

Crystal structure of particulate methane monooxygenase

Raquel L. Lieberman and Amy C. Rosenzweig

*Departments of Biochemistry, Molecular Biology, and Cell Biology and of Chemistry,
Northwestern University, Evanston, IL 60208, USA*

Methanotrophic bacteria are a unique family of gram negative eubacteria that utilize methane as their sole source of carbon and energy. The first step in their metabolic pathway is the oxidation of methane to methanol by methane monooxygenase (MMO) enzyme systems. There are two types of MMO systems, a soluble cytoplasmic complex (sMMO) and a membrane-bound particulate system (pMMO). All methanotrophs produce pMMO, and several strains also produce sMMO under copper-limiting conditions. The crystal structure of the sMMO hydroxylase, which contains a carboxylate-bridged diiron center, has been known for more than a decade. By contrast, most questions surrounding the biochemistry, structure, and mechanism of the predominant methane oxidation enzyme, pMMO, have remained unanswered despite considerable research efforts in the last 20 years. In particular, the pMMO metal ion composition and stoichiometry have been controversial. We have determined the crystal structure of pMMO from the methanotroph *Methylococcus capsulatus* (Bath) to 2.8 Å resolution. The enzyme is a 300 kDa trimer, comprising three copies each of the pmoB, pmoA, and pmoC subunits. Two metal centers, modeled as mononuclear copper and dinuclear copper, are located in the soluble regions of each pmoB subunit, which resembles cytochrome *c* oxidase subunit II. A third metal center, occupied by zinc in the crystal, is located within the membrane. The crystallographic model for the metal centers is supported by spectroscopic data obtained for purified pMMO.

