Modeling The Conversion Of Lignocellulose Into Medium-chain Carboxylates

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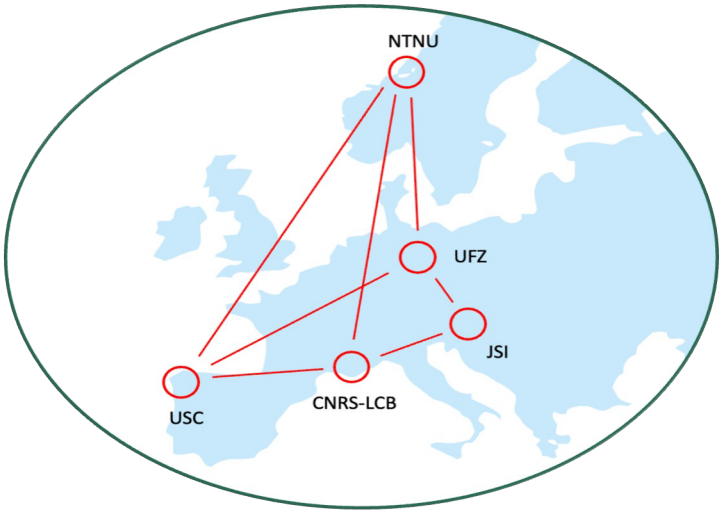
Medium-chain carboxylates are compounds with numerous applications, including in medicine, agriculture, and biofuel production [1]. In the so-called **carboxylate platform**, they can be produced from insoluble polysaccharides by an undefined microbial consortium. This facilitates the use of more sustainable feedstocks, such as agricultural **biowaste**, as substrates for their production. By combining experimental data with **genome-scale metabolic modeling**, we aim to guide the design of a defined synthetic consortium with optimal productivity.

THE CELL4HEM CONSORTIUM

The Cell4Chem project is a collaborative work under the ERA CoBioTech umbrella. With a combined effort, meta-omics, and tools from bioinformatics and systems biology, we will uncover new information about the community. The responsibilities in the project are shared by the project partners, who are based in various institutions across Europe.

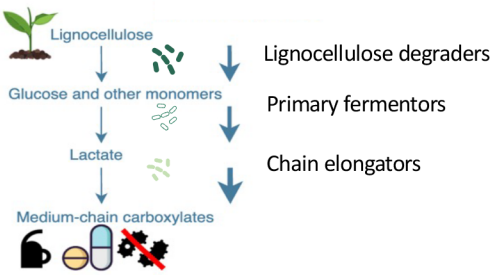


CHALLENGES

To increase yields from the traditional carboxylate platform, certain challenges must be overcome.

This includes:

- Reducing carbon flux through **competing pathways**.
- Establishing a **stable community**.
- Overcoming pathway **bottlenecks**.



APPROACH

Our approach involves applying a concept from systems biology called **genome-scale metabolic models (GEMs).** GEMs are species-specific reconstructions of an organism's metabolic network.

Their mathematical nature facilitates the use of **mathematical optimisation** to predict:

- The **genotype- metabolic phenotype** - relationship
- **Sensitivity to perturbations** in the environment

With the emergent use of **microbial communities** in industrial applications, the concept of genome-scale models has also been extended to the community level[2]. The **'community models'** can be applied to simulate the exchange of metabolites between the community members and the metabolic capacity of the community as a whole. Rather than viewing a community member as a black box, community models also offer advanced insights into its specific function and potential.

PROJECT PLAN AND METHODS

1. Building genome-scale metabolic models
   - Draft reconstruction and functional annotations of proteins and reconstruction of network with CarveMe [3]. Reconstruction of main pathways.
2. Model calibration with mono-culture data.
   - Determining kinetic parameters from experimental data and simulating growth in different environments with constraint-based methods.
3. Microbial community simulation
   - Applying constraint-based methods for community simulation.
4. Optimisation of microbial consortia.
   - Applying constraint-based methods, to find the desired community composition.

WORK PROGRESS

Building draft models with CarveMe for various community members.

Collecting resources on metabolic phenotypes and reconstructing main pathways.

Simulating growth in various media data from literature and partner experiments.

References

[1] V. D. Groof et al. (2019), "Medium chain carboxylic acids from complex organic feedstocks by mixed culture fermentation," *Molecules*, vol. 24, a.n. 398

[2] A. V. Colarusso, et al. (2021) "Computational modeling of metabolism in microbial communities on a genome-scale," *Current Opinion in Systems Biology*, vol. 11, p. 46-57.

[3] D. Machado et al. (2018)., Fast automated reconstruction of genome-scale metabolic models for microbial species and communities, *Nucleic Acids Research*, vol. 46, p. 7542–7553

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