ERA CoBioTech (ERA-Net Cofund on Biotechnologies)

ACHEMA2018

Kick-off session: "Biotechnology for a sustainable bioeconomy"

Project name: **Investigating large scale bioreactor effects in microbial application**

Project acronym: **ScaleApp**

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant 722361

Frankfurt am Main, 14.06.2018

Project partners

Technische Universität Berlin

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Stefan Junne

Puratos
Reliable partners in innovation

Coralie Lefebvre
Marie Carmen Alvarez Morales

gymetrics
VALUES THAT COUNT

Michael Ferguson

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Marco Oldiges (coordinator)
Eric von Lieres

- Total project budget: 2.720 k€
- Project start: 01.07.2018

Microbial cell factories for Bioprocesses: A hell of a job

„Force a complex organism optimized to survive under natural conditions to do:

non-natural high product formation,

in a **non-natural** environment,

with **non-natural** ultimate efficiency,

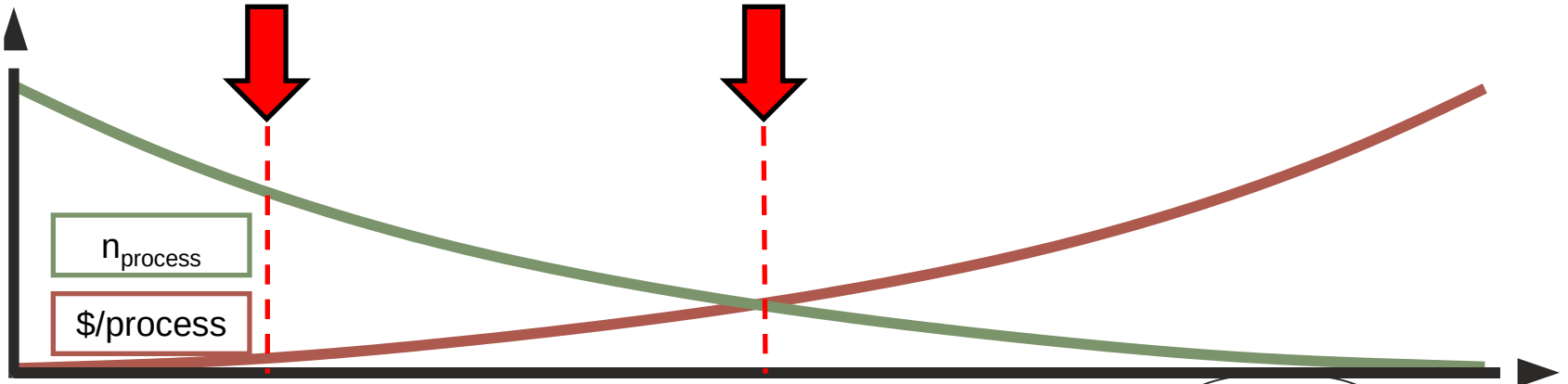
without being stressed! “

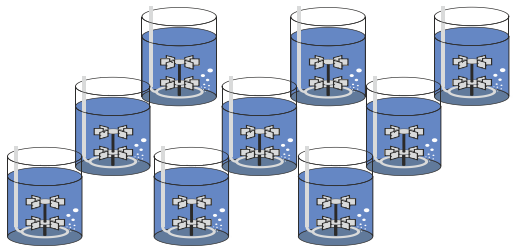
Who can do this job?

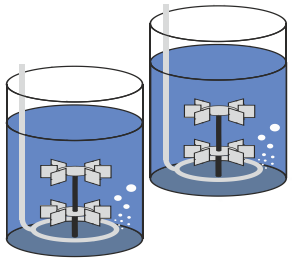
Important critical decisions :

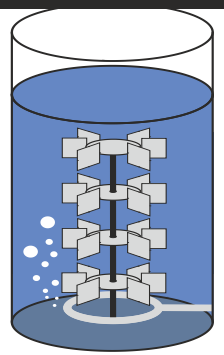
- optimal chassis organism
- tailored metabolic network design
- bioprocess design parameters
- **bioprocess scale-up (metabolic robustness !!!)**

Scale-up of biotechnological processes









lab scale
[~ 1 L]

pilot scale
[~ 10^2 L]

production
[~ 10^5 L]

optimization → **prove** → **conservation**

Bioprocess development depends on lab-scale optimization.

Process transferability between scales

Uncertainty between scales

lab scale
[~ 1 L]

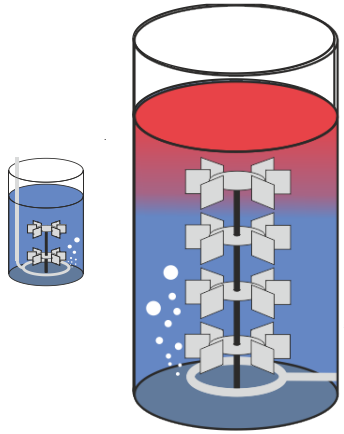
production
[~ 10^5 L]

laboratory scale:

oxygen transfer, OTR
→ 300-500 mmol L^{-1} h^{-1}

volumetric power input, P_V
→ 40-60 kW m^{-3}

mixing time, θ
→ seconds

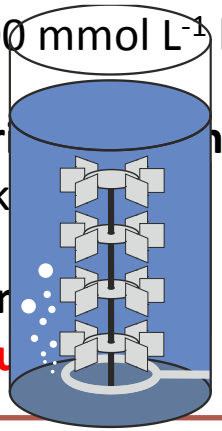


production scale:

oxygen transfer, OTR
→ < 100 mmol L^{-1} h^{-1}

volumetr… …nput, P_V
→ < 2 k…

mixing tir…
→ minu…



lab scale
[~ 1 L]

X

production
[~ 10^5 L]

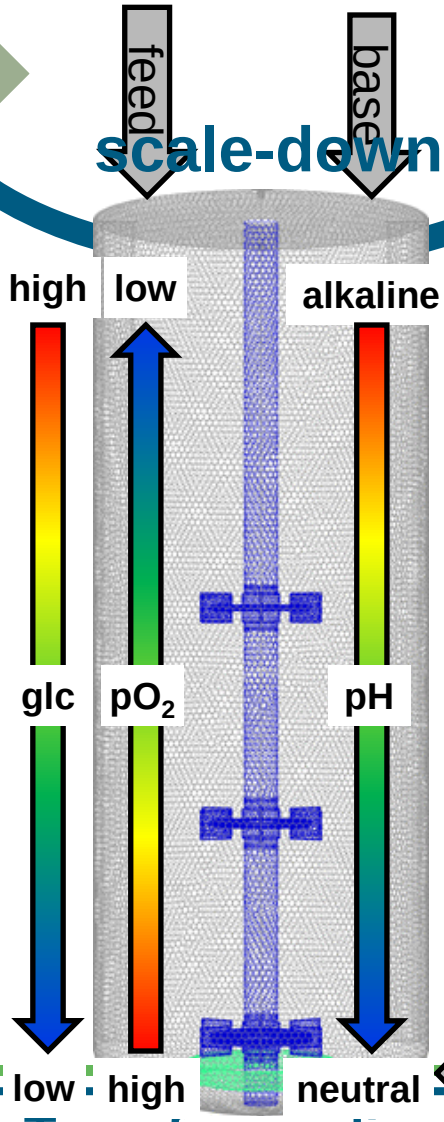
low mixing performance / energy dissipation result in inhomogeneities

Gradient formation in large-scale bioreactor

lab scale
[~ 1 L]

production
[~ 10^5 L]

scale-down



expected gradients:

- major gradients
  - **pO_2**
  - **substrate**
  - **pH**

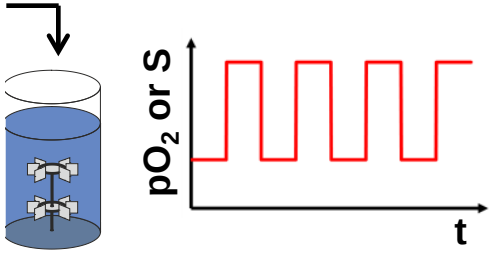
expected effects:

- less biomass formation
- lower product yields
- byproduct formation
- stress response

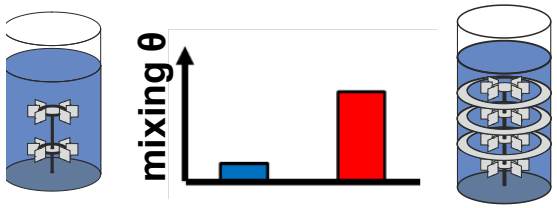
Scale-Down: Transfer gradients into lab scale

Experimental devices for Scale-down simulation

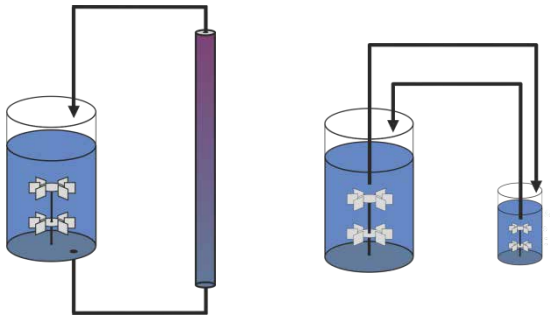
Feed



pulse reactors

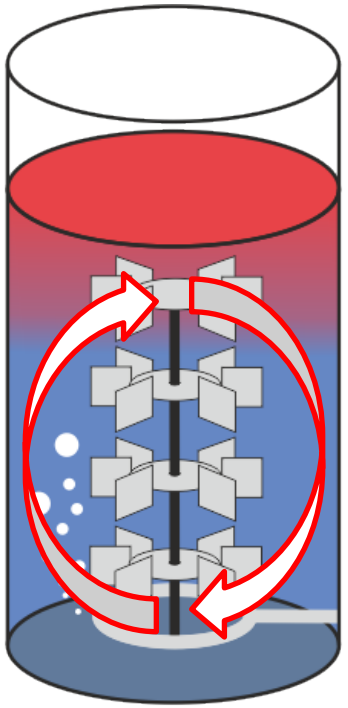


handicap reactors



compartment reactors

production scale



gradient + mixing

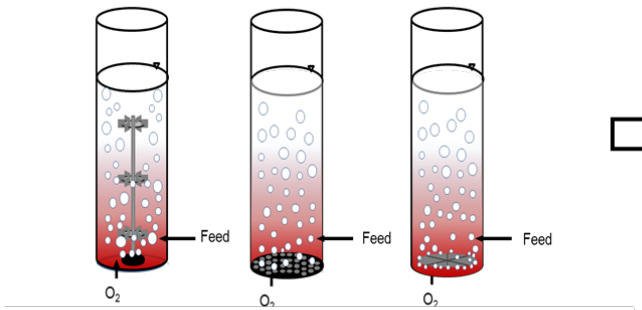
complex oscillation

Two compartment scale-down devices most frequently used

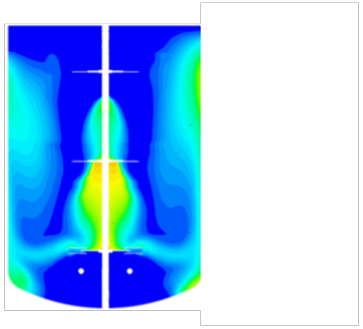
Metabolic phenotyping in separate compartments

ScaleApp objective

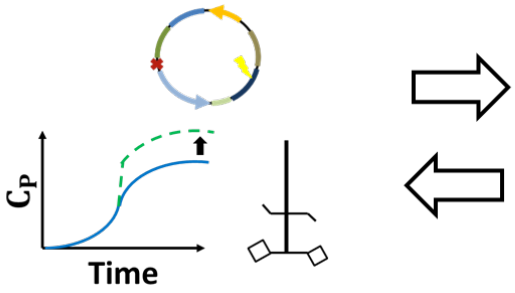
Gradient detection in industrial cultivations



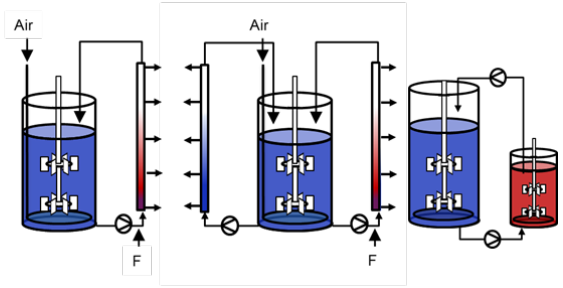
CFD combined with kinetic models



Process optimization



Scale-down cultivations

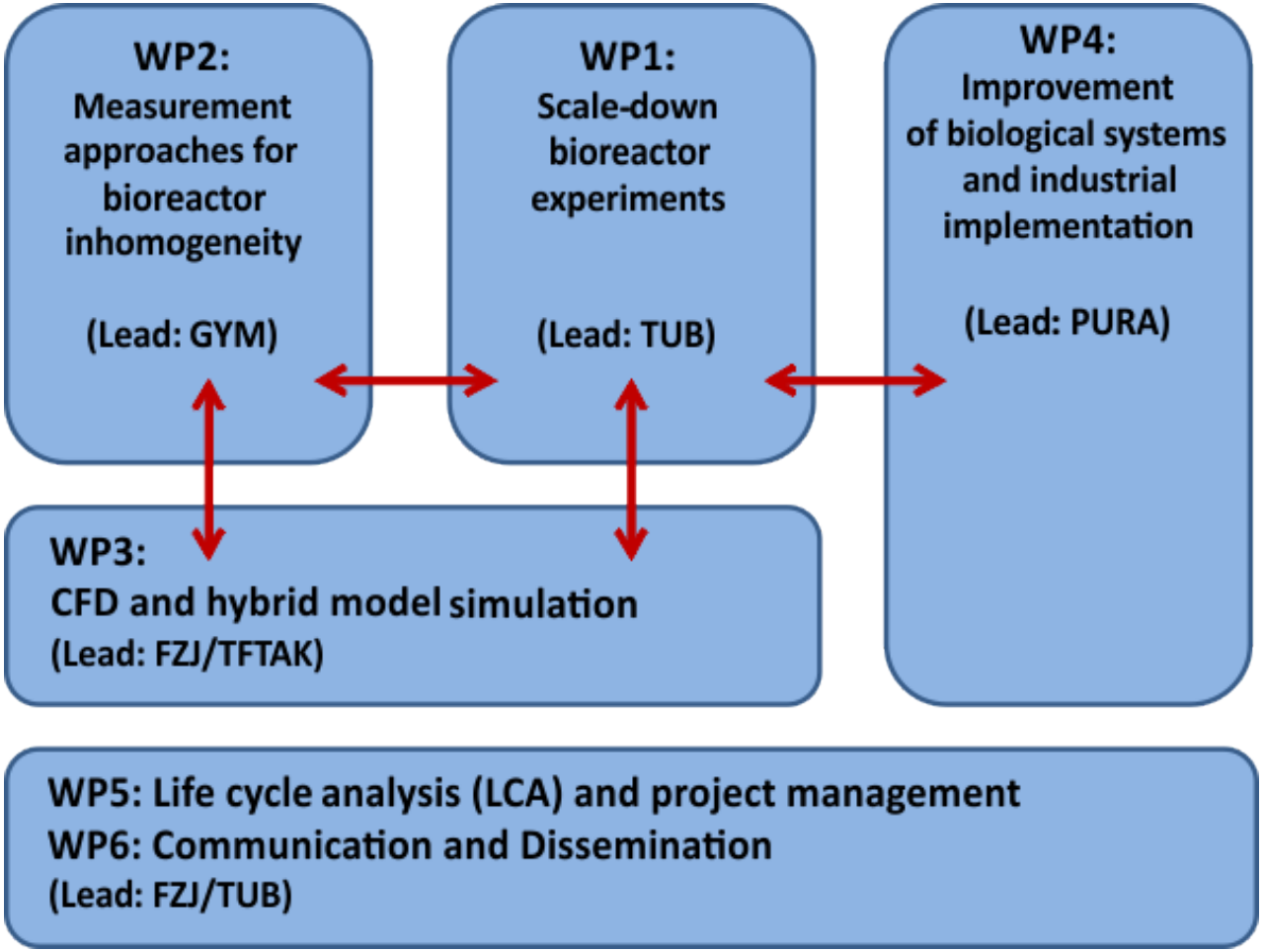


Target processes/products:

- Sec-mediated secretory formation of commercial enzyme
- Yeast biomass formation and derived products

Tailor-made design of scale-down bioreactor setup for several industrial bioreactor configurations and scales

Project plan



Summary: Expected outcomes

- *Development of multi-position monitoring tools and their application for in situ measurement of gradients in aerated bioreactors*
- *Design of suitable scale down bioreactors, which mimic more precisely true conditions in the industrial scale*
- *Investigation of the microbial response to gradient formation to identify targets for improvement of strain and process*
- *Hybrid modelling with CFD based on gradient measurements and metabolic modelling for the prediction of scale up effects*

Summary: Implementation of results

- *Support of industrial biotechnology partners in establishing improved large-scale cultivation processes.*
- *Generating commercially exploitable IP on cellular metabolism, scale-up/down and PAT technologies.*
- *Training of skilled researchers in large-scale cultivation and scale-up/down strategies for the industrial biotechnology and bioprocessing industries.*
- *Provision of learning material for courses dedicated to the topic of scale up/scale down and an increased knowledge of the interdisciplinary biotechnological and process engineering disciplines.*
- *Information about relevance of industrial biotechnology and improvement of its societal acceptance*

Contact details

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