Biomanufacturing Platform

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Why?

- Activities in biomanufacturing have been steadily increasing in Switzerland in recent years
  - Vaccines, protein and cell & gene therapeutics
- 3 UASs, 9 working groups with expertise
- Modern equipment for complete biopharma-ceutical production processes
- Lead: Regine Eibl & Thomas Villiger

Activities in 2023(1)

Projects

- Intensified and continuous IgG production based on novel SUT
  - Research (complete single-use USP line with Dynadrive 50 L)
    - ✓ High seed fed-batch productions
    - ✓ Continuous productions
  - Results
    - ✓ Webinars
    - ✓ Conference contributions
    - ✓ Further publications in progress

Chemie Ingenieur Technik

These are not the final page numbers! ↘↘

Research Article 1

Process Intensification Using a One-Step Inoculum Production and High-Seeded Fed-Batch Processes

Jan Müller[1]*, Vivian Ott[1], Noémi Weiss[1], Peter Neubauer[2], Dieter Eibl[1], and Regine Eibl[1]

DOI: 10.1002/cite.202200097

Various approaches to process intensification are currently being investigated to ensure time and cost savings when producing biopharmaceuticals. In the present study, a one-step inoculum production was established based on an ultra-high cell density working cell bank with immunoglobulin G producing Chinese hamster ovary cells. Cryovials were used for direct inoculation of 1-L wave-mixed perfusion bioreactors. When reaching around 180 · 10^6 cells mL^{-1} in N-1 perfusion mode, low-seed and high-seed fed-batch experiments in shake flasks were inoculated, as was the case for 250-mL stirred single-use bioreactors. Additionally, proof-of-concept runs at 50-L and 200-L scale were successfully performed. The intensification approach presented allows manufacturing capacity to be increased by up to 50 %.

Keywords: Chinese hamster ovary cells, Monoclonal antibody, N-1 perfusion, Ultra-high cell density

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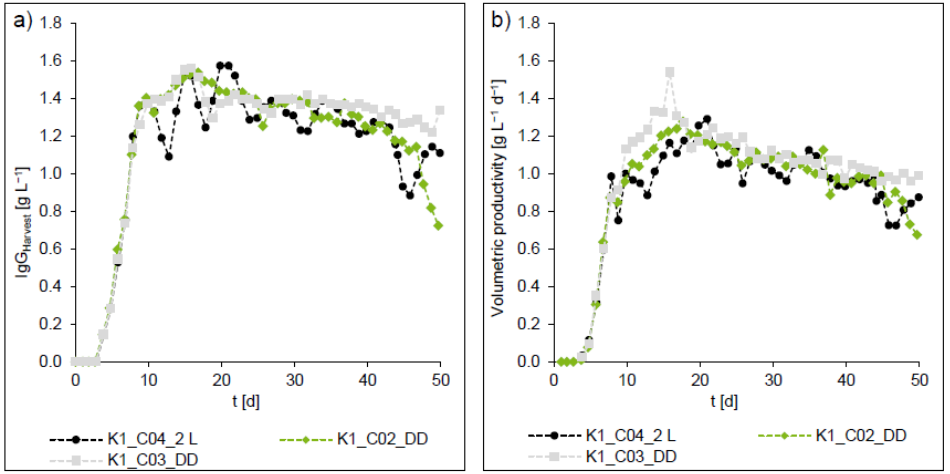
Project

- Continuous mab production

- IgG antibody
  - 50 d, productivity > 1 g L^{-1} d^{-1}
  - 50 L Dynadrive S.U.B. (start: 5 L) with ATF module and Raman spectrometer



28th ESACT MEETING European Society for Animal Cell Technology

30 min talk planned

Activities in 2023(2)

Events

- 2x DECHEMA Meetings (Wädenswil, Wuppertal)
- ECI Single Use Technologies VI (Boston)
- 10th Summer School (Wädenswil)
  - Cell expansion and protein expression in standard and single-use bioreactors
- Himmelfahrtstagung on Bioprocess Engineering (Weimar)

Publications

- 5 Research articles / Reviews
- 3 Book chapters

Activities in 2023(3)

- Improving the process understanding and efficiency of IB refolding processes
- PAT for IB fermentations
- Chromatography modeling

Publications

- Rolinger, Laura, Jürgen Hubbuch, and Matthias Rüdt. "Monitoring of ultra-and diafiltration processes by Kalman-filtered Raman measurements." Analytical and Bioanalytical Chemistry 415.5 (2023): 841-854.

Activities in 2023(4)

Projects/Publications

- Raman spectroscopy to control glycosylation
  (https://onlinelibrary.wiley.com/doi/10.1002/biot.202300318)
- Co-current filtrate flow in TFF to improve filtration in perfusion
  (https://onlinelibrary.wiley.com/doi/epdf/10.1002/bit.28589)
- Bleed recycling of perfusion processes
  (https://www.sciencedirect.com/science/article/pii/S1369703X23000682)

Efforts in connection with sustainability(1)

- Use of single-use technology dominates and continues to increase due to increased sustainability (BioPlan Associates)
- Project work by students in the 5th semester of Biotechnology (Bachelor) on the topic of sustainability of single-use systems
- Use of sustainable single-use materials (plant-based biopolymer)

Source: https://www.needpix.com/photo/1556089/ (12/2023)

Efforts in connection with sustainability (2)

The "Effic-IB" project aims to significantly reduce water consumption, energy requirements and wastewater pollution and thus improve the ecological and economic footprint of protein refolding processes at an industrial partner.

- Apply biophysical and statistical methods to improve understanding of IB refolding
- Use the obtained knowledge to find more sustainable process conditions
- Develop fast analytical methods for process development

Planned activities 2024(1)

- Testing and use of sustainably produced single-use systems
  - Green Elephant Biotech and their CellScrew
- 2 talks at 28th ESACT Meeting (Edinburgh)
- Continuation of collaboration with ThermoFisher for further 2 years

Planned activities 2024(2)

Projects

- Bayesian inference for chromatography modelling
- Real-time control of chromatography equipment
- PAT and model-predictive control for non-standard fermentations (IB & PHB)
- PAT and model-predictive control in collaboration with an OEM (funding pending)

Others

- Biotech Days in Basel
- Bio International Convention in San Diego

Planned activities 2024(3)

Projects

- We will continue to work with Merck on perfusion processes and PAT (Raman/IR etc)
- We will start a three-year project with Lonza in the realm of digitalization and modeling of continuous processes
- Focus of continuous / intensified processes in combination with PAT is being applied to viral vector processes (AAV)

Events

- Continuous chromatography course sept 2024 at FHNW
- Probably an ISPE event and some industrial events
- ESACT with talks/posters
- HES-SO visit in Feb 2024
- Biotech Days in May


Q&A