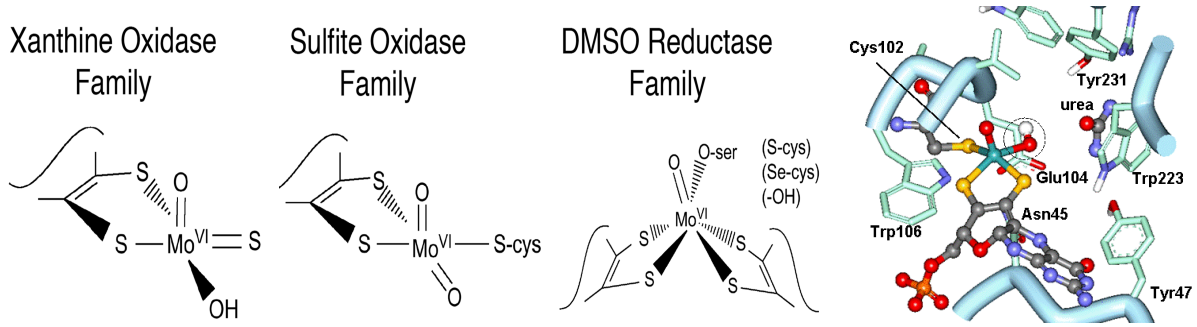
Molybdenum enzymes studied by X-ray absorption spectroscopy



Typical Mo coordination in the molybdenum cofactor (moco) in the three families of enzymes (left) and XAS-based model of the moco in a new enzyme (YedY) from *E. coli* (right).

Summary:

Enzymes carrying a molybdenum cofactor (Moco) exist in all organisms. They catalyze reactions in the global C-, N-, and S-metabolisms. Until today, more than 40 enzymes containing Moco have been described. Most of them undergo redox reactions. In particular, the Moco is the active site of three enzymes which are of crucial importance in human metabolism. Sulfite oxidase (SO) is involved in the degradation of sulfur-containing amino acids. Xanthine dehydrogenase (XDH) and aldehyde oxidase (AO) are complex metallo-flavoproteins that contain Moco, two [2Fe2S] clusters and FAD cofactors, and catalyze a large range of hydroxylation reactions using NAD^+ or O_2 as electron acceptors.

Of prime interest, e.g. in the context of human diseases (Moco-deficiency, isolated sulfite oxidase deficiency), is the mechanism of Moco modification and insertion into the enzymes by chaperones during maturation. Information on the atomic and electronic structure of the Mo atom and its ligand environment, on the reaction dynamics (structural and oxidation state changes, substrate interactions), and on the changes at the Mo during Moco synthesis/assembly, modification, insertion, functioning, and maintenance of the cofactor is required. Such information may lead, e.g., to medical therapies using tailored Moco's and may unravel general principles of metal cofactor insertion during maturation of enzymes.

Tracking the Moco transfer between the various proteins and monitoring of the changes of the ligand environment and oxidation state of the Mo atom during cofactor synthesis, maturation, transfer, and functioning was one of the main subjects of this project. X-ray spectroscopy has provided essential information on the ligand coordination and oxidation state, as well as on the assembly of the metal centers in various Mo-enzymes.