Protein design towards SAF production for R. toruloides

Summary

The project aims to advance the state of the art in the field of enzyme design and strain engineering. The effort is going to be directed at the engineering metabolic steps for the biosynthesis of energy-rich molecules (lipids and terpenes) that are fit to be used as raw material in aviation fuel production.

Research field:	Chemistry and biotechnology
Supervisor:	Prof. Dr. Petri-Jaan Lahtvee
Availability:	This position is available.
Offered by:	School of Science Department of Chemistry and Biotechnology
Application deadline:	Applications are accepted between June 01, 2024 00:00 and June 30, 2024 23:59 (Europe/Zurich)

Description

The aviation industry represents 7.8% of final oil consumption worldwide and accounts for 2.5% of global CO# emissions. When calculated for the total historic release, it has contributed around 4% to global warming to date. The industry is heavily dependent on non-renewable and diminishing energy sources. The industry is in urgent need of developing a more sustainable supply model. A promising avenue is the conversion of wastes, sidestreams, and low-value byproducts into aviation fuel.

Naturally occurring bioprocesses are optimized via competition, selection, and evolution to benefit individual organisms in a “selfish“ way. High production rates of fuels for internal combustion engines are unlikely to be encountered in wild-type strain as those high production rates do not provide comparable advantages to a host organism as they provide to transportation vehicles.

Advances in AI tools in the field of protein engineering have been impressive. Available AI packages allow a range of opportunities to predict enzyme activity under pre-defined conditions and towards specific substrates and or products. However, the speed of computation prediction outpaces the ability to implement and test the enzyme variants in vivo. The discord between the potential of computation biology and the reality of the implementation offers a great possibility to innovate and advance synthetic biology fields. Issues to address include (but are not limited to) efficacy in synthesizing libraries of alternative gene variants or success rate in generating recombinant DNA strains using the libraries.

The candidate for the PhD position will undertake a throughout integration of computation design, library construction, strain engineering, and strain characterization.

1. Computation design. Working with bioinformaticians, available packages will be explored aiming for the prediction of novel/improved function. All enzymatic steps in the biosynthesis of lipids and terpenes will be considered. Strategies for identifying and removing existing bottlenecks with and without novel metabolic steps, will be evaluated for implementation feasibility.
2. Library construction. A variety of prediction packages can generate a large number of potential alternatives (e.g., different genes, a gene with changes in critical amino acids...). Developing a pipeline to define the critical set of changes that can realistically be tested, while preserving as high library diversity as possible.
3. Strain engineering. R. toruloides is considered a non-conventional yeast and molecular tools for engineering the species is lagging compared to S. cerevisiae and other common laboratory yeasts. Nonetheless, protocols for transformation are established to a sufficient level for improvement. The PhD candidate will implement additional solutions aimed at increasing transformation efficacy and throughput of the procedure via automation.

4. Strain characterization. Successfully generating recombinant strains from complex libraries has to be characterized. The more efficient is the procedure for generating recombinant strain, the more burdening is load to characterize all of the strains. The automation platform for strain characterization will be codeveloped to reflect strain engineering success rate.

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