

## MODELLING BIOCATALYTIC PROCESSES TO ACCELERATE ENZYME AND PROCESS DEVELOPMENT

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Biocatalysis has developed enormously in recent years and today represents a potentially powerful method for the sustainable synthesis and production of many new compounds. Nevertheless, in most cases, successful industrial implementation will require significant biocatalyst and process development. One of the most useful tools to guide us through the development stages is process modelling. Industrial implementation relies upon production at a suitable scale and with an adequate cost margin. This means the productivity and reaction yield must be adequate. For a sustainable process, three additional requirements must also be met: the process must use a renewable feedstock, be operated under mild conditions, and be produced at high enough concentration. Even at an early stage of process development and scale up it is very instructive to see whether these five demands can be met. Their relative importance depends on the value and scale of production [1]. Thus, the use of simplified metrics can be very useful at the lowest level of modelling. It can also guide protein engineering and decisions about process configuration [2]. Once the key metrics are met, then work needs to focus on optimization and reactor selection. Here knowledge of enzyme kinetics and rate laws are important. Combined with mass balances, they provide the basis for establishing the design of the process and a model which can inform a techno-economic analysis. Today there are several aspects of modelling within this development cycle requiring further attention. First, kinetic models need to incorporate all aspects of biocatalysis, including the effects of localizing multiple enzymes. Secondly, enzyme kinetics and stability need to be modelled using parameters obtained under suitable operational conditions. Thirdly, the effects of scale, including the effects of concentration gradients in large reactors are rarely modelled. Finally, the use of short-cut methods is still often overlooked, despite the possibilities this can bring to focus development. In this lecture, I will describe the general framework for process modelling of biocatalytic processes and outline areas which require particular research in the future.

[1] Woodley, J.M. 2022. Ensuring the sustainability of biocatalysis. *ChemSusChem*. e202102683.

[2] Meissner, M.P. and Woodley, J.M. 2022. Biocatalyst metrics to guide protein engineering and bioprocess development. *Nature Catal.* **5**, 2-4.