ERA CoBioTech

BioTech Research & Innovation Hack

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ERA CoBioTech Funded Projects at A Glance: ContiBio

Continuous bioprocessing of microbial co-cultures: directing population by nutrient pulsing based on single cell data

PART OF EUROPEAN BIOTECH WEEK

INNOVATION IS IN OUR GENES

ContiBio

Continuous bioprocessing of microbial co-cultures: directing population by nutrient pulsing based on single cell data

Researchers with the EU-funded Contibio project will design a cell-machine interface for controlling the simultaneous cultivation of multiple microbial species within the same continuous cultivation device for improved bioprocessing conditions.

Project coordinator:

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Consortium

Dr Christian Dusny, Helmholtz-Centre for Environmental Research –UFZ Leipzig, (Germany)

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Project duration:

01 May 2021 - 30 April 2024

The use of microbial co-cultures for advanced bioprocessing

The ambition of the ContiBio project is to build-up on these research efforts and extend the concept, i.e. control of microbial population, and more specifically co-cultures, based on dynamic single cell data, for the transition from batch bioprocesses to continuous ones. Indeed, for designing sustainable bioprocesses, the cultivation mode resulting in the highest time-space yield should (TSY) be promoted. Despite the several benefits coming with fed-batch, including high product concentrations and easy application, the time dependence of product quality is still a major problem. Time dependent product quality leads to high batch to batch variations in all branches of biotechnology. Furthermore, if the variations are too high, the batch does not pass quality control (QC) and has to be discarded, leading not only to economic, but also to environmental problems. Also, the fact that co-culture will be considered will demonstrate the usefulness of the approach for controlling very complex microbial systems where cells belonging to different species are interacting. Ultimately, not only the process itself will be significantly improved, but also the capabilities of the biological systems (increase of metabolic potential, population stability…).

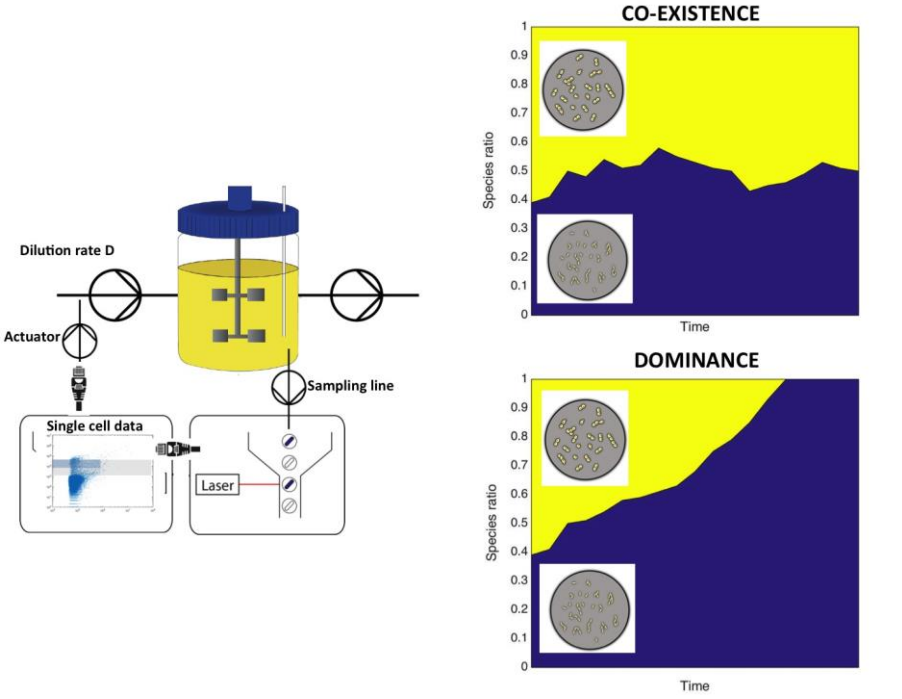

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Figure 1: Cell-machine interface for directing microbial co-culture

A recurrent feature is that population stability cannot be ensured in classical chemostat systems. On the other hand, the very same studies have shown that applying nutrient pulses at given interval during continuous cultivation, promoted proteome and subpopulations stabilization.

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This effect, known as periodic forcing, has also been shown to be efficient in stabilizing the activity of synthetic gene networks. Whereas the molecular mechanisms behind population stabilization through periodic forcing are still unknown, the application of nutrient pulses at given frequency and amplitude during continuous cultivation seems to be a new paradigm for ensuring cellular stability during continuous biomanufacturing. Thus, ContiBio project aims to contribute towards the control of synthetic co-cultures in continuous bioreactors by assembling a modular computational framework to address phenotypic and genetic instabilities arising at a single cell level. This modular computational framework will then be used to analyze the solution space for three different types of co-cultures operated in continuous cultivation mode.

Contibio project will provide technologies enabling stability of co-cultures in continuous cultivation devices by addressing issues related to phenotypic and genetic diversification of microbial populations. The main expected outcomes are:

- Tools and methodologies to directly implement complex microbiological systems on existing and novel applications. The tools, mainly relying on automated single cell technologies, will be implemented through an Artificial Intelligence (AI) program, allowing its direct application on any kind of bioprocesses. The universality of the tool will be assessed by addressing three different case studies covering a broad range of biotechnological application from sourdough to recombinant protein production. The effectiveness of the knowledge generated will be evaluated internally within consortium partners and the success rates will be used to provide the first quantitative lifecycle estimates of the effectiveness of implementing novel technologies (e.g. PURATOS estimates 20% increase in the sourdough market).
- Optimized knowledge on the interactions in and the stability of co-cultures of current fermentation processes based on ContiBio technologies will yield new stable microbial systems, fermented products with new or improved functionalities, stability, or efficiency and new innovative bio-based products (Partner : PURATOS, as well as associated partners : SYNGULON and ABInbev).
- Templates for starter cultures, biorefineries, fermentation, probiotics and antibiotics raising awareness potential. By introducing the use of co-cultures and by enabling continuous processes, ContiBio will encourage diversification

Project website: https://contibio-cobiotech.com/
Twitter: @Contibio_eu

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