Research projects at the Microbial and Enzyme Technology Lab

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Multicopper oxidases are multidomain enzymes that use the distinctive redox ability of copper ions. These enzymes are encoded in the genomes of organisms in all three Domains of Life – Archaea, Bacteria and Eukarya. The multicopper oxidases couple the oxidation of a range of substrates to the reduction of dioxygen to water, serving as paradigms for other enzymes that couple one-electron reductant to a four-electron oxidant, most notably cytochrome c oxidase. Copper proteins play central roles in Fe, Cu and O2 metabolism, are related to a range of genetic diseases, and are important in biotechnology, detoxification, and to the elimination of greenhouse gases. Moreover, understanding copper biochemistry on a molecular level provides mechanisms to improve or inhibit these processes and enhance drug design.

Research projects at MET will focus on the structural and biochemical characterization of multicopper oxidases from hyperthermophilic microorganisms. We propose to use site-directed, saturation and random mutagenesis, followed by robotic screening, in order to dissect their structure, activity and stability by using an integrated and multidisciplinary approach. Catalytic characterization by steady-state and transient-state kinetics will be assessed providing detailed information on the enzymatic reaction mechanisms and rate-limiting steps. Different spectroscopic techniques will be used to characterize the redox centers and elucidate the spectral features of wild type and variant enzymes. This integrated approach is expected to contribute for the elucidation of key aspects of MCOs. Furthermore, we will take the opportunity to get deep insight over the hyperthermostable nature of multicopper oxidases under study as the data obtained could assist the design by protein engineering techniques of optimized and stable bacterial laccases for biotechnological applications.

Two positions are available: (1) Turning a metallo-oxidase into a laccase by directed evolution (understanding the specificity towards the reducing substrate at the T1 Cu site), (2) Can multicopper oxidases accept other substrates than dioxygen as electron acceptors? (elucidating the catalytic mechanism at the T2/T3 Cu center)