A Small-Scale Bioreactor Concept with Magnetically Levitated Stirrer

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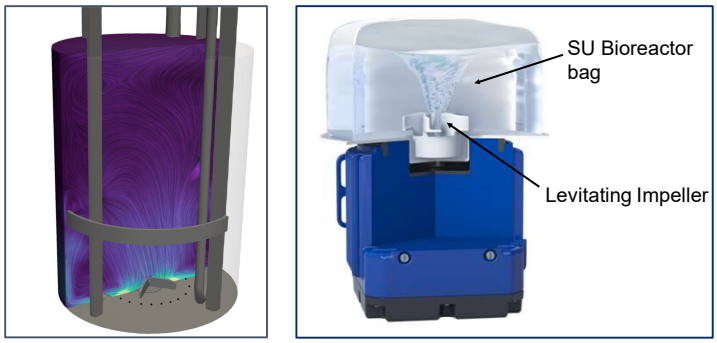
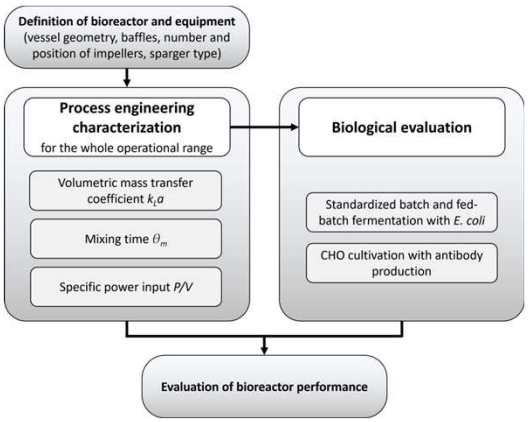
Introduction

Stirred bioreactors are essential for developing and commercializing biopharmaceuticals using microbial or mammalian systems, such as recombinant *Escherichia coli* or CHO cells (Chinese hamster ovary cells). These organisms differ significantly in morphology, metabolism, and process requirements, often necessitating tailored bioreactor designs with specific geometries, stirrers, and energy input strategies. Recent trends in process development favor miniaturized, parallelized cultivation systems to enhance throughput, reduce material consumption, and improve process understanding.
To support this, a collaborative project with Levitronix GmbH focuses on developing a universal, seal-less, magnetically driven bottom-stirrer system suitable for microbial and cell culture applications. The system is scalable from mL to L benchtop formats and aims to simplify bioreactor selection while maintaining flexibility across diverse production organisms and process conditions.
The current results presented here are based on a bioreactor setup with a 600 mL working volume and the PMS-i30 magnetic mixer drive from Levitronix GmbH, demonstrating its suitability for small-scale, high-performance bioprocessing.



Methods

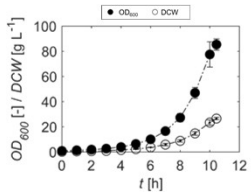
- Process engineering characterization according to DECHEMA's recommendations [3].
- Batch and fed-batch fermentations with *E. coli* W3110 and Biener's medium according to DECHEMA's recommendations and further specifications by Schirmer et al. [2,4].
- CHO cell cultivations with ExpiCHO-S 6H8 and ExpiCHO™ Stable Production Medium and Efficient Feed C+ (ThermoFisher). Reference cultivations were carried out in the HyPerforma Glass Bioreactor (ThermoFisher).

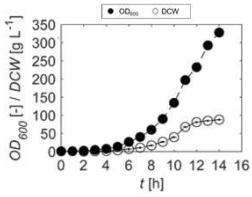


Results and Discussion

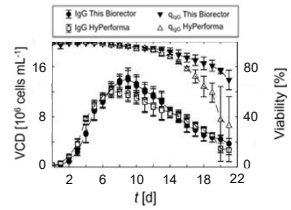
- Easy to handle bioreactor system.
- A possible stirrer speed range of up to 7730 rpm, enabling power inputs ranging from 2.2×10^{-5} kW m^{-3} to 53.4 kW m^{-3}.
- Mixing times for CHO cultivation conditions with ca. 16 s are achieved at stirrer speed of 430 rpm (15 W m^{-3}) and can be further decreased to 0.5 s at maximum speed. Thus, microbial requirements (<10 s) are already met at power inputs above 1 kW m^{-3}.
- A maximum volumetric mass transfer coefficient kLa of 672 h^{-1} could be achieved.
- Optical densities of OD600>80 (>24 g/L dry weight) were achieved in batch operation and OD600>328 (>88 g/L dry weight) in fed-batch operation with *E. coli* at stirrer speeds of 7730 rpm.
- Mass propagation of CHO cells resulted in a maximum viable cell density (VCD) of 14.3×10^6 cells/mL (day 9) and an IgG concentration of 3.5 g/L by the end of the cultivation. Comparable cultivation results and similar cell-specific IgG production rates (qIgG) were observed in the reference system HyPerforma Glass.

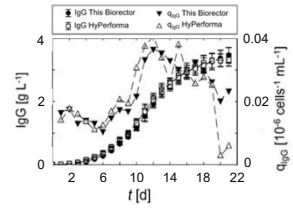
E. Coli





CHO cells





Conclusions

Due to the contactless agitator design, no harmful shear or frictional forces are transmitted to the production organisms, and the absence of a shaft feedthrough significantly reduces the risk of contamination. The magnetic drive system effortlessly adapts to varying environmental and cultivation requirements without the need for modifications or different bioreactor setups. It supports a wide operational range, from low (2.2×10^{-5} kW m^{-3}) to high power inputs (53.4 kW m^{-3}), enabling flexible use for diverse applications. Process engineering data confirm that the newly developed bioreactor system is suitable for cultivating both shear-sensitive animal cells and robust microbial strains. Batch fermentations with *E. coli* and fed-batch processes achieved high cell densities (OD_{600} of >80 and >328, respectively). During the cultivations of CHO cells in a chemically defined medium, a cell density of 14.3×10^6 cells/mL was reached, and the target IgG concentration (≈3 g/L) was exceeded, reaching nearly 3.5 g/L. The reference cultivations in a commercially available standard cell culture system also showed comparable results.

References

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