

Comparability between Mobius® CellReady 3L Bioreactor and 3L glass bioreactors



INTRODUCTION

Millipore's Mobius® CellReady 3L bioreactor is a single-use stirred tank bioreactor ideal for cell culture process development. Arriving pre-assembled and gamma irradiated, the CellReady 3L bioreactor significantly reduces the assembly time, down time and maintenance time associated with traditional glass bioreactors. To ensure maximum operational flexibility, the CellReady 3L bioreactor comes standard with pre-fitted weldable tubing lines, two available sparging options, a vent line, and integrated side sampling, addition, and drain ports. Designed to replace traditional bench-scale glass bioreactors, the CellReady 3L bioreactor is compatible with most standard controller configurations.

To demonstrate comparable functionality, the 3L CellReady single-use bioreactor was evaluated against the 3L Applikon® glass bioreactor in head to head cell culture performance and vessel characterization experiments. The criteria examined in these experiments were CHO cell growth, viability, productivity, and the volumetric mass transfer coefficient for oxygen (kLa). For each of these criteria, the experimental results reported in this paper verify that the CellReady 3L bioreactor performs comparably and is suited to replace traditional glass.

- Single-use 3L stirred tank bioreactor
- Pre-assembled and gamma irradiated
- Compatible with your existing controller

CELL CULTURE

Data Summary

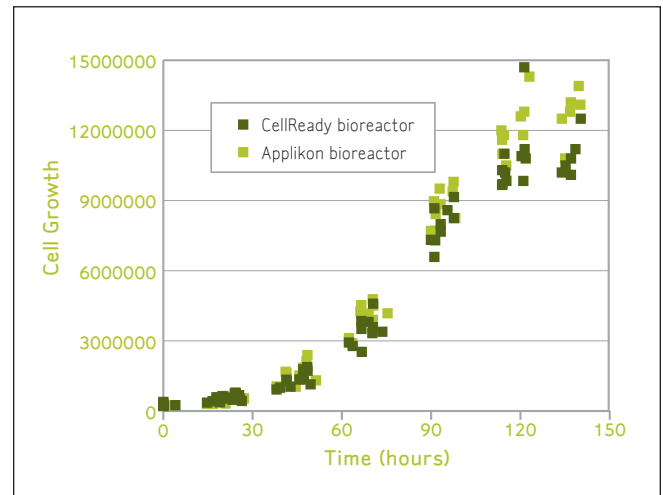
- A total of fourteen cell culture performance experiments indicated comparable cell growth, viability, and productivity for CHO cells in the CellReady 3L single-use and Applikon 3L glass bioreactors.
- The integrated side-sampling port on the CellReady 3L bioreactor made the sampling process easier and more efficient by eliminating the need to purge the sample line prior to drawing the sample.

Methods

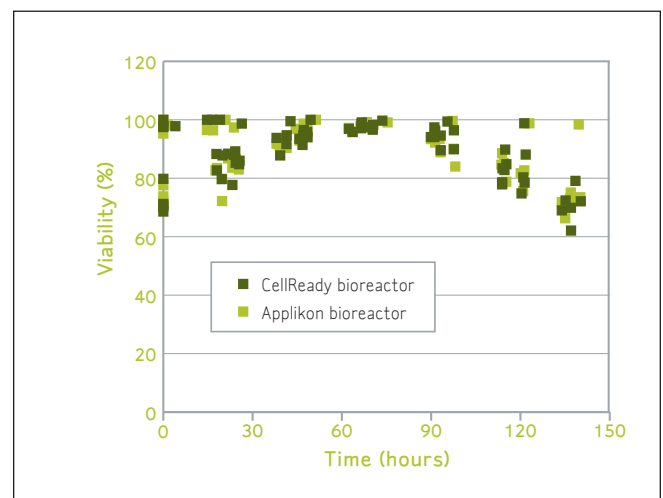
- Seven 3L Applikon glass bioreactors and seven 3L CellReady single-use bioreactors were inoculated and maintained under identical cell culture process conditions using Applikon ez-Controllers. Process conditions are outlined in the table below.
- Cell number and viability were determined by trypan blue exclusion using a Vi-Cell® counter, and IgG levels were determined using an ELISA specific for murine IgG. The bioreactors were sampled and assayed twice daily for cell number, viability, and protein titer until the viability dropped below 75% for 2 consecutive points.

Operating Parameter	Set point Values
Cell Type	CHO –S
Seeding Density	2×10^5 cells/mL
pH	6.95 + 0.05
Temperature	37.0° C + 0.5
Dissolved Oxygen	30%
Gas Flow Rate	0.1 vvm (air)
Agitation Rate	200 rpm
Culture Medium	GIBCO® Opti-CHO 8mM Glutamine 0.2% (v/v) Pluronic® F68 50 ppm anti-foam C

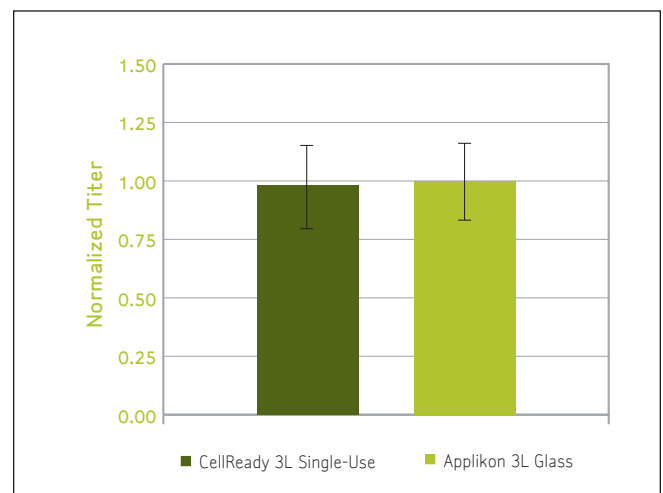
Comparability of CHO Cell Growth in Bioreactor Vessels



Comparability of CHO Cell Viability in Bioreactor Vessels



CHO Cell Productivity in CellReady Bioreactor vs. Glass Bioreactor



Volumetric Mass Transfer Coefficient for Oxygen (kLa)

Data Summary

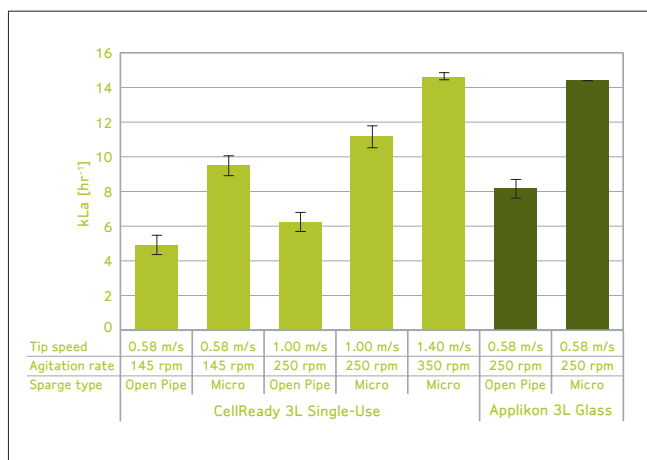
- Bubble size, sparge rate, impeller design and agitation rate are key operating variables that impact kLa.
- The CellReady bioreactor axial flow impeller has larger diameter curved blades compared to Applikon bioreactor's standard axial flow impeller.
- Accounting for these differences, kLa data for the CellReady 3L bioreactor was collected at several agitation rates and tip speeds while maintaining a constant sparge rate.
- By adjusting the agitation rate as appropriate for the impeller design, comparable kLa values were achieved in the CellReady 3L single-use bioreactor and the Applikon 3L glass vessel.

Methods

- kLa was determined via the static gassing out method for both the CellReady 3L single-use and the Applikon 3L glass bioreactors. Each experiment was performed at the same ez-Controller station using the same DO probe.
- The standard Applikon bioreactor configuration includes a 15 micron microsparger or a seven-hole open pipe sparger both made of stainless steel and placed centrally below the impeller. The CellReady bioreactor comes standard with a 15-30 micron polyethylene microsparger or a single-hole open pipe built into the bottom of the vessel.

- Aside from the thermowell and DO probe, each experiment was performed with a pH probe installed to simulate the baffling that occurs during a cell culture process.
- The DO probe was initially calibrated to 100% at air saturation, and was brought down to < 2% with N₂ before each experiment commenced.
- The sparge rate was set at 0.2 vvm with air and no overlay was applied.
- Each experiment was performed in 37°C water and repeated in triplicate.

kLa in CellReady Bioreactor vs. Glass Bioreactor



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