(Form 5)

Forefront Physics and Mathematics Program to Drive Transformation (FoPM)
Report for the International Research Experience

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Period	From 4/1/2024 to 5/31/2025

I had the privilege of spending seven months at the California Institute of Technology as a visiting student researcher in Professor Frances H. Arnold's group. Professor Arnold received the 2018 Nobel Prize in Chemistry for her groundbreaking work on the directed evolution of enzymes for use in biotechnology. The Arnold group is internationally recognized for pioneering directed evolution, a method to enable the engineering of enzymes to create new-to-nature catalysts with applications ranging from green chemistry to medicine. The group combines experimental evolution, machine learning, and high-throughput screening to design enzymes with novel functions, all with the overarching goal of advancing sustainable chemistry and biocatalysis. The lab brings together a highly diverse community of students and postdoctoral researchers with backgrounds in organic synthesis, protein engineering, machine learning, and bioinformatics. I found it incredibly inspiring to be part of such a collaborative and intellectually vibrant environment.

During the internship, I was part of the project that focused on developing a generalizable, machine learning–based pipeline to identify promiscuous hydrolases capable of degrading environmental contaminants. These pollutants, commonly found in wastewater sludge, are challenging to remediate using conventional methods. We prioritized some model compounds due to their prevalence and putative toxicity; however, a key bottleneck in experimentally validating the machine learning predictions was the cost and time required to synthesize multiple full-length gene constructs. To address this, we developed a cost-effective gene assembly strategy and software package to assemble short overlapping DNA fragments into full length genes. This approach, combined with our in-house sequencing tool (LevSeq), enabled us to construct and test a diverse set of enzyme variants at reduced cost and with higher throughput. By integrating the experimental workflow with our machine learning predictions, we screened over 50 candidate enzymes for catalytic activity against the degradation of our model compounds. We found some enzymes with initial activity, which were further engineered with directed evolution. This combined computational experimental pipeline could serve as a scalable platform for enzyme discovery in bioremediation applications.

To complement and accelerate this computational-experimental workflow, I also explored ways to identify promising enzyme candidates more efficiently by developing high-throughput detection assays using biosensors. Current detection of degradation relies on high-performance liquid chromatography (HPLC), which, while precise, is low-throughput and unsuitable for large-scale or field-deployable applications such as wastewater monitoring. To address this limitation, I utilized computational tools to identify binding proteins capable of sensing intermediates or end-products of the catalytic activity. Based on differential scanning fluorimetry results, I identified a promising candidate binder for the intermediate and final degradation products. This work allowed me to collaborate with leading nicotine biosensor expert Professor Henry Lester at Caltech to create a fluorescence-based sensor capable of detecting either product in a high-throughput format with fluorescence. This will enable rapid and scalable screening of enzyme libraries for catalytic activity, significantly accelerating our discovery workflow and integrating my expertise from the Campbell Lab with that of the Arnold and Lester labs.

Overall, I had an amazing seven months surrounded by talented and passionate scientists, which allowed me to explore the interdisciplinary integration of experimental protein engineering with computational methods, an area I had long wished to experience. Caltech itself was an amazing place to be: a quiet yet vibrant community that fostered both focus and creativity. I also attended numerous seminars and symposia, which gave me the chance to interact with professors and students from across departments, broadening my perspective and building new connections. I was fortunate to meet inspiring mentors whose passion and dedication to science are qualities I aspire to carry forward in my own career. These experiences reinforced for me that being a successful researcher requires not only technical expertise and intellectual ability but also strong communication, collaboration, and critical thinking skills. My time at Caltech has shaped both my current PhD work and my long-term vision as a scientist, emphasizing the importance of independence, teamwork, and interdisciplinary engagement in world-class research.

I would like to sincerely thank Frances for welcoming me into her laboratory and all of the members for their invaluable mentorship throughout my internship. I am also grateful to the Caltech community for creating such a supportive and stimulating environment. Finally, I would like to express my gratitude to FoPM and SPRING-GX for providing the financial and institutional support that made this international research experience possible.



Beautiful sunset from the Caltech campus



Weekend trip to Santa Monica beach



Arnold Group at ACS San Diego, celebrating Professor Frances Arnold's receipt of the Priestley Medal