

Presented By:

Matt Liptak

Department of Chemistry,
University of Vermont

Non-Canonical Heme
Oxygenases: A New Chapter
of Heme–Oxygen Chemistry

October 5, 2018
SMLC 102 - 4:00 PM



A diverse array of chemical transformations in biological systems is carried out by the combination of heme and oxygen. *Mycobacterium tuberculosis* MhuD and *Staphylococcus aureus* IsdG are representative members of two classes of enzymes that use molecular oxygen to convert heme to mycobilin and staphylobilin, respectively. These products cannot be rationalized based upon known heme–oxygen chemistry, leaving several open questions regarding the mechanism by which these enzymes activate oxygen for regiospecific oxygenation of the heme substrate. We have employed a variety of optical and magnetic spectroscopies, along with single- and multi-reference electronic structure calculations, to characterize substrate binding and the activation of two key enzymatic intermediates. We have discovered that two essential second- sphere amino acids work in concert to catalyze the first oxygenation of the heme substrate. The second-sphere interactions bring a peroxo moiety close to the site of heme oxygenation, and increase the electrophilicity of this carbon. I will discuss the major implications of our data with respect to heme–oxygen chemistry, and outline the future directions of our research.