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Computational redesign of transaminase active site

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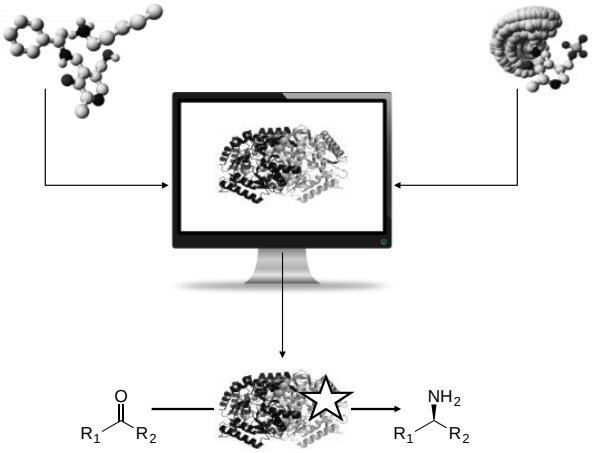
Aminotransferases are widely exploited in simple as well as more elaborate multi-enzymatic cascade reactions as an environmentally friendly alternative to transition metal catalysis. However, efficient selective conversion of numerous targets is a great limitation to date [1]. Attempts to improve substrate scope have been undertaken by generation and screening of large mutant libraries, which is very time-consuming and raises costs concerns [2]. Recent approaches explored the use of molecular docking of demanding substrates, followed by energy minimization and/or MD simulations [1;3]. Still, the best results have been obtained by extensive mutagenesis and screening.

Here we report our efforts aimed at developing a computational strategy for the redesign of the active site of *Vibrio fluvialis* ω-transaminase by CASCO (Catalytic Selectivity by Computational design) to obtain a toolbox of variants for ketone amination [4]. The approach should make it possible to perform the high-throughput generation and screening of multiple mutations only by computational tools and to design only a small number of promising variants to be verified in the laboratory. Furthermore, this workflow should not have substrate limitation but offer a standardized protocol applicable to any reasonable target.



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