? Carl Lippenberger was a chemical engineer and is now a litigation attorney.

WRM 97

Food and Drug Administration laws and regulations - Food Safety - How chemists are involved

Elizabeth S Furukawa, elizabeth.furukawa@fda.hhs.gov. Center for Food Safety and Applied Nutrition, Office of Food Additive Safety, Division of Food Contact Notification, Food and Drug Administration, College Park, MD 20740, United States

U.S. FDA develops regulations based on the laws set forth in the Federal Food, Drug, and Cosmetic Act (FD&C Act) or other laws under which FDA operates, such as the National Environmental Policy Act (NEPA). This talk will give a brief background of U.S. FDA Laws and Regulations, and discuss how chemists are involved in regulatory aspects of premarket approvals for food safety. Specifically, the role of a chemist trained to facilitate information exchange by interpreting FDA laws, rules, regulations, and guidance documents to governmental authorities, trade associations, industry, and consumers with emphasis on food safety.

WRM 98

Beyond the bench: Careers in patent law for chemists

Kimberly Bolin, kbolin@mofo.com. Patent Prosecution Group, Morrison & Foerster LLP, Palo Alto, CA 94304, United States

Have you ever wondered why scientists leave the bench and what it is they do? Are you wondering what a patent agent does, and how to get started? Please join us to learn the answer to these questions as our presenter discusses her reasons for leaving the bench, how she got started in patent law, and what she enjoys most about being a patent agent.

WRM 99

Pathways to Intellectual Property: Options for Scientists

Jeffrey A Lefstin, lefstinj@uchastings.edu. Hastings College of the Law, University of California, San Francisco, CA 94102, United States

Dr. Jeffrey Lefstin is a former molecular biologist who is now Professor of Law at UC Hastings College of the Law.

Professor Lefstin will discuss the intellectual property landscape and programs that provide training in intellectual property law.

WRM 100

A Day in the Life: Patent Attorney

Sandra Thompson, sthompson@buchalter.com. Buchalter Nemer, Irvine, CA 92612, United States

Patent attorneys fit in two basic subfields – those who litigate and those who draft and file patent applications (prosecution). Dr. Sandra Thompson is a patent attorney who works primarily in prosecution and will discuss her background in chemistry, what it takes to be a patent attorney, and what a day in the life of a patent attorney looks like.

WRM 101

Electrocatalytic Reduction of H⁺ and CO₂ by a Series of Iron Carbonyl Clusters

Louise A. Berben, laberben@ucdavis.edu. Department of Chemistry, University of Davis, Davis, CA 95616, United States

Selective reactivity of an electrocatalytically generated catalyst—hydride intermediate toward the hydrogen evolution reaction (HER) or reduction of CO₂ is key for a CO₂ reduction electrocatalyst. Under appropriate conditions, Et₄N[Fe₄N(CO)₁₂] (Et₄N-1) is a catalyst for the HER or for CO₂ conversion at —1.25 V vs SCE using a glassy carbon electrode.

WRM 102

Using redox-active ligands to promote multi-electron reactivity at electrophilic metal centers

Alan F Heyduk, aheyduk@uci.edu, Aaron Hollas, Rui Munha, Janelle Lora. Department of Chemistry, UC Irvine, Irvine, CA 92697, United States

Redox-active ligand platforms have been used to access multi-electron chemistry at electrophilic, early transition metals. While Group 4 and 5 metal ions do not normally support multi-electron, small-molecule activation reactions, tridentate redox-active pincer ligands, denoted [ONO] or [NNN], have been shown to enable nitrene- and oxo-transfer. New results on O₂ activation to form reactive tantalum oxo species will be presented alongside kinetic and thermodynamic studies of imido and oxo reactivity.

WRM 103

Group 10 Metal-Mediated N-O Bond Activation

Joshua S Figueroa, jfigu@ucsd.edu. Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA 92093, United States

Nitrosoarenes have been used for decades as spin-trapping reagents for paramagnetic metal centers. Nevertheless, only limited information is available concerning the molecular and electronic structure of the resultant metal-bound nitroxide radicals. In this presentation, a series of Group 10 metal nitroxide radicals are discussed in the context of one-electron N=O activation and weak spin-spin interactions between multiple metal-bound nitroxide radical centers. Details of the solution phase dynamics of Group 10 metal nitroxide radicals are presented. These studies are shown to have uncovered transformations that lead to the complete, formally four-electron, scission of nitrosoarene N=O bonds. Synthetic, structural and spectroscopic studies aimed toward the generation of a new class of nitroxide-based mixed-valence materials are also presented.

WRM 104

Two-Step Electroreduction of CO₂ to Ethanol Catalyzed by Oxide-Derived Metal Nanoparticles

Matthew Kanan, mkanan@stanford.edu. Department of Chemistry, Stanford University, Stanford, CA 94305, United States

Electrochemical reduction of CO₂ provides a link between renewable electricity and carbon-based fuel. Catalysts suitable for a fuel-producing electrolytic device must reduce CO₂ and its derivatives with high selectivity and energetic efficiency using H₂O as the H⁺ source and produce a fuel of choice. Metal electrodes in their bulk form are inefficient and unselective CO₂ reduction catalysts. This talk will describe our development of "oxide-derived" metal nanoparticle electrocatalysts. Oxide-derived metal nanoparticles are prepared by reducing metal oxide precursors, which kinetically traps metastable nanoparticle structures that are uniquely enabling for catalysis. I will describe examples of these catalysts that electrochemically reduce CO₂ to CO at potentials close to the thermodynamic minimum as well as a catalysts that selectively reduce CO to multi-carbon oxygenates. The catalysts operate in water at ambient temperature and pressure and are remarkably robust. The structural origins of the catalytic activity will be discussed based on diffraction and high-resolution electron microscopy. Oxide-derived metal nanoparticles enable a two-step electrochemical conversion of CO₂ to ethanol that could make CO₂ a valuable feedstock for synthetic liquid fuel.

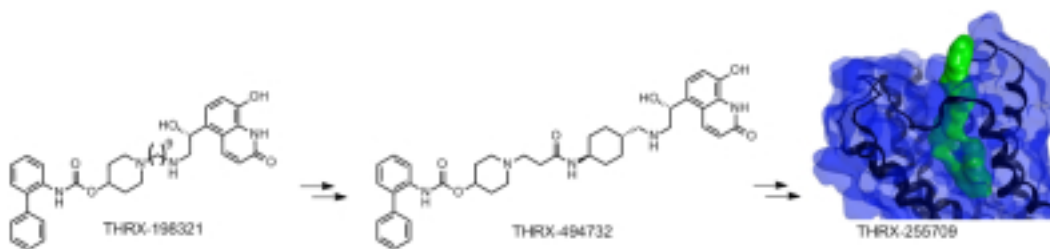
WRM 105

Discovery of Muscarinic Acetylcholine receptor antagonist and Beta 2 adrenoceptor agonist (MABA) dual pharmacology molecules

Adam D Hughes¹, ahughes@theravance.com, Erin K Bradley², Yan Chen¹, Sharath S Hegde³, Jeffrey R Jasper⁴, Tae-Weon Lee⁴, Alexander McNamara³, Mathai Mammen¹, M. Teresa Pulido-Rios³, Tod Steinfeld⁴. (1) Department of Medicinal Chemistry, Theravance, Inc., South San Francisco, United States (2) Computational Chemistry, LigDCipher, United States (3) Department of Pharmacology, Theravance, Inc, United States (4) Department of Molecular & Cellular Biology, Theravance, Inc., United States

Inhaled beta-2 adrenergic receptor (β_2) agonists and inhaled muscarinic acetylcholine antagonists are the most frequently used bronchodilators in the treatment of Chronic Obstructive Pulmonary Disease (COPD). While short-acting agents (4–6h) serve as 'rescue' therapy, long-acting (12–24h) bronchodilators can reduce the incidence and number of exacerbations, as well as improve

lung function. Due to the complementary nature of the two mechanisms, combinations of the two classes provide even greater improvement in lung function than either mechanism alone. By applying our multivalent approach to drug discovery, we sought to design muscarinic acetylcholine receptor antagonist and β_2 agonist dual pharmacology bronchodilators. Our initial discovery efforts and early structure activity relationships including the selection of muscarinic and β_2 pharmacophores as well as the significance of the linker moiety will be described. Several MABA molecules exhibiting bronchoprotection and extended duration of action in our animal models will be highlighted. The proposed multivalent bimodal orientation for these molecules will also be discussed.



WRM 106

Discovery of NAMPT inhibitors with favorable physicochemical properties as potential treatments for cancer

Mark Zak¹, mzak@gene.com, **Nicolas Skelton**¹, **Tom O'brien**¹, **Bianca M Liederer**¹, **Justin Ly**¹, **Leslie Wang**¹, **Deepak Sampath**¹, **Jason Oeh**¹, **Weiru Wang**¹, **Kenneth W Bair**², **Xiaozhang Zeng**², **Yen-Ching Ho**², **Timm Baumeister**², **Po-wai Yuen**³, **Peter S Dragovich**¹. (1) Genentech, South San Francisco, CA 94080, United States (2) Forma Therapeutics, Watertown, MA 02472, United States (3) Pharmaron, Beijing, China

Nicotinamide phosphoribosyltransferase (NAMPT) serves as a key mediator of tumor metabolism by participating in a biosynthesis pathway of nicotinamide adenine dinucleotide (NAD).

Specifically, NAMPT catalyzes the conversion of nicotinamide (NAM) and phosphoribosyl pyrophosphate (PRPP) to nicotinamide mononucleotide (NMN), a precursor to NAD. As a co-factor of enzymes required for cell metabolism and DNA repair, NAD is particularly important to rapidly proliferating cells. Inhibition of NAMPT and downstream depletion of NAD may, therefore, represent a novel approach to cancer chemotherapy. Herein we describe the identification and optimization of small molecule NAMPT inhibitors with favorable physicochemical properties.

Structure- and properties-based drug design techniques were employed to identify a lead compound with potent biochemical and cell-based NAMPT inhibition activity, good oral bioavailability in multiple preclinical species, and excellent efficacy in mouse xenograft studies. The SAR surrounding the lead series as well as the biological characterization of the lead compound will be described. Crystal structures of small molecule inhibitors in complex with the NAMPT protein will also be discussed.

WRM 107

Increasing target residence time in drug discovery; Optimization via covalent reversible interactions

Timothy D Owens, tim.owens@principiabio.com. Medicinal Chemistry, Principia Biopharma, South San Francisco, CA 94080, United States

The concept of drug-target residence time has emerged in the past decade as a critical, yet under scrutinized parameter in drug development. The efficacy gained by prolonged target engagement and the promise of improved safety profiles due to the low circulating plasma concentrations required make slow off-rate inhibitors attractive. Irreversible covalent binding of targets, either by drugs incorporating a strategically placed electrophile (*i.e.* EGFR and BTK inhibitors, proteasome inhibitors) or where metabolic transformation produces a reactive metabolite (proton pump inhibitors) provide one route to achieving long residence times and efficacy, although safety concerns have been raised for this approach. Alternatively, for certain targets, a conformational

change upon ligand binding can lead to slow off rates and extended residence time through non-covalent interactions. However, discovery of these inhibitors typically requires a specialized screening effort and is difficult to design a priori. A general methodology that would allow the design of compounds with extended target residence time is therefore highly desirable. This seminar will highlight Principia's reversible covalent technology which enables the design of potent, selective and durable inhibitors for targets containing cysteine residues in their binding pocket.

WRM 108

The potential of boron-containing small molecules in medicinal chemistry.

Yang Liu, yliu@anacor.com. Department of Medicinal Chemistry, Anacor Pharmaceuticals Inc., Palo Alto, CA 94303, United States

The element boron is underexploited in medicinal chemistry and has tremendous potential in drug discovery. The reactive empty P-orbital of boron interacts with enzyme targets in a manner that is not achievable with traditional carbon-based chemistry and leads to highly potent enzyme inhibitors. Despite this advantage and considerable effort within the industry on boronic acids inhibitors, only the proteasome inhibitor Velcade has reached the market. This is attributed to the poor drug-like properties of boronic acids. Anacor has overcome these limitations by creating a boron-containing compound collection that combines the P-orbital reactivity of the boron with chemical/metabolic stability and selectivity characteristics so that the resulting compounds have intrinsic drug-like properties. The compounds retain their ability to react with active site functional groups in proteins, but do so in a very selective manner. Anacor's boron-containing library is a rich source of chemical matter with demonstrated utility in inflammatory and infectious diseases. The structure-based design and optimization around the benzoxaborole scaffold has led to the discovery of novel bacterial LeuRS inhibitors that represent a new class of Gram-negative antibacterial agents. One further SAR investigation has provided new promising benzoxaboroles for the treatment of serious Gram-positive antibacterial infections including methicillin-resistant *Staphylococcus aureus* (MRSA).

WRM 109

Targeting the Immunoproteasome

Dustin L McMinn, dmcminn@onyx.com. Medicinal Chemistry, Onyx Pharmaceuticals, South San Francisco, CA, United States

Protein homeostasis plays a critical role in several cellular functions and is governed in part by proteasome-mediated degradation of polyubiquitinated protein. Two proteasome isoforms, the constitutive (cP) and the immunoproteasome (iP), are diversified in substrate specificity and function by consequence of sequence differences in select respective proteolytic subunits. The cP is found in all tissues, whereas iP harbors in hematopoietically-derived cells and can be induced in peripheral tissues following exposure to inflammatory cytokines (i.e. IFN- γ and TNF α). Whereas dual inhibition of cP and iP with agents such as Carfilzomib drives caspase 3/7 activation and induces cell death, selective inhibition of iP has been shown to regulate cytokine production and T-cell plasticity with no effect on cell survival. ONX-0914, a selective small-molecule inhibitor of the $\beta 5i$ subunit specific of the iP, is efficacious in animal models of autoimmune disorders. The crystal structure of ONX-0914 bound to murine cP and iP has revealed a structural basis for selectivity driven primarily by interactions within the S1 pocket of $\beta 5i$. However, computational modeling has indicated that the closely related analogue, PR-924, adopts a distinct binding mode that enhances selectivity for the human $\beta 5i$ subunit. Together, these data have potentiated the design of lead structures with excellent selectivity for the immunoproteasome.

WRM 110

Inhibiting protein-protein interactions

Julio C Medina¹, Steven H Olson¹, Yosup Rew¹, Felix Gonzalez Lopez De Turiso¹, Michael D Bartberger¹, Hilary P Beck¹, Jude Canon³, Ada Chen¹, Jeff Deignan¹, Brian Fox¹, Ana Z Gonzalez¹, Darin Gustin¹, Xin Huang¹, Xianyun Jiao¹, Lixia Jin², Frank Kayser¹, David Kopecky¹, Yihong Li¹, Jonathan D Oliner³, Tao Osgood³, Xuelei Yan¹, Qiuping Ye², Dongyin Yu³, Daqing

Sun¹. (1) *Therapeutic Discovery, Amgen, South San Francisco, CA 94080, United States* (2) *PKDM, Amgen, United States* (3) *Oncology Research, Amgen, United States*

Protein-protein interactions play a fundamental role in mediating cellular processes. However, due to their inherent nature, identifying drugs that disrupt these interactions remain challenging. The majority of protein-protein interaction drug targets are not accessible to biologics and inhibition with small-molecule drugs is difficult given the lack of suitable binding pockets. Among these targets, disruption of the MDM2-p53 protein-protein interaction is recognized as promising due to its role in regulating apoptosis, cell cycle arrest and senescence. This presentation will describe the structural based de novo design of molecules that inhibit the MDM2-p53 complex. We will also discuss our efforts towards the optimization of potent and selective inhibitors with favorable pharmacokinetic properties, leading to the discovery of AM-8553.

WRM 111

NNSA Radiochemistry Center of Excellence at the University of Tennessee

Howard L Hall, howard.hall@utk.edu. *Institute for Nuclear Security, University of Tennessee, Knoxville, TN 37996, United States*

In 2013, the National Nuclear Security Administration (NNSA) funded the establishment of a Radiochemistry Center of Excellence at the University of Tennessee. This center principally focuses on advanced radiochemical separation methods and the application of radiolabelled particle tracking (via PET) for validating computational fluid dynamics simulations. The center's research objectives and its early results are reviewed.

This work is supported by the NNSA Stewardship Sciences Academic Alliances program.

WRM 112

Real-world application of nuclear chemistry in a time of crisis; A summary of analytical support to the DOE Fukushima response by the Lawrence Livermore National Laboratory

Steven A Kreek, *Nathan G Wimer, Bryan B Bandong. Lawrence Livermore National Laboratory, Livermore, CA 94550, United States*

The Lawrence Livermore National Laboratory was the principal consequence management lab analysis capability supporting the U.S. Department of Energy response to the Fukushima Daiichi incident. Over the span of several months, LLNL was tasked to perform thousands of analysis of physical samples and *in situ* gamma-ray spectra that were collected by U.S. field teams in the region over the same period. The scale and duration of the response strained even our significant capability and highlighted the need for additional surge capacity, robust processes and illustrated the benefit of applying corroborative techniques to support and affirm technical conclusions.

Details of the analysis performed and the impact to the overall dose assessment will be described. This work performed under the auspices of the U.S. Department of Energy by Lawrence Livermore National Laboratory under Contract DE-AC52-07NA27344. LLNL-ABS-641738.

WRM 113

Experimental nuclear and radiochemistry at Lawrence Livermore National Laboratory: A radiochemistry renaissance

Dawn A Shaughnessy¹, shaughnessy2@llnl.gov, *Kenton J Moody*¹, *Roger Henderson*¹, *Narek Gharibyan*¹, *Patrick Grant*¹, *John Despotopoulos*². (1) *Chemical Sciences Division, Lawrence Livermore National Laboratory, Livermore, CA 94551, United States* (2) *University of Nevada, Las Vegas, NV, United States*

Radiochemistry has been a part of Lawrence Livermore National Laboratory (LLNL) since its founding in 1952. In recent years, the Experimental Nuclear and Radiochemistry Group has been involved in many different research projects, which include chemistry development for nuclear forensics, radiochemical diagnostics for the National Ignition Facility (the world's largest laser), chemical automation, and discovery of the heaviest chemical elements. In 2012, the laboratory and city were honored with the naming of element 116 as Livermorium. In this presentation, we will present an overview of the current experimental nuclear and radiochemistry program at LLNL,

including new advances for the inertial confinement fusion program and the future of heavy element studies.

WRM 114

Target fabrication & characterization for nuclear experiments at LLNL

Roger A Henderson, henderson55@llnl.gov. *Department of Experimental and Nuclear Radiochemistry, Lawrence Livermore National Laboratory, Livermore, CA 94550, United States*
Recent nuclear target making activities at LLNL have focused on double-sided foils for use at the DANCE and CHI-NU experiments located at the Lujan Neutron Science Center of the Los Alamos National Laboratory. A mixed-isotope $^{239/242}\text{Pu}$ target has been prepared and fielded at DANCE, and a large (93 mg) ^{239}Pu target assembly has been prepared and fielded at the CHI-NU experiment. The ^{239}Pu targets consist of ten large-area (4-cm) targets, where the uniformity of the deposit is a desired quantity of measure. The Target Record Player has been constructed to carry out these measurements, and results of the determinations are shown. The system now has the additional capability to serve as an inert foil thickness gauge, where the spectra of alpha particles passing through a foil to be measured are compared to a reference spectrum, whereby the energy loss and hence foil thickness can be determined. Results of a measurement of a 2.5 μm rolled Al foil are shown.

WRM 115

Radioanalytical Method Development for Nuclear Forensics and Safeguards: New Challenges and Old Familiars

Ralf Sudowe, ralf.sudowe@unlv.edu. *Department of Health Physics & Diagnostic Sciences, University of Nevada Las Vegas, Las Vegas, NV 89154-3037, United States*

The fast and reliable analysis of radioactive samples is of uttermost importance for nuclear forensics and safeguards. A fast quantification of the amount of radioactivity released is for example necessary to estimate the exposure risk to the public and to allow for swift and informed decision making in the immediate aftermath of the incident. Most current radioanalytical methods, particular for analysis of actinide elements and pure beta emitters, require however a substantial amount of sample preparation and chemical separations before the radionuclide of interest can be measured. It is therefore necessary to develop new sample analysis procedures that allow for a quick turnaround time and increased sample throughput with a minimum of deviation between samples. Another challenge stems from the fact that most current procedures have been developed for the analysis of air, water, soil and bioassay samples. While these protocols build the foundation of operational environmental monitoring, they are not necessarily suitable for the analysis of samples that will be encountered in the aftermath of a nuclear incident involving an improvised nuclear device or a dirty bomb. Of particular interest for emergency response and nuclear forensics are therefore methods that can be applied to the analysis of steel, concrete, melt glass, asphalt and bone samples.

WRM 116

Heavy element research at Texas A&M University

Charles M. Folden, Folden@comp.tamu.edu. *Cyclotron Institute, Texas A&M University, College Station, TX 77843-3366, United States*

A program to study the chemistry and physics of heavy elements is in progress at Texas A&M University. The Cyclotron Institute there houses two accelerators capable of producing beams with energies near the Coulomb barrier, and the Momentum Achromat Recoil Spectrometer has been developed for use as a separator for these experiments. Recent work has focused on nuclear reactions leading to the production of spherical, shell-stabilized nuclei near the $N = 126$ shell. This work has shown a clear dependence of the reaction cross section on the difference in neutron binding energy and fission barrier height. Further experimental work is focused on the development of novel extraction systems for the study of the chemistry of the transactinide elements and their homologs. Additionally, a new gas stopper has been designed and fabricated, and a nationwide collaboration has been formed to coordinate future online chemistry experiments. The most recent results of this work will be presented, along with personal reflections of the influence of Prof. Darleane C. Hoffman on the career of the author.

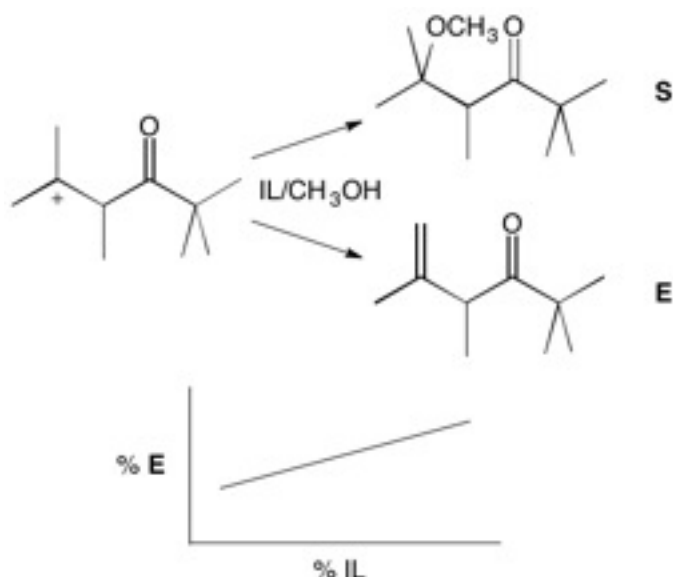
WRM 117

Effect of ionic liquid cosolvent on the methanolysis of pivaloyl triflate

Beth D. Kochly, *bkochly@mills.edu*, Susan Citrak, Nelius Gathondu, Gabriella Amberchan.

Department of Chemistry & Physics, Mills College, Oakland, CA 94613, United States

The effect of ionic liquid cosolvent on the k_{Δ} methanolysis of pivaloyl triflate was studied. The expected substitution and elimination pathways were observed, and product ratios determined by ^1H NMR spectroscopy. It was found that the ratio of elimination to substitution product increased linearly with increasing mole fraction of ionic liquid cosolvent. This trend is consistent among the ten ionic liquids studied. It was further determined that the rate of increase of elimination product correlates to the hydrogen bond donating and accepting ability of the solvent system, i.e. the Kamlet-Taft solvatochromic parameters α and β .



WRM 118

Water soluble Verdazyl Radicals synthesized from Aldoses

Thanh Ngoc T Le, *thanhngoc.le@sjsu.edu*, David J.R. Brook. Department of Chemistry, San Jose State University, San Jose, CA 95112, United States

Verdazyls are a series of heterocyclic, stable free radicals that are less well known than nitroxides. Verdazyl radicals are attractive targets for the development of spin probes and fluorescence quenchers because they have three variable substituents at the 1, 3, and 5 positions that may be used for molecular interaction, and they are easily synthesized from aldehydes. Our aim is to synthesize water soluble verdazyl radicals that can be developed into biological probes. Aldose provide an ideal starting point for water soluble verdazyl because they have both aldehyde and polyhydroxy functionality. We report a series of verdazyl radicals synthesized from aldo-pentoses and aldo-hexoses. These products were characterized by UV-vis, NMR, LCMS, and HPLC.

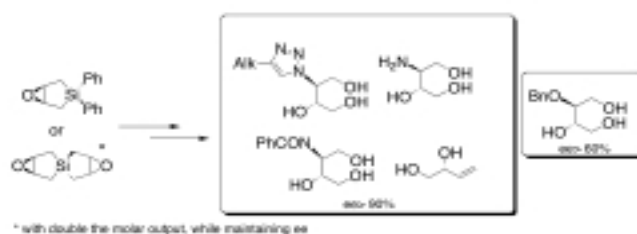
WRM 119

Multiplying the catalytic output of reactions through bifunctional substrates

Makan Kaviani-Joupari, *makan.kaviani@gmail.com*, Michael P. Schramm. Department of Chemistry and Biochemistry, California State University, Long Beach, Long Beach, California 90840, United States

The preparation of enantiopure building blocks is a fundamental area of importance for synthetic chemistry. We became particularly interested in asymmetric ring opening of silylcyclopentene

oxides with different nucleophiles such as azide and acetate using Jacobsen's catalysts. Silylcyclopentene oxide is amenable to several distinct asymmetric catalytic transformations providing access to enantio-enriched tetraols, triol-azides and triol-amines. The sequences employed allow for selective protection of one amine or alcohol from the four heteroatoms that are introduced into the carbon scaffold. We have now turned our attention towards utilizing bifunctional substrates containing two cyclopentene oxide rings in an attempt to double the molar output of these reactions, while reducing the waste created by spectator ligands. It turns out that the two asymmetric transformations work independent of the other functional groups present on the substrate and high enantioselectivity and good yield was achieved. This new type of atom economy may have other applications to multiplying catalytic output using polyfunctional substrates.



WRM 120

An efficient approach to the total synthesis of acylfulvenes, a class of potent antitumor agents

Ihsan Erden, ierden@sfsu.edu, *Jingxiang Ma*. *Chemistry and Biochemistry, San Francisco State University, San Francisco, California 94132, United States*

Acylfulvenes comprise a class of semisynthetic drugs that exhibit considerable antitumor activity and are related to the naturally occurring illudins. Although there are three reported total syntheses of the hydroxymethylacylfulvene, none of these involves a classical fulvene synthesis and are rather lengthy. We have developed a direct approach to acylfulvenes employing tandem acylation-intramolecular condensation reactions with the cyclopentadienyl anion. Applications of this methodology to smaller or larger ring systems, as well as the synthesis of acylfulvene analogs will also be discussed.

WRM 121

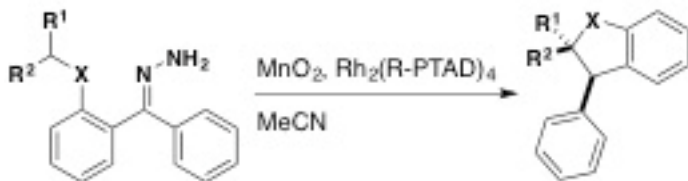
Asymmetric synthesis of 2,3-dihydrobenzofurans via Rh(II) catalyzed C-H insertions

Kellan N. Lamb, kncandee@ucdavis.edu, *Cristian Soldi, Richard Squitieri, Jared T. Shaw*.

Department of Chemistry, University of California, Davis, Davis, California 95616, United States

The first examples of Rh-catalyzed asymmetric C-H insertions involving a donor-donor carbene are reported. The carbenoid precursor, a diazo compound, is formed in situ by MnO₂ oxidation of

a diaryl hydrazone. A chiral catalyst, $\text{Rh}_2(\text{R-PTAD})_4$, is added in one pot to afford various 2,3-dihydrobenzofurans. Highlights of this reaction include no necessary isolation of the diazo intermediate and low catalyst loading (0.5 mol %). Excellent yields of up to 95%, with dr >95:5 and er up to 99:1 have been observed for a variety of substrates. Efforts towards applying this methodology to the total synthesis of the resveratrol dimer *E*- ω -viniferin are underway.



WRM 122

Cation Stabilizing Strategies for Sc-catalyzed Enantioselective [3+2] Carbocycle Annulations with Allylsilanes

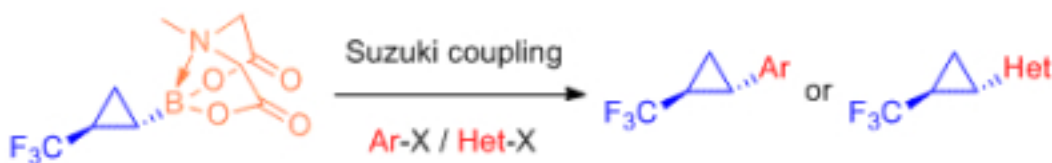
Nicolas Ball-Jones, nballjon@gmail.com, Joseph J Badillo, Brittany M. Anderson, Annaliese K. Franz. Department of Chemistry, University of California, Davis, Davis, CA 95616, United States
Herein we disclose the first catalytic asymmetric [3+2] allylsilane annulation for the synthesis of cyclopentanes containing a quaternary spirocenter. The annulation reaction is catalyzed with a scandium(III)-indapybox complex where the presence of a BArF anion plays an important role in the catalytic activity and stereoselectivity. Formation of a lactone product via trapping of the β -silyl carbocation provides support for an ester-stabilized carbocation intermediate. Mechanistic insight through NMR spectroscopy will also be presented. The utility of the optimized conditions will also be presented for the diastereoselective synthesis of functionalized cyclopentanes derived from coumarin and simple malonates. Transformations of the annulation products provide access to NH spirooxindoles and demonstrate that the silyl group can be converted a hydroxyl moiety using Tamao-Fleming oxidation conditions.

WRM 123

Synthesis of *trans*-2-(trifluoromethyl)cyclopropanes via Suzuki cross-coupling reactions with a MIDA boronate

Matthew A J Duncton, mattduncton@yahoo.com, Rajinder Singh. Department of Chemistry, Rigel, Inc., South San Francisco, CA 94108, United States

Motifs with three-dimensional topology are of interest to medicinal chemists. The *trans*-2-(trifluoromethyl)cyclopropyl motif, which combines the well-known cyclopropyl and trifluoromethyl groups in a unique three-dimensional arrangement, is a potentially attractive fragment for medicinal chemists. In this paper, we describe the synthesis and use of an easily prepared building block - *trans*-2-(trifluoromethyl)cyclopropylboronic acid MIDA ester - which can be used to introduce the 2-(trifluoromethyl)cyclopropyl fragment in to aromatic and heteroaromatic systems via a Suzuki reaction. In particular, we have focused on introducing the 2-(trifluoromethyl)cyclopropyl motif in to templates frequently encountered by medicinal chemists



WRM 124

Towards a PLA for durable goods

Allison Flynn, aflynn@lapol.net, Lennard Torres. Lapol, LLC, Santa Barbara, CA, United States

While polylactic acid is probably one of the most popular bio-derived resins being explored, it has distinct problems when compared to fossil-derived resins. PLA is generally brittle and exhibits a low softening temperature, thus making it unsuitable for applications that require flexibility, toughness, or heat resistance. The predominantly used and commercially available resins used for improving some of the properties of PLA are often derived from petroleum. Lapol, LLC, a renewable biopolymer resin technology company, offers solutions to these problems and limitations of PLA by creating cost effective, biodegradable products that not only improve the properties of PLA but also reduce environmental burdens. Lapol, LLC sells its resins to end-user converting companies that seek biodegradable/compostable and renewable/sustainable polymer applications for products such as: containers, food service disposables, electronic components, credit cards, toys and a variety of other products that are injection molded, thermoformed, blow molded, extrusion coated or extrusion cast films. This presentation gives an overview and status of the current Lapol, LLC technology.

WRM 125

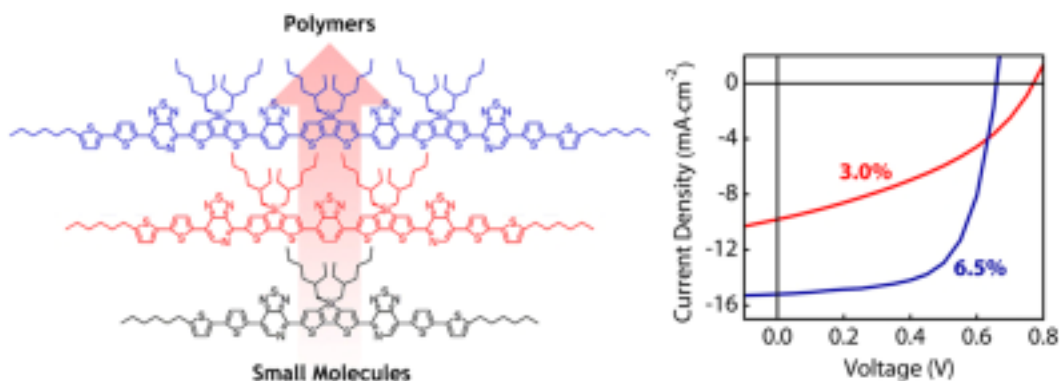
Extended donor-acceptor alternating narrow band-gap molecules for organic photovoltaics: Bridging between polymers and small molecules

Xiaofeng Liu, xliu@chem.ucsb.edu, **Guillermo C. Bazan**, *Center for Polymers and Organic Solids, University of California Santa Barbara, Santa Barbara, California 93106, United States*

Narrow band-gap conjugated polymers and small molecules have both been drawing significant contribution in organic solar cells. Intrinsic advantages and disadvantages relevant to solution processable photovoltaics are often contrary between these two classes of materials. In particular, small molecules possess monodispersity in chemical structures and higher crystallinity, while on the other hand, poorer film formation properties and lower thermal stabilities, as compared with their polymeric counterparts. More importantly, solar cell devices based on small molecular materials are extremely sensitive towards chemical impurities, of which polymers are relatively more tolerant.

Considering the fact that polymers and small molecules provide complementary material properties, we have designed molecular frameworks with successive extension of donor-acceptor characteristics. Materials synthesized following these frameworks are able to adopt some of the most important merits from both polymers (e.g., film quality and thermal robustness) and small molecules (e.g., structural monodispersity and crystallinity). Fabrication of solar cell devices with these materials does not require delicate control over solvent additives or post-deposition treatment, yet reaching power conversion efficiencies close to the highest reported value

obtained for discrete molecules to date (6~7%). When integrated in field effect transistors, the most extended molecular system shows device thermal stability beyond 200 °C.



WRM 126

Novel amphiphilic and super absorbent cellulose nanofibril aerogels

Feng Jiang, fjiang@ucdavis.edu, **You-Lo Hsieh**, *Department of Fiber and Polymer Science, University of California, Davis, Davis, California 95616, United States*

Cellulose nanofibrils (CNFs) with 1-2 nm widths and up to 1 μm lengths have been robustly derived from rice straw cellulose at 96.8% yield and assembled into aerogels with tunable densities as low as 1.7 mg/cm^3 and porosities up to 99.9%, far superior than organic super-absorbents and approaching those of silica and carbon aerogels. These CNF aerogels are uniquely amphiphilic and demonstrate superior absorbency towards both polar and non-polar liquids (e.g., 210 g/g water and 375 g/g chloroform), unprecedented for aerogels. In water, these CNF aerogels display outstanding resilience at 0.8 compressive strain and full recovery within 4s and over 100 cycles. The absorption capacity toward saline solution (0.9 wt% NaCl) is as high as 210 g/g, far superior to the less than 50 g/g of acrylic-based superabsorbents. Modification with triethoxyl(octyl) silane further enhanced the oleophilicity of these aerogels to absorb 139-356 times of non-polar hydrocarbons, polar aprotic solvents and oils, surpassing all polymeric super-absorbents as well cellulose and carbonaceous aerogels by 2 to nearly 20 times and approaching the best performing carbon nanotube and graphene aerogels. The absorbed hydrocarbons could be fully recovered from saturated aerogels that still retain over 50% of its original absorption capacity after 6 cycles.

WRM 127

Biodegradable Plastic Produced by Bacteria

Allison J. Pieja, allison@mangomaterials.com, Mango Materials, Palo Alto, California 94302, United States

Mango Materials produces biodegradable plastics from methane that are economically competitive with conventional petroleum-based plastics. Mango Materials uses excess methane gas from wastewater treatment plants or landfills to produce pellets of polyhydroxyalkanoate (PHA), a valuable polymer that is converted into a variety of high margin or high volume, eco-friendly plastic products such as children's toys, electronic casings, water bottles, and food packaging containers. Due to a rising preference for green products from both consumers and government agencies, demand for biodegradable and non petroleum-based plastics is growing rapidly. The competition uses either petroleum, which is low cost but produces non-biodegradable plastic, or sugars, which are expensive but produce biodegradable plastic. In contrast, Mango Materials uses affordable methane gas and a process that competes favorably with petroleum-based plastics to produce low-cost, biodegradable plastics. Currently, Mango Materials is in the process of scaling up from small bench-top reactors to a demonstration facility that will produce commercial samples of PHA. This technology gives methane producers another profitable use for their waste biogas while transforming a greenhouse gas into a valuable commodity. This presentation will discuss the concept of using methane to produce a biodegradable plastic.

WRM 128

Torrefaction of agricultural by-products: Effects of temperature and time

Bor-Sen Chiou¹, bor-sen.chiou@ars.usda.gov, **Cristina Bilbao-Sainz**¹, **Diana Valenzuela-Medina**¹, **Artur Klamczynski**¹, **Rebecca Milczarek**², **Roberto Avena-Bustillos**², **Wen-Xian Du**², **Syed Imam**¹, **Greg Glenn**¹, **William Orts**¹. (1) Bioproduct Chemistry and Engineering, U.S. Department of Agriculture, Albany, CA 94710, United States (2) Processed Foods Research, U.S. Department of Agriculture, Albany, CA 94710, United States

Agricultural by-products, such as apple, grape, olive, and tomato pomaces as well as almond and walnut shells, were torrefied at different temperatures for various times. Torrefaction involves heating at 200°C-300°C under inert atmosphere to remove volatiles and produce materials with lower moisture contents and higher energy values. Raw tomato pomace had the highest energy value due to its high lignin and fat contents. Also, raw grape and olive pomaces had high energy values due to their high fat contents. All samples had relatively high energy yields when torrefied at 230°C, but had reduced energy yields at higher temperatures and times.

WRM 129

Optimizing the value of agriculturally-derived fibers based on their source & properties

William J. Orts¹, bill.orts@ars.usda.gov, **Gregory M. Glenn**¹, **Eliton S. Medeiros**², **Eliangela de M. Teixeira**³, **Adriana de Campos**³, **Morsyleide F. Rosa**⁴, **Luiz H.C. Mattoso**³. (1) USDA-ARS, Western Regional Research Center, Albany, CA 94710, United States (2) Centro de Tecnologia,

Universidade Federal da Paraíba, João Pessoa, PB 58050-900, Brazil (3) Laboratório Nacional de Nanotecnologia para o Agronegócio, Embrapa Instrumentação Agropecuária, São Carlos, SP 13560-970, Brazil (4) Embrapa Agroindústria Tropical, Fortaleza, CE 60511-110, Brazil

After years of delay, biorefineries that convert cellulose to biofuels are starting to come on line; however, this emerging industry has a long way to go until it can profitably meet its targeted production levels. Cellulosic-ethanol production has been delayed by technical challenges. The industry needs assurances that technology exists to convert agriculturally-derived fibers to value-added products.

The USDA research team from Albany, California is developing biorefinery strategies relevant to the Western US by utilizing biomass feedstocks that are prevalent in the West. Beyond biofuels, it is critical to produce multiple products from these feedstocks. Data will be presented on development of (1) novel enzymes and microbes, and (2) novel chemical/mechanical methods for making value-added chemicals and polymer composites from these same feedstocks.

Specifically, this presentation focuses on production of products from agriculturally-derived fiber sources and compares their functionality as it relates to fiber source. Applications include creation of drop-in-replacement biodegradable polymers, sustainable composites, and novel nanocomposites. This presentation also represents a successful collaboration between USDA and Brazilian researchers whereby we compare results for fibers traditionally found in North America with those more prevalent in the tropics (i.e. sisal, jute and coconut fiber). In one study, for example, blends of sisal fiber with biopolymers of starch and poly(caprolactone), a degradable biopolymer, showed increases in both tensile strength by as much as 30% and elastic modulus (resilience) by 2-fold with the addition of 5% and 10% fiber. These results were significantly different from those obtained using flax fiber, a traditional fiber found in North America. In another study, nanocrystalline cellulose derived from coconut husks reveal longer fibrils than those obtained from rice straw, wheat straw, or cotton. Implications of these property differences will be discussed.