

Scale-up/down of microbial processes

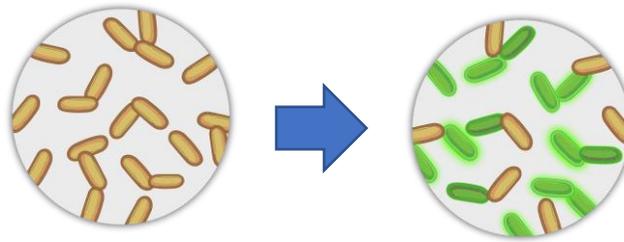
A modern light on an old issue

Frank Delvigne

F.Delvigne@uliege.be

MiPI research topics

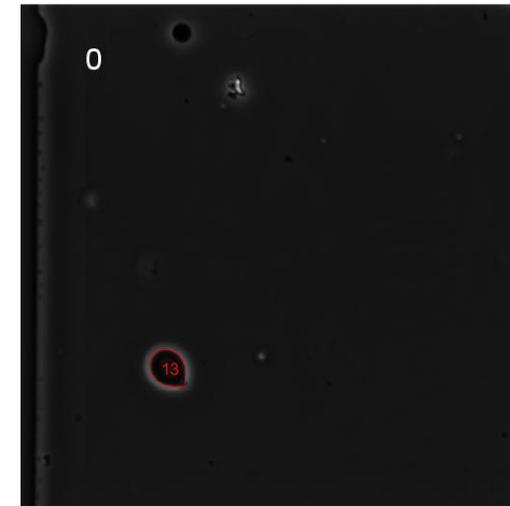
Main topic: diversification strategies of microbial population under fluctuating environmental conditions



Outcomes :

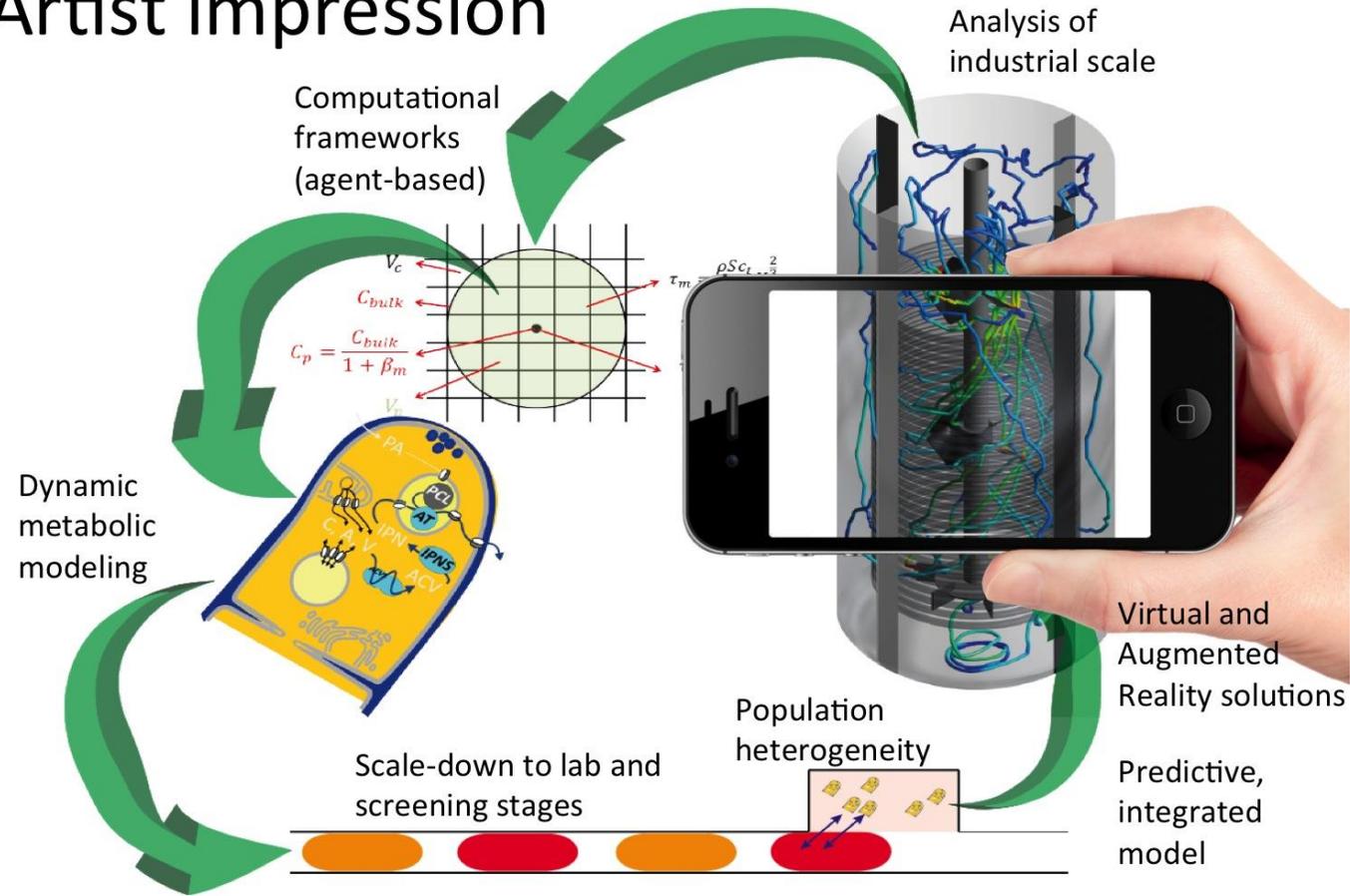
- Control of gene expression in continuous cultivation devices
- Scale-up/down
- Biofilm switching in *Pseudomonas sp.*
- Bet-hedging in yeast
- Microbial interactions and stabilization of co-cultures

Experimental devices



1. Scale-up/down framework: extracellular perturbations drive cell physiology

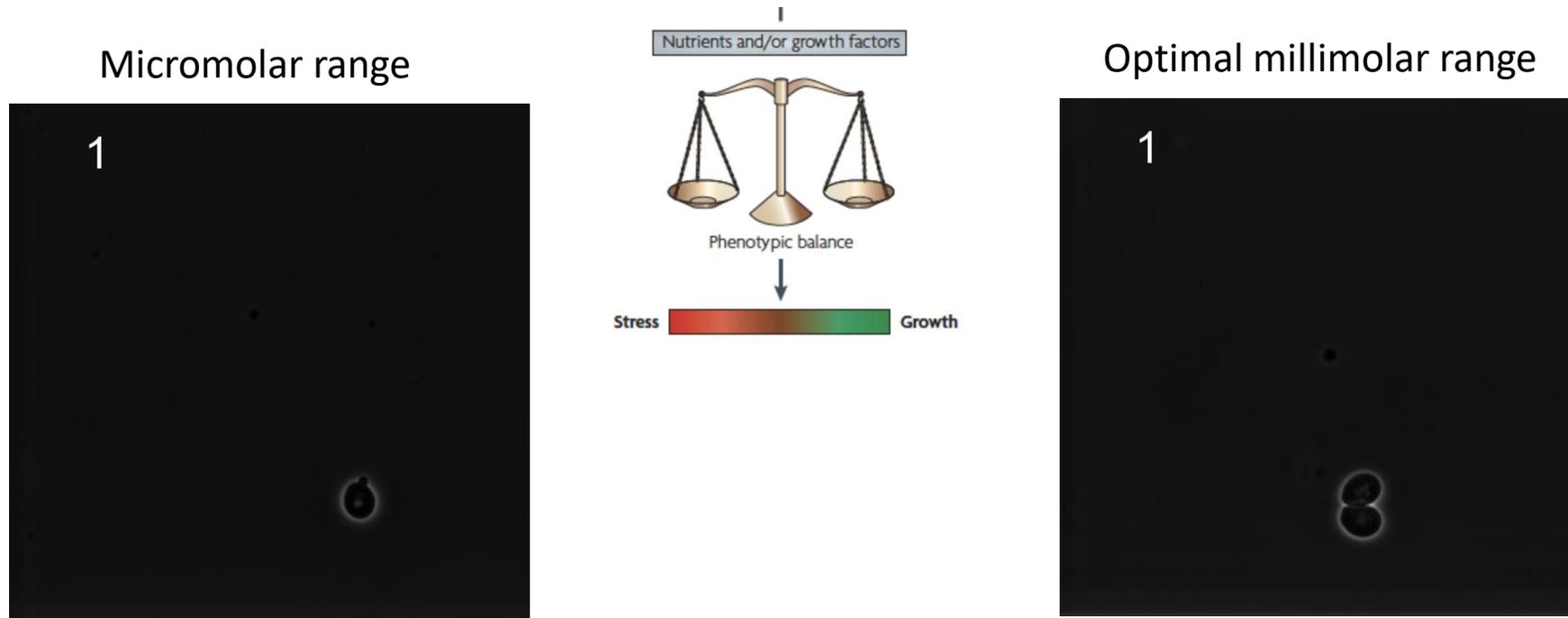
Artist impression



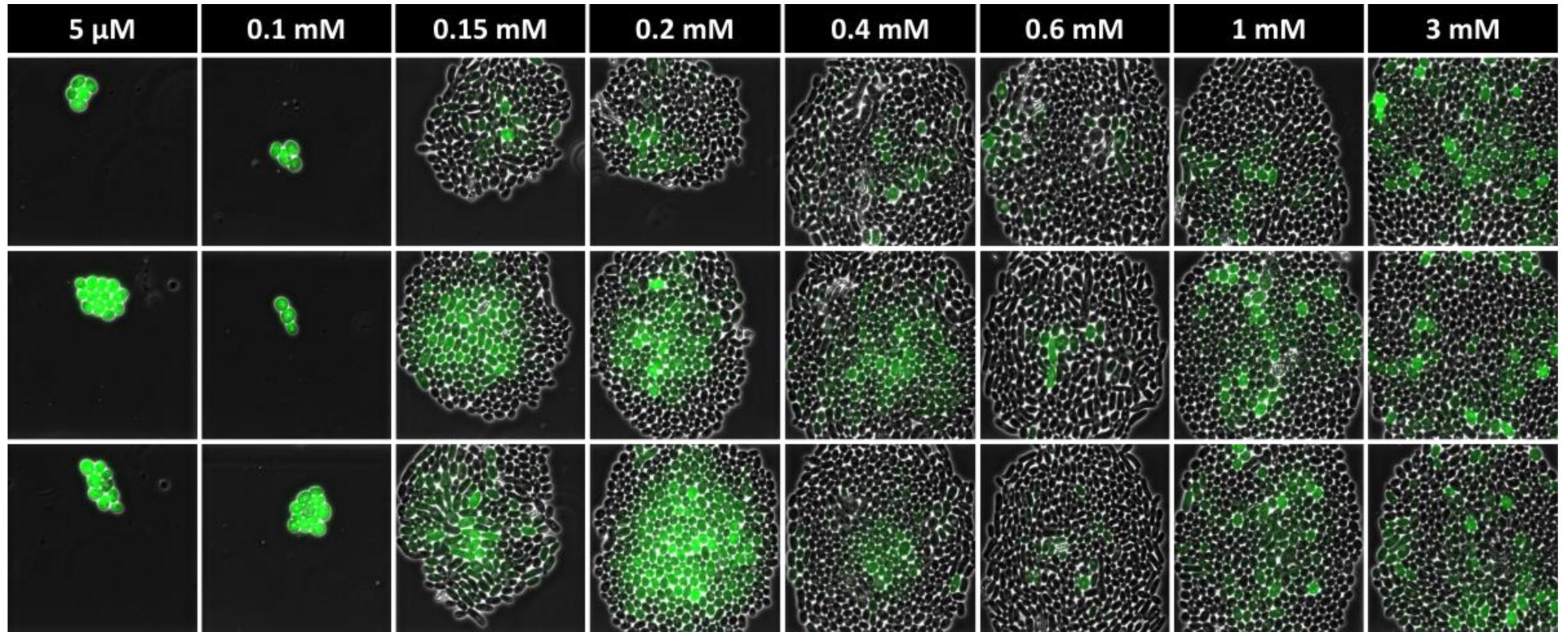
Delvigne F, Noorman H. Scale-up/Scale-down of microbial bioprocesses: a modern light on an old issue. *Microb. Biotechnol.* 2017;10:685–7

2. Let's take it from another perspective: anticipation of environmental perturbations by cell population

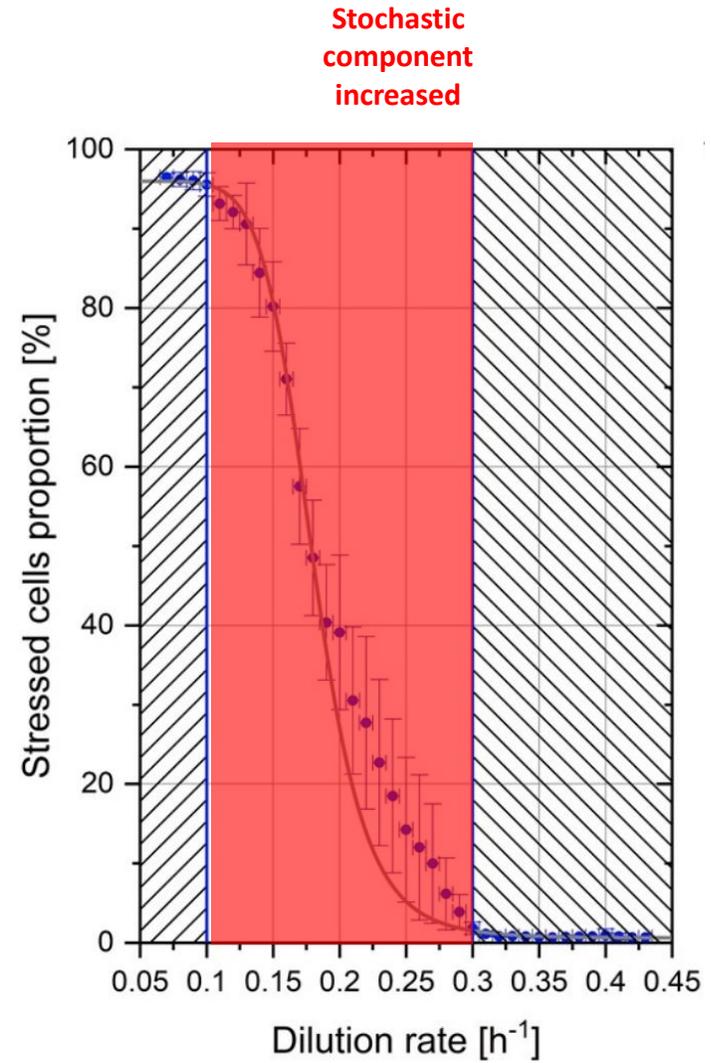
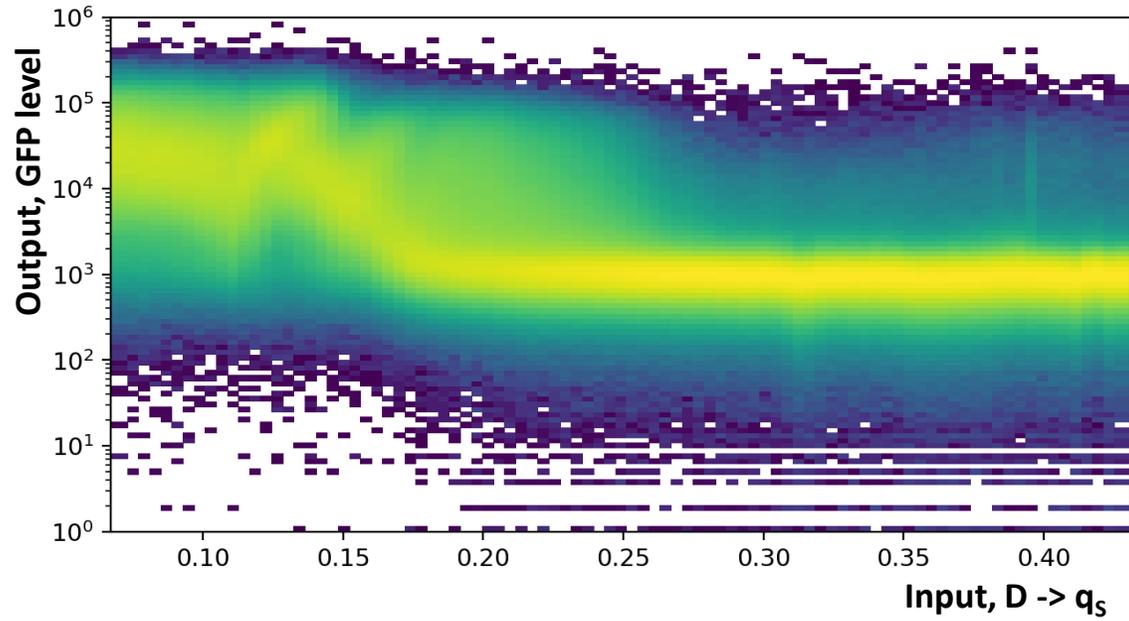
Case study: *Saccharomyces cerevisiae* CEN.PK113-7D trade-off between growth and stress resistance

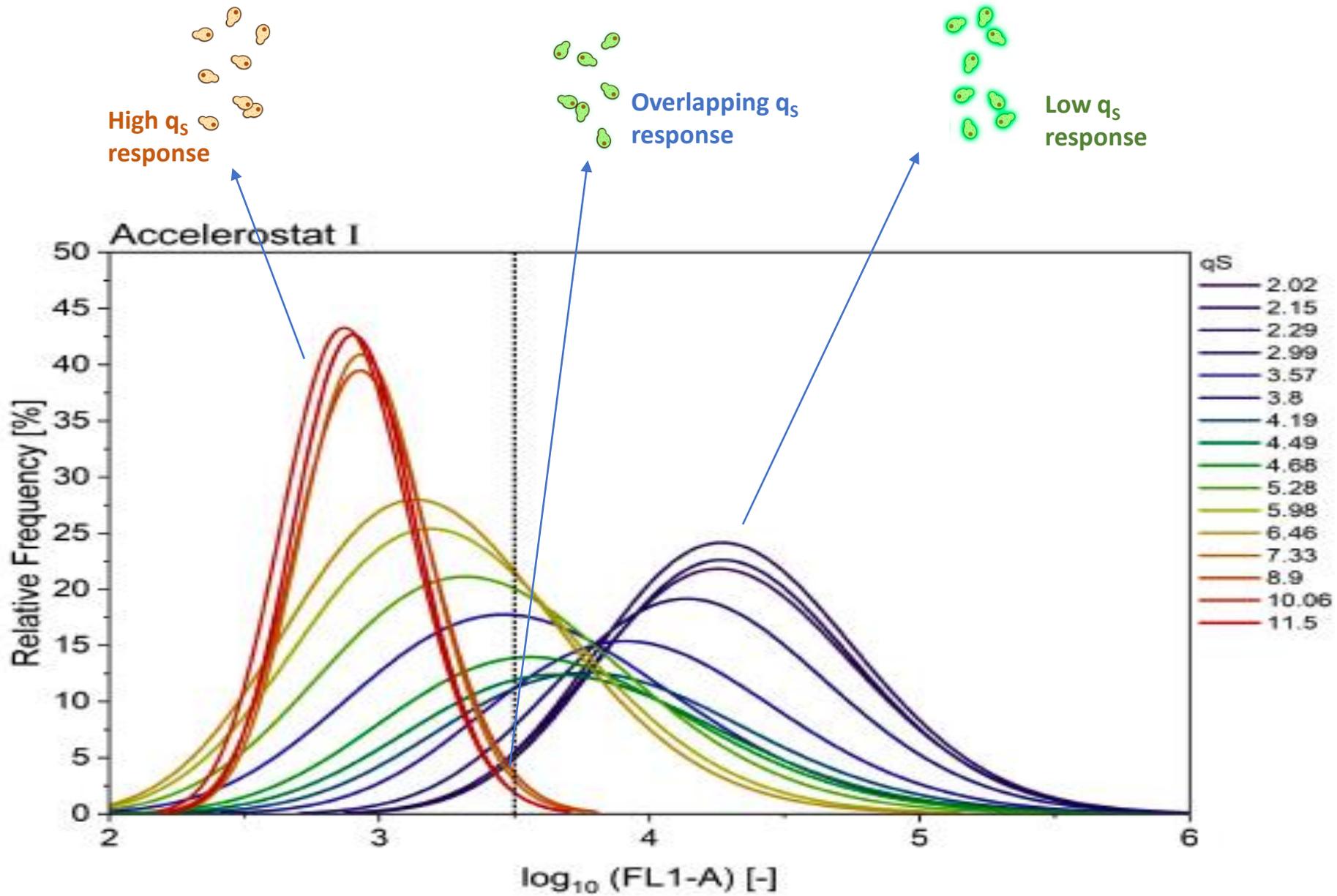


Microfluidics cultivation experiments under constant substrate (glucose) conditions

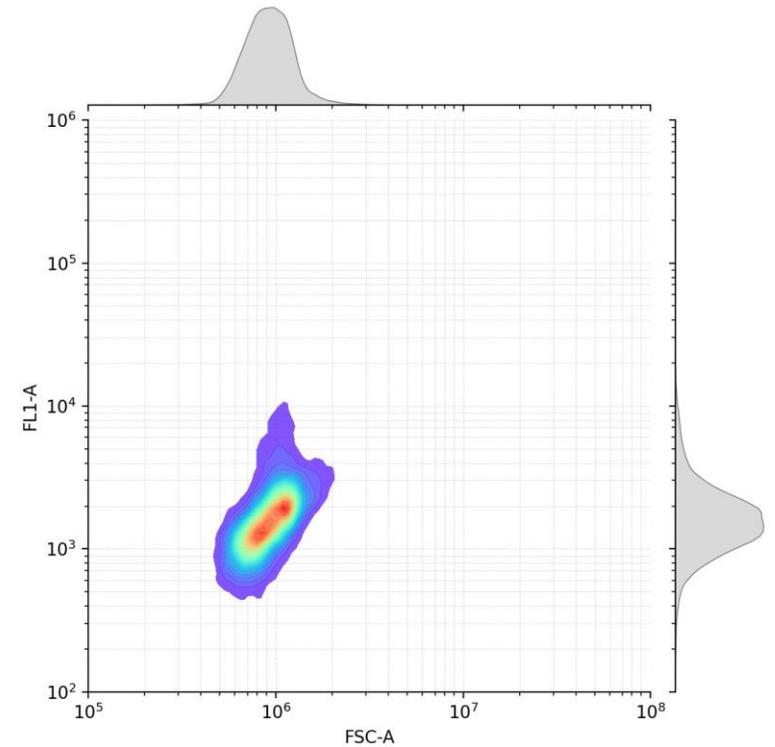
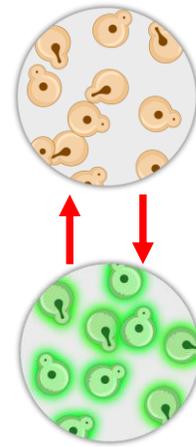
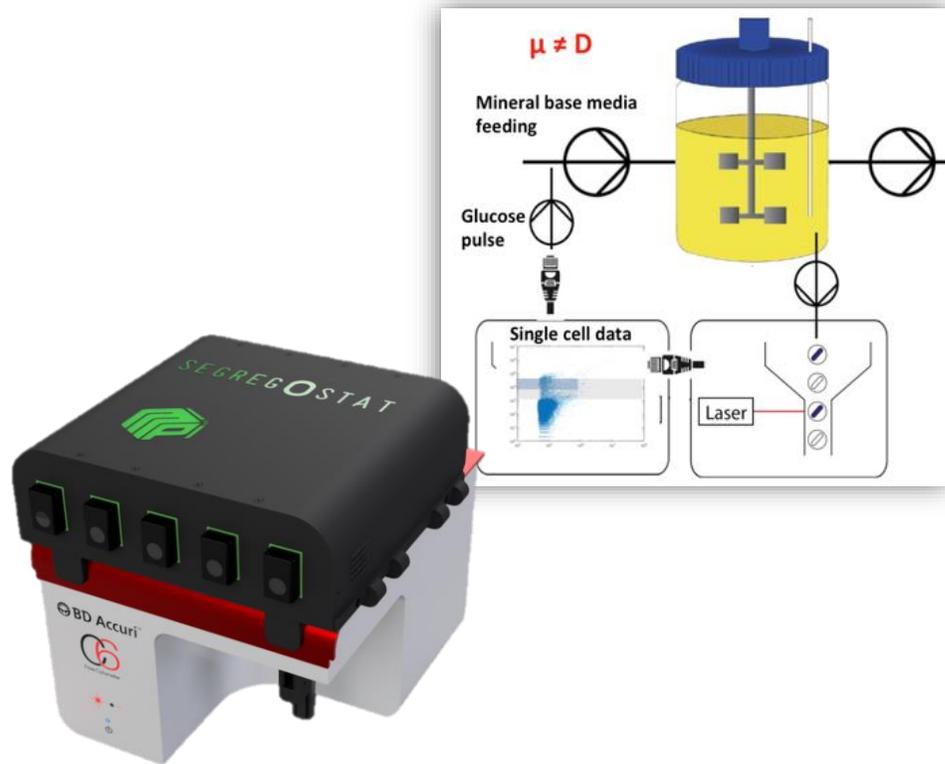


A-stat experiments -> cell population exhibits increasing q_s

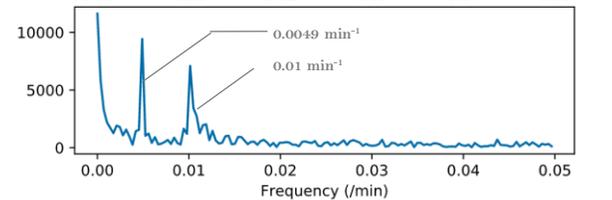
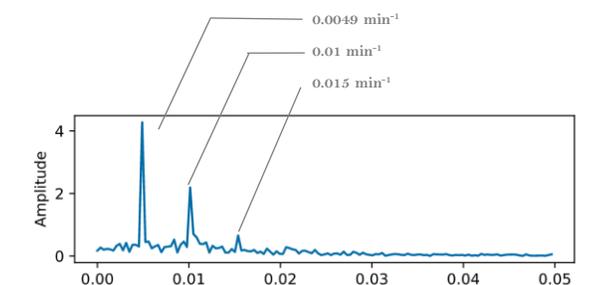
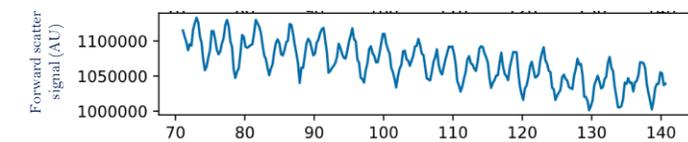
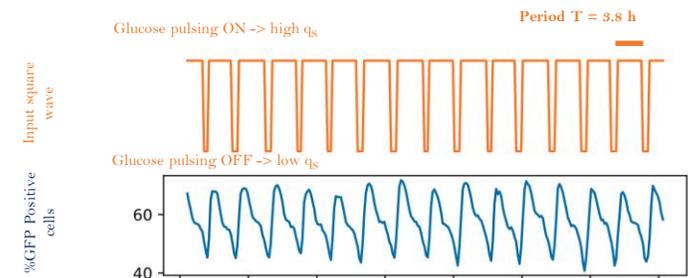
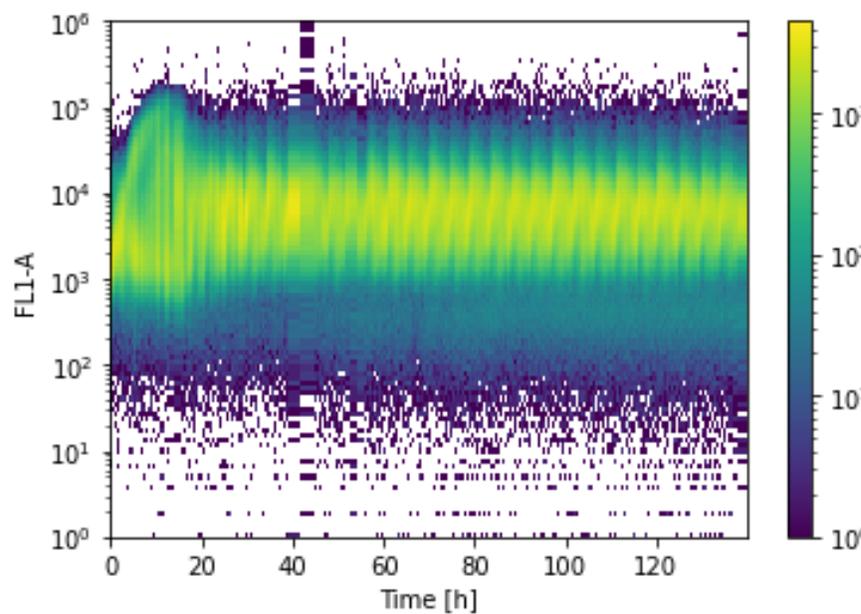
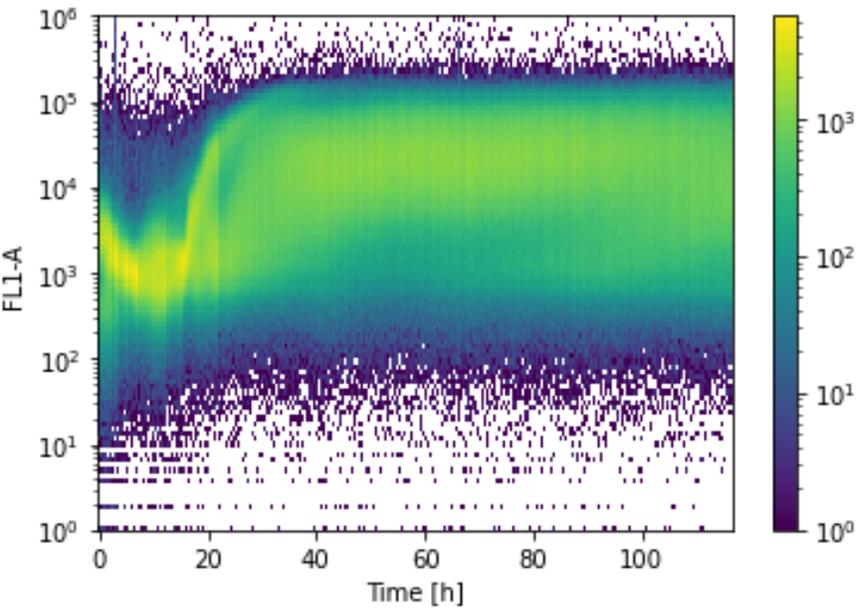
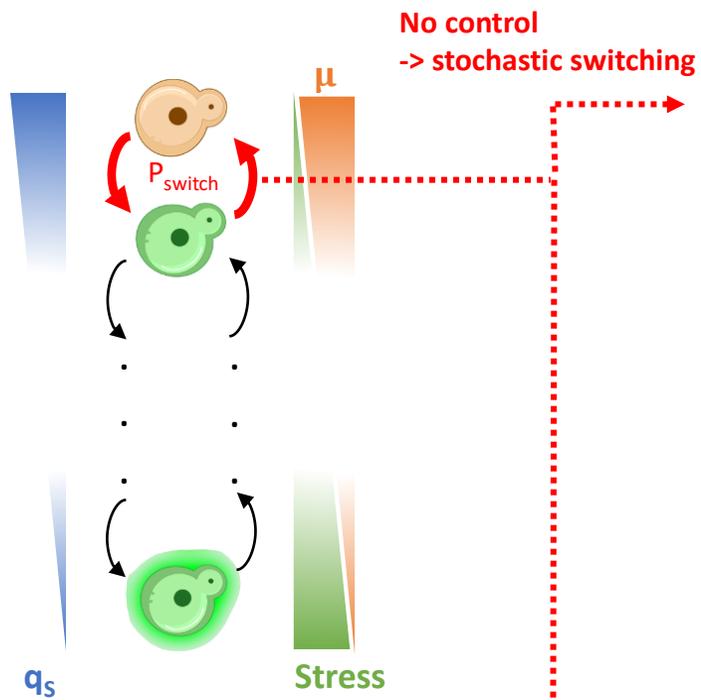




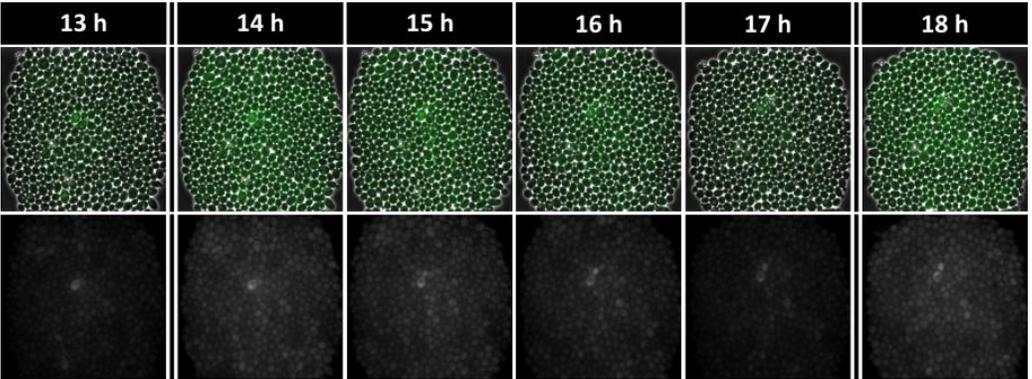
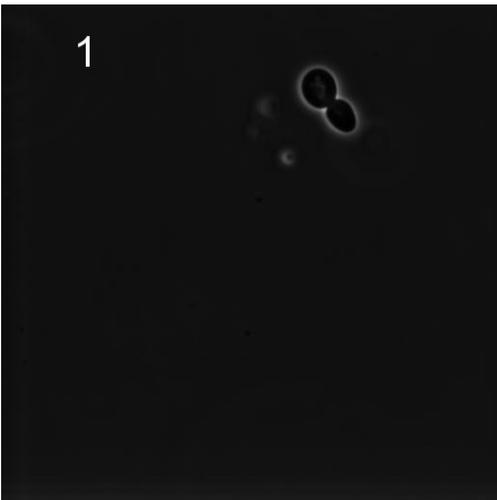
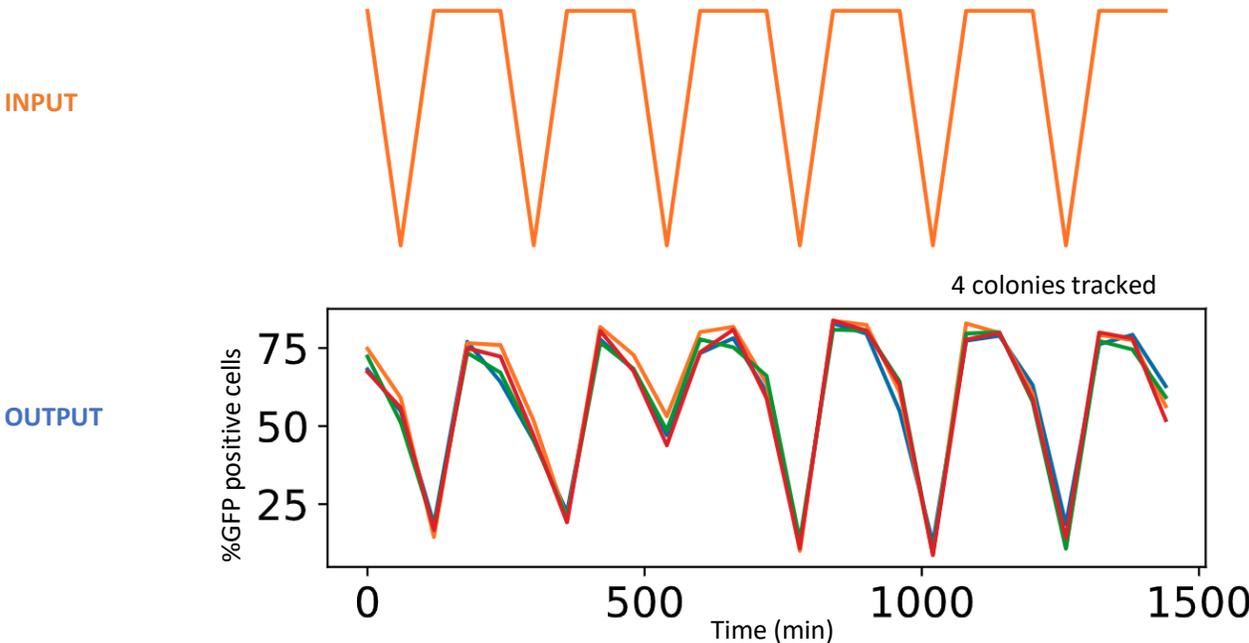
3. Turning stochastic switching into a fully responsive one?



Sassi *et al.* [2019] Microbial Biotechnology
Nguyen *et al.* [2021] Biotechnology and Bioengineering



Microfluidics cultivation experiments with fluctuations between $q_{S,low}$ and $q_{S,high}$



4. Segregostat control is robust to scale-down conditions

Is it possible to apply « segregostat » for controlling microbial population under large-scale conditions ?

Under large-scale conditions, three regimes :

- **Regime 1**: $q_s/q_{s,max} > 0.2$, Ethanol production
- **Regime 2**: $0.05 < q_s/q_{s,max} < 0.2$, Glucose limitation
- **Regime 3**: $q_s/q_{s,max} < 0.05$, Low glucose availability (possibly ethanol consumption)

Haringa *et al.* [2017] Chemical Engineering Science

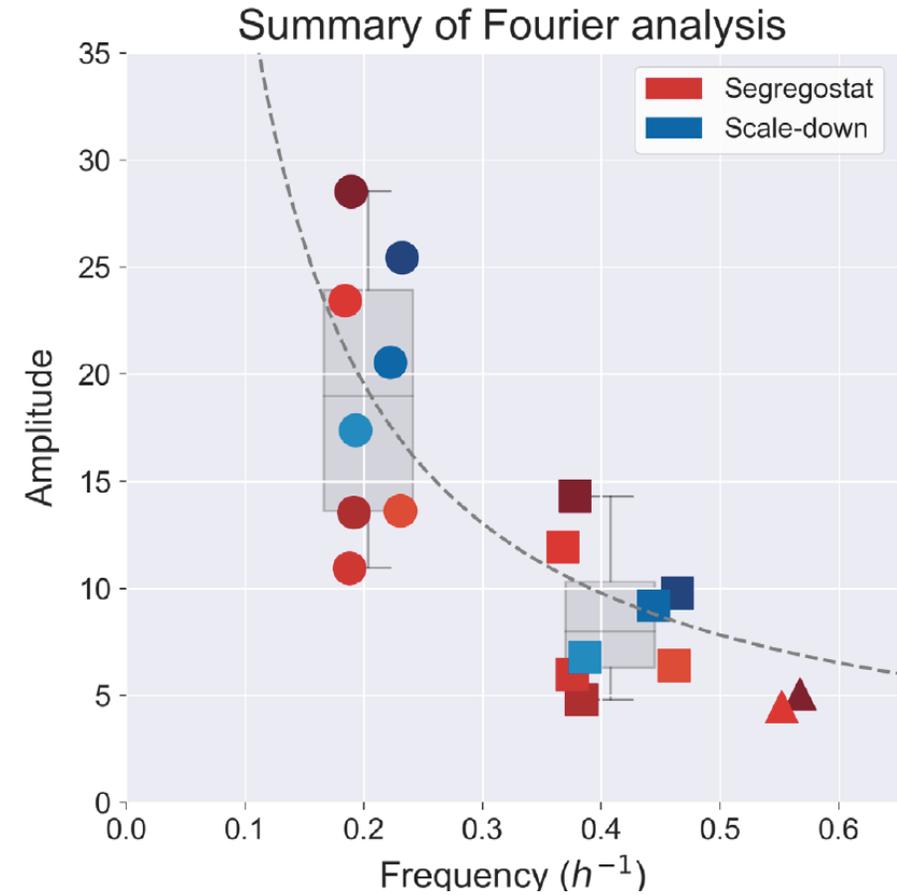
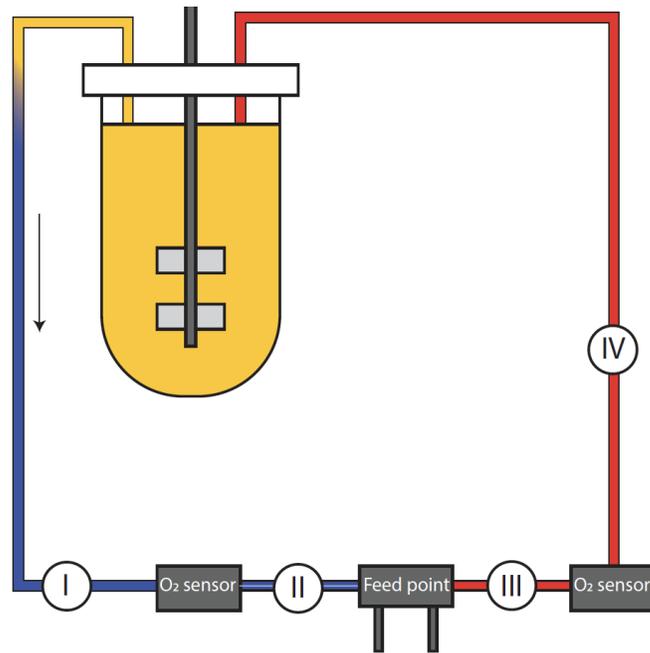


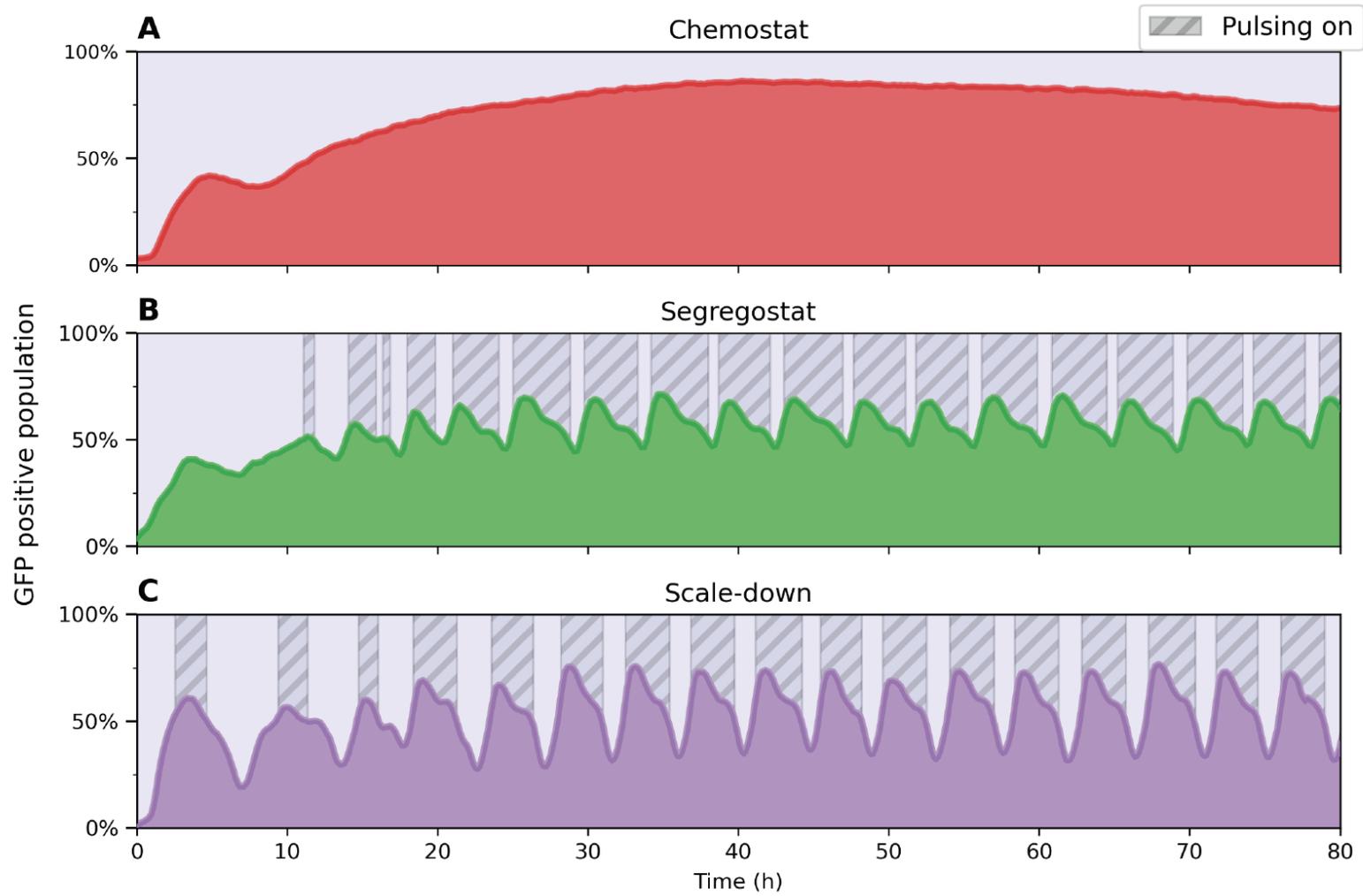
Correspond to our $q_{s, intermediate}$ regime -> high diversification in this range

Scale-down experiments

Conditions tested :

- $V_{STR} = 900 \text{ mL}$; $V_{plug-flow} = 100 \text{ mL}$; $t_{res} = 2 \text{ min}$
- $V_{STR} = 800 \text{ mL}$; $V_{plug-flow} = 200 \text{ mL}$; $t_{res} = 4 \text{ min}$
- $V_{STR} = 800 \text{ mL}$; $V_{plug-flow} = 200 \text{ mL}$; $t_{res} = 8 \text{ min}$





Acknowledgements

University of Liège – Gembloux Agro-Bio Tech:

Samuel Telek
Andrew Zicler
Lucas Henrion
Mathéo Delvenne
Fabian Moreno Avitia
Boris Zacchetti
Juan Andres Martinez
Ghazal Bajoul
Maximilian Tieke

University of Bielefeld/ FZ Jülich:

Alexander Grünberger
Sarah Täuber

TU Delft:

Cees Haringa

ComRaDes consortium:



Segregostat is now available in a DIY format

