MASS TRANSFER in the CELL-tainer® DISPOSABLE BIOREACTOR

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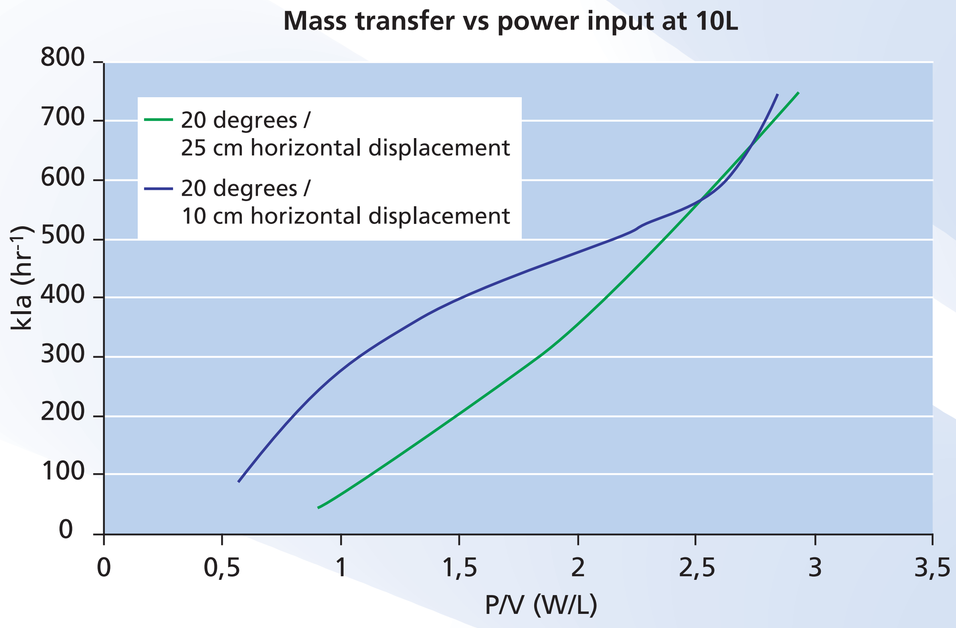
Summary
The CELL-tainer® disposable bioreactor ensures due to its movement in two directions a superior mass transfer in comparison to traditionally stirred cell-culture bioreactors or the wave type bioreactors. The CELL-tainer® is applicable in a wide range of cultivations ranging from sensitive mammalian cells to more robust bacterial cultures.

Introduction

In production of biopharmaceuticals the use of disposable type of bioreactors become more and more common. Advantages are for example large cost-saving in validation of equipment, reduction of contamination risk and easiness of operation. For this purpose wave-type bioreactors have been introduced. A clear disadvantage of these reactors is the restricted mass transfer capacity. By introducing another type of induction of a wave movement, the mass transfer capacity can be increased significantly and such a wider range of applications is possible.

Results

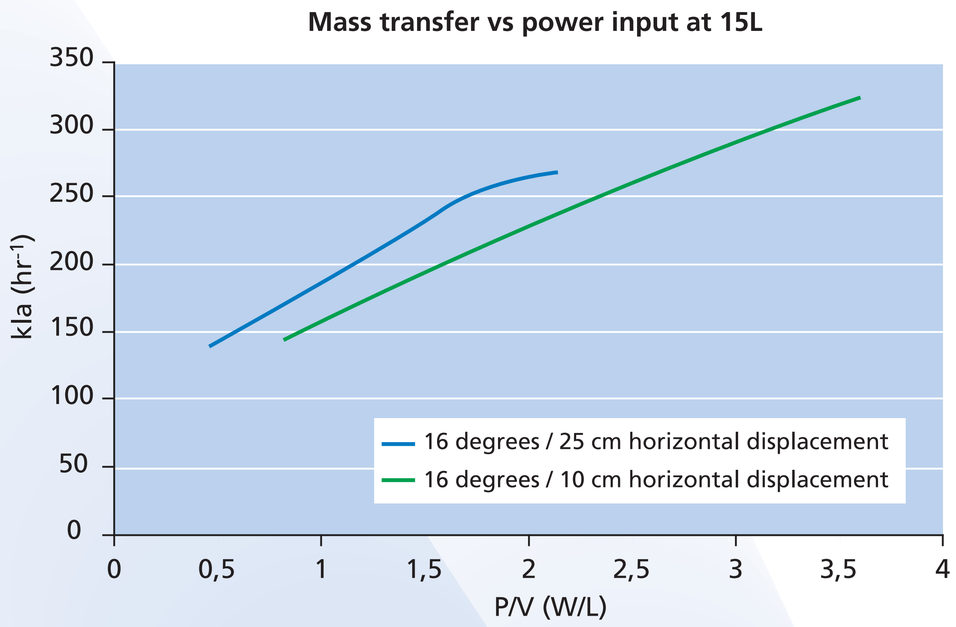
Mass transfer investigations using the dynamic method (in tapwater, 20˚C), show that the capacity for mass transfer (oxygen and CO_2) in the CELL-tainer® equipment is superior to that in a stirred bioreactor (kla = 10-20 hr^{-1}) and far above the mass transfer of a Wave bioreactor (kla = 4–8 hr^{-1}).
The mass transfer and mixing is induced by using a two-dimensional movement: a horizontal displacement as well as in combination herewith a rocking motion.

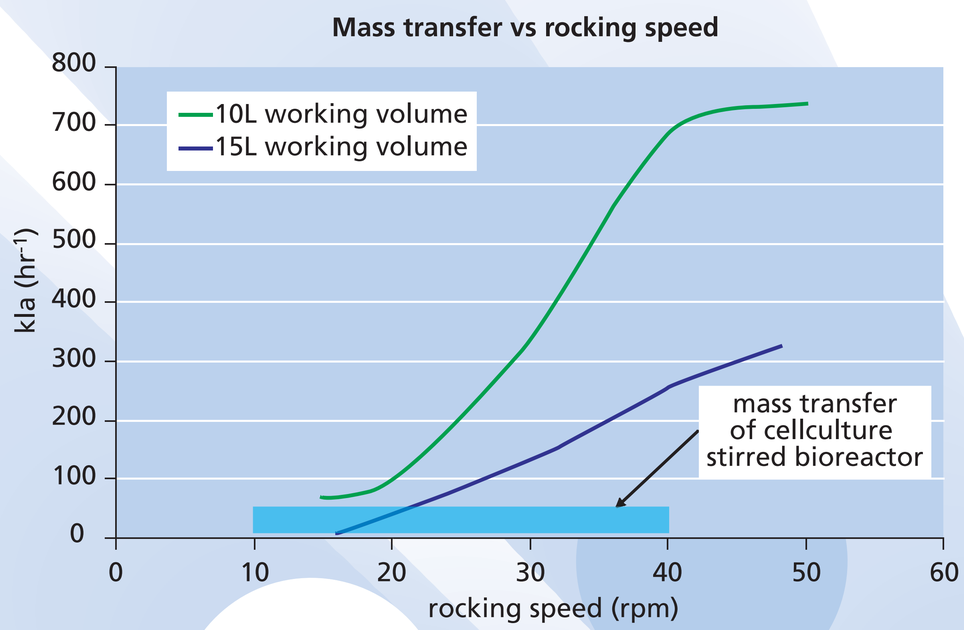


The mass transfer in the CELL-tainer® is influenced by wavelength, shaking speed and shaking angle. The horizontal displacement has a significant effect on the mass transfer capacity. These parameters are the basis for the design of larger scale bags and proper scale-up. By keeping the mass transfer characteristics as well as the fluid flow forces constant when scaling-up, the micro-environment of the cell will be kept uniform, thus making it easy to predict large scale behavior of the cells from small scale experiments.

The mass transfer in the CELL-tainer® disposable bioreactor ranges kla -values up to 700 hr^{-1} depending on liquid volume and rocking speed. The power-input to the liquid is comparable to standard stirred bioreactors as applied for microbial cultures (1 - 3 W/L).

In comparison with the traditional stirred bioreactor for mammalian cell-culture, the CELL-tainer® is superior in mass-transfer. The mass transfer is strongly effected by volume. However at a working volume of 15L the kla still can be up to 300 hr^{-1} which is sufficient to support oxygen consumption of most microbial applications and certainly for cell-culture.





Conclusion

Using a double movement, mass transfer in wave-type disposable bioreactors can be increased significantly in comparison to a movement in a single degree of freedom.
This means that the system overcomes the natural barrier of oxygen supply and CO^2 - removal of the standard equipment for cell-culture. Also microbial cultivation can be performed in the CELL-tainer® disposable bioreactor. Such way the bioreactor can support much higher cell-densities as usually applied.

Literature: WO2007/001173, Method and apparatus for cultivating cells using wave motion, Heiden, Pieter van der, at al., 2007.