



Custom CDMO Services

**Perfusion Hollow Fiber Bioreactors
and Instrumentation**

GMP-CNC & GLP production

ISO 9001:2015 certified



Contract Manufacturing Division

- Cell, protein, & antibody production
- GMP-CNC, and GLP/RUO manufacturing
- Custom cell culture and biomanufacturing
- Over 1,700 customers served globally
- Experience with 2,650+ cell lines



Instrument Division

- Perfusion hollow fiber bioreactors
- Automated, closed, single-use
- Manufacturing, distribution, service
- Diagnostic, pharma, food, vet health

Minneapolis-based since 1981

Custom CDMO Services

Contract manufacturer of
monoclonal antibodies,
recombinant proteins, & cells






Contracted Services Offered

Upstream Services	Downstream Services	
<ul style="list-style-type: none">• Cell bank (MCB/WCB) generation and characterization (5 – 300+ cryovials per batch)• Cell culture services- whole cell pellets, lysates, nuclear extraction preps, formalin fixation, formaldehyde cross-linking• Upstream process development• Cell line optimization• Traditional cell culture protein production (<200 L)• Bioreactor cell culture protein production (200 L -3,000 L)	Purification	Analytics
	<ul style="list-style-type: none">• Purification process development• Affinity chromatography (including IgG and IgM)• Cation/anion polishing• TFF/diafiltration• Custom services	<ul style="list-style-type: none">• Qualification and validation• SDS-PAGE• HPLC/UPLC - size exclusion and affinity chromatography• A280• ELISA• Custom Services

- Traditional Cell Culture Methods
 - Batch sizes up to 200 L in spinner flasks
 - Batch sizes up to 200 roller bottles
 - Multi-layered cell culture flasks (e.g. CellStacks)
- Bioreactors
 - Hollow fiber perfusion bioreactors
 - Batch sizes ranging from 200-3,000 L
 - Automated, single-use, closed system
- Why Hollow Fiber?
 - Decreased labor and material costs
 - Improved scalability of upstream processes
 - High batch-to-batch consistency
 - Improved yields for low-expressing cell lines



Process Development	Research Use Only	GMP Controlled Not Classified
<ul style="list-style-type: none">- Tech transfer to C3- Scale up or down- Process optimization- Process development for upstream, downstream, and analytical testing	<ul style="list-style-type: none">- GLP documentation- Low price point- Fast turnaround- Custom production methods and labeling	<ul style="list-style-type: none">- GMP documentation under C3's QMS- Controlled production space- Commonly used for <i>in-vitro</i> diagnostics and analyte specific reagents
		

Cell Types

- Hybridoma
- Mammalian
- Insect
- Cancer
- iPSC
- Custom engineered cell lines

Common Cell Lines:

- HEK293
- HeLa
- NSO
- Vero
- Sf9, Sf21, High Five

Expression Systems

- Stable cell lines
- Hybridoma
- Transient Transfection (protocol required)

Common Proteins:

- IgG and IgM
- Recombinant Proteins

Difficult to Express

- Suppressed protein expression due to protein or metabolomics interference/inhibition
- Unnatural proteins (i.e., Bi- or Tri-specifics, fusion proteins, etc.)
- Low titer expression
- Shear sensitive protein or cell line

Reduce Working Capital & Turnaround Time

- Locked-in Price
 - Guaranteed price per mg
 - Cost savings over time
- Safety Stock
 - Just-in-Time Shipments
 - Safety Stock
- Protect Quality
 - ISO/GMP Capabilities
 - Custom documentation
- Vault of Value
 - Defer manufacturing costs
 - Eliminate inventory expense
 - Pay upon consumption



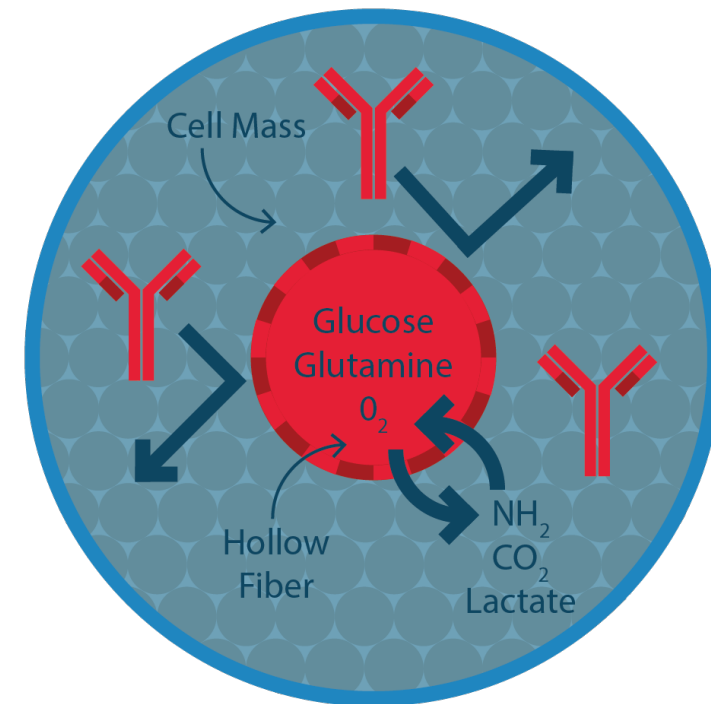
mAbVault
Lock-in Price. Secure Supply. Protect Quality.

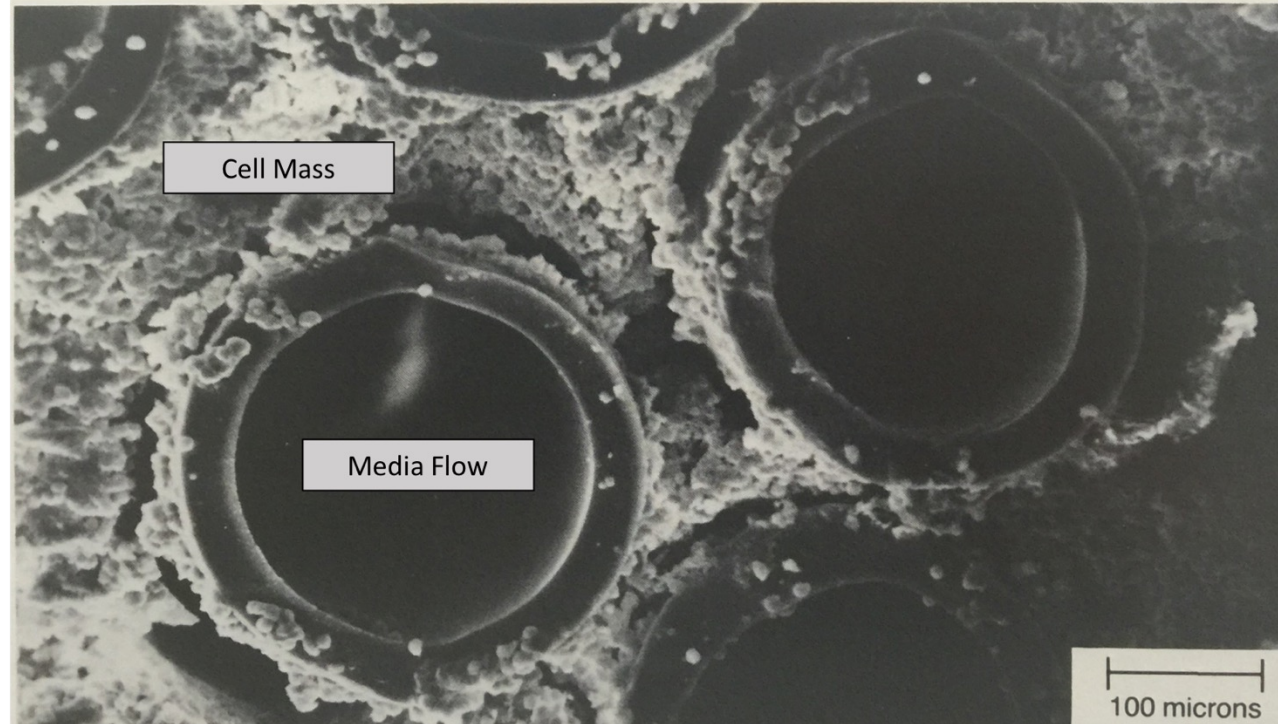
Perfusion Hollow Fiber Bioreactors and Instrumentation

Continuously fed, single-use
bioreactors scaled to meet and
grow with your needs



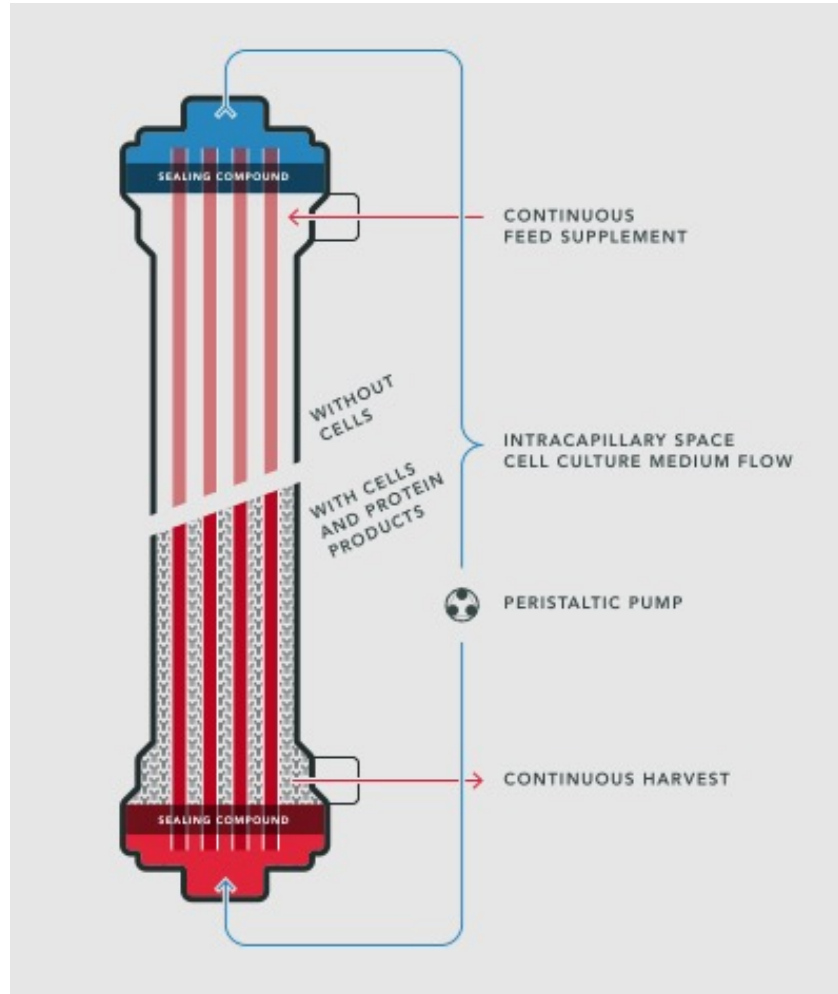
- Hollow fibers are semi-permeable with a MWCO of ~55kDa
- Media flows through the IC space
- Cell grow to high density (~ 10^9 cells) outside the hollow fibers
 - Protected from shear stress
 - Product is retained in EC space
- Tiny pores in the hollow fibers allow limited diffusion across the membrane





Thousands of tiny, semi-permeable hollow fibers create separate chambers. Above is an Electron Micrograph image of a transected hollow fiber cartridge. Media flows through the interior of the hollow fibers and the cells grow to a high density outside the hollow fibers.

Hollow Fiber Bioreactors



Perfusion

Maintain cell health and protein production for longer with constant fresh media delivery.



Single-Use

Reduce labor by decreasing cleaning time and contamination risks with easy-to-use disposable cartridges.



Automated

Ensure reproducibility, reduce labor, and decrease contamination risk with automated monitoring and control.



Linearly Scalable

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



Continuous Manufacturing

Achieve high-quality protein production by continuously harvesting product throughout the run and consolidating upstream process steps.

Scalability

AcuSyst hollow fiber bioreactors can be linearly scaled by adding cell culture cartridges in parallel

AutovaxID®
Benchtop



AutovaxID



Maximizer



Xcellerator (6-20)

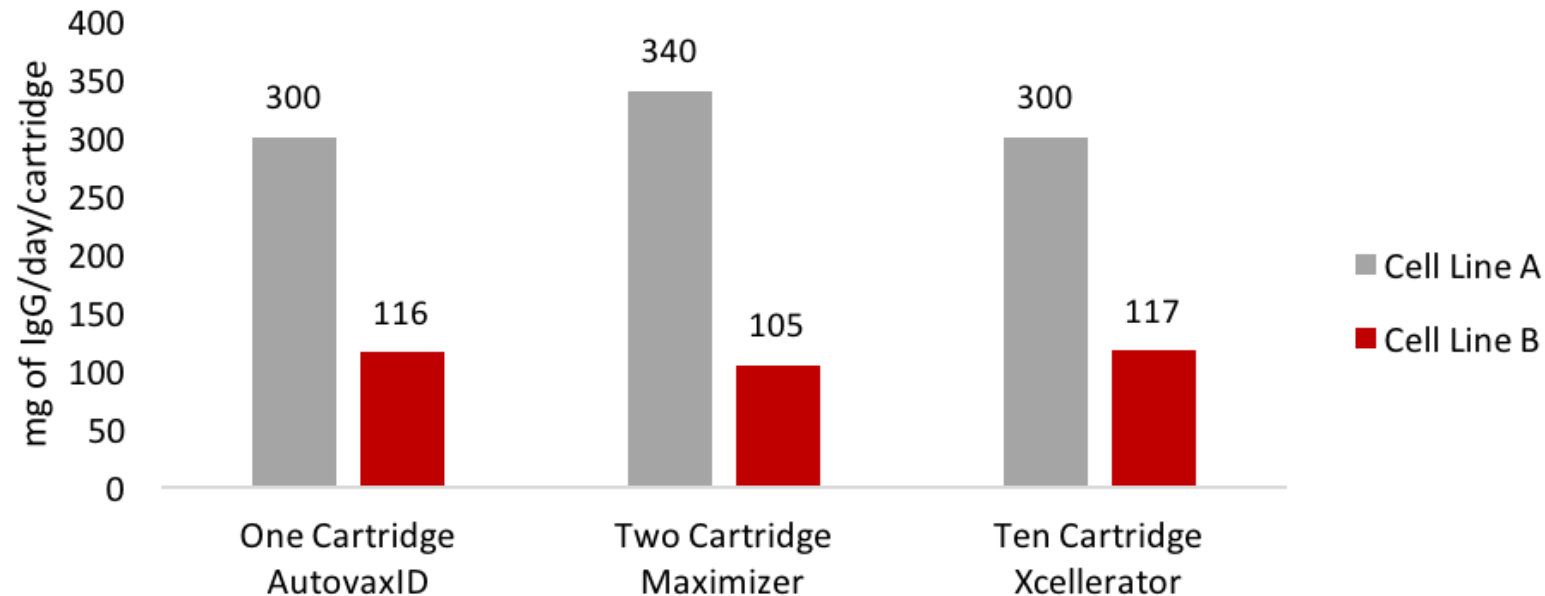


AcuSyst XCELLERATOR™
On casters, about the size of a refrigerator

AcuSyst-MAXIMIZER®
Benchtop

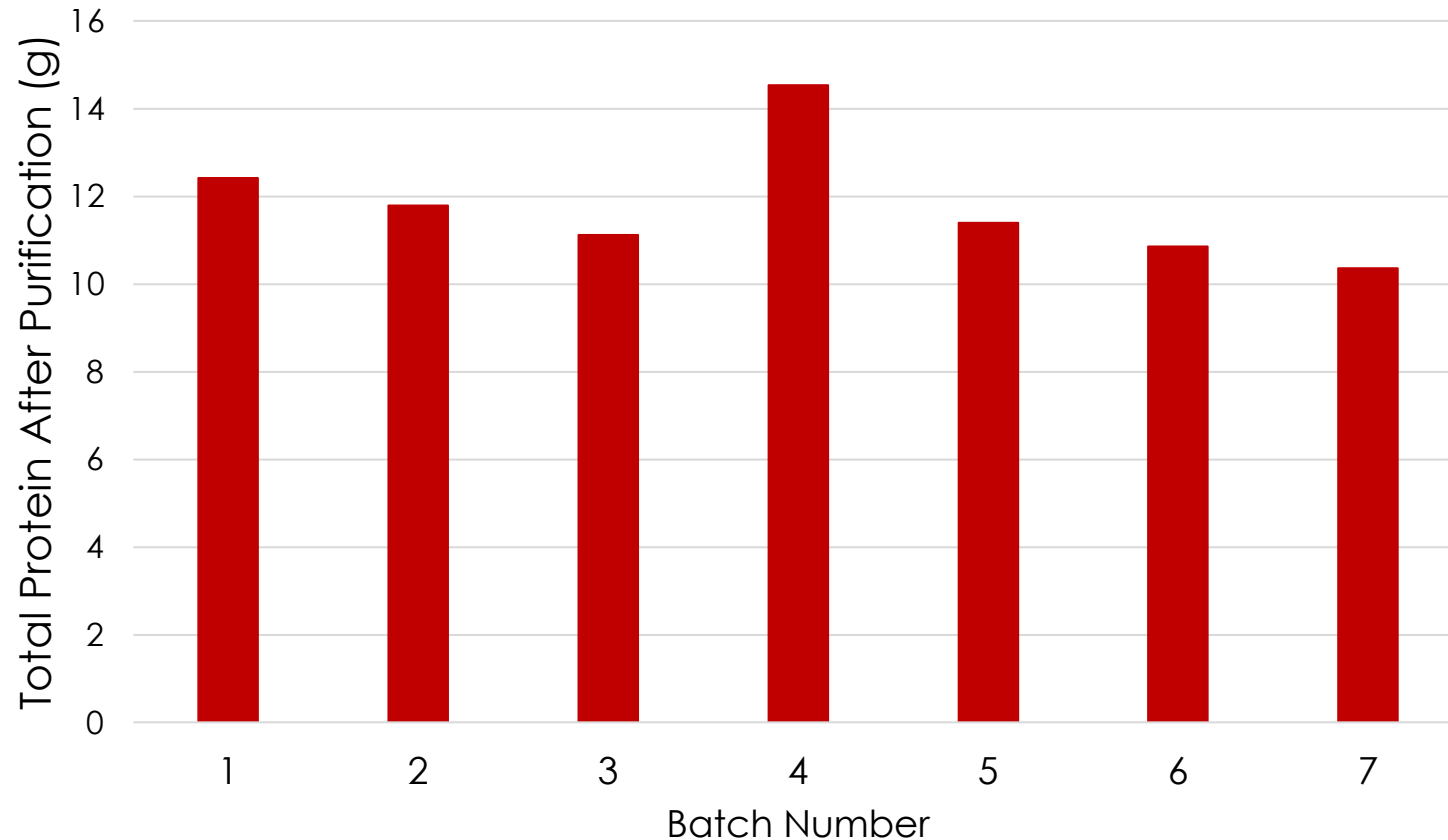


Normalized Production Rate



The graph above shows data from two low-expressing mammalian cell lines (A and B) that were each run in three bioreactors with progressively more culture cartridges. Data is normalized to total mgs of IgG/day/cartridge to show consistency, even as cartridges are added. Productivity per cartridge remains within +/- 12%.

Batch-to-Batch Consistency

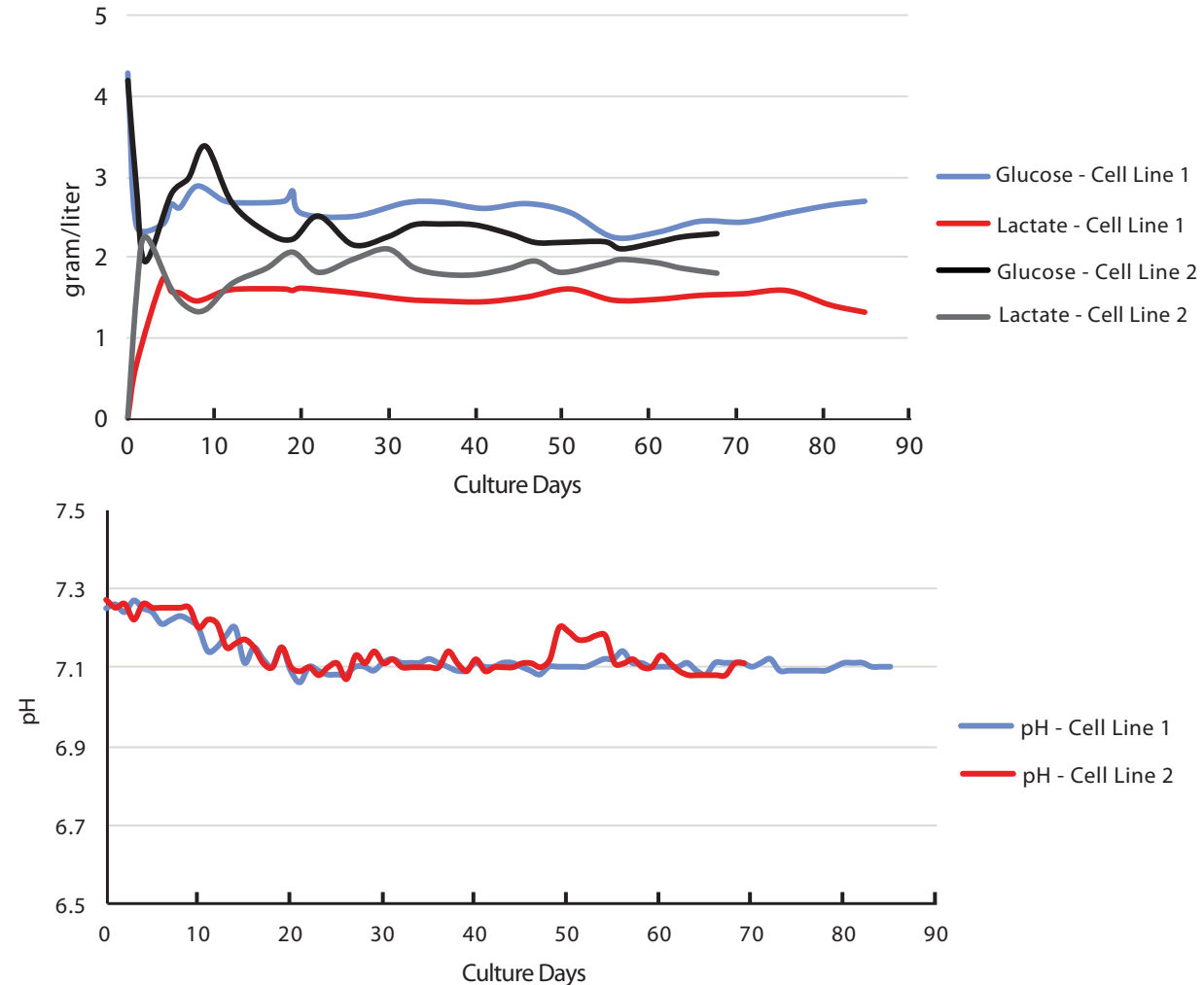


Total protein yield after purification for 7 repeat batches performed over 10 years. Each culture was performed in an AcuSyst Xcellerator.

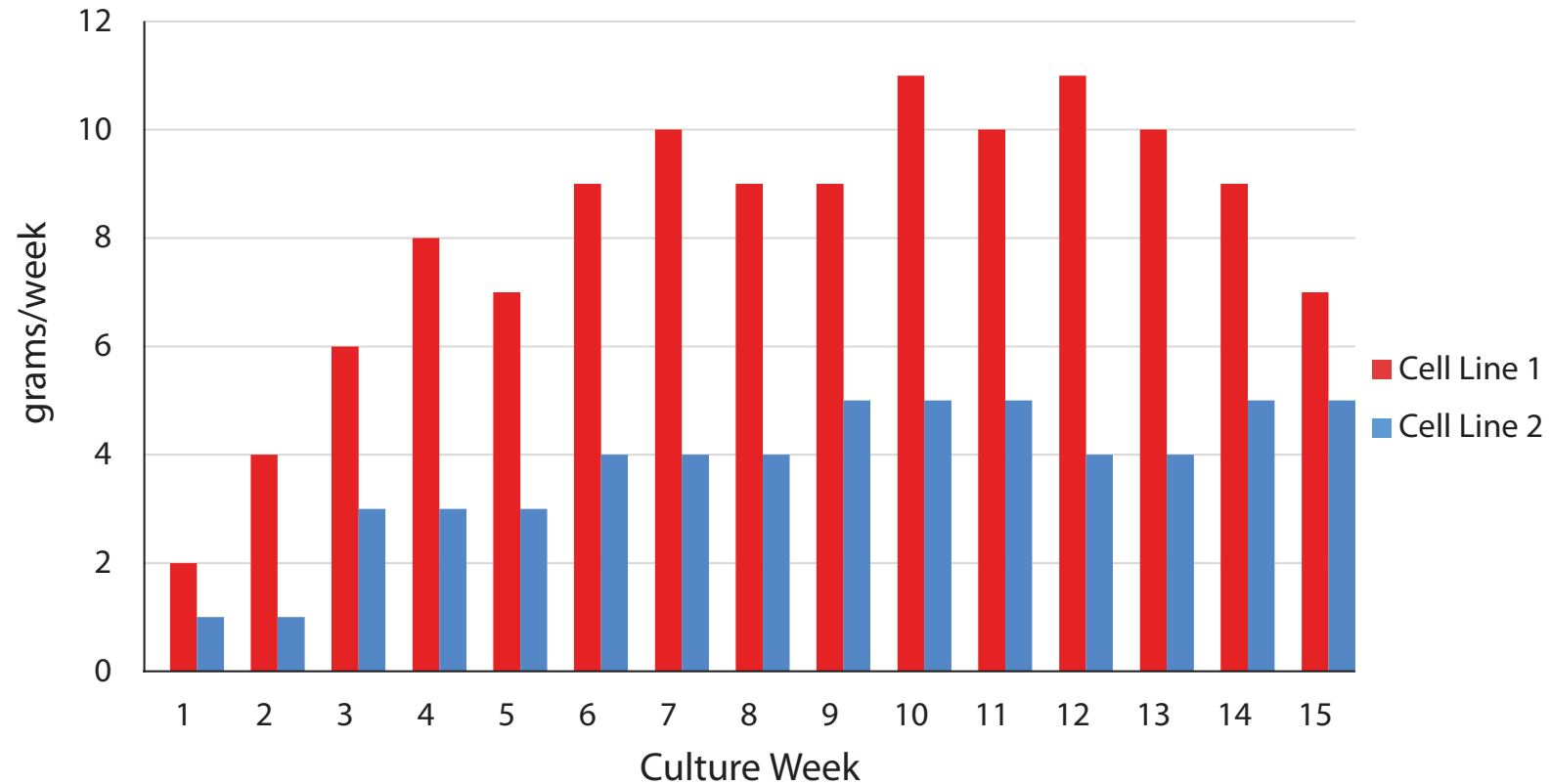
Steady-State Protein Production

AcuSyst bioreactors maintain cell health for long run durations.

Two mammalian cell lines were run for >60 days. After the initial growth phase, glucose, lactate, and pH remained stable for both cell lines for the run duration.

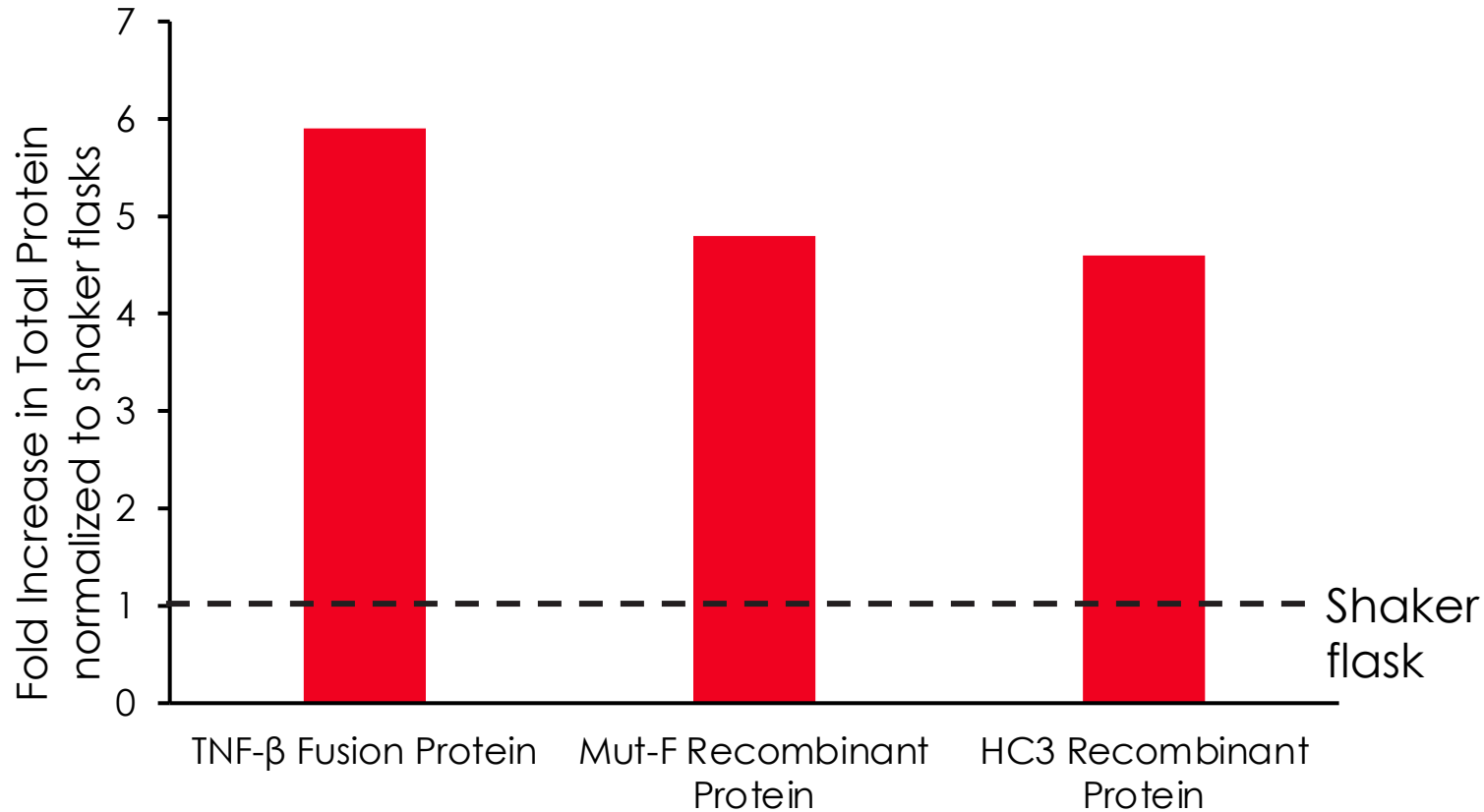


Steady-State Protein Production



Two low-expressing hybridoma cell lines were cultured in an Xcellerator for 15 weeks. Both runs had consistent protein yields for the run duration.

Improve Hybridoma Cell Line Titer



Proteins with low titers are efficiently produced in AcuSyst bioreactors. Data are presented as fold change in yield for actual AcuSyst culture runs over calculated stirred tank runs. Relative stirred tank yields are represented by the dotted line. Stirred tank yield was calculated using known titer values in spinner flasks and extrapolating up to equivalent media usage to the AcuSyst bioreactor runs.

Why Use Perfusion Bioreactors

- Reduced supplementation, automation, and ease of scale-up reduces costs
- Fewer downstream process steps needed
- Enhanced production with low-expressing cell lines
 - Increase in titer with optimization
 - More protein due to continuous manufacturing
- Linear scalability
 - Lower validation requirements
 - Predictable yields across milestones
 - Flexibility
- Reduced seed-train requirements
 - Lower operations costs

