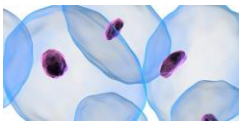

Model-driven optimization of synthetic methylotrophy and formatotrophy

Supervisors: Sara Benito Vaquerizo MSc, Dr. Nico J. Claassens.

Researchers involved: Sara Benito Vaquerizo MSc and Dr. Maria Suarez Diez, Systems and Synthetic Biology (SSB).

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Type of thesis: Computational

Required competences:

- Master student in Bioinformatics or Biotechnology, with sufficient background in modelling and bioinformatic analysis.
- The student must have followed the course: 'Metabolic engineering of Industrial Microorganisms' or another one related.

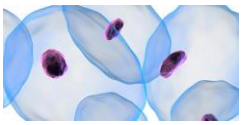
Acquired competences:

- Porgramming skills: Python/Matlab, R.
- Metabolic modelling:
    - Genome-scale metabolic models.
    - Constraint-based reconstruction and analysis techniques: COBRApy, COBRA Toolbox.
    - Flux Balance Analysis.
- Comparative transcriptome analysis.
- Microbial physiology and genetics.

Date: 25-01-2021date the project was proposed

Description

A key challenge in bioproduction is the need to use more sustainable substrates, independent of agricultural resources. Highly promising substrates include the reduced one-carbon molecules formate and methanol, which can be generated via electrochemical production from abundantly available CO2 and renewable electricity (Cotton et al., 2020). However, most 'chassis' organisms in synthetic biology and metabolic engineering cannot grow on these substrates. In addition, in terms of ATP-



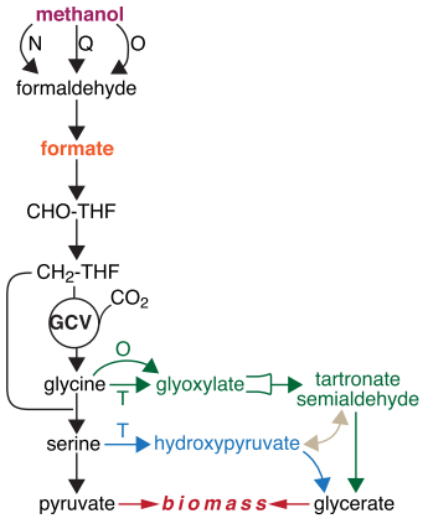


Figure 1: Metabolic map of variants of the reductive glycine pathway

consumption, limiting the potential product yields from these one-carbon substrates. A few years ago, a highly ATP-efficient linear pathway was designed for the assimilation of formate and methanol: the reductive glycine pathway (Figure 1) (Bar-Even et al., 2013). This pathway was recently engineering into the model bacterial host *Escherichia coli* (Kim et al., 2020). However, so far the growth rates of the engineered *E. coli* strain on formate and methanol are still relatively low, and also yields should be further improved to realize a platform strain for efficient C1-based bioproduction. In this project you will used genome-scale metabolic modelling methods, as well as analysis of transcriptome data sets to predict engineering targets to further optimize this strain. These analysis should result in a model-driven engineering strategy that can later be implemented by experimental partners in the lab.

References

Bar-Even, A., Noor, E., Flamholz, A., & Milo, R. (2013). Design and analysis of metabolic pathways supporting formatotrophic growth for electricity-dependent cultivation of microbes. *Biochimica et Biophysica Acta - Bioenergetics*, *1827*(8–9), 1039–1047. https://doi.org/10.1016/j.bbabio.2012.10.013

Cotton, C. A. R., Claassens, N. J., Benito-Vaquerizo, S., & Bar-even, A. (2020). Renewable methanol and formate as microbial feedstocks. *Current Opinion in Biotechnology*, *62*, 168–180. https://doi.org/10.1016/j.copbio.2019.10.002

Kim, S., Lindner, S. N., Aslan, S., Yishai, O., Wenk, S., Schann, K., & Bar-Even, A. (2020). Growth of *E. coli* on formate and methanol via the reductive glycine pathway. *Nature Chemical Biology*, *16*(5), 538–545. https://doi.org/10.1038/s41589-020-0473-5