How Bacteria Convert Methane to Methanol at the Diiron Center in Methane Monooxygenase

Abstract
A fundamental goal in catalysis is the coupling of multiple reactions to yield a desired product. Enzymes have evolved elegant approaches to address this grand challenge. A salient example is the biological conversion of methane to methanol catalyzed by soluble methane monooxygenase (sMMO), a member of the bacterial multicomponent monooxygenase (BMM) superfamily. sMMO is a dynamic protein complex of three components: a hydroxylase, a reductase, and a regulatory protein. The active site, a carboxylate-rich non-heme diiron center, is buried inside the 251-kDa hydroxylase component. The enzyme processes four substrates: $O_2$, protons, electrons, and methane. To couple $O_2$ activation to methane oxidation, timely control of substrate access to the active site is critical. Recent studies of sMMO have begun to unravel the mechanism, details of which will be described. The mechanism is quite different from that adopted by cytochromes P450, a large class of heme-containing monooxygenases that catalyze very similar reactions as the BMM enzymes. Understanding the timed enzyme control of substrate access has implications for designing artificial catalysts. To achieve multiple turnovers and tight coupling, synthetic models must also control substrate access, a major challenge considering that nature requires large, multimeric, dynamic protein complexes to accomplish this feat.

Research interests:
- biological interactions involving metal ions, focusing on reactions and physical and structural properties of metal complexes. Such complexes can be useful as cancer drugs and as models for the active sites of metalloproteins. Metal ions also promote key biological reactions in enzymes and metal complexes can be employed to sense biological signaling agents.

Website: http://web.mit.edu/lippardlab/