

# PHYSICAL CHEMISTRY SEMINAR



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Monday, October 24<sup>th</sup>, 2022  
 4:00 PM | YH 4222

Bhaumik Collaboratory  
 Yoo Seminar & Conference Room

## Rare Event Sampling, Protein Dynamics in Enzymatic Catalysis and Directed Evolution: Lessons in Artificial Enzyme Design



**Abstract:** Remarkably, after many decades of study, the way enzymes so magnificently catalyze chemical reactions is still a matter of significant debate. In addition, artificial protein catalyst design has proven elusive. Years ago, we proposed the concept of the “promoting vibration,” a rapid protein motion which is a central part of the reaction coordinate and hence the mechanism of chemistry and reaction rate enhancement. Over the years, these motions have been found by a variety of groups in a variety of enzymes that catalyze diverse chemical reactions. In addition to theoretical work, experimental work has strongly supported this concept. More recently we have examined the development of such motions in laboratory evolved enzymes, finding initial protein designs lacking in such motions followed by appearance via the evolution process. These developments suggest that at least one of the reasons for the failure of theoretical enzyme design to create functional catalysts has been a focus on the creation of only static structures that are complementary to transition states. This talk will first briefly review early work on the discovery of promoting vibrations along with our Transition Path Sampling methods and reaction coordinate identification algorithms. We will then discuss how evolution introduces promoting vibrations and how this creates functional catalysts. We will finally speculate on how such ideas may be introduced into de novo enzyme design.