Characterization of orbitally shaken single-use bioreactors for plant cell cultivation

AACHENER VERFAHRENSTECHNIK

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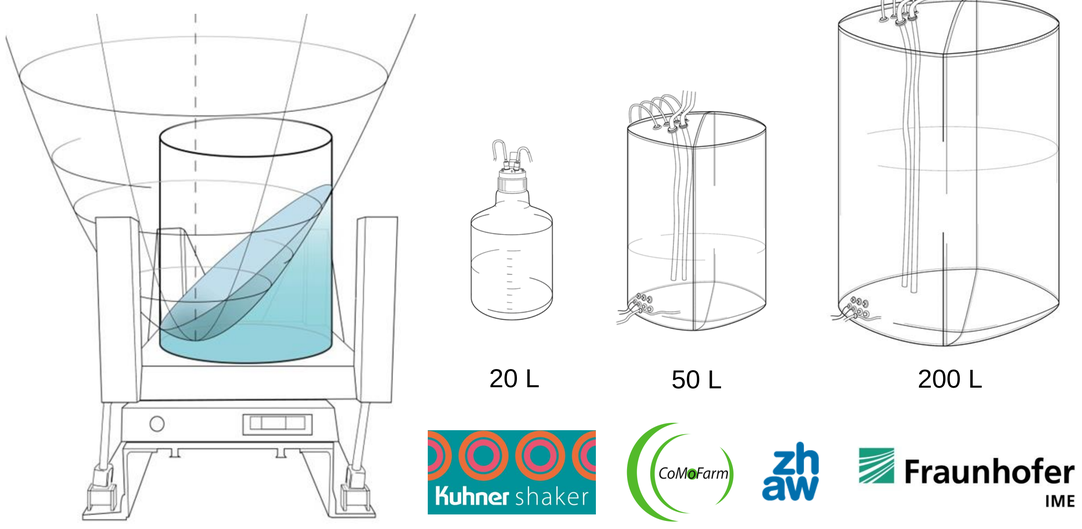
Introduction

CoMoFarm - Contained Molecular Farming

- EU project in the Seventh Framework Programme
- Development of contained systems for plants and plant cells
- Use of orbitally shaken single-use bioreactors



Materials and Methods

- Transfer of the **R**espiration **A**ctivity **Mo**nitoring **S**ystem (RAMOS) from shake flasks to orbitally shaken bioreactors
- Integration of a torque sensor for power input measurements

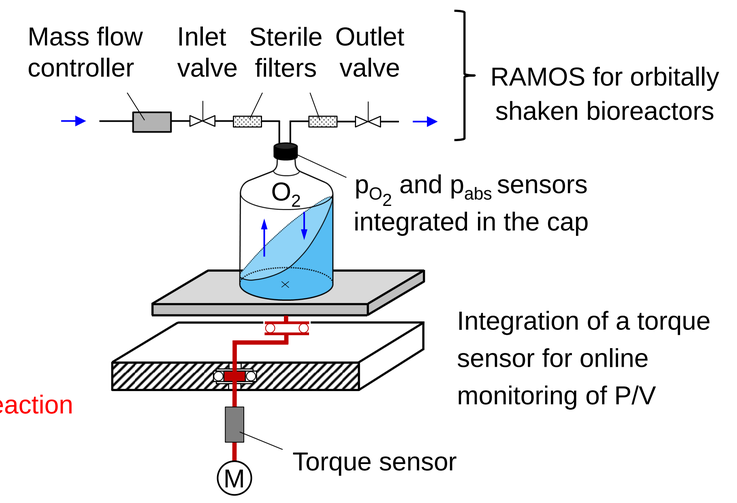
RAMOS to measure the OTR in shake flasks

$$OTR = k_L \cdot a \cdot (c_L^* - \cancel{c_L})$$

$c_L \approx 0$; reduced with sulfite reaction

$$SO_3^{2-} + 0.5 \cdot O_2 \xrightarrow{Co^{2+}} SO_4^{2-}$$

$$\hookrightarrow \quad k_L \cdot a = \frac{OTR_{max}}{c_L^*}$$



$$\frac{P}{V} = \frac{1}{V} \cdot 2 \cdot \pi \cdot n \cdot (M_{liquid} - M_{solid})$$

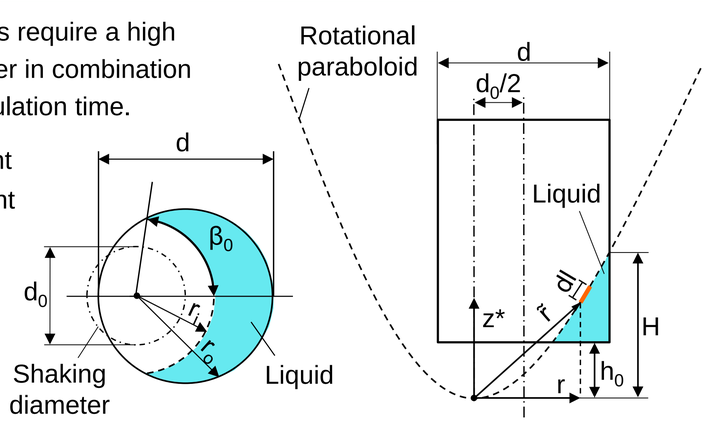
Results Hydrodynamics

Calculation of the liquid distribution

CFD simulation of a 20 L reactor V_L = 8 L; 180 rpm by Sören Werner

CFD simulations require a high computing power in combination with a long simulation time.

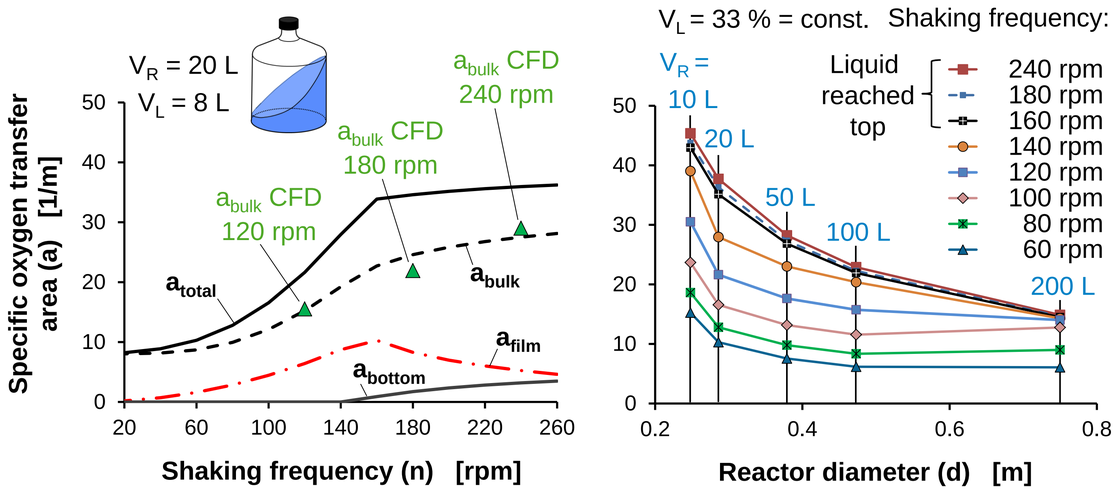
→ Development of a time efficient calculation method.



$$z^* = \frac{(2 \cdot \pi \cdot n)^2}{2 \cdot g} \cdot r^2$$

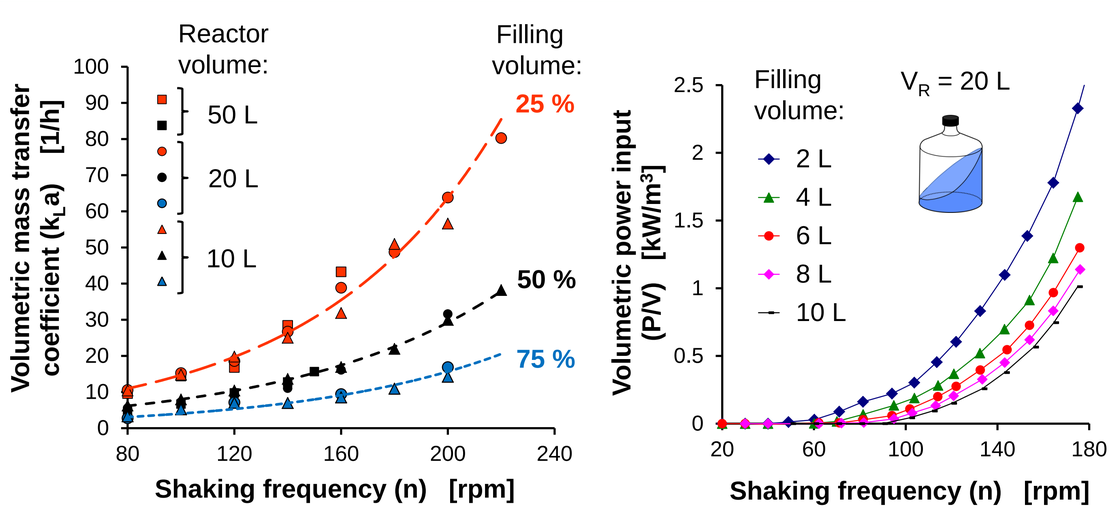
$$A_{bulk} = 2 \cdot \int_0^{\beta_0} \int_{r_i}^{r_o} 2 \cdot r \cdot \frac{(2 \cdot \pi \cdot n)^2}{2 \cdot g} \cdot \sqrt{\frac{g^2}{(2 \cdot \pi \cdot n)^4} + r^2} \cdot dr \cdot d\beta$$

Results of the liquid distribution model



Results for $k_L a$ and P/V

Influence of filling volume and shaking frequency



Increasing $k_L a$ with decreasing filling volume

Similar $k_L a$ values for the same relative filling volume at different scales!

Increasing P/V with decreasing filling volume

P/V values are in a similar range as values in stirred tank reactors.

Conclusion

- Successful integration of online monitoring systems for power input and oxygen transfer in orbitally shaken bioreactors.
- Volumetric oxygen transfer areas were calculated with the proposed mathematical model and validated with CFD data.
- ➢ Values for $k_L a$ and P/V were used to adjust optimized conditions for the cultivation of plant cell suspensions

See poster: **Scale-up production of pharmaceutical proteins in plant cell suspensions with orbitally shaken disposable bioreactors**

Literature

[1] Raven N, Klöckner W, Anderlei T, Rasche S, Kühn C, Büchs J, Schillberg S: **Scale-up production of pharmaceutical proteins in plant cell suspensions with orbitally shaken disposable bioreactors**, Poster presentation ESACT conference, 23-26 June 2013, Lille, France

[2] Klöckner W, Diederichs S, Büchs, J: **Orbitally shaken single-use bioreactors.** In: R. Eibl and T. Eibl (Eds.): Disposable Bioreactors II, Springer, 2013

[3] Klöckner W, Tissot S, Wurm F, Büchs J: **Power input correlation to characterize the hydrodynamics of cylindrical orbitally shaken bioreactors.** Biochemical Engineering Journal, 2012, 65, 63-69