CONTROLLED BIOCATALYTIC SYNTHESIS OF METAL NANOPARTICLE-ENZYME HYBRIDS: DEMONSTRATION FOR CATALYTIC H_2-DRIVEN NADH OR FLAVIN RECYCLING

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Having control over the shape and size of metal nanoparticles (NPs) is key for making them suitable for specific applications: ranging from drug delivery, biosensing to catalysis. This has given rise to substantial effort into exploring different synthesis routes for improving the control over the NPs polydispersity as well as the sustainability of the process.[1] Here, we demonstrate the controlled synthesis of metal NPs under mild conditions using isolated enzymes (**Fig. 1A** and **2A**). We also demonstrate the activity of the resulting metal NP-enzyme hybrids as H_2-driven NADH or flavin recycling systems (**Fig. 1B** and **2B**): for an enantio-selective ketone reduction with an alcohol dehydrogenase and for a chemo-selective alkene reduction with an ene-reductase, respectively.

In both systems we have observed the enzymes' compatibility with the metal NPs; we hope this is an area which can help bring about new reactivities for more sustainable processes by using both the enzyme and metal NP properties either in a cascade reaction or synergistically.

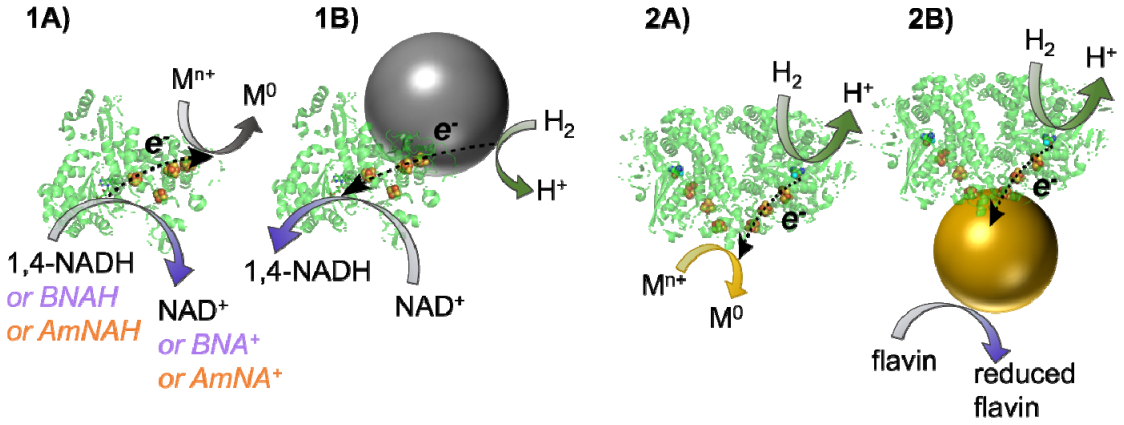

Figure. 1A) NAD^+ reductase is used to make metal NPs by oxidizing NADH or cheaper, synthetic cofactors: BNAH or AmNAH.[2] **1B)** The resulting metal NPs are used to oxidize H_2, supplying electrons back to the enzyme which selectively reduces NAD^+ to 1,4-NADH. **2A)** Hydrogenase is used to make metal NPs by oxidizing H_2. **2B)** The resulting metal NP-enzyme hybrids show increased flavin reduction rates, in comparison to the enzyme alone.

[1] J. E. Ortiz-Castillo, R. C. Gallo-Villanueva, M. J. Madou, V. H. Perez-Gonzalez, *Coord. Chem. Rev.* **2020**, *425*, 213489.

[2] H. A. Reeve, J. Nicholson, F. Altaf, T. H. Lonsdale, J. Preissler, L. Lauterbach, O. Lenz, S. Leimkühler, F. Hollmann, C. E. Paul, K. A. Vincent, *Chem. Commun.* **2022**, *58*, 10540-10543.