

Lipid phosphoinositides are essential regulators of many cellular processes, including growth, proliferation, membrane trafficking, and cytokinesis. The generation of lipid phosphoinositides through the action of lipid kinases and phosphatases must be tightly regulated. The misregulation of these enzymes are frequently involved in numerous human diseases, including cancer, viral infection, and inflammation. I will discuss our work examining the regulation of phosphatidylinositol 4 kinases (PI4K) and phosphoinositide 3-kinases (PI3K), and the molecular basis of how they are regulated by both host proteins and viral proteins in disease. A specific focus will be on our synergy of X-ray crystallography, Hydrogen deuterium exchange mass spectrometry, and functional biochemical assays to probe enzyme structure, dynamics, and function. These enzymes all act on membrane surfaces, and I will also focus on our development of novel biophysical tools to examine membrane-signalling complexes in their native lipid environment, and how disease linked mutations change interactions with membrane surfaces.