DEPARTMENT OF CHEMISTRY AND ENVIRONMENTAL SCIENCE
SEMINAR SERIES
SPRING 2023

WEDNESDAY, APRIL 5, 2023
TIERNAN HALL – LECT. HALL 2
1:00PM-2:20PM

GUEST SPEAKER

Dr. Peng Liu
Chemistry Department
University of Pittsburgh
Pittsburgh, Pennsylvania

TOPIC

Computational Studies of
Catalytic C–H Bond and Olefin Functionalization
— Strategies, Insights, and Predictions

ABSTRACT

Due to limited mechanistic insights and the complexity of catalyst-substrate interactions, catalyst design and optimization in transition metal catalysis and biocatalysis are often based on chemical intuition and experimental trial-and-error. I will discuss our recent efforts towards a streamlined computational approach to understand and predict the reactivity and selectivity of various C–H bond and olefin functionalization reactions, catalyzed by both transition metal complexes and bioengineered metalloenzymes.

We use computational tools to investigate reaction mechanisms and steric, electronic, dispersion, and strain effects of the transition metal catalyst. We utilized energy decomposition analysis (EDA) methods to quantitatively analyze different types of covalent and non-covalent interactions between the transition metal catalyst and the substrate. These studies provided a straightforward way to identify the dominant factor controlling reactivity and selectivity. We demonstrated these theoretical insights can facilitate catalyst discovery in collaborations with synthetic organic chemistry groups. Recently, we have applied these computational approaches to conformationally flexible catalyst systems, including transition metal catalysts with conformationally flexible and hemilabile ligands, asymmetric ion-pairing catalysis, and organic reactions in solution. These approaches have been further extended to study enzymatic reactions to explore the behaviors of short-live radical intermediates in asymmetric biocatalysis.

References:

1. Fu, Y.; Zerull, E. E.; Schomaker, J. M.; Liu, P.: "Origins of Catalyst-Controlled Selectivity in Ag-Catalyzed Regiodivergent C−H Amination," *J. Am. Chem. Soc.*, **2022**, *144*, 2735–2746. DOI: 10.1021/jacs.1c12111
2. Fu, Y.; Bernasconi, L.; Liu, P.: "*Ab Initio* Molecular Dynamics Simulations of the S_N1/S_N2 Mechanistic Continuum in Glycosylation Reactions," *J. Am. Chem. Soc.*, **2021**, *143*, 1577–1589. DOI: 10.1021/jacs.0c12096
3. Mai, B. K.; Neris, N. M.; Yang, Y.; Liu, P.: "C–N Bond Forming Radical Rebound Is the Enantioselectivity-Determining Step in P411-Catalyzed Enantioselective C(sp^3)–H Amination: A

Combined Computational and Experimental Investigation," *J. Am. Chem. Soc*. **2022**, *144*, 11215–11225. DOI: 10.1021/jacs.2c02283
4. Fu, Y.; Chen, H.; Fu, W.; Garcia-Borràs, M.; Yang, Y.; Liu, P.: "Engineered P450 Atom-Transfer Radical Cyclases are Bifunctional Biocatalysts: Reaction Mechanism and Origin of Enantioselectivity," *J. Am. Chem. Soc*. **2022**, *144*, 13344–13355. DOI: 10.1021/jacs.2c04937
5. Lu, G.; Liu, R. Y.; Yang Y.; Fang, C.; Lambrecht, D. S.; Buchwald, S. L.; Liu, P.: "Ligand-Substrate Dispersion Facilitates the Copper-Catalyzed Hydroamination of Unactivated Olefins," *J. Am. Chem. Soc*. **2017**, *139*, 16548–16555. DOI: 10.1021/jacs.7b07373

BIO

Peng Liu is a Professor of Chemistry at the University of Pittsburgh. He received his B.S. degree from Peking University in 2003 and M.Sc. degree from the University of Guelph in 2006. He completed his Ph.D. study and performed postdoctoral research at UCLA. He joined the University of Pittsburgh as an Assistant Professor in 2014 and was promoted to Associate Professor in 2019 and Full Professor in 2022. Since 2015 he has been an adjunct faculty member in the Department of Chemical and Petroleum Engineering at the University of Pittsburgh. He is currently a member of the Pittsburgh Quantum Institute and the Computational Modeling and Simulation program at Pitt. He has mentored 26 graduate students, 5 postdocs, and 27 undergraduate and high school students. His research accomplishments have been recognized by a number of awards, including the NSF CAREER award (2017), the Journal of Physical Organic Chemistry Award for Early Excellence (2018), the NIH Maximizing Investigators' Research Award (2018), Innovation in Education Award (2020), and Chancellor's Distinguished Research Award (2020). He has published over 200 manuscripts, including 76 in *J. Am. Chem. Soc.*, the flagship journal of the American Chemical Society.

Prof. Liu's research focuses on addressing the grand challenges in computational studies of catalytic organic reactions. He introduced transformative computational approaches to the organic chemistry community to study catalytic reaction mechanisms and catalyst effects on reactivity and selectivity. He has significantly expanded the capabilities of utilizing computational studies to provide chemically meaningful insights into complex mechanistic scenarios. Prof. Liu's research has led to new understanding of several important, but often overlooked factors in catalysis, including catalyst–substrate non-covalent interactions, catalyst flexibility, substrate ring strain, and solvent effects.

Prof. Liu have employed next-generation computational tools in various catalytic systems, including transition metal catalysis, polymerization, glycosylation, photoredox catalysis, and biocatalysis with engineered metalloenzymes. These catalytic reactions enabled selective synthesis of functionalized molecules via novel bond formation strategies. The mechanistic insights from Prof. Liu's computational studies provided the theoretical foundation of new experimental methodology development and practical catalyst design principles to accelerate experimental discovery.

Seminar Coordinator:
Dr. Genoa Warner – grw4@njit.edu
Dr. Lijie Zhang - lijie.zhang@njit.edu