HAMAC
Hybrids: Artificial metalloenzymes for Asymetric catalysis
CP2D 2008

AGENCE NATIONALE DE LA RECHERCHE ANR

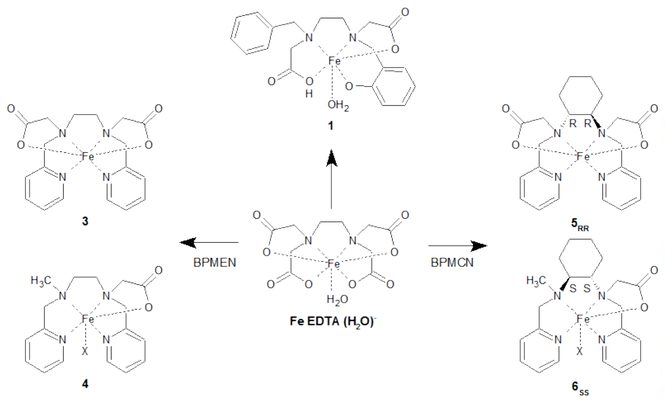
Collaborative project between Laboratoire de Chimie et Biologie des Métaux (UMR 5249)/ BioCE team (Principal investigator Dr. Stéphane Ménage) and IBS(UMR 5075) / Metalloprotein Group (Dr. Christine Cavazza)

he combination of biomolecules and inorganic catalysts for a sustainable chemistry

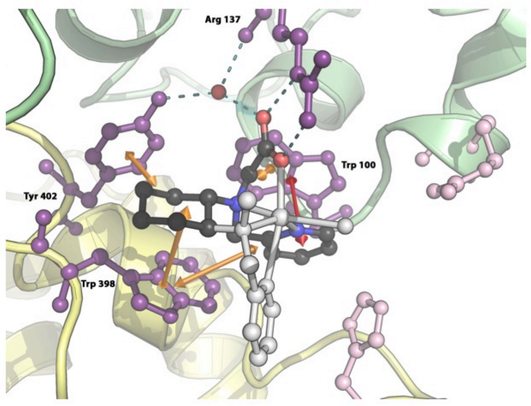
Biocatalysis represents an accurate answer to green chemistry but suffers from the limited access to chemical transformation. The combination of a stable protein, affording the specificity of the substrate and an inorganic complex dictating the reactivity represents a great alternative for these biocatalysts optimization. The HAMAC Project deals with the design of these artificial metalloenzymes by embedding an iron catalyst into a protein, NikA. The construction of an artificial oxygenase for sulfides and aromatic rings is a main breakthrough in the field and lead us to propose an original method for the design of such hybrids. The success of the project is based mainly on the knowledge at the molecular level of the interactions between the catalyst and the protein thanks to protein crystallography.

Artificial metalloenzyme design

We have used the periplasmic nickel-binding protein NikA from *Escherichia coli* and iron complexes in which N_2Py_2 ligands have been varied in terms of charge, aromaticity and size. Five “NikA/iron complex” hybrids have been characterized by X-ray crystallography and their interactions were studied using quantum calculations and determined that weak tryptophan-ligand CH/π H-bonds finely modulate the stability differences between hybrids. our study aims at the complete characterization of the factors that conditions the interaction of an artificial ligand and a protein and their implications for catalysis.



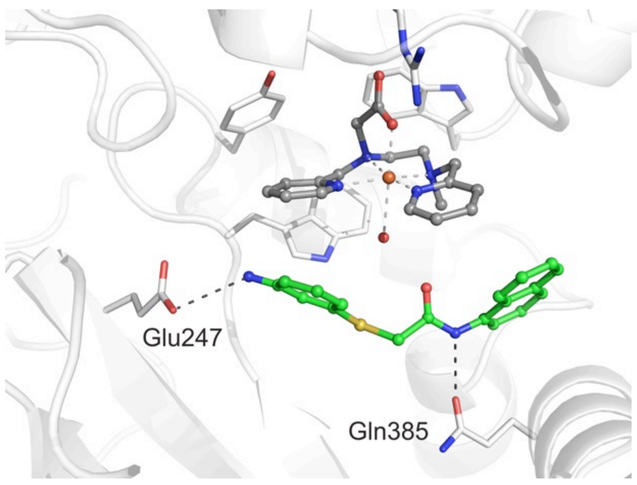
Eur.J. Inorg. Chem.(2012) 85-96

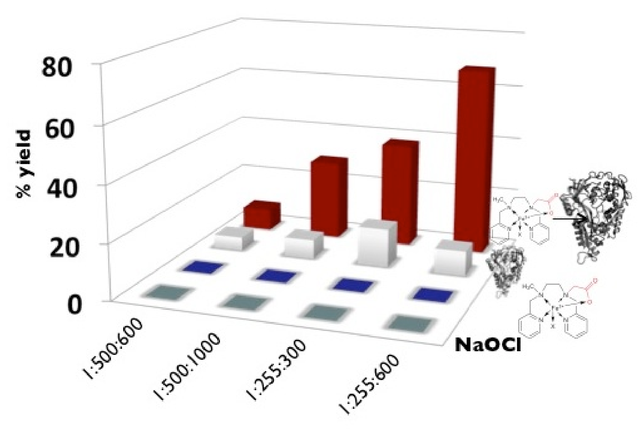


J. Biol. Inorg. Chem. (2012) 17, 817-829

Search for substrates for sulfide oxidation

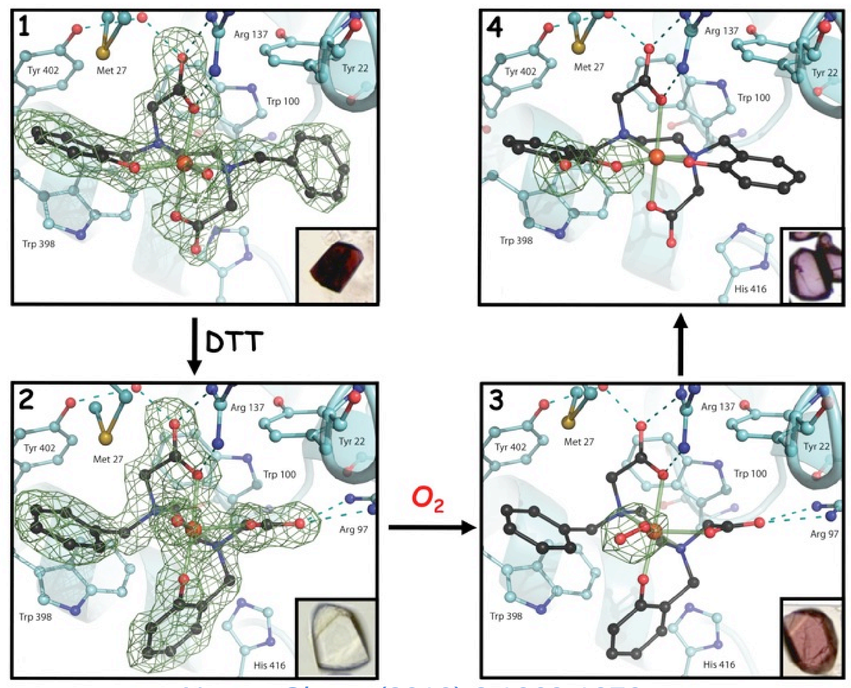
Molecular docking simulations were conducted to screen molecules that could be potential substrates able to be catalytically oxidised by our hybrids. We found a family of substrates specific to our newly synthesized artificial oxygenases and highlighted the importance of the synergetic effect of the different partners, i.e. the protein, the inorganic complex and the substrate.





How to decipher reactions catalyzed by an inorganic complex using a protein matrix

Model chemistry and protein crystallography were combined to unravel the catalytic cycle of an aromatic dihydroxylation by complex 1 bound to NiKA. The protein-bound, arene-containing iron complex was able to activate dioxygen, which led to the formation of a catechol as a sole product. Structure determinationon flash-cooled crystals were used to characterize four intermediates and the end product of O_2-mediated aromatic hydroxylation.



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