

A SINGLE-USE BIOREACTOR FOR BOTH CELL AND MICROBIAL CULTURES: A DREAM BECOMES REALITY

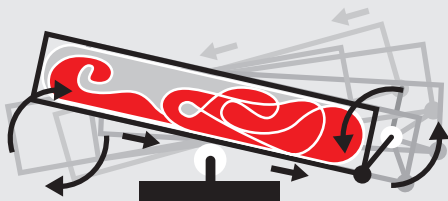
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Introduction

Application of single-use equipment is common practice in the biopharmaceutical industrial and academic field. Compared to the traditional glass or stainless steel bioreactors, single-use bioreactors offer clear advantages: a quicker turnaround time; minimal utilities required; greatly reduced risk of cross contamination; more operational flexibility; reduced validation requirements. However, until recently, single-use bioreactors could only be used for animal cell cultures, due to limitations in mixing and mass-transfer.

As single-use technology not only has significant benefits for cell culture processes, but clearly also for microbial fermentation processes and for seed-trains, process development and small scale production, there is a strong need for single-use bioreactors supporting more demanding bioprocesses.

Fig. 1



CELL-tainer® 2-D Movement for superior Mixing and Mass Transfer

Design Parameters

To meet this need, we decided to develop a single-use bioreactor with the following design parameters:

- Multi-purpose: supporting both cell and microbial cultures
- Gamma stable single-use pH and DO sensors
- In-line measurement for glucose & lactate
- Integrated process control, hook-up to scada-systems
- Easy to operate, scalable and robust

Mixing and Mass Transfer

The obtained $k_L a$ values make the CELL-tainer® suitable for both high density cell cultures and microbial fermentation. Figure 2 shows the measured $k_L a$ values as a function of movement

Fig. 2

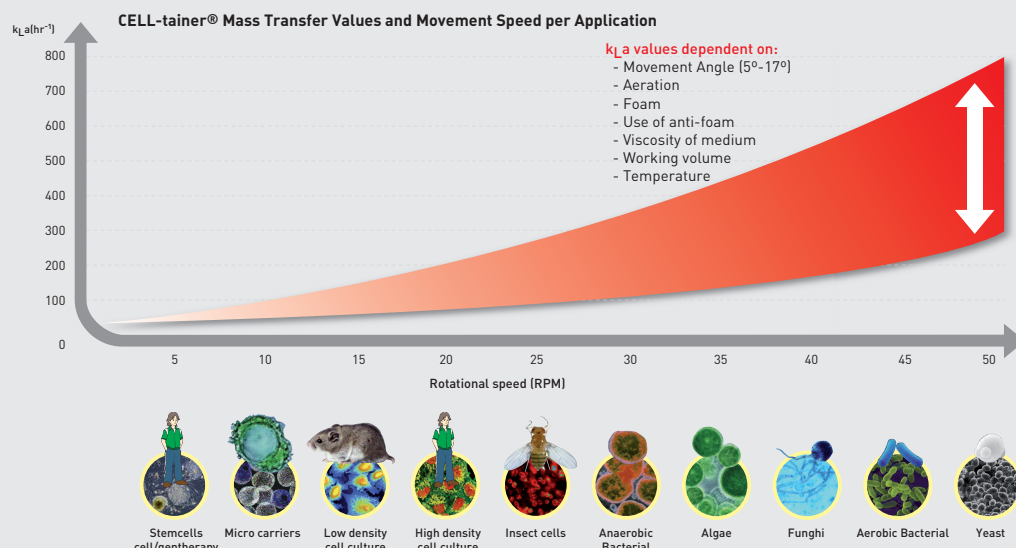
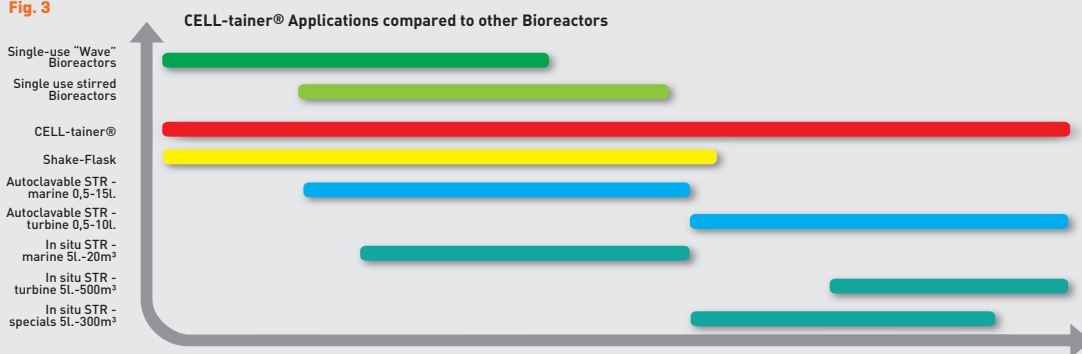


Fig. 3



CELL-tainer®: Multi-purpose Single-use Bioreactor for Full Spectrum of Culture Organisms

speed [rpm]. The range in $k_L a$ value per rpm value is caused by variations in movement angle, aeration, viscosity of medium, foam formation, working volume, use of anti-foam, and temperature.

Applications and Results

Figure 3 shows an overview of the applications of the CELL-tainer® compared to other single-use and conventional bioreactors. In terms of viable cell density and protein production of cell-lines, like CHO-cells, PER.C6®-cells, insect-cells, we measured superior results compared to first generation single-use bioreactors and comparable results as in conventional stirred bioreactors. Also microbial organisms like *E.coli* and *Corynebacterium* show comparable results as in conventional stirred bioreactors. This is shown in figure 4.

Working Volume

The cell-culture bioreactor bag has special segmentation strips, making it possible to expand

in one-and-the-same bag from 250mL up to 15L. The microbial bag has a working volume of 500ml up to 12L. Bags of 2L-30L working volume are also available.

Process Control

The CELL-tainer® is a complete bioreactor system, including:

- A closed cabinet ensuring precise temperature control without gradients
- Precision flow meters for Air, O₂, CO₂ and N₂
- Peristaltic pumps for pH and feed control
- Integrated process control and online measurement of pH, DO and glucose/lactate
- Full SCADA options
- Electrical glass door protecting light sensitive cultures

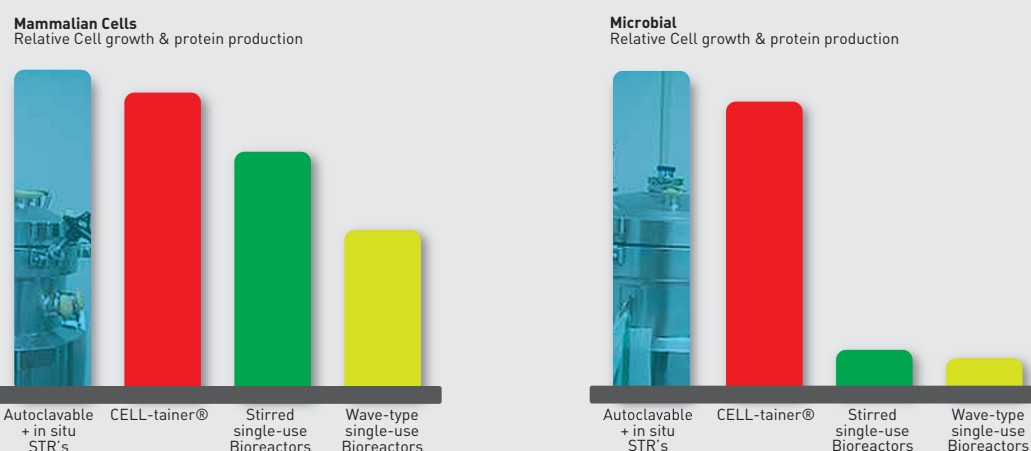
Conclusion

As $k_L a$ values and other vital process parameters can be controlled, the CELL-tainer® is the ideal multi-purpose equipment for:

- Process development
- Preculture
- Cell-banking and Starter cultures
- Small scale production

The CELL-tainer® bioreactor has opened a new era for bioprocesses optimization. A real multi-purpose single-use bioreactor is now available for a complete spectrum of culture organisms, offering you a wide range of process conditions and volumes and overall control in one single piece of equipment.

Fig. 4



Maximal Cell-Growth + Protein Production of Single-use Bioreactors compared to Conventional STR's