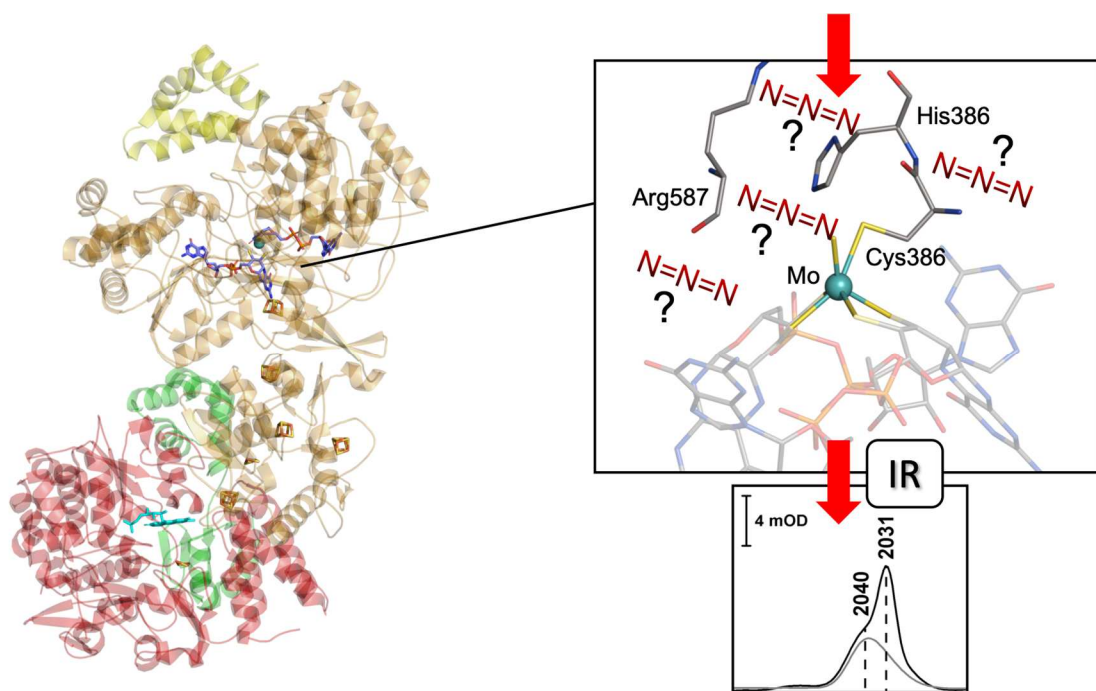


Unveiling the role of the second coordination sphere in inhibitor binding in a formate dehydrogenase from *Rhodobacter capsulatus*

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In the last decades the worldwide energy demand continuously increased, calling for the development of alternative energy sources. As most of the known metalloenzymes exhibit a substantial catalytic activity their mechanistic understanding is highly relevant for the development of potential bio(inspired)-technological applications. One of these metalloenzymes is the Mo-containing CO₂-reducing formate dehydrogenase (FDH) from *Rhodobacter capsulatus*. The R_cFDH and its active site (Moco), a bis-MGD cofactor, is capable of catalyzing the oxidation of formate (HCO₂⁻) and the reduction of CO₂.



The enzyme contains further cofactors, which are involved in the reaction and electron transfer, e.g. five [4Fe4S] and two [2Fe2S] clusters as well as a FMN prosthetic group, that act as the natural electron acceptor. However, the underlying mechanism at the Moco is not fully understood, yet. Hence, the research groups of Silke Leimkühler, Maria-Andrea Mroginski and us accomplished a multidisciplinary approach combining IR spectroscopy, DFT calculations and enzyme kinetics to elucidate the potential interaction of an IR-sensitive inhibitor, iso-electronic to CO₂, with the active site and its surrounding second coordination sphere. For this purpose, multiple conserved amino acid residues were exchanged in order to clarify their role in inhibitor/substrate binding.