Process engineering tools to guide implementation and scale-up of transaminase cascades

Pär Tufvesson,[a] Krešimir Janeš,[a] Naweed Al Haque,[a] Joana Lima-Ramos,[a] Paloma de Gracia Andrade Santacoloma,[a] Watson Neto,[a] John M Woodley[a]
[a] *DTU Chemical and Biochemical Engineering, Soltofts plads, 2800 Kgs. Lyngby, Denmark*
e-mail: pt@kt.dtu.dk

Biocatalysis is gaining ground in the pharmaceutical and fine chemical industry as a selective and potentially green technology to help synthesize industrially interesting products. In particular in the last decade the application of transaminases (E.C. 2.6.1.X) has gained particular attention as a means to synthesize optically pure chiral amines from prochiral ketones using an amine donor. Chiral amines can also be synthesized by other routes but the importance of the compounds mean that a variety of routes will be required to cover the synthesis of many different chiral amines of different properties and values.

A major challenge in the transaminase catalysed synthesis of chiral amines is the unfavourable equilibrium position [1]. There are several solutions to such equilibrium problems, including the use of *in-situ* product removal (ISPR) and cascade reactions to degrade or recycle the co-product formed. Such techniques, especially those using cascades can be a great tool to overcome the thermodynamic hurdle, but also present some new challenges with respect to compatibility of reaction conditions, recycling of co-factors and last but not least, the added cost of the cascade system components [2].

In this lecture we will present several process engineering tools including the use of mathematical modelling, uncertainty and sensitivity analysis [3] as well as economic evaluation and defined experimental protocols to help evaluate the feasibility of new biocatalytic cascades. The concepts will be illustrated with data from transaminase catalysed syntheses we have been modelling and studying experimentally at DTU.

Acknowledgement
The authors acknowledge the support of project AMBIOCAS, financed through the European Union 7th Framework Programme (Grant agreement no.: 245144)

References
[1] P. Tufvesson, J. Lima-Ramos, J. J. Skibsted, N. Al-Haque, W. Neto, J. M. Woodley, *Biotech. Bioeng.* **2011**, *108*, 1479-1493
[2] P. Tufvesson, J. Lima-Ramos, M. Nordblad, J. M. Woodley, *Org Process Res Dev*, **2011**, 15, 266-274
[3] P. G. Andrade Santacoloma, G. Sin, K. V. Gernaey, J. M. Woodley, *Org Process Res Dev*, **2011**, *15*, 203-212