

Hollow Fiber Bioreactors

Proven Technology, Cost-Effective Production

Hollow Fiber Bioreactors are used globally for GMP- and ISO-regulated products
Cell Culture Company is a world leader in Hollow Fiber Bioreactors (since 1981)



Why Hollow Fiber Bioreactors?

Since 1981, Cell Culture Company (C3) has designed and distributed Hollow Fiber Bioreactors worldwide. C3 features these bioreactors in our GMP and GLP manufacturing suites. Our instruments improve the quality of mammalian and insect cell culture by creating in vivo-like conditions which lead to higher protein expression and greater yields. We use our Hollow Fiber Bioreactors at scales from 1g - 500g.

Benefits of Hollow Fiber Bioreactors



Perfusion

Maintain cell health and extend protein production with consistent fresh media delivery, removal of waste, and continuous harvesting.



Single-Use

Reduce labor and contamination with simple disposable cartridges.



Automated

Improve reproducibility with automated monitoring and control.



Linearly Scalable

Enable predictable scale-up and reduce validation time by adding cartridges in parallel.



Continuous Manufacturing

Harvest protein throughout the run and consolidate process steps.

Predictable Protein Manufacturing

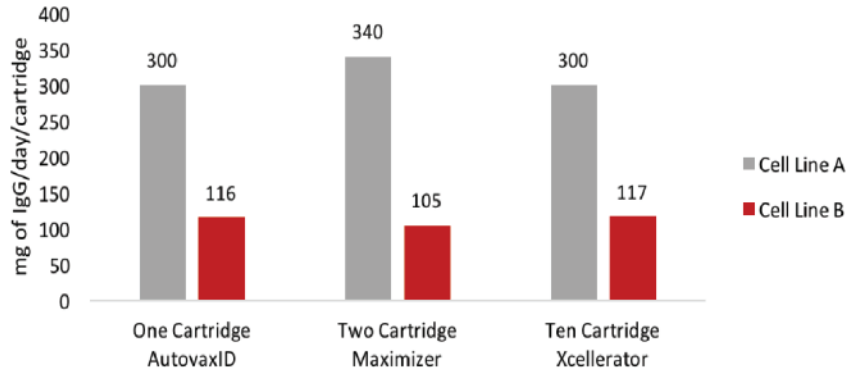


Figure 1: Cell lines A and B were each grown in three Hollow Fiber Bioreactors. Both cell lines had consistent production, even when cartridges were added in parallel for scale-up.

Figure 2: Two cell lines were grown in Hollow Fiber Bioreactors for >80 and 70 days (cell line 1 and 2, respectively), and maintained consistent metabolic parameters for the length of their runs.

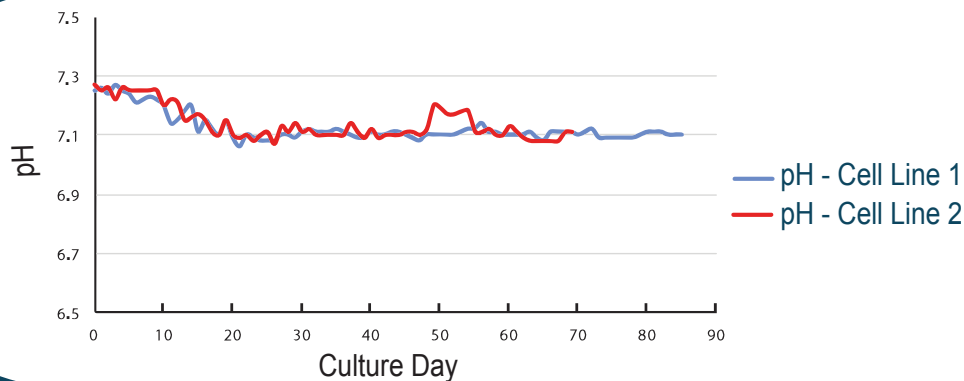
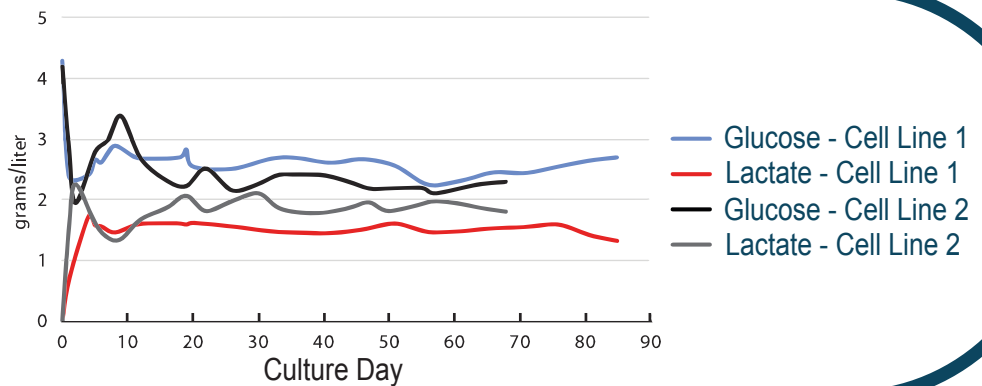
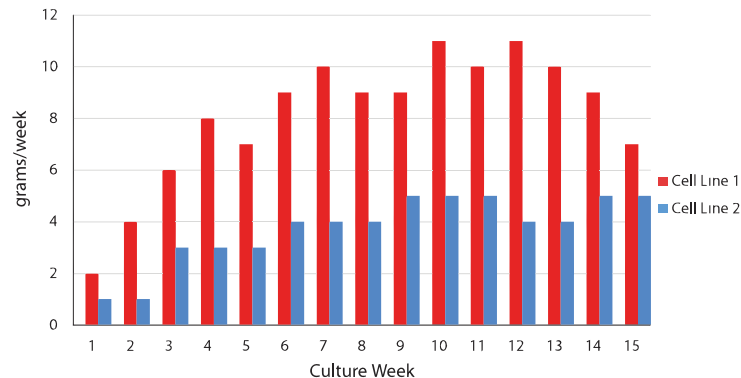
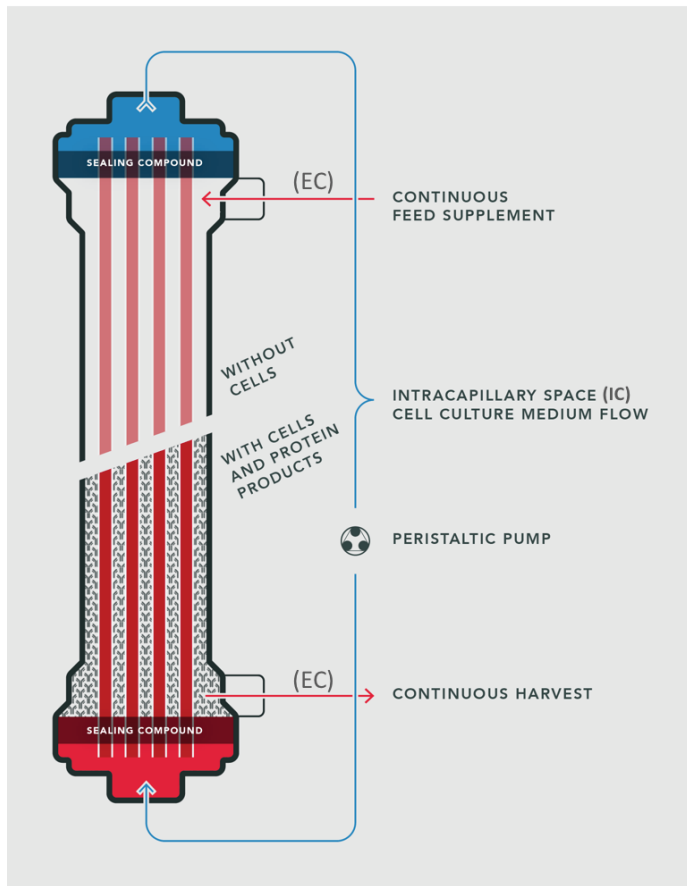


Figure 3: The same cell lines as in Figure 2 also maintained consistent pH for the duration of the run.

Figure 4: Two cell lines were grown for 15 weeks and IgG production was monitored throughout. Protein titers remained high and consistent through the duration of each run.



How Do They Work?



Circuit diagram of a hollow fiber cartridge showing two flowpaths: EC (cell side) and IC (media side).

- Hollow fibers are semi-permeable capillary tubes made of polymers about 200µm in diameter.
- The hollow fiber creates two spaces (see left):
 - The extracapillary (EC) "cell side" where cells are grown to high densities (2×10^{11} cells)
 - The intracapillary (IC) "media side" where media flows at a high rate.
- The semi-permeable walls of the hollow fibers allow essential nutrients to feed the growing cells from the IC to the EC (see below).
- Waste flows from the cell side to the media side to be washed away, but the hollow fiber pore size restrictions retain cells and cell products.
- Protein product can be continually harvested into a refrigerated harvest container as a concentrated, cell-free supernatant that is ready for downstream purification.
 - Decreases risk of protein degradation
 - Essentially eliminates downstream concentration steps

Features

Single-Use

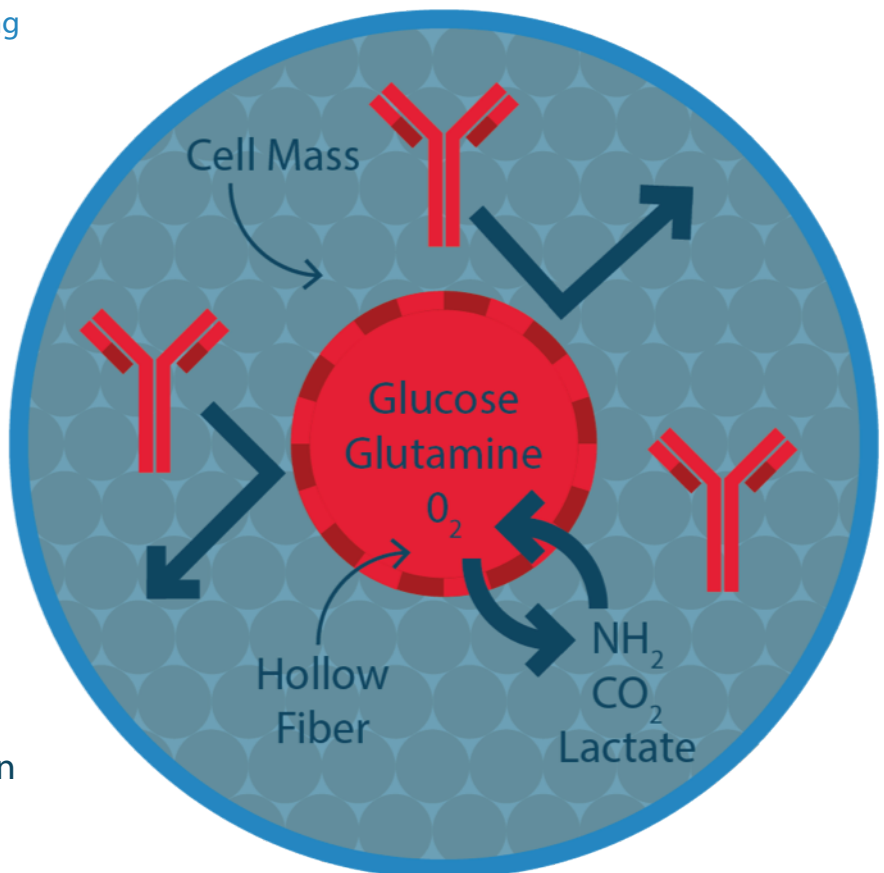
- Supplied sterile and ready to use
- No cleaning validation expense
 - Easy set-up and take-down

Closed System

- Ensures product segregation
- Minimizes contamination risk

Automated

- Decreases labor
- 30 minutes to start run
- 10 hours of labor per month to maintain



Bioreactor Line



HF Primer™

- Single-use, manual perfusion bioreactor for high density cell culture
- Uses high-efficiency oxygenator and faster circulation rates to provide better oxygenation than the competition
- Supports $\sim 5 \times 10^{10}$ cells
- Dimensions: 12cm x 20cm x 33cm
- Requires a peristaltic pump, 2 pump heads, and a CO₂ incubator

SCALE-OUT

AutovaxID®

- Benchtop production scale bioreactor
- Integrated refrigeration for continuous harvest
- Automated control and monitoring of pH, temperature, tissue perfusion rate (EC Cycling) and harvest rate
- Touch screen with remote monitoring
- Supports 1×10^{11} cells
- Benchtop: 51cm x 51cm x 48cm



SCALE-OUT



AcuSyst-Maximizer®

- Benchtop 80L-200L perfusion bioreactor
- Automated control of pH, temperature, tissue perfusion rate, and harvest rate
- Supports cell culture from weeks up to months
- 1 or 2 cultureware cartridges at a time
- Supports 2×10^{11} cells
- Benchtop: 70cm x 66cm x 52cm

SCALE-OUT

AcuSyst-Xcellerator™

- Fully automated pH, lactate, oxygen, temperature monitoring and control
- 21 CFR Part 11 Compliant
- Integrated refrigeration for continuous harvest
- Touch screen with remote monitoring
- 6x-20x cultureware cartridges at a time
- Size of a refrigerator: 134cm x 85cm x 203cm





Kyle Biesecker, PhD
Business Development Director
8500 Evergreen Blvd | Minneapolis, MN | 55433
kbiesecker@cellcultureco.com | www.cellculturecompany.com