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# IN SILICO ENZYME DISCOVERY AND OPTIMIZATION FOR UNNATURAL REACTIONS

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## PURPOSE OF THE ABSTRACT
Enzymes have the potential of increasing the sustainability of industry by substituting polluting chemical processes with environmentally friendly reactions. This is possible thanks to the wide spectrum of reactions natural enzymes can perform as well as the inherent catalytic features many of them own, like specificity and enatioselectivity. However, these capabilities are often not sufficient to satisfy industrial needs, and natural enzymes need to be tuned, which is usually a slow and costly process addressed by directed evolution campaigns. These strategies have revealed over the last decades how distal mutations can be the key to boosting enzymatic properties [1]. In the last years, and with the advance of computation, the scientific community has tried to understand the fundamentals for predicting distal mutations [2], so that directed evolution studies, which are tedious, expensive and depend on efficient screening approaches, can be outperformed.

Still, engineering approaches are often insufficient, in particular, when natural catalysts for specific abiological reactions do not exist or have not yet been discovered. Genomic and metagenomic-based techniques are the strategies of choice for identifying enzymes with novel biocatalytic activities [3]. However, such genome-mining techniques are typically time-consuming and laborious, highlighting the need to develop novel high-throughput enzyme discovery technologies capable of matching the pace of business.

In Zymvol, we have focused our efforts in covering these two hurdles, aiming to speed up the application of biocatalysts to industry and therefore its transition towards greener practices. In particular, we have developed ZYMEVOLVER (ZYV), able to boost the enzymatic properties through targeting both active site and distal mutations; and BIOMATCHMAKER (BMM), that combines bioinformatics with reliable physics-based simulations at distinct theoretical levels to perform enzyme discovery for abiological reactions. Here, the capabilities of both ZYV and BMM pipelines will be discussed, highlighting various case studies that have led to the identification and optimization of novel enzymes for non-biological reactions that are of high interest for the chemical and pharmaceutical industries.

## FIGURES

**FIGURE 1**

**FIGURE 2**


## KEYWORDS

Enzyme engineering | Enzyme discovery | Computational tools


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