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Oxygen transfer rates and requirements in oxidative biocatalysis

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Biocatalytic oxidation reactions offer several important benefits such as regio- and stereoselectivity, avoiding the use of toxic metal based catalysts and replacing oxidizing reagents by allowing the use of oxygen. However, the development of biocatalytic oxidation processes is a complex task which requires simultaneous consideration of several issues regarding the process design and operation.

In this work, the oxygen requirements are analysed for different process scenarios, considering different biocatalyst formats and variation of the desired productivity. Also, the applicability of two different oxygen supply methods (bubbling and membrane aeration) investigated. Hollow fibre membrane contactors present an interesting alternative for reactor aeration, creating large specific areas (area/volume) of the gas/liquid interface. The modular design of membrane contactors, scaling-up is relatively straight forward (Gabelman and Hwang, 1999), and membrane contactors are implemented for various industrial applications (Klaassen *et al.*, 2005).

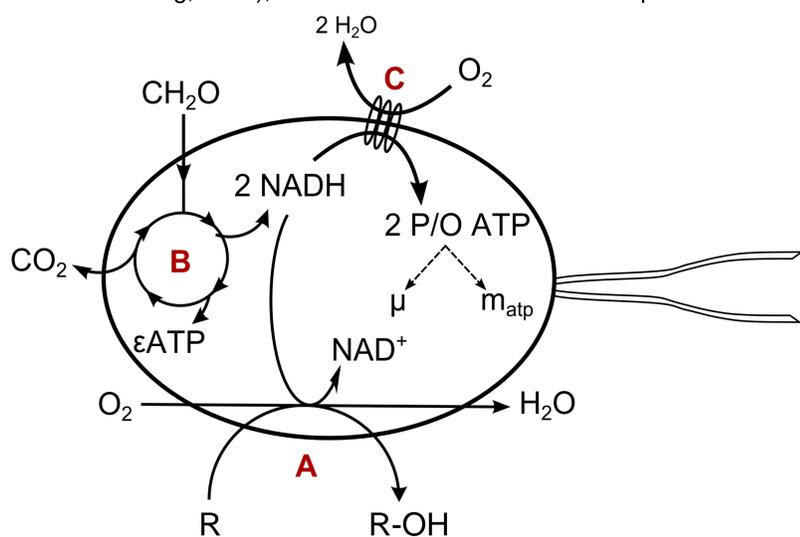


Figure 1. Illustration of a cell that catalyze a specific hydroxylation reaction (A), generates energy via the citric acid cycle (B) and the electron transport chain (C). The energy enables maintenance of cellular function (m_{atp}) and growth (μ).

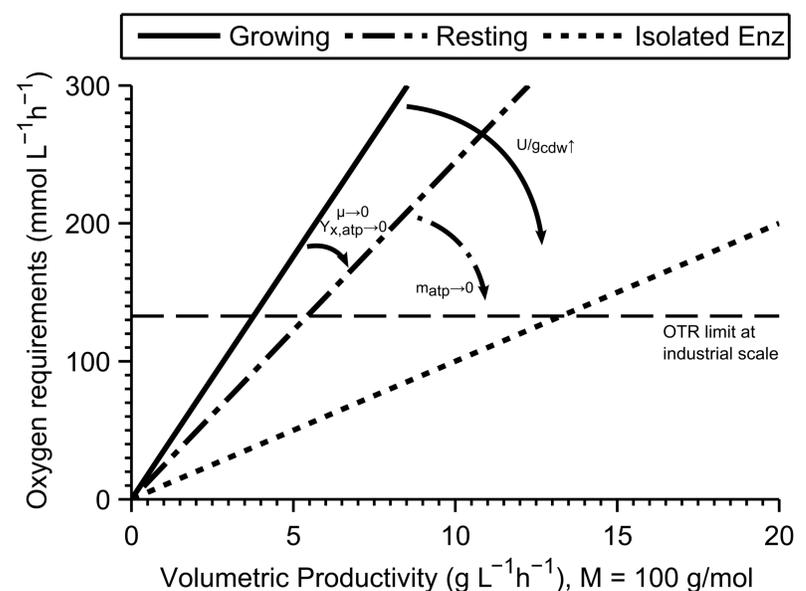


Figure 2 Oxygen requirements of different types of biocatalysts carrying out an oxidation reaction. The calculations are based on *E. coli* and the following parameter values: $A_{cat} = 50 \text{ U/g}_{cdw}$, $\mu = 0.2 \text{ h}^{-1}$, $\epsilon = 2/3$, $P/O = 1.5$, $Y_{xNADH} = 16.97 \text{ mmol/g}_{cdw}$, $Y_{xatp} = 70.2 \text{ mmol/g}_{cdw}$, $m_{atp} = 7.9 \text{ mmol/g}_{cdw/h}$ (Ingraham *et al.*, 1983; Varma and Palsson, 1994). The maximum oxygen transfer rate (OTR) for bubble aeration at industrial scale is estimated using a k_a of 500 h^{-1} (Villadsen *et al.*, 2011). The OTR limit is based on the use of air.

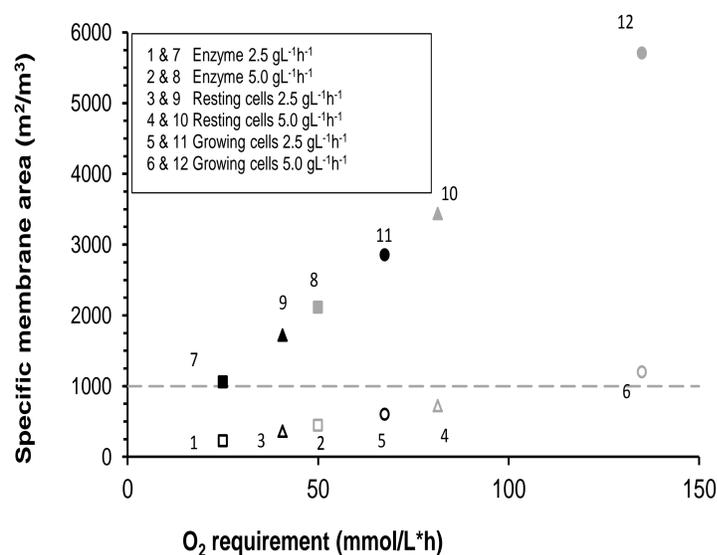
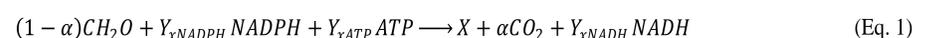


Figure 3 Examples of the estimated specific membrane area required for aeration of bio-oxidation processes, based on a volumetric productivity of $2.5 \text{ gL}^{-1}\text{h}^{-1}$ (black) or $5 \text{ gL}^{-1}\text{h}^{-1}$ (grey) respectively. Calculations are based on either the use of oxygen (open symbols) or air (closed symbols). The calculation were conducted as described previously (Côté *et al.*, 1988), assuming an oxygen mass transfer coefficient of $3.8 \text{ g m}^{-2}\text{h}^{-1}\text{bar}^{-1}$ for a polypropylene hollow fibre (Côté *et al.*, 1989) and operation at 1 bar. The dashed line represents a level where the design of commercial may become a limiting factor.

Oxygen requirements

Figure 1 illustrates the overall metabolic processes of a cell catalysing a biooxidation reaction. By combining these catabolic reaction with the anabolic reaction for biomass synthesis (Eq. 1) a model for the oxygen consumption can be derived (Eq. 2) (Villadsen *et al.*, 2011).



$$r_{O_2} = A\mu + B + C r_{cat} \quad (\text{Eq. 2})$$

$$A = \underbrace{\frac{Y_{xATP} - Y_{xNADH} P/O}{\epsilon + 2P/O} + \frac{1}{2} Y_{xNADH}}_{\text{Growth}} \quad B = \underbrace{\frac{m_{ATP}}{\epsilon + 2P/O}}_{\text{Maintenance}} \quad C = \underbrace{\frac{1}{2} + \frac{P/O}{\epsilon + 2P/O}}_{\text{Biocatalysis}}$$

Membrane aeration

Because enzymes can be inactivated by gas/liquid interfaces (Bommarius & Karau, 2005), bubble-less aeration through membranes may improve the operational stability of the enzyme. Figure 2 shows the estimated specific membrane areas necessary in order to reach given productivities using different forms of the biocatalyst.

Conclusions

- The maximum achievable productivity is greatly influenced by the oxygen requirement set by the biocatalyst.
- Maximum productivities of 3.5 and $5 \text{ gL}^{-1}\text{h}^{-1}$ were estimated for growing and resting cells respectively, using conventional bubble aeration.
- Membrane aeration is limited in terms of the maximum oxygen flux. Thus, the use of pure oxygen may be necessary in order to support the desired productivity.
- Bubble-less aeration would be particularly relevant to systems using sensitive enzymes. It may also be beneficial in order to minimize the evaporation of volatile components.

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"Developing a validated technology platform for the application of oxygen dependent enzymes in synthesis and transformation of alcohols"