Quantitative Assessment of Process Robustness for a Mutualistic Microbial Co-Cultivation Using a Mechanistic Model

Peter Götz, Berliner Hochschule für Technik, Bioprocess Engineering

Mixed microbial cultures as well as defined co-cultivations are a common tool in food technology for obtaining fermented products. Another well known application of undefined mixed cultures is their use in wastewater treatment, employing the largest bioreactor systems existing. Harnessing the potential of co-cultivations in non-food processes has evolved in the last decades, yet large-scale applications are scarce. Here are a few examples (Schmidt 2021):

- Dark fermentative hydrogen production
- Photoautotrophic production of polyhydroxyalkanoates
- Propionic acid production from whey

Two basic concepts are currently driving research and development of co-cultivations:

- Assembling new metabolic pathways within a defined microbial consortium
- Activating silent genes for secondary metabolites through interactions within a microbial consortium

The latter can be aimed at discovery and production of antimicrobial therapeutics, an important task in view of the rise of resistant pathogenic strains. GMP production of the respective substance for pharmaceutical application requires a deep process understanding, which may be incomplete due to the complexity of interactions, even in two-species co-cultivations.

To analyze inherent problems with low reproducibility caused by interactions in a microbial consortium, we developed a mathematical model for the mutualistic co-cultivation of *Lactococcus lact*is and *Candida kefyr* using lactose as substrate. After estimating model parameters from batch, fed-batch and continuous cultivations of the pure strains and defined mixtures of the two species, simulations of the co-cultivation model allow investigation of various process conditions.

Main goal of this work is investigating the influence of variations of initial conditions in different operating modes. The continuous process model exhibits multiple steady states, which translates for batch and fed-batch co-cultivations into regions of high sensitivity to process conditions, where small perturbations may change the outcome of the process drastically. Final result will be finding these parameter regions and defining rules to avoid pitfalls in process development.

Schmidt, S. (2021). Applications of mixed microbial cultures in industrial biotechnology. In R. Kourist, & S. Schmidt (Eds.), The Autotrophic Biorefinery: Raw Materials from Biotechnology (pp. 353-384). De Gruyter. https://doi.org/10.1515/9783110550603-013