Disruptive Technologies Transforming Upstream Process Intensification for All Modalities

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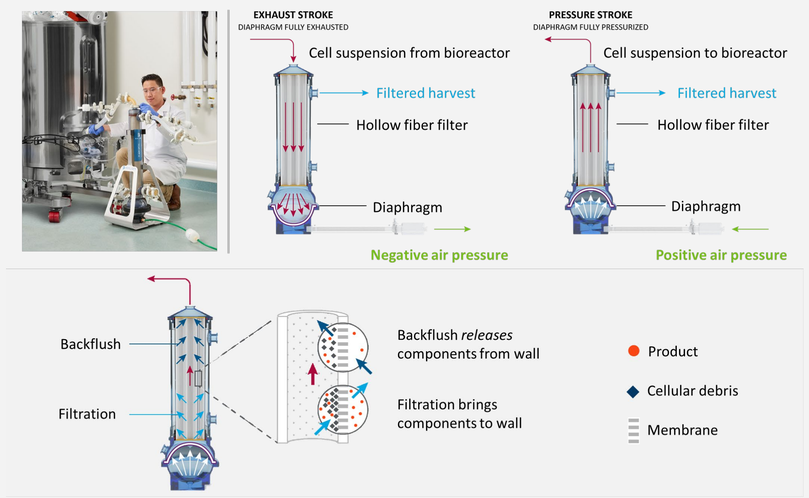
Abstract

The global pipeline of biologics continues to grow and diversify. The emergence of more complex modalities such as multi-specific antibodies, antibody drug conjugates (ADCs), fusion proteins, cell and gene therapies are presenting unique challenges in the development and manufacturing of these biologics. Additionally, the growing biologics pipeline is resulting in increased demand of global manufacturing capacity. The bioprocessing industry continues to invest in new manufacturing technologies that will enable efficiency and productivity for their existing facilities. Because of these drivers, there has been increased adoption of process intensification strategies such as intensified cell culture enabled by perfusion. Benefits of this approach include increased cell density and volumetric productivity, flexible manufacturing with single use technologies, reduced cost of goods, and smaller facility footprint while increasing throughput. Perfusion using alternating tangential flow (ATF) has been implemented for upstream process intensification for the bioprocessing of biologics in the last decade to achieve and maintain viable cell densities in excess of 100 million cells/mL over extended periods of time. This poster will highlight the use of XCell® ATF perfusion-based technology over a range of process steps (N-1, N, and harvest) and modalities (monoclonal antibodies, vaccines, plasmid DNA, and cultivated food). Case studies will include intensification of CHO and SF9 cell growth and vaccine manufacturing.

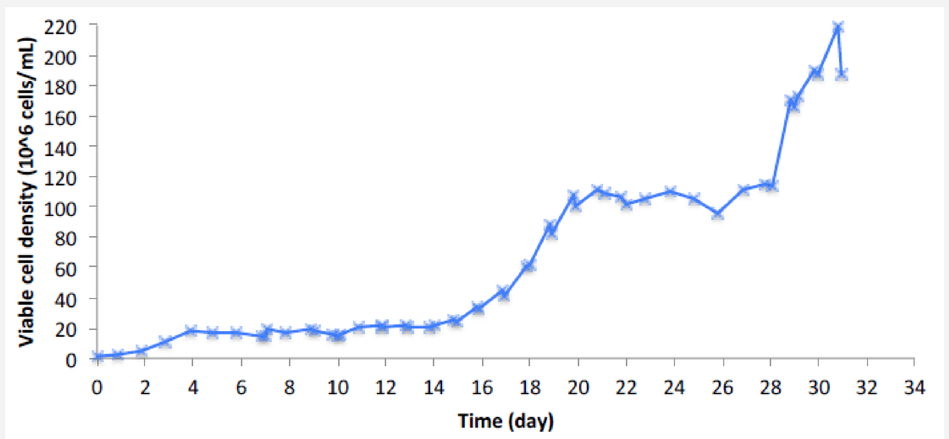
How It Works

Alternating tangential flow (ATF) is attained by the action of a diaphragm pump moving upward (pressure stroke) and downward (exhaust stroke). The backflush as a result of ATF cleans the filter, which allows for higher viable cell density and longer filter life.

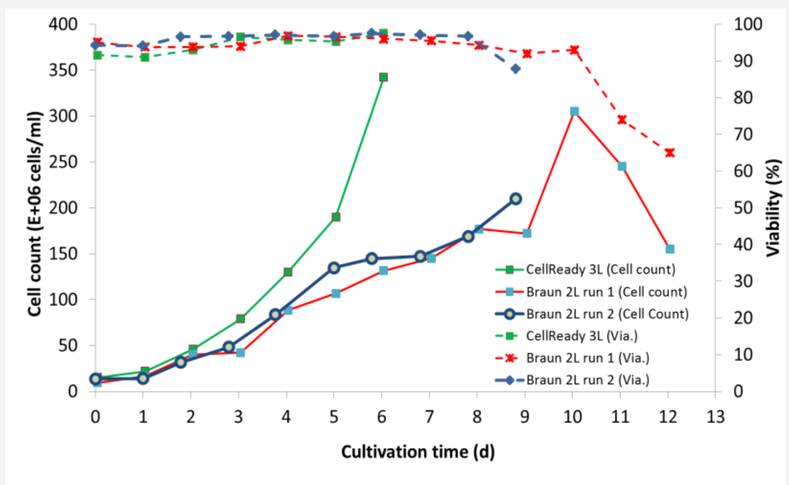


CHO Cell Growth

In this CHO perfusion experiment, VCD was maintained at ~20 million cells/mL for 10 days and then increased to ~100 million cells/mL for days. A maximum VCD of >200 million cells/mL was able of be achieved.

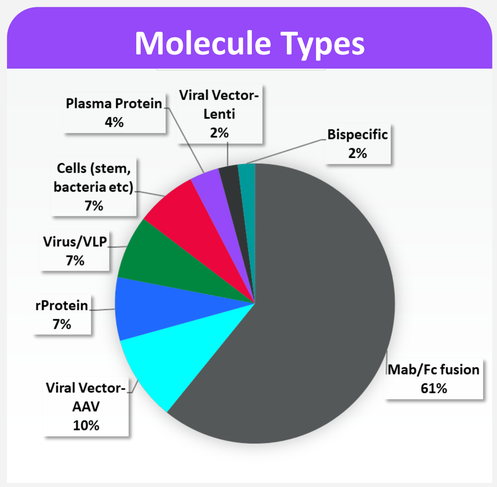


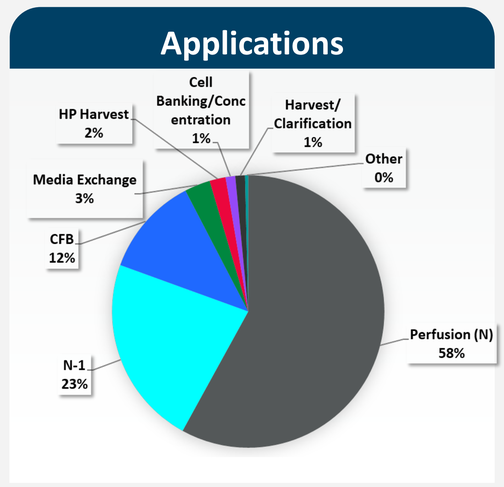
SF9 Cell Growth



The XCell® ATF System was used with two different bioreactors growing SF9 cells. In the CellReady reactor, a maximum VCD of ~350 million cells/mL was reached while maintaining >90% viability.

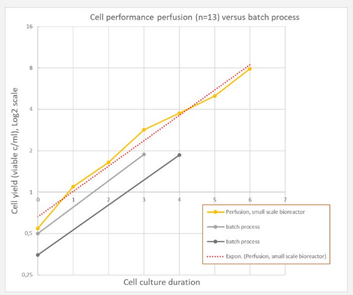
XCell® ATF System Adoption Across Multiple Platforms

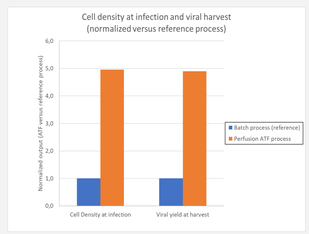




- The XCell® ATF System is actively used at >500 sites globally for a variety of molecule types
- Over 40 commercial processes in nine countries use the XCell® ATF System as part of the upstream process
- Intensification has been proven on >2 5 different cell types including CHO, HEK-293, SF9, Per.C6, iPSC, hPSC, and cultivated food

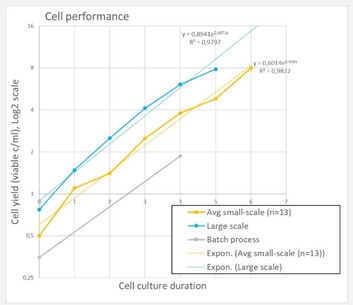
N-1 & N for Vaccine Manufacturing[1]

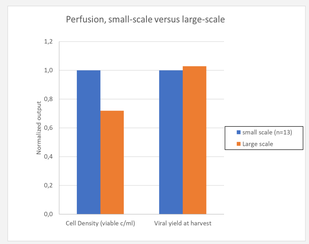




N-Stage Intensification

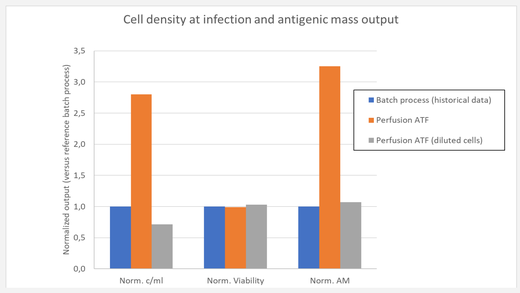
Perfusion with the XCell® ATF System was compared to the batch process. 5-fold higher cell density and 5-fold higher viral yield was observed.





Scale-Up: ATF 2 to ATF 10

Cell density and viral yield were comparable between the two scales. Higher volumetric output per batch translates to more efficient plant utilization.



N-1 Intensification

- High density seeding of the production reactor (N) with N-1 intensified cells resulted in a 3-fold increase in both cell density and viral output
- Intensified N-1 cells performed comparably to historical batch data when using the reference seeding density

Conclusion

The growing global biologics pipeline is driving the need for increased manufacturing capacity across a diverse group of complex modalities. XCell® ATF has enabled robust perfusion operation for cell culture intensification to meet these demands through increased cell densities and volumetric productivities across 25 cell types. This published work highlights the capability of ATF technology to increase viable cells densities above 200 million cells/mL with CHO cells and 350 million cells/mL with SF9 cells as well as improve viral yield in vaccine manufacturing by 3-5x with N and N-1 perfusion applications. These intensification strategies implemented result in flexible manufacturing, reduced cost of goods, and smaller facility footprints while increasing throughput to meet the global biologics pipeline demands.

References

[1]Hans de Hoog et al., Investigation of XCell® ATF Perfusion Technology for virus manufacturing process intensification at MSD Animal Health, Repligen Whitepaper, 2022 (https://www.repligen.com/Products/xcell-atf/technology/resources/white_paper/Animal_Vaccine_Mnfg_Whitepaper_20JUL2022.pdf)

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