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VABILO NA PREDAVANJE V OKVIRU DOKTORSKEGA ŠTUDIJA KEMIJSKE ZNANOSTI / INVITATION TO THE LECTURE WITHIN DOCTORAL PROGRAMME IN CHEMICAL SCIENCES

Prof. Dr. Andreas S. Bommarius

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z naslovom / title:
Biocatalyst development – without protein engineering but with dimensionless numbers and ML

v petek, 17. 5. 2024 ob 13.30 uri /
on Friday, 17. 5. 2024 at 13.30
v predavalnici 1 v 1. nadstropju Fakultete za kemijo in kemijsko tehnologijo, Večna pot 113 **/ in lecture room 1,** 1st floor at the Faculty of Chemistry and Chemical Technology, Večna pot 113

Vljudno vabljeni! / Kindly invited!

Abstract:

Biocatalysts often are highly selective but too frequently are not sufficiently stable for process readiness. Besides increased specific activity towards a desired substrate, increased stability is the next most frequent goal of protein engineering. This presentation will argue that activity and stability can be jointly developed if outcome is measured by the total turnover number (TTN), a dimensionless number characterizing the average number of turnovers per active site over the enzyme's lifetime.[1] We will demonstrate that TTN can be viewed from the angle of classical dimensionless numbers, highly useful in science and engineering.[2]

Baeyer-Villiger monooxygenases (BMVOs), highly useful for converting ketones into esters or lactones but too unstable for process use, can be optimized both without and with the help of protein engineering; this presentation will demonstrate both.[3,4]

Assessing an enzyme's specific activity often seems straightforward. However, in semisynthetic β-lactam manufacture, penicillin G acylase (PGA) and an alternative enzyme, α-amino ester hydrolase (AEH), face selectivity issues (synthesis vs hydrolysis), inhibition by substrate, and, in our reactive crystallization process, inhibition by crystal surfaces. We will develop a kinetic reaction scheme that holds up a high degree of conversion.[5,6] The kinetic data will be analyzed both by classical fitting routines as well as by machine-learning based techniques.

Lastly, we will stabilize AEH via computational protein engineering techniques and find that there is a strong trade-off between increased activity and increased stability.[7]

References

[1]   AS Bommarius, Chem. Ing. Tech./Chem. Eng. Tech. 2023, 95(4), 491-497 (doi: 10.1002/cite.202200177)
[2]   AS Bommarius, unpublished
[3]   LCP Goncalves et al., Adv. Synth. Catal. 2017, 359, 2121-2131 (doi: 10.1002/adsc.201700585)
[4]   H Mansouri et al., ACS Catalysis 2022, 12, 11761−11766 (doi.org/10.1021/acscatal.2c03225)
[5]   PGA: PR Harris et al., Biotech. Bioeng. 2022, 119, 3117-3726 (doi: 10.1002/bit.28214)
[6]   AEH: CE Lagerman et al., Chem. Eng. J. 2021, 426, 131816 (doi.org/10.1016/j.cej.2021.131816)
[7]   CE Lagerman et al., Protein J. 2023, 42, 675–684 (doi: 10.1007/s10930-023-10155-z)