

Modelling *Clostridium Kluuyveri* to enhance its selectivity to medium-chain fatty-acids.

Level: MSc

Keywords: Metabolic modelling, Genome scale metabolic models, COBRA Toolbox (MATLAB)/COBRAPy (Python), Medium-chain fatty acids (MCFA).

Medium-chain fatty-acids (MCFA) are saturated monocarboxylic acids that can be used as antimicrobials, biodiesel precursors, corrosion inhibitors or for bioplastic production. *Clostridium Kluuyveri* is known as the unique clostridia able to grow anaerobically on ethanol and acetate as the sole carbon sources producing MCFA (Seedorf et al. 2008). The main fermentation products are butyrate, caproate and small traces of caprylate (Reddy et al. 2018).

The thesis project aims to enhance the selectivity to higher medium-chain fatty-acids (caproate (C6), caprylate (C8)) in *C. Kluuyveri* following an 'in silico' approach.

Due to the development of bioinformatic tools and metabolic engineering techniques, the availability of sequenced genomes has increased, leading to the reconstruction of predictive models of cellular metabolism and their analysis using constraint based-modeled techniques. Genome scale metabolic models (GEMs) are reconstructions used to get insight into the metabolic features and capabilities of organisms.

The genome scale metabolic model of *C. Kluuyveri* was reconstructed (Zou et al. 2018) and served to understand the metabolic potential of *C. Kluuyveri* elucidating novel pathways.

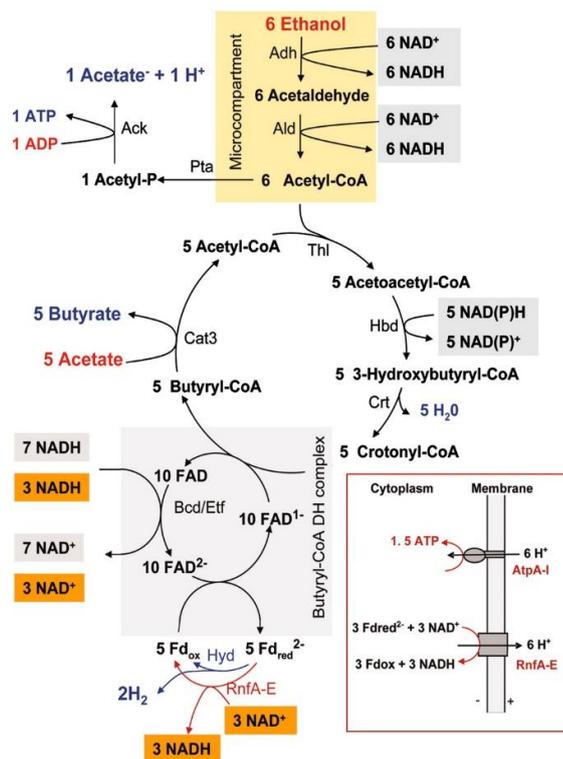


Figure1. Butyrate synthesis pathway from ethanol / acetate fermentation in *C. Kluuyveri* (Seedorf et al. 2008).

Thesis project:

- Exploration and validation of the GEM of *C. Kluyveri*.
- Simulation with different carbon sources and ratios to study the different product range.
- Introduction of new pathways to extend the product range to higher medium-chain fatty-acids.
- Apply algorithms to find possible genetic interventions that could increase the selectivity to the desired products.

COBRApy (Python) or COBRA Toolbox (MATLAB) will be applied as the constraint based modeled techniques.

Contact Details: **Sara Benito Vaquerizo**
Laboratory of Systems and Synthetic Biology
Computational Systems Biology Group

Stippeneng 4
6708 WE Wageningen
Room number: 6037
e-mail: sara.benitovaquerizo@wur.nl

References

- Reddy, M. V., Mohan, S. V., & Chang, Y.-C. (2017). Medium-Chain Fatty Acids (MCFA) Production Through Anaerobic Fermentation Using *Clostridium kluyveri*: Effect of Ethanol and Acetate. *Applied Biochemistry and Biotechnology*, 185(3), 594–605. doi: 10.1007/s12010-017-2674-2
- Seedorf, H., Fricke, W. F., Veith, B., Bruggemann, H., Liesegang, H., Strittmatter, A., ... Gottschalk, G. (2008). The genome of *Clostridium kluyveri*, a strict anaerobe with unique metabolic features. *Proceedings of the National Academy of Sciences*, 105(6), 2128–2133. doi: 10.1073/pnas.0711093105
- Zou, W., Ye, G., Zhang, J., Zhao, C., Zhao, X., & Zhang, K. (2018). Genome-scale metabolic reconstruction and analysis for *Clostridium kluyveri*. *Genome*, 61(8), 605–613. doi: 10.1139/gen-2017-0177