2025

Glenn T. Seaborg Symposium

Abstract Book

UCLA CNSI AUDITORIUM

Many thanks to all of our participants and Applicants!

2025 Glenn T. Seaborg Symposium

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Regioselective Au(III) mediated metalloenzyme arylations

Nima Adhami, Michael Rebelo, Parathorn Teptarakulkarn, Sofia H. Ando, Eileen J. Olivares, Michael R. Sawaya, Thomas Louie-Goff, Tyler A. Kerr, Jose A. Rodriguez[1,2], Alexander M. Spokoyny[1,2]

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Metalloenzymes play a central role in countless biological processes, yet understanding their precise mechanisms remains a formidable challenge due to inherent limitations in existing research methods. Bioconjugation chemistry has emerged as a transformative tool, allowing us to attach functional probes to specific biomolecular sites and study these macromolecules in their native environments. While the field has advanced significantly for various biomolecules, metalloenzymes have remained underexplored as substrates. Unlocking strategies that selectively and bioorthogonally targeting these systems promise to shed light on their intricate functions and broader roles in cellular processes. In this work, we address these challenges by developing a Au(III)-mediated platform for selective arylation of cysteine residues in metalloenzymes, focusing on Fe and Ni Rubredoxin—metalloproteins notable for containing five cysteine residues. By employing a range of Au(III) reagents, we achieved unprecedented regio- and chemoselectivity with quantitative yields, a first in the metalloenzyme conjugation space. Remarkably, the reactions proceed rapidly and under mild conditions, making it both practical and broadly applicable. Structural and functional characterization, through cyclic voltammetry and circular dichroism, confirm that Rubredoxin conjugates retain their native structure and function. Notably, this work showcases the first single crystal X-ray structure of a directly arylated metalloprotein, opening the door to new structural and mechanistic insights. These findings highlight the specificity, efficiency, and versatility of our Au(III)-mediated strategy as an invaluable tool for site-selective metalloenzyme modifications.

Authors: Ajmera, P., Chaturvedi, S. S., Vargas, S., Goswami, A., Qian, B., Petersen, A., Alexandrova, A.N.
Affiliation and Funding: UCLA Department of Chemistry and Biochemistry | NIH, NSF
Title: Evolution of Electric Fields for Catalyzing Enzyme Reactions
Abstract: Electrostatic preorganization is widely considered to be a key factor for the efficiency of natural enzymes to catalyze reactions. Electric fields are a well-defined descriptor to gauge the preorganization at the enzyme's active site. We have previously found that a 3-dimensional, dynamic description of active site electric fields is an information-rich approach to understanding the electrostatic landscape necessary for a reaction. The methods we have developed to analyze the time-dependent nature of these electric fields allows us to understand the evolution of enzymes, both natural and lab-based. We introduce an open-source adaptable framework for such analyses, applicable across various classes of enzymatic reactions. We illustrate that the directed evolution of protoglobin for a non-native cyclopropanation reaction modulates the enzyme's inherent electric field, optimizing it for the non-native chemistry. Additionally, we observe across families of chorismate mutase enzymes, all which catalyze the Claisen rearrangement, a variety of favorable electric fields that evidently stabilize the transition state. Our research highlights the intricate ways in which natural and evolved enzymes tailor the electric fields at their active sites for optimized catalysis.

Poster Abstract

Title: Magnesium Isotopic Composition of Igneous Rock Standards via MC-ICP-MS
Affiliations: University of California, Los Angeles
Authors: Yara Fahmy Boutien, Cage Zhou, Peng Ni

Abstract

Magnesium isotopes play a vital role in geochemistry, serving as tracers for mantle-crust interactions, biogeochemical cycling, planetary differentiation, and the origin of life. As a key component of silicate rocks, Mg undergoes isotopic fractionation during magmatic, metamorphic, and sedimentary processes, making it essential for understanding Earth's geochemical reservoirs' evolutionary patterns over time. Our lab has recently focused on high-precision Mg isotope analysis for sub-μg Mg samples using multi-collector inductively coupled plasma mass spectrometry (MC-ICP-MS), to enhance inter-laboratory reproducibility. We measured the δ^{24}Mg, δ^{25}Mg, and δ^{26} Mg (relative to standard reference DSM-3) of geochemical reference materials (BHVO-2 and BCR-2), along with the synthesized standard solution.

To improve Mg purification, we implemented a newly calibrated step involving the addition of $HNO_3 + HF$, which enhances the removal of matrix elements such as Li, Na, Zn, and Ti by shifting their elution peaks away from Mg, reducing contamination. Our method follows the general approach established in previous studies but employs a micro-column for Mg separation and collection. The results from MC-ICP-MS confirm the viability of this micro-column method for analyzing low-Mg samples, demonstrating high Mg recovery while maintaining measurement accuracy and precision. This validation highlights the effectiveness of the micro-column approach in refining Mg isotope analyses and improving data consistency across laboratories.

Title: Leveraging cooperative dual Ni catalysis for photoredox-enabled alkyl–alkyl cross-coupling

Authors:
Melecio A. Perea,[§,‡] Erin M. Bucci,[§,‡] Remy F. Lalisse,[†‡] Poulami Mukherjee,[†‡] T. Judah Raab,[‡] Lakshmy Kannadi Valloli,[¶] Matthew J. Bird,*[,¶] Osvaldo Gutierrez,*[,†‡] and Abigail G. Doyle*[,‡]

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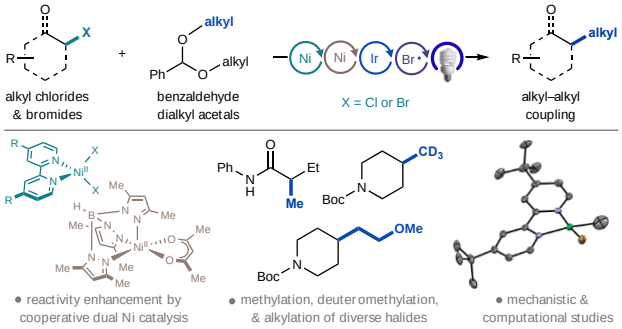
[§]These authors contributed equally

Abstract body:

The installation of alkyl substituents, such as methyl groups, is a crucial tactic for the synthesis and diversification of medicinal compounds with improved pharmacological profiles. However, strategies that leverage methyl radical for C(sp^3) methylation remain underdeveloped due to the challenge of obtaining cross-selectivity between fleeting aliphatic radicals and alkyl electrophiles. We report a conceptually-novel mechanistic framework for C(sp^3)–Me bond formation using two different Ni catalysts capable of cross-coupling diverse alkyl halides (chlorides and bromides) with methyl radical generated photocatalytically from benzaldehyde dimethyl acetal. Notably, this strategy is effective at methylating a variety of primary and secondary alkyl halides with diverse steric and electronic profiles. Furthermore, by modifying the alkyl substituents on the acetal coupling partner, we demonstrate cross-couplings beyond methylation to access an array of 1°–1° and 1°–2° alkyl–alkyl bonds with complementary selectivity to S_H2-guided pathways. Experimental and computational mechanistic studies provide support for a presumptive, in situ-generated (bpy)Ni^{I}(X) catalyst, which facilitates C–C bond formation, while a (Tp*)Ni^{II}(acac) co-catalyst cooperatively stabilizes and shuttles methyl radical for chemoselective cross-coupling.



Dissecting the Regulation and Bypass of Translation Termination

Izaiah Cole, Michael Lawson

Abstract:

Translation termination, as the final step of the central dogma of biology, is complex process that requires many proteins working in tandem to properly release synthesized peptides or mark for degradation by nonsense mediated decay. Release of the peptide chain from the ribosome has currently been stated to be the work of release factors eRF1, and eRF3; however, our interest of influential factors resides primarily in dissociable regulatory factors such as ABCE, the identity of the terminal amino acid, and mRNA sequence/modifications. We will investigate how these factors influence termination of translation via an in-vitro reconstituted yeast translation system and single-molecule fluorescence spectroscopy to track the impact of these various factors in real time. This research will contribute to our understanding of how these various factors influence the rate of translation termination, along with other coordinating processes, such as regulation of ribosomal traffic, recycling, and stop codon readthrough.

Funded by UCLA CBI Training Grant (T32GM136614)

Embedded Heterocyclic Functionality Enables Passive Permeability of Complex Peptidomimetic Macrobicycles

Cooper, G. I. D.; Durham, N.; Walker, G. L.; Yu, H.; Harran, P. G.*

Abstract

Peptidic macrocycles can bind protein targets with greater affinity and selectivity than traditional small molecules. However, their therapeutic utility is often limited by poor cellular uptake, low oral bioavailability, and rapid metabolism. General strategies for improving the passive membrane permeability of peptidic macrocycles remain elusive. Our lab has recently discovered that complex polyfluorinated macrobicycles bearing bridging heterocyclic residues demonstrate high permeability, with several exceeding that of orally bioavailable small molecules, diclofenac and chloramphenicol ($P_{app} \geq 5.0 \times 10^{-6}$ cm/s). Evaluation of structure in relation to observed permeability supports transannular hydrogen bonding shielding peripheral polar surface area. We hypothesize this gives amphiphilic character to our structures, thus enabling passive membrane permeability.

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Funding

This work has been supported by the NSF (CHE-2246856 to P.G.H.), the NIH grant (1S10OD028644 to UCLA), and major equipment grant NSF CHE-1048804 is acknowledged.

Authors: Jiaming Ding, Allison T. Hands, Lucas A. Wein, Nathan J. Adamson, John M. Billingsley, Yi Tang and Neil K. Garg*.

Department of Chemistry and Biochemistry, University of California, Los Angeles

Title: Concise Total Synthesis of (–)-Pensubrubine Using an Interrupted Fischer Indolization Strategy

Abstract: Natural products that possess the pyrrolidinoindolines motif have drawn significant attention from the chemical community. Recently, the Tang lab at UCLA has identified a family of new pyrrolidinoindolines, named the subrubines, which feature a unique diaza[3.3.3]propellane core. This presentation will describe our synthetic efforts toward this class of natural products, which has led to the completed total synthesis of (–)-pensubrubine. The synthesis features a key diastereoselective interrupted Fischer indolization reaction to rapidly introduce a quaternary stereocenter and assemble the challenging C3–C2–C3' stereotriad. The total synthesis of (–)-pensubrubine was achieved in only seven steps from known compounds and allowed for the unambiguous establishment of the natural product's absolute stereochemical configuration. These studies not only provide access to the natural product, but also highlight the utility of interrupted reactions for the rapid introduction of structural complexity.

Funding Source: National Science Foundation CHE-2246904

Elucidating key steps of ribosomal collisions and rescue utilizing an *in-vitro* reconstituted yeast translation system

Author Names: Aubrey J. Emmi[1], Dr. Michael R. Lawson[1,2]

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Abstract:

RNA quality control mechanisms mediating protein synthesis are signaled by the stalling and collision of ribosomal subunits. The delay in processive ribosomal elongation can be due to many defects in the mRNA, eventually leading to aberrant mRNA and nascent protein degradation, as well as ribosomal rescue. Quality control mechanisms, like no go decay and the ribosomal quality trigger, are crucial for suppressing the formation of harmful proteins and have been implicated in many neurodegenerative diseases. While these processes are essential to maintaining the proteome, many questions remain regarding the mechanism, kinetics, and crosstalk between these quality control systems. In Aim 1 of this project, the factors responsible for surveillance of ribosomal collisions, Hel2 and Cue2, will be monitored in the presence of different mRNA stalling sequences using single-molecule assays. Tracking these quality control factors using total internal reflection fluorescence (TIRF) microscopy will allow the control and resolution to monitor the dynamics of these proteins over time. In addition to elucidating the dynamics of ribosomal collision sensing, Aim 2 will investigate ribosomal subunit splitting in the presence of an aberrant mRNA. The coordination of the no go decay factors, Dom34, Hbs1, and Rli1, will be monitored in the presence of normal and cleaved mRNA. Characterization of ribosomal collisions and subunit splitting in the presence of an aberrant mRNA can be compared to the canonical process of termination, highlighting the kinetics of crucial ribosomal quality control mechanisms.

Funding Sources: This work is supported by the National Institute of Health under Award Number T32GM145388.

Abstract:
Phosphoranyl radicals provide a unique mode of reactivity to activate strong bonds under the mild conditions conferred by photoredox catalysis. Using the α-scission pathway of a phosphine-photoredox dual system, we have developed a catalytic strategy for the N-H activation of a variety of azoles, forming anti-Markovnikov selective N-alkylated products with unactivated olefins. Current work aims to further explore the selectivity and scope of this intermolecular hydroamination method.

Authors:
Kassandra Sedillo[1], Flora Fan[2], Robert R. Knowles[1], Abigail G. Doyle[2]
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External Funding:
NIH

Nine Novel Small Molecule Modulators That Inhibit Mitochondrial Import of Mutant Alanine-Glyoxylate Aminotransferase via High Throughput Screening of Human Cell Models of Primary Hyperoxaluria Type 1

Peter Fernandez[1], **Jonathan Shirley**[1], Jordan Tibbs[1,2], Robert Damoiseaux[4], and Carla Koehler[1,3]

[1]Department of Chemistry and Biochemistry, [2]Biochemistry, Biophysics, and Structural Biology, [3]Biochemistry, Molecular, and Structural Biology, [4]Molecular Screening Shared Resource, University of California, Los Angeles, Los Angeles, CA 90095

Primary Hyperoxaluria Type 1 (PH1) is a metabolic disorder caused by autosomal recessive mutations that culminate in End Stage Renal Disease (ESRD). Pathologically, point mutations in the protein alanine-glyoxylate aminotransferase (AGT) result in either mislocalization of a metabolically active protein, typically from peroxisomes to mitochondria, or aggregation in other cellular compartments. Physiologically, the mislocalization disrupts AGT's detoxification role, causing oxalate buildup and kidney stones characteristic of ESRD. Current treatments, like kidney stone removal, dialysis, and renal allografts, do not fully attenuate PH1, and mortality from complications remains high, especially in younger patients. Our project aims to ameliorate PH1 by using small molecules to relocate mutant AGT from mitochondria to peroxisomes and restore its function. Compounds like MitoBloCKs have been shown to inhibit mitochondrial import and redirect mutant AGT P11L-G170R. We endeavor to investigate multiple drug classes as potential treatments. We developed a human liver model using a HepG2 FlpIn cell line expressing mutant AGT P11L-G170R for high-throughput screening. AGT is fused to a C-terminal GFP (AGT-GFP11), while the remaining GFP1-10 is targeted to peroxisomes. Upon small molecule treatment, successful protein relocation to peroxisomes is confirmed by green fluorescence upon GFP reconstitution. After screening ~55,000 compounds, we discovered nine capable of rescuing mutant AGT and producing a phenotype comparable to wildtype cells. Peroxisome numbers also appeared to double when certain compounds were screened compared to wildtype AGT, suggesting peroxisomal biogenesis may be implicated in the rescue mechanism. Our work highlights the potential of mitochondrial import inhibitors for treating diseases of similar pathology, with our high-throughput screening protocol offering a promising approach to identifying drug targets and understanding disease mechanisms.

Authors: Caitlyn Fick, Advait Holkar (Chemical and Biomolecular Engineering, UCLA), and Samanvaya Srivastava (Chemical and Biomolecular Engineering, UCLA)

Advisor: Samanvaya Srivastava (Chemical and Biomolecular Engineering, UCLA)

Abstract: Synthetic complex coacervates have been proposed as an exciting platform for protocellular enzymatic reactors, protein encapsulants and stabilizers, and additives in cosmetics and consumer care products. However, rapid droplet coalescence in complex coacervate dispersions limits their utility. As such, developing coacervate-water interfacial stabilizers remains a long-standing challenge. To this end, our previous work demonstrated robust stabilization of complex coacervate microdroplets against coalescence by using comb polyelectrolytes (cPEs). In this poster, we will assess the critical comb polymer characteristics and architectures that govern coacervate emulsion stability. Synthesizing an extensive library of cPEs with varying backbone lengths, sidechain lengths, and sidechain densities facilitates an exploration of the key parameters and the necessary concentrations that dictate droplet stability and size distributions, achieving robust stabilization. We envision that this research will pave the way for establishing design rules to create coacervate-water amphiphiles, macromolecules that have a strong affinity towards the coacervate-water interfaces.

This research was supported by the National Science Foundation under grant no. DMR-2048285.

Authors: Sarah A. French[1] Allison M. Clark,[1] Luca McDermott,[1] Zach G. Walters,[1] Jiaming Ding,[1] Andrew V. Kelleghan,[1] K. N. Houk,[1] Neil K. Garg.[1]

Affiliation: [1]Department of Chemistry and Biochemistry, University of California, Los Angeles, CA 90095, USA.

Title: Addressing the anti-Bredt olefin synthesis problem.

Abstract: The π-bonds in unsaturated organic molecules are typically associated with having well-defined geometries that are conserved across diverse structural contexts. Nonetheless, these geometries can be distorted, leading to heightened reactivity of the π-bond. Although π-bond–containing compounds with bent geometries are well utilized in synthetic chemistry, the corresponding leveraging of π-bond–containing compounds that display twisting or pyramidalization remains underdeveloped. A notorious class of geometrically distorted molecules that contain π-bonds are anti-Bredt olefins. These olefins have been known since 1924, and conventional wisdom maintains that anti-Bredt olefins are difficult or impossible to access. This presentation will focus on a new approach towards these strained intermediates which uses relatively mild reaction conditions to generate the anti-Bredt olefin. As a result, functional group tolerance in trapping reactions is expanded and the scope of possible trapping adducts is broadened. Ultimately new insight can be gained about the fundamental reactivity of these exotic organic molecules.

Emma J. Greene[1] and Patrick G. Harran[1*]

Department of Chemistry and Biochemistry, University of California, Los Angeles[1]

Abstract

Spiroketals have garnered significant interest due to their presence in a variety of natural products exhibiting potent pharmacological activities. Such compounds include, but are not limited to, antitumor compounds, glycocidase inhibitors, and antibiotics. The rigidity of these spiroketal motifs and the conformational constraints they impose make them common pharmacophores in these biological systems. Despite their biological relevance, the synthesis of functionalized spiroketals remains hindered by the need for specific catalytic systems and substrates, elevated temperatures, and lengthy reaction times. Herein, we present a novel, Lewis acid-free, diastereoselective methodology utilizing exocyclic enol ethers and Micheal acceptor containing vicinal tricarbonyls to access a broad range of functionalized spiroketals under mild conditions. This offers an efficient introduction of diverse functional groups at strategic positions on the spiroketal framework, enhancing their structural diversity and applicability to natural product synthesis. Applications of this methodology in the synthesis of bioactive natural products such as Reveromycin B and AL-1 are underway. This methodology offers a versatile alternative to previous techniques and straightforward pathways to a variety of spiroketal-based compounds.

Authors: Morgan Grimes[1], Michael Lawson[1,2]
Advisor: Dr. Michael Lawson[1,2]

Ribosomal recycling, the final step of cellular protein synthesis, ensures ribosomes are quickly and efficiently removed to prevent collisions near stop codons. Defects in this process have been linked to neurological diseases such as autism spectrum disorder. Previous research has uncovered many of the factors involved in ribosomal recycling, however much of the kinetics of this process remain unresolved. This proposal aims to further elucidate the dynamics of ribosomal recycling through an in-vitro reconstituted yeast system analyzed by single molecule fluoresce microscopy. Using a suite of biochemical techniques, fluorescent tags will be precisely added to essential factors for real-time tracking of ribosomal recycling events. This research aims to (1) resolve the dynamics of 60S subunit removal by Rli1, (2) elucidate the mechanism and timing of P-site tRNA removal, and (3) discover the factors involved in the removal of the 40S subunit. This research will improve our understanding of the transition from termination to recycling as well as elucidate the choreography and composition of factors on the ribosomal complex during each stage of recycling. The dysregulation of translation at any stage can wreak havoc on a cell and often result in disease phenotypes. Its importance to nearly all other cellular processes makes our understanding essential for identifying possible therapeutic targets and mechanisms.

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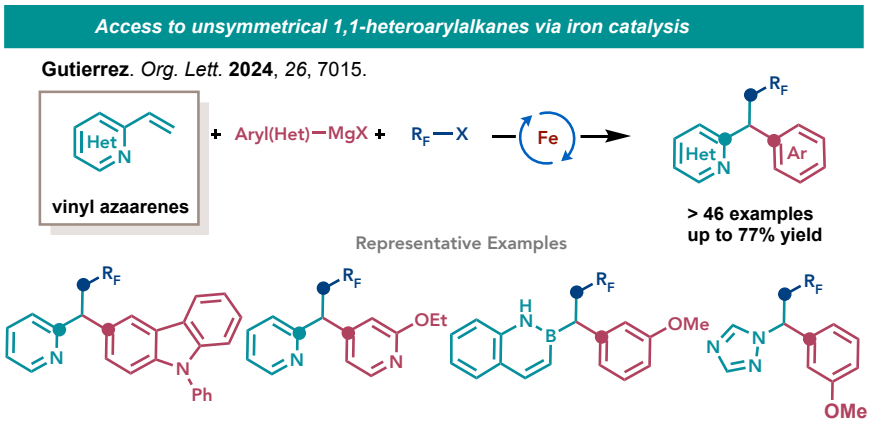
Dicarbofunctionalization of Vinyl Azaarenes Using a Multicomponent Iron-Catalyzed Cross-Coupling Approach to Synthesize 1,1-Diarylalkanes

Macayla Guerrero (UCLA), Angel Renteria-Gomez (UCLA), Deborshee Das (UCLA), Osvaldo Gutierrez* (UCLA)

Abstract:

1,1-diarylalkanes are valuable scaffolds in several fields of chemistry. Although they are important compounds, the dicarbofunctionalization of vinyl azaarenes using a multicomponent iron-catalyzed cross-coupling approach to access this moeity is still underdeveloped. Herein we report a protocol using commercially available iron salts, bisphosphine ligands, fluoroalkyl halides, and Grignard reagents to perform a multicomponent dicarbofunctionalization of vinyl azaarenes to yield functionalized 1,1-diaryl alkanes using mild conditions. This multicomponent approach leads to the successful synthesis of three-component products in good yields and regioselectivity. Further functionalization of the three-component azaarene substrates can be performed to yield synthetically relevant azaarene 1,1'-diaryl compounds such as pyridine N-oxides.



Funding Sources: NIH NIGMS (R35GM137797)

Poster Authors:

Yuyang Han,[1,3] Adeline Sun,[2] Cameron Movassaghi,[1,3] William Prater,[1] Aaron Meyer,[4] Chong Liu[1] and Anne M. Andrews[1,2,3,4,5*]

[1]Department of Chemistry & Biochemistry, University of California, Los Angeles (UCLA);
[2]Department of Neuroscience; [3]California NanoSystems Institute, UCLA;
[4]Department of Bioengineering, UCLA;
[5]Department of Psychiatry and Biobehavioral Sciences, Semel Institute for Neuroscience and Human Behavior, and Hatos Center for Neuropharmacology, UCLA

Poster Abstract:

Dopamine and serotonin signaling in brain extracellular environments play important roles in neuropsychiatric and neurological disorders, including major depressive and anxiety disorders, schizophrenia, substance use disorder, and Parkinson's disease. Several types of voltammetry have been used to measure neurotransmitter concentrations *in vivo*. Fast-scan cyclic voltammetry (FSCV) has most often been used to study phasic changes in dopamine and serotonin, which are rapid (tens of milliseconds to seconds). Nonetheless, FSCV suffers from the need for background subtraction. To retain key information in capacitive currents and enable determination of basal neurotransmitter levels, our group developed a non-background-subtracted voltammetry method called rapid pulse voltammetry (RPV).

Principal components regression (PCR) has been used for FSCV to make analyte concentration predictions. Another dimensionality reduction method widely used in chemometrics is partial least squares regression (PLSR), which improves predictive accuracy *vs.* PCR for FSCV and RPV data. In PLSR, experimental parameters are merged to form a 2-D matrix (2-mode tensor), sacrificing experimental context reflected by the data structure. Tensor-PLSR reduces multidimensional data. Both FSCV and RPV data can be interpreted as 3-D tensor models with tensors representing voltage, time, and injection sample IDs. Here, we use PLSR and tensor-PLSR to analyze RPV data for co-detecting serotonin and dopamine and comparing prediction accuracies and data interpretability. Evaluation of model performance includes the ability to discriminate neurotransmitter concentrations from pH and cation concentration changes anticipated *in vivo*.

Understanding the effects of nanostructuring and elemental doping on nickel-rich cathode materials for fast charging lithium-ion batteries

Grace Y. Kim, Casey Cornwell

UCLA Department of Chemistry and Biochemistry

Advisor: Dr. Sarah Tolbert

$LiNi_{0.8}Co_{0.1}Mn_{0.1}O_2$ (NMC811) is a nickel-rich layered oxide cathode that is commonly used for EV applications but commercially used NMC811 bulk materials are typically made of large agglomerated particles (~40um diameter), resulting in prolonged charging times due to long Li+ diffusion pathways. One strategy to improve the charging speed is to nanostructure NMC811 (~200nm diameter) to reduce the Li+ diffusion distances. Additionally, nanostructuring will have higher surface areas, providing more electrolyte penetration into the electrode but can be detrimental to the performance because it has a reactive surface that promotes SEI formation and high charge transfer resistances. Additionally, a limiting factor of NMC811 is cation mixing, where Ni escapes into the lithium layer, resulting in structural degradation and poor cycling stability.

In this work, we address these drawbacks by synthesizing nanostructured NMC811 with elemental doping using a sol-gel method. There are two different methods of doping into NMC811 by either inserting into the transition metal slab with Al or into the Li slab with Zr. When doped with Al, it has a local strengthening effect across the transition metal layer and reduces cation mixing, proven using X-ray Diffraction. Diversely, Zr increases the height of the Li slab and gives rise to higher Li^+-ion diffusion while preventing structural collapse. Using Rietveld refinement, we reveal that doping with Al or Zr will have a wider Li+ diffusion layer thickness and X-ray photoelectron spectroscopy shows less kinetically unfavorable rock-salt phases on the surface. High-rate galvanostatic cycling shows nanostructured NMC doped with Al or Zr both achieve high charging rates of up to 60 mAh/g at a C-rate of 64C, where bulk materials are unable to hold any capacity at this rate. We use a combination of different surface and structural properties of Al or Zr doped nanostructured NMC811 to understand how they manifest in fast-charging capabilities.

Autonomous Catalyst Explorer: Accelerating Data-Driven Optimization of Electrocatalysts for Electrochemical CO_2 Reduction

Yi-An Lai[†], Muxin Xiong[†], Aijian Huang[†], Yaming Hao[†], Chris Pierno[†], Hao Ming Chen[††], Matthew Nava[†], Chong Liu[†*]

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Abstract

We introduce "Catalyst Explorer," an autonomous platform that accelerates electrocatalyst discovery by surpassing the limitations of conventional grid search. It integrates automated synthesis, electrochemical characterization in an H-cell setup, gas product quantification, and machine learning-driven closed-loop optimization. The system employs a multi-objective Bayesian optimization methodology to investigate the synthesis of copper catalysts, the composition of CO_2 feedstock, and ionic liquid additives to improve CO_2 solubility and capture. It successfully found optimal conditions for maximizing Faradaic efficiency and current density of carbon monoxide, exploring CO production metrics in two days. This platform significantly reduces the number of experiments required compared to conventional methods, which typically require hundreds of trials to achieve similar optimization and construct a Pareto front illustrating the trade-off between Faradaic efficiency and current density in a multi-dimensional space. Built on open-source software and modular hardware, the Catalyst Explorer offers a scalable, cost-effective solution for high-throughput experimentation and activity mapping across multiple factors. This platform advances autonomous laboratories, accelerating data-driven innovations in electrocatalysis and enhancing energy storage through catalyst efficiency and stability optimization.

Funding Acknowledgements

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On the Origin of Red Emission in Protein-Stabilized Copper Nanoparticles: Evidence for Cu^{I}-Metallothionein-like Cluster Formation

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Abstract

Nanoparticles (NP) formed or placed in a biological environment will form a shell composed of biomolecules, most commonly proteins, around the core. The interaction of the protein shell with the NP core remains poorly resolved, particularly for NP based on biometals. Red emissive copper nanoclusters (**RCuNC**), serves as a model for the Cu^{0} NP-protein interface, and have been developed as biocompatible sensors, wherein its origin of the red emission remains unknown. Herein, we identify that the red emission from **RCuNC** does not originate from the Cu^{0} NP but from Cu^{I}-metallothionine(MT)-like clusters. Emission decay measurements, Cu^{I}-quantification assays, direct protein metalation with Cu^{I}, and native polyacrylamide gel electrophoresis imaging experiments support at least two distinct populations of Cu that form during the reduction of Cu^{II} in the presence of proteins. Furthermore, the rapid oxidation of the reduced Cu under air destroys the red emission with concomitant protein degradation. Our findings reveal that approximately 47% of the total Cu is present as Cu^{I} in the as prepared bovine serum albumin-stabilized **RCuNC**. Our results underscore the need for the scrutiny of the assignment of emitting species in copper-treated protein samples under reducing conditions, while revealing the opportunity for the development of protein-based sensors with red-emitting embedded Cu^{I}-MT-like clusters.

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Self-assembling molecular aggregates allow for the construction and control of extended structures with modifiable building blocks. Biology takes advantage of self-assembling systems to create large-scale extended structures such as light harvesting nanotubes from small-scale monomeric subunits. A better understanding of self-assembly mechanisms allows for better control for tuning molecular aggregate structure from the monomeric building blocks. There are pronounced differences in the photophysical properties between J-aggregate and monomer due to both local interactions between chromophore building blocks and the overall topology and long-range structure of the aggregate. The actual mechanisms underlying self-assembly, however, are still hard to resolve. However, we take advantage of two well-studied prototypical cyanine molecular aggregates TDBC and C8S3 to demonstrate changes in absorption spectra, emission lifetimes, and structure (measured via electron microscopy and dynamic light scattering) can reveal local and extended aggregate formation, growth, disorder annealing, and defect curing. We find that carefully monitoring changes in photophysical observables of chromophore-based (supra-)molecular complexes in conjunction with computational spectroscopy can illustrate a more comprehensive picture of the growth and kinetics of self-assembly, providing insight into multiple growth regimes with different dominant mechanisms over the course of the first three

hours of aggregation. This can be used to better design and create complex structures for a wide range of applications such as SWIR imaging, light harvesting, or energy transport.

Lotuzas, Aleksandras[1]; Hsu, Hung Kai[1]; Pan, Hope[1]; Zhang, Jeffrey[1]; Eisenberg, David[1]; Harran, Patrick G.[1]*

Insoluble fibrils of the microtubule associated protein tau accumulate in neurons as dementia becomes apparent in Alzheimer's patients. Neurofibrillary tangles (NFTs) of tau are recognized as the single best predictor of AD-related cognitive loss. The correlation of fibrillar tau with cognitive impairment inspires our premise to develop a chemical disaggregator of fibrillar tau, and argues that disaggregators of this established, yet challenging drug target could be key to halting AD-related dementia. EGCG is a naturally occurring flavonoid abundant in green tea that has been shown to be a potent tau disaggregant during *in-vitro* studies. Unfortunately, this small molecule suffers greatly from poor pharmacological properties and oxidative instability therefore making it a challenging drug target. We propose that creating analogs of EGCG attached to a nanobody carrier that is able to penetrate the blood brain barrier could enable this drug to disaggregate tau inside neurons of Alzheimer's patients, therefore improving cognitive decline.

The Eisenberg lab has determined a cryoEM structure of an intermediate of brain-extracted tau fibrils following incubation with EGCG. Building upon this structural insight, we have designed and synthesized EGCG analogs that outperform the natural compound in tau fibril seeding assays. These analogs incorporate a stable PEG-lyated diyne extension, allowing them to be selectively conjugated to a brain penetrant nanobody. Current efforts are focused on testing the bioconjugates in *in-vivo* brain penetrance studies. This presentation will cover the chemistry for selective derivatization of EGCG and conjugation of resultant analogs to carrier systems.

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Cancer is an extremely deadly and common disease, making it one of the largest markets for therapeutics. Therefore, it's crucial to develop new drugs that are both cost efficient and effective for a range of cancers. Portimine is a marine dinoflagellate-derived natural product of great interest due to its potent apoptotic activity against Jurkat T-lymphoma cells and mouse embryonic fibroblast cells. Portimine's unique property lies in its ability to induce apoptosis at low concentrations without causing cellular damage or necrosis. Despite being structurally reminiscent of certain neurotoxins, portimine exhibits markedly lower acute toxicity in systemic administration to mice. Because its mode of action is in question and its natural abundance is low, we are proposing an enantioselective route of portimine that would allow for the production of ample amounts for mode-of-action studies and further derivatization. A scalable and diastereoselective sequence to produce a linear precursor containing all the carbons present in the portimine has already been developed, and current efforts are ongoing to close the macrocyclic structure utilizing a Diels-Alder reaction. Through the use of a pyrroline heterocycle, we hope to utilize it as an effective dienophile, which would rapidly lead to the natural product after a few late-stage manipulations. This project anticipates the accessibility of synthetic portimine for cell culture studies, emphasizing potential synergy with Bcl-2 antagonists and Smac mimetics. Additionally, we hope to unravel the mode of action through genome-wide profiling experiments and molecular labels, paving the way for the development of experimental therapeutics with selective apoptosis induction.

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TITLE: Cleavable Fluorous Tags for Reversible Solubilization of Therapeutic Drugs in Perfluorocarbon Nanoemulsions

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Fluorous nanoemulsions, droplets of fluorous solvent stabilized by stimuli-responsive polymer surfactants, are a powerful tool for bioorthogonal, targeted drug delivery[1]. Although the unique properties of the fluorous phase provide many advantages, such as being abiotic, chemically inert, and having improved payload retention compared to traditional oil-in-water emulsions, a key challenge is developing reliable methods to solubilize payloads into the fluorous cores of the system. Historically, solubility has been achieved through the non-cleavable attachment of fluorous chains to payloads[2]. However, this approach is unsuited for therapeutics, whose activity and localization can be negatively impacted by large perfluorocarbon chains. Thus, to achieve fluorous solubility in the fluorous phase, whilst retaining payload activity, a series of cleavable fluorous tags have been developed. These tags are designed to utilize simple chemistry to append short fluorous chains commonly found functional handles common on therapeutic drugs, such as alcohols, amines, thiols, and carboxylic acids. Upon exposure to specific endogenous stimuli, these tags are designed to be cleaved, removing the fluorous chains from the payload, releasing them from the fluorous phase in active form. By expanding the ability to solubilize different drug payloads into fluorous solvent, this project aims to increase the flexibility of fluorous nanoemulsions as a platform for bioorthogonal drug delivery.

References

(1) Kaneda, M. M.; Caruthers, S.; Lanza, G. M.; Wickline, S. A. Perfluorocarbon Nanoemulsions for Quantitative Molecular Imaging and Targeted Therapeutics. *Ann Biomed Eng* **2009**, *37* (10), 1922–1933.

(2) Vincent, J. M.; Contel, M.; Pozzi, G.; Fish, R. H. How the Horváth Paradigm, Fluorous Biphasic Catalysis, Affected Oxidation Chemistry: Successes, Challenges, and a Sustainable Future. *Coord Chem Rev* **2019**, *380*, 584–599.

Seaborg Symposium 2025 Poster Abstract

Unexpected changes in reaction mechanisms characterized in $(Mo,W)O_2$ and $(Mo,Nb)O_2$ Li-ion battery host materials

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Abstract: Despite persistent increases in demand for Li-ion batteries, understanding the mechanisms that govern device performance, such as charging times and longevity, remains an active area of investigation. Creating mixed transition metal electrode materials is a common approach to improve energy storage and is central to current industrially relevant battery chemistries. Crucially, performance changes in mixed transition metal systems are typically attributed to changes in bulk composition- without consideration of local ordering of transition metals which can range from a fully mixed solid solution to nanodomains of monometallic phases. Here, using substituted rutile-like MoO_2 as a model system, we clarify the importance of the local arrangement of transition metals within Li host materials on achieving high-power density and cycle life. Surprisingly, we show; by synthetically controlling the ordering of transition metals within the host lattice, a wide range of device performances can be observed in similar sized materials that have identical elemental compositions and refine to the same space groups. Through dynamic structural observation using *operando* synchrotron diffraction, differences in performance can be correlated with changes in the often kinetically-limiting phase transition which typically accompanies Li insertion/removal. In nominally similar samples, we give examples of both improved and impaired electrochemical Li kinetics and relate these differences with changes in the structural pathways followed during (de)insertion of Li guests. We find that locally mixed materials are able to react more uniformly with smaller changes in host unit cell volume- accompanied by enhanced Li reaction kinetics and reversibility. Overall, this work gives new structure-property insights for the design of battery host materials and highlights that understanding local structure is critical for improving charging speeds and device longevity.

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Unveiling the Structure-Activity Relationship for Cobalt-based Spinel Oxide with Superior Acidic OER Performance

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Climate change has become an urgent issue due to the high carbon emission from various industrial sectors. As a result, achieving carbon neutrality has become a priority for society. Hydrogen is widely used in various industries and stands out as a promising zero-carbon energy carrier. However, most hydrogen is currently produced from steam reforming of natural gas, which is unsustainable due to its consumption of fossil fuel and the enormous amount of CO_x and NO_x by products released. Water electrolysis presents an attractive alternative for clean hydrogen production when coupled with renewable electricity. In recent years, the proton exchange membrane water electrolyzer (PEMWE) has received significant attention due to its ability to produce hydrogen at high rate, high efficiency, and high purity. The current bottleneck of PEMWE technology comes from its reliance on pricey Ru or Ir-based catalysts with limited durability. Thus, finding a low-cost catalyst with high activity and stability for the acidic oxygen evolution reaction (OER) on the anode is crucial for the next generation PEMWE products.

Co_3O_4, as an alternative to Ru and Ir-based catalysts, has attracted much attention due to its low cost, good activity, and acid tolerance. A significant amount of effort has been devoted to further improving the performance of Co_3O_4 and related spinel oxides, in order to reach the superior performance of noble-metal-based catalysts[1]. However, the maintenance of both high activity and acid corrosion resistivity has remained challenging. These two factors are closely related to the OER reaction mechanism, and direct oxo coupling (DOC) has been proposed as an ideal mechanism that optimizes both activity and stability[2]. Nevertheless, the DOC mechanism requires tight control of lattice parameters and metal site distances[3,4], consequently non-noble-metal-based spinel oxide structures that enable acidic OER via the DOC mechanism have not been reported.

In this work, we present a facile method of hydrothermal synthesis that produces aggregated needle-like spinel $NiCo_2O_4$ nanostructures. In 0.5M H_2SO_4, the $NiCo_2O_4$ nanostructure exhibits

remarkable activity and record-high durability for acidic OER. *In-situ* x-ray absorption spectroscopy revealed a higher stability during acidic OER catalysis of the Co and Ni coordination environment in $NiCo_2O_4$ compared to its less stable Co_3O_4 counterpart. This observation indicates the formation of fewer oxygen vacancies on $NiCo_2O_4$ under reactive potential, avoiding the critical structural deformation that would impair catalyst durability. Furthermore, we conducted density functional theory calculations to confirm the decreased OER overpotential arising from replacement of Co with Ni in octahedral lattice sites and to learn the preferred reaction pathway for DOC.

In conclusion, this research presents $NiCo_2O_4$ as an acidic OER catalyst with superior activity and stability. This investigation into $NiCo_2O_4$ provides insights into the design of anode catalysts for PEMWE, advancing toward sustainable hydrogen production with high yield and low cost.

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References

1. Yang, X.; Li, H.; Lu, A.-Y.; Min, S.; Idriss, Z.; Hedhili, M. N.; Huang, K.-W.; Idriss, H.; Li, L.-J., Highly acid-durable carbon coated Co_3O_4 nanoarrays as efficient oxygen evolution electrocatalysts. *Nano Energy* **2016**, 25, 42-50.
2. Wang, L.-P.; Van Voorhis, T., Direct-Coupling O_2 Bond Forming a Pathway in Cobalt Oxide Water Oxidation Catalysts. *The Journal of Physical Chemistry Letters* **2011**, 2 (17), 2200-2204.
3. Fang, Y.-H.; Liu, Z.-P., Mechanism and Tafel Lines of Electro-Oxidation of Water to Oxygen on RuO_2(110). *Journal of the American Chemical Society* **2010**, 132 (51), 18214-18222.
4. Lin, C.; Li, J.-L.; Li, X.; Yang, S.; Luo, W.; Zhang, Y.; Kim, S.-H.; Kim, D.-H.; Shinde, S. S.; Li, Y.-F.; Liu, Z.-P.; Jiang, Z.; Lee, J.-H., In-situ reconstructed Ru atom array on α-MnO_2 with enhanced performance for acidic water oxidation. *Nature Catalysis* **2021**, 4 (12), 1012-1023.

Computational investigation on the origin of enantioselectivity in thiol peptide mediated asymmetric hydrogen atom transfer (HAT) reactions

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This work presents a computational study to reveal the origin of hydrogen atom transfer (HAT) with synthetic tetrapeptide Cys in enantioselective hydroamination[1] and hydrodifluoalkylation[2] of alkenes. We identified that the pro-chiral radical intermediate bind the thiol peptide catalyst via a specific conformation facilitated by non-covalent interactions (π-π stacking in hydroamination, C-H … O hydrogen bond in hydrodifluoalkylation). Such non-covalent interaction is only preserved in one of the subsequent asymmetric HAT transition states, leading to high product enantioselectivity controlled by substrate distortion energy.

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[1] Hejna, B. G.; Ganley, J. M.; Shao, H.; Tian, H.; Ellefsen, J. D.; Fastuca, N. J.; Houk, K. N.; Miller, S. J.; Knowles, R. R., *Journal of the American Chemical Society,* **2023**, *145*, 16118 – 16129

[2] Pinto Pereira, M. V.; Geunes, E.; Shao, H.; Zhang, Y.; Cheng, J.; Magpantay, S. V.; Mercado, B.; Mayer, J. M.; Houk, K. N.; Knowles, R. R.; Miller, S. J. *Manuscript under review*

“Turn-On” Sialic Acids for Noncovalent Cell Surface Labeling

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Cells communicate with receptors and ligands on their glycan–covered surfaces. Metabolic glycoengineering is a strategy that can help us better understand this communication by introducing designer receptors. When cells are fed synthetically modified carbohydrates, inherent cellular scavenging pathways uptake the sugars and incorporate them into biomolecules on the cell surface. With small modifications such as azides, we can further elaborate these sugars with biorthogonal reactions. Known as the chemical reporter strategy, this two-step approach can be used to decorate cell surfaces with fluorescent dyes or ligands. Thus far, slow reaction kinetics or chemical instability of reacting partners have limited the translation of metabolic glycoengineering from cells and simple organisms to complex animals like mice. A noncovalent approach to metabolic glycoengineering could accomplish this translation by capitalizing on inherently stable and high affinity host-guest complexes to achieve selective labeling of modified sialic acid on cell surfaces.

Cucurbiturils (CB) are biocompatible, synthetic macrocycles that bind small molecule guests with exceedingly high affinities which rival the biotin-avidin complex. We have chosen to pursue the trimethylsilyl methylamine motif which is known to have a remarkably high affinity for CB[7] given its small size. Previous work in the Sletten Group found that the catioinic amine has prevented successful incorporation of this modified sugar onto cell surfaces. This work aims to mask the amine as an azide to facilitate incorporation, followed by an *in situ* “turn-on” reduction to the high affinity amine. Subsequent CB binding will achieve noncovalent complexation–enabled metabolic glycoengineering. Progress toward the synthesis of multiple sialic acid analogues modified with trimethylsilyl methylazide, cell viability in the presence of the modified sugars, and incorporation efficiency are reported herein.

Title: Automated research of concerted proton coupled electron transfer in aquo/hydroxo/oxo Osmium complexes

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Abstract. Transition metal centers play a crucial role in proton-coupled electron transfer (PCET) reactions, where subtle non-covalent interactions beyond the first coordination shell are believed to influence the mechanism and reactivity. Electrochemical techniques, such as cyclic voltammetry, have been instrumental in discerning between stepwise and concerted mechanisms of PCET processes, particularly by evaluating the pH-dependence of the apparent charge-transfer rate constant. However, the labor-intensive nature of systematic investigations across various pH conditions limits the comprehensive exploration of parameters such as proton donor/acceptor types and concentrations. Here, we propose an automated electrochemical research platform as a transformative strategy to address these limitations and enhance efficiency. We developed *AutoEchem*, an integrated experimentation platform that automates electrochemical testing and enables high-throughput exploration of various conditions. *AutoEchem* employs flow chemistry for automated liquid solution delivery in batch mode for solution preparation, titration mode for pH adjustment, and in situ electrochemical reactivation of the working electrode. The platform utilizes Python-controlled hardware and software for precise control and data analysis. We successfully validated *AutoEchem* by reproducing pH-dependent kinetics of $[Os^{II}(bpy)_2py(OH_2)]^{2+}$ from previous studies, confirming a stepwise PCET process in line with Laviron's model. Additionally, our results indicate a correlation between phosphate buffer concentration and the propensity of concerted pathways, suggesting the potential impact of buffer composition on PCET mechanisms. These findings highlight the reliability and utility of automated electrochemical research in elucidating fundamental insights into PCET processes in aqueous environments.

Antimicrobial polylysine-phage conjugates for improved biocompatibility

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The rise of antibiotic resistance necessitates the development of alternative treatments, such as antimicrobial polymers and phage therapy, which utilizes viruses specific to bacteria. However, these approaches face opposite shortcomings, as many polymers lack specificity for bacterial cells resulting in poor biocompatibility, while phages are restricted to a very narrow host range. To circumvent this, we modified M13 bacteriophage to act as a polymer delivery platform, comparing the efficacy of polylysine of various lengths and method of attachment.

First, the receptor binding protein of M13 was modified to express a short chain variable fragment (scFv) of an antibody known to bind poly-N-acetylglucosamine (PNAG), a common surface polysaccharide found on both gram negative and positive pathogens. Binding of the recombinant phage to PNAG-producer *S. aureus* was confirmed through enzyme-linked immunosorbent assays (ELISAs).

Second, a library of lysine homopolymers of various lengths were tested for antimicrobial activity, finding broad spectrum activity towards gram positive and negative species, with longer polylysine being effective at lower concentrations. Three polylysines of different lengths were loaded on the PNAG-binding phage through either electrostatic interactions or EDC crosslinking; both methods of attachment improved potency by lowering the minimum inhibitory concentration (MIC) ten-fold towards species with high levels of PNAG. When tested at the same concentration as the MIC, higher levels of cell viability were observed for polylysine-phage conjugates produced by EDC crosslinking than electrostatic loading, yet both conjugates exhibited superior biocompatibility compared to polylysine alone. Thus, chemical conjugation of antimicrobial polymers to genetically modified phages can effectively target a broader range of bacteria while minimizing harm to human cells.

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Beyond Cell Types: Unveiling the Active Neurons Behind Behavior

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The functional anatomy of the brain has historically served as the foundation for understanding cognition and behavior. With the rise of molecular medicine and the pursuit of precision treatments, it is crucial to integrate cellular and molecular characteristics with their spatial context. **A**tlas-scale **T**ranscriptome **L**ocalization using **A**ggregate **S**ignatures (ATLAS) is a high throughput, image-based, single-cell transcriptomic technology. Leveraging aggregate cell type signatures, ATLAS captures single-cell spatial distribution and transcriptional identities across the whole mouse brain within one week. To identify functional regions, a signature of immediate early genes (IEGs) is incorporated to assess neuronal activity. mRNA *in situ* hybridization (FISH) with hybridization chain reaction (HCR) is applied to amplify the detection signal. When integrated with ATLAS sample processing, fos and fosb expression exhibited clear differences between generalized seizure and baseline conditions, with fos significantly enriched in the amygdala and L2 IT-PPP-APR Glut and STR-PAL Chst9 Gaba subclasses. To improve detection dynamic range, we designed a probe set of ten baseline-normalized high-discrepancy IEGs, selected from single-cell RNA sequencing results of activated and baseline cortex, to ensure maximum variance between active and resting neurons. This optimized approach enables whole-brain neuronal activity mapping while preserving cell type identity, offering 3D functional compartmentalization and transcriptional profile at single-cell resolution, serving as a powerful tool for cognitive and behavioral neuroscience.