Oxygen Dependent Biocatalytic Processes

Enzyme catalysts have the potential to improve both the process economics and the environmental profile of many oxidation reactions especially in the fine- and specialty-chemical industry, due to their exquisite ability to perform stereo-, regio- and chemo-selective oxidations at ambient temperature and pressure. A significant number of enzymes carrying out redox reactions (oxidoreductases) requiring molecular oxygen as an electron acceptor – those termed oxidases, monoxygenases and dioxygenases. These enzymes catalyze a range of industrially relevant reactions, such as oxidation of alcohols to aldehydes and ketones, oxyfunctionalization of C-H bonds, and epoxidation of C-C double bonds. Although oxygen dependent biocatalysis offers many possibilities, there are numerous challenges to be overcome before an enzyme can be implemented in an industrial process. These challenges require the combined effort of protein engineering (i.e. modification of the amino acids sequence to improve activity, stability and selectivity) and reaction engineering (i.e. modification of reaction conditions to increase the yield and productivity) to be solved. The most important reaction engineering challenge is the requirement for oxygen, because the transfer of oxygen from the gas-phase (typically air) to the aqueous phase, where the reaction takes place, is notoriously slow due to the low aqueous solubility of oxygen at ambient conditions. Therefore, vigorous agitation and aeration is required to create a large interfacial area for mass transfer, which is not only expensive but also sets a limit to the maximum productivity of the reactor. The oxygen transfer problem is further complicated by gas-liquid interface induced enzyme deactivation, large dependency of the catalytic rate on the oxygen concentration in solution and stripping of volatile organic compounds from the reaction mixture.

In this thesis, the supply of oxygen and the implications on the biocatalyst performance are studied. The important kinetics of the reaction between enzyme and oxygen are described in detail. In fact, it is found that most enzymes operate far below their potential maximum catalytic rate at industrially relevant oxygen concentrations. Detailed knowledge of the enzyme kinetics are therefore required in order to determine the best operating conditions and design oxygen supply to minimize processing costs. This is enabled by the development of the tube-in-tube reactor (TiTR) setup, capable of performing fully automated kinetic characterization of oxygen dependent enzymes - at oxygen concentrations allowing full saturation of the enzyme. The development of the TiTR enables us to characterize a range of enzyme variants developed through protein engineering. This not only exemplifies the importance of knowing the full enzyme kinetics when choosing an enzyme variant for further development, but also that it is in fact possible to change the oxygen reactivity of an enzyme through substitution of amino acid residues.

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