

CHEMISTRY AND BIOCHEMISTRY COLLOQUIUM

Modulating protein interactions to map information flow in cell signaling

Abstract. Cellular communication or signaling employs vast interconnected networks of proteins, with varying patterns of transient interactions that translate diverse extracellular stimuli to distinct cellular responses. While much is known about the structure and function of the individual components of signaling networks, a systems understanding of the decision-making process employed by the cell and its spatio-temporal deployment is still in its infancy. Our lab is focused on engineering protein interactions *in vitro*, in live cells, and in whole organisms, in order to bridge the gap between our structural understanding of proteins and their emergent cellular function. The seminar presentation will examine four layers of information that are subtly embedded in any protein interaction cascade. *Conformation* – Protein engineering of a functional bio-sensor that detects G protein-selective conformations of a GPCR. *Selection* – Translating GPCR conformation to function by systematically modulating the GPCR-G protein interaction in live cells. *Multi-domain interactions* – Mapping a homomeric interface in Protein Kinase C that selectively regulates its cellular function. *Multi-protein interactions* – Mechanical communication in molecular motor ensembles revealed by artificial myosin filaments. The studies presented employ DNA nanotechnology and a genetically encoded ER/K linker. Broad applications of these technologies and their impact on selective modulation of key drug targets will be briefly discussed.



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