The Next Generation of XCell® ATF Controllers for High Cell Density Perfusion Cell Culture

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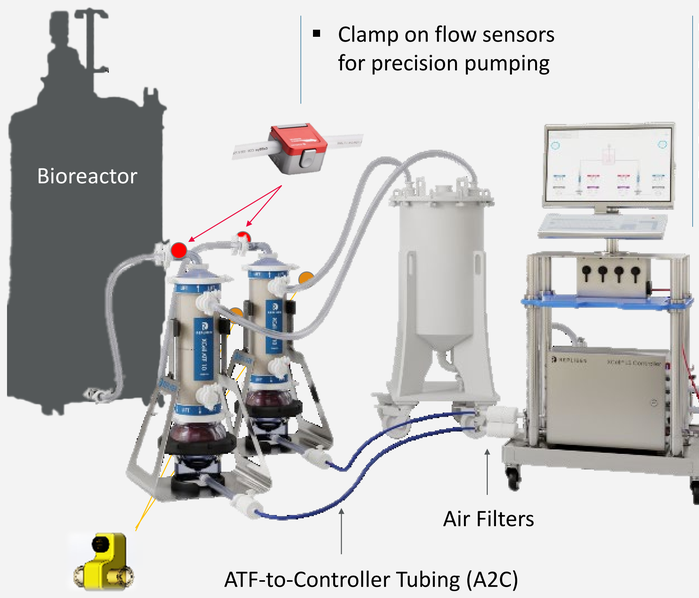
Introduction

Scalability is one of the most important factors to commercial viability in the biotech industry; scaling up bioprocesses from bench scale to manufacturing scale could be challenging without the right technology or information. With close to two decades of process intensification experience, Repligen's XCell® ATF has been successfully implemented in various upstream bioprocess applications including recombinant proteins, mAbs, cell therapies, plasmid DNA, vaccines, and cultured meat. Benefits of intensification include significant improvements in volumetric productivity, flexible manufacturing with single use technologies, reduced cost of goods, and smaller facility footprint while increasing throughput. With a focus on scalable and innovative improvements to optimize and intensify bioprocesses, Repligen recently launched the next generation large-scale (LS) controller.

XCell® LS Controller added new features to the well adopted ATF technology in the bioprocessing industry. One controller unit has the capability of controlling up to two ATF devices (ATF 4, 6, and 10) using a single controller unit, allowing for a reduction in overall facility footprint. These new systems incorporate flow sensors for accurate diaphragm pumping and permeate pressure sensors to monitor filter fouling. In this poster, we will highlight setup examples of the new controller and connections to the upstream bioprocess workflow. Also, we will present data showing the use of the new large-scale controller in high performance cultures – up to 4.5 cP viscosity and 8 psi of bioreactor head pressure.

Enhanced User Experience



- Clamp on flow sensors for precision pumping
- Control two ATF devices using one controller
- In line permeate sensor to monitor filter health

- Industrial touchscreen HMI
- Headless "No HMI" option available
- Remote control via DeltaV/DCS
- Data acquisition/recording
- 21 CFR compliant with audit trail
- Windows 10 Domain Security

Designed for Scalability

Bench Scale Development → Pilot Scale Development → Clinical Production → Commercial Production

XCell® Lab Controller

XCell® LS/Plus Controller

2 Device Formats

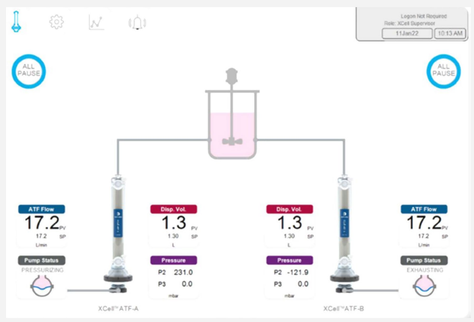
XCell® Lab Controller
ATF 1, ATF 2, ATF 4

XCell® LS/Plus Controller
LS: ATF 4, ATF 6
LS Plus: ATF 6, ATF 10

Single-use **Stainless Steel**

- XCell® ATF is actively used at >500 sites globally for a variety of molecule types
- Over 40 commercial processes in nine countries use ATF as part of the upstream process
- Intensification proven on >25 cell types including CHO, HEK-293, SF9, Per.C6, iPSC, hPSC, and cultivated food
- 6+ XCell® LS Controller installations in late-stage clinical/commercial settings

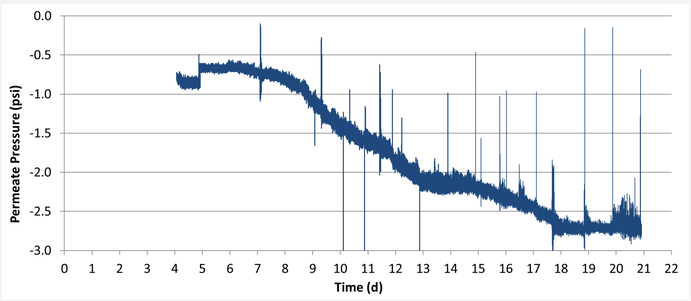
New Feature – Dual Channel and Flexible Device Operation



- Each XCell® LS/Plus Controller can be used for two ATF devices
- Both ATFs connected to one bioreactor or one ATF each connected to its own bioreactor
- XCell® LS Controller for ATF 4 and/or ATF 6
- XCell® LS Controller Plus for ATF 6 and/or ATF 10
- Reduces equipment footprint

New Feature - Permeate Pressure Monitoring

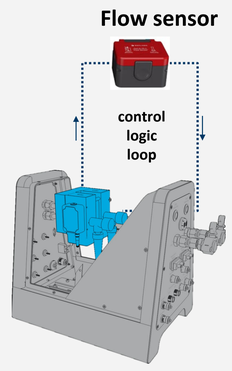
- In-line permeate pressure sensor monitors filter health throughout the process, giving operators valuable information to change filter when it is needed



- Permeate pressure plot for a 21-day CHO perfusion culture
- No alarms triggered and no filter swap needed for this run

- Two alarm levels can be customized based on process knowledge gained during development runs

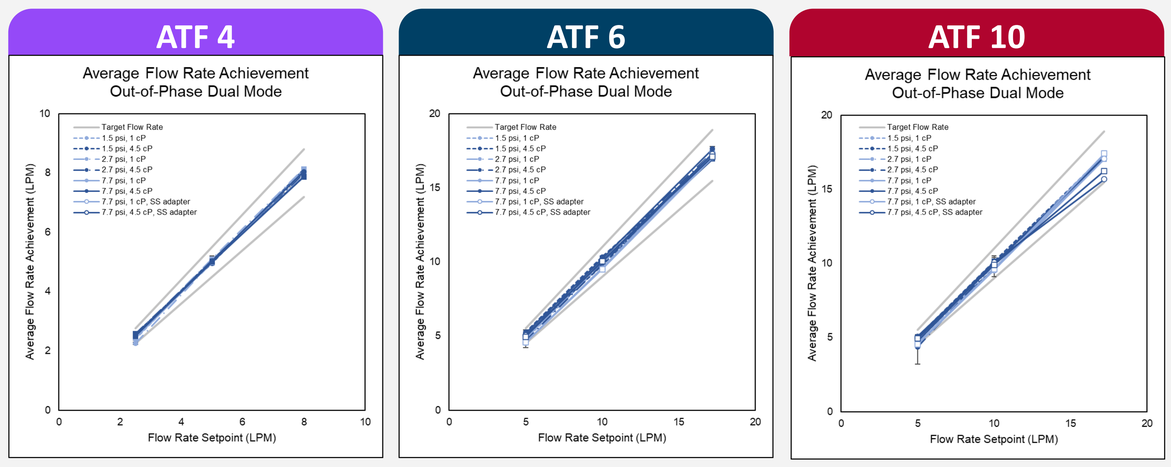
New Feature – Flow-based Feedback Control of ATF Rate



- Non-product contact, clamp on flow sensor provides feedback to enable precision pumping, ensuring stable ATF rate through processes
- Proprietary technology to read bi-directional flow and compensate for higher gassing rates in intensified cultures

Consistent Performance in Challenging Culture Conditions

- XCell® LS Controller enables consistent ATF operation even with high culture viscosities (up to 4.5 cP; seen in high density perfusion cultures) and high head pressures (up to 8 psig; seen in taller bioreactors)



Conclusion

Repligen continues to improve upon the XCell® ATF technology to meet challenges of next generation processes, including higher densities and larger single-use bioreactors. The XCell® LS Controller incorporates:

- Dual channel to reduce equipment footprint
- Flexible device operation for modular facilities
- Permeate pressure sensors for monitoring filter health
- Flow sensors for precision pumping

With scalability in mind, processes can be developed with the XCell® Lab and then scaled up for pilot and commercial manufacturing with the XCell® LS Controller, using a range of filter devices that accommodates cultures ranging from 0.5L to 5000L.

Learn more at **repligen.com**