# ENABLING BRIGHTER LIVING BY ENZYME ENGINEERING: FROM STRUCTURE INSPIRED TRIAL AND ERROR TO STRUCTURE GUIDED DESIGN

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Enzymes evolve in nature to enable life. They can provide a competitive edge to organisms to survive under changing environmental conditions. In industry, we apply enzymes under conditions and for reactions that can be quite different from those for which the enzyme evolved in nature. For this reason, enzyme properties are often not fit for the intended industrial applications. Enzyme engineering is therefore an important tool to overcome these limitations and unlocks the potential of enzymes for many applications.

This presentation will provide an overview of different enzyme applications developed by us and enabled by Enzyme Engineering. Examples are selected to show how enzyme engineering methods have evolved over time since our first commercial production of non-animal derived chymosin in 1988 [1].

One of the early enzyme engineering work to enable “Green Routes” for beta-lactam antibiotics was the directed evolution of a glutarylacylase into an adipylacylase. In a first mutagenesis round sites contributing to the adipyl activity where explored followed by saturation mutagenesis of these residues. Only in hindsight, the identified mutations could be rationalized based on the enzyme structure [2].

Another interesting example of enzyme engineering was the development of a thermostable phytases. The developed `consensus approach' showed that sequence information of homologous, mesophilic enzymes contains sufficient information to allow rapid design of a thermostabilized, fully functional phytase [3].

More recently, we apply computational methods to create “smart libraries” with more reliable predictions of beneficial mutations. Together with the University of California in San Francisco, we designed a new computational tool for the Rosetta computational design software package, which out-performs previous design tools [4]. Such methods are especially important for enzyme engineering problems in which the throughput of the applied screening methods is limited, for example, due to the complexity of matrices we apply for food enzyme developments.

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