

Artificial Metalloenzymes for *in vivo* Catalysis: Challenges and Opportunities

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Artificial metalloenzymes (ArMs) result from the incorporation of an abiotic metal cofactor within a host protein, Figure 1. Thanks to the remarkable supramolecular affinity of biotin for streptavidin ($K_D > 10^{-13}$ M), linking a biotin anchor to an organometallic catalyst ensures that, upon addition of streptavidin, the abiotic cofactor is quantitatively incorporated within the streptavidin. Alternatively, human carbonic anhydrase has proven equally versatile for the development of artificial metalloenzymes relying on aryl-sulfonamide anchors to ensure the localization of the abiotic metalcofactors within the host protein. The catalytic performance of the resulting ArMs can be optimized either by chemical (variation of the anchor-spacer-ligand moiety) or genetic- (mutation of the host protein) means. These chemo-genetic schemes were applied to optimize the performance for thirteen different catalyzed transformations as well multiple reaction cascades in the presence of natural enzymes, either *in vitro* or *in vivo*.

This presentation will highlight the group's effort to implement and evolve artificial metalloenzymes with activities that are complementary to natural enzymes. These include: C–H activation, hydroxylation, olefin metathesis, imine reduction, cross-coupling reactions etc.

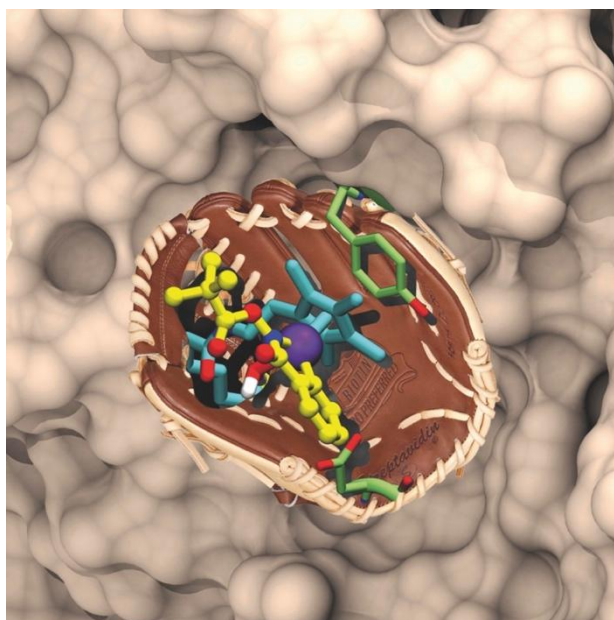


Figure 1. Endowing organometallic catalysis with a genetic memory. In a Darwinian spirit, anchoring an abiotic metal cofactor within a host protein allows to implement directed evolution schemes to optimize the performance of organometallic catalysts.