Universität Basel

Research Project

Optimization of Artificial Keto-Reductases Based on the Biotin-Avidin Technology:Theoretical and Practical Aspects

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Project title Optimization of Artificial Keto-Reductases Based on the Biotin-Avidin Technology:Theoretical and Practical Aspects
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Optimization of Artificial Keto-Reductases Based on the Biotin-Avidin Technology: Theoretical and Practical Aspects

In the past three decades, homogeneous and enzymatic catalysis have evolved independently to provide the necessary tools for the synthesis of high value added products. These two approaches are complementary in many respects. With the aim of exploiting the advantages of both fields, artificial metalloenzymes have recently attracted increasing attention. Such hybrid catalysts result from combining an organometallic moiety, typical of homogeneous catalysts, with a protein, reminiscent of an enzyme. Following this approach, several artificial metalloenzymes have been designed, optimized and structurally characterized.

Within this project, it is proposed to combining both in-silico (computer-based) and in-vitro (experiment) screening of artificial metalloenzymes. For this purpose, mixed quantum mechanical/classical mechanics (QM/MM) calculations of artificial ketoreductases based on the biotin-avidin technology will be carried out. Because QM/MM is computationally a very demanding technique, also force field-based approaches will be further developed. One of them - VALBOND-TRANS - is specifically designed for treating metal centers in particular bonding topologies. Until now, VT has only been parametrized for octahedral complexes and we seek to extend this to square planar compounds. Finally, the insight obtained from the computational studies will be applied towards the chemogenetic optimization of artificial keto-reductases

This project aims at providing alternative catalytic solutions with

potentially broad (industrial) applications. Artifical enzymes have the potential to combine some of the attractive features of both homogeneous and enzymatic catalysis. Here we try to pursue a targeted approach that is inspired by how nature addresses such problems and that is guided by reliable computations.

Keywords computational chemistry, catalysis, biomimetic, biotin-avidintechnology, QM/MM simulation, metalloenzymes, trans effect, ligand binding, x-ray, force fields
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