BILFINGER INDUSTRIETECHNIK SALZBURG

Development of an end-to-end process train for continuous manufacturing of bio-based products

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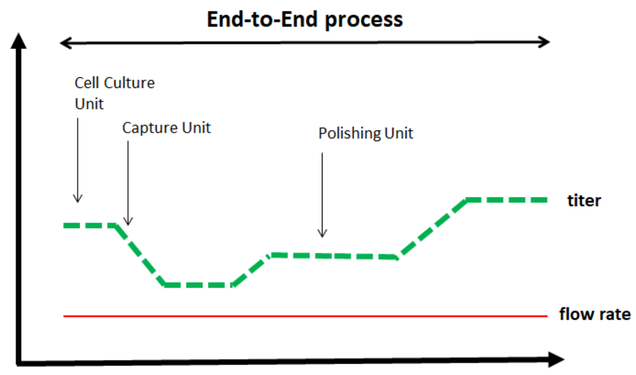
Background

Integrated continuous bio-manufacturing is the future trend in the bio-pharmaceutical industry. Reduced plant sizes, more flexibility, less occupation of resources and reduction of cost of goods (CoG) are the anticipated benefits. Together with the University of Natural Resources and Life Sciences, Vienna, Bilfinger Industrietechnik Salzburg launched the **End2End Project** in October 2019 to develop an automated end-to-end process skid for ICB.

The End2End Project

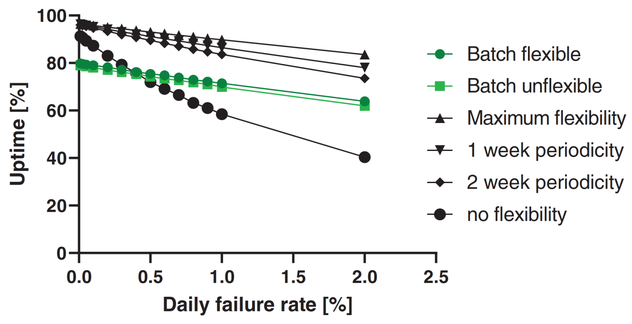
Mass Flow

- Truly continuous
- Uninterrupted
- No bind & elute step



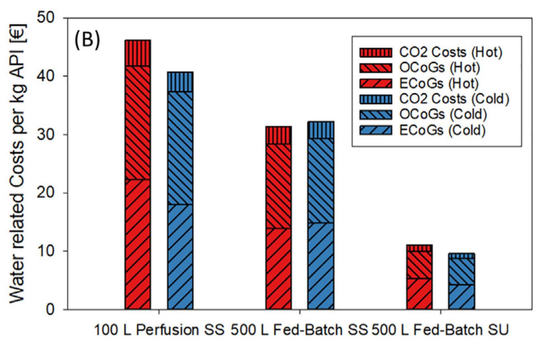
Economics

- Lot definitions & scheduling[2]
- CoG impact evaluation
- Full Scale Study



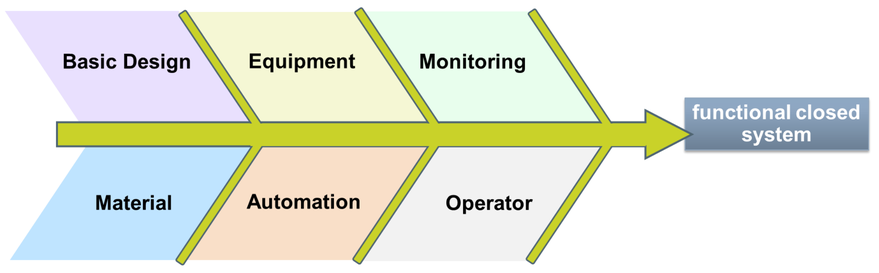
Ecological Footprint

- CO2 Impact (WARIEN)[1]
- Mass Process Intensity simulations
- Floor space reduction



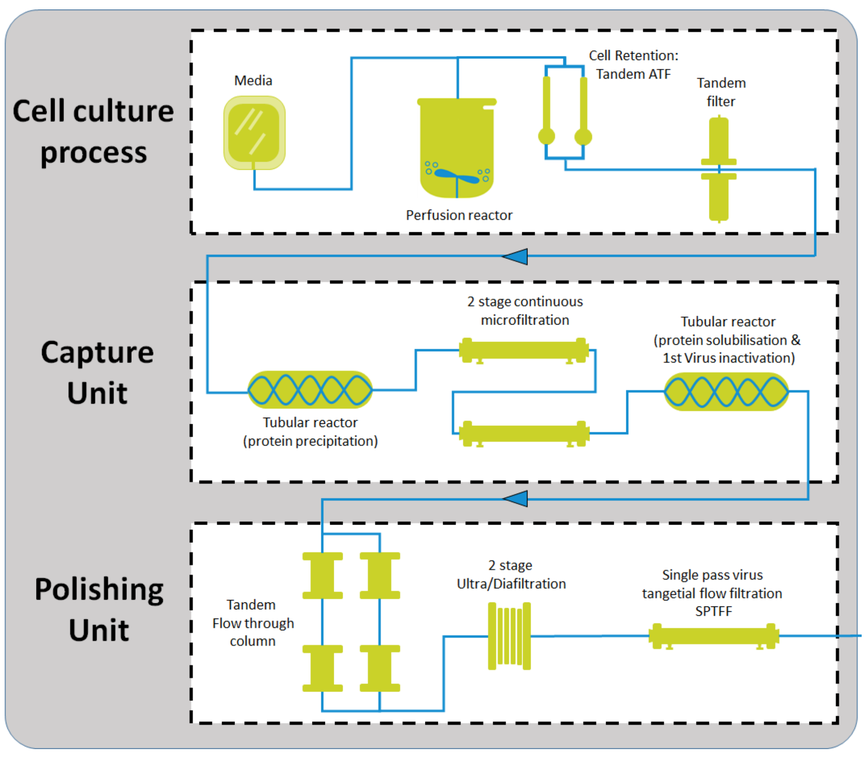
Design

- Functional Closed System*
- Compact Design
- In-Process Maintenance



End-to-End Prototype

- Three major interconnected units
- Precipitation as the capture step
- Incl. 2nd virus inactivation



Showcase

- CHO cell culture producing industrial relevant monoclonal antibody
- 2 – 100 L Scale
- Head-to-Head comparison with batch-wise production
- Integration of USP with capture unit (2 L scale) had been already established

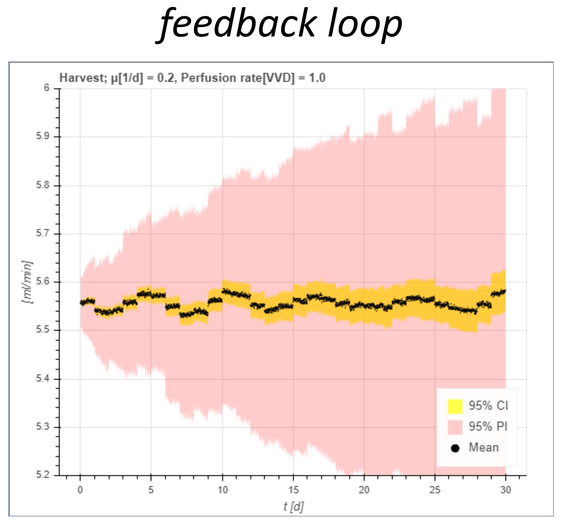
Traceability

- narrow residence time distribution
- Avoiding surge tanks
- Multiple error species simulation*

Control

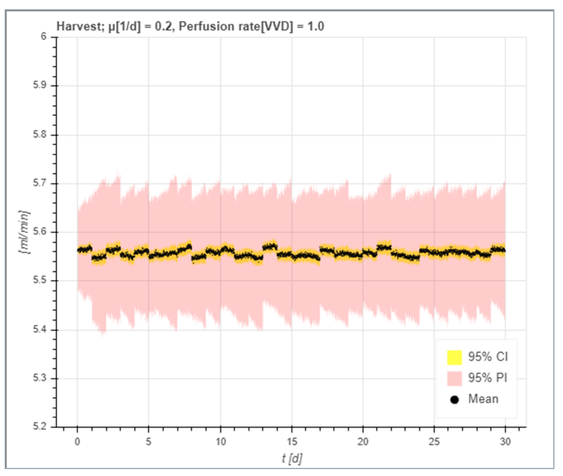
- Fully automated system
- Interconnected control strategy
- Error propagation simulations*

feedback loop



vs

one-step ahead prediction



Monitoring

- Establishment of a comprehensive process monitoring
- CQA & CPP Soft Sensors*
- Development of product quality monitoring tools[3]

1) Cataldo A.L., Sissolak B., Metzger K., Budzinski K., Shirokizawa O., Luchner M., Jungbauer A., Satzer P., (2020), *Water related impact of energy: Cost and carbon footprint analysis of water for biopharmaceuticals from tap to waste*. Chemical Engineering Science: X, Volume 8
2) Satzer, P., Komuczki, D., Pappenreiter, M., Cataldo, A.L., Sissolak, B. and Jungbauer, A. (2021), *Impact of failure rates, lot definitions and scheduling of upstream processes on the productivity of continuous integrated bioprocesses*. J Chem Technol Biotechnol.
3) Lhota G., Sissolak B., Striedner G., Sommeregger W., Vorauer-Uhl K, (2021) *Quantification of glycated IgG in CHO supernatants: A practical approach*. Biotechnol Prog.
* Manuscript in preparation

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