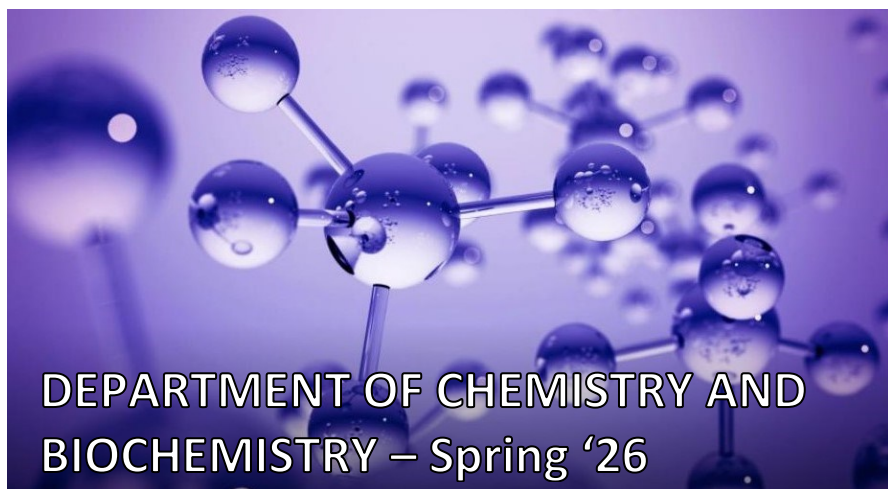




THE SALZBERG CHEMISTRY SEMINAR SERIES



The City College
of New York



Monday, May 11 2026 @ 12:00 noon – MR1027

Investigating DNA Binding and Protein Structure with De Novo Proteins

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Abstract: The ability to design proteins *de novo* offers a transformative pathway toward creating enzymes and scaffolds with functions not found in nature. This seminar will primarily detail the design and experimental validation of a novel, *de novo* DNA-binding protein. Unlike natural DNA-binding motifs, which are often difficult to study due to their evolutionary history and alternate functions (e.g., recruitment of other proteins, response to regulatory signals), our design utilizes a modular framework optimized for high-affinity recognition of specific sequences. We describe the iterative process of scaffold stabilization and active site grafting, resulting in a protein that exhibits both programmable sequence specificity and indirect readout. These results demonstrate that sophisticated enzymatic functions can be engineered from scratch using first-principles design. Building upon these principles of modularity and stability, the final portion of the talk will highlight the recent development of a highly stable, *de novo* β -barrel protein. While the β -sheet topology remains a challenge for design due to the complexities of edge-to-edge interactions, our recent work shows that strictly defined geometric constraints can produce exceptionally robust architectures. We will discuss the structural characterization of this barrel and its potential as a rigid scaffold for future ligand-binding applications. Together, these projects illustrate a burgeoning era in protein engineering where both complex function and extreme structural stability are no longer emergent properties, but predictable outcomes of rational design.

Biography: Dr. Lee Solomon is an associate professor of Chemistry and Biochemistry at George Mason University, with an affiliate appointment in the Institute for Bio-health Innovation. His research focuses on protein, biomaterial and peptide design. He seeks to understand the foundational biophysics of many common natural functions so they can be incorporated into abiological technologies. Solomon earned his Bachelors and Masters in Biological Sciences at the State University of New York at Buffalo in 2006. He then received his Ph.D. in Biochemistry and Molecular Biophysics from the University of Pennsylvania in 2013. His postdoctoral research was carried out at Argonne National Laboratory (2014-2017). Before beginning his appointment at Mason in 2019, he was awarded an AAAS Science and Technology Policy Fellowship to serve in the United States Department of Energy. His research has been recognized by a number of awards including an NSF CAREER award.

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