Artificial biocatalysis with biologically or chemically synthesized molybdenum cofactors

Co-supervisor 1: Ingo Zebger, TU Berlin

Co-supervisor 2: Silke Leimkühler, University of Potsdam

1 Abstract:

The highest level of complexity is reached when the catalytic metal center of a biocatalyst is replaced by a chemically synthesized compound, ideally exhibiting a different reactivity and improved stability compared to the original biocatalyst. Bioinorganic model chemistry is a very useful tool in order to support the biological investigations helping to clarify questions of the natural active sites regarding the role of ligands and the electronic structure. Model chemistry for the molybdenum cofactors (Moco) so far has been challenging and a “perfect” structural model compound for any of these enzymes is still missing due to the complexity of the molybdopterin moiety and the lability of the Moco. To overcome this problem, it is possible to biologically synthesize different forms of Moco using purified enzymes, making use of the biosynthesis machinery, or alternatively to extract the cofactors from purified molybdoenzymes and place them back into the active site of different apo-enzymes after purification. In the center of this project is the trimethylamine-*N*-oxide (TMAO) reductase from *Escherichia coli,* which will be analyzed biochemically and spectroscopically with respect to the relevance of different ligands at the metal center for the enzyme’s reactivity. Further, artificial enzymes with Moco model compounds inserted into the apo-protein will be prepared to provide active enzymes containing an artificial, chemically synthesized cofactor.