

Corning® Ascent® Fixed Bed Reactor System

Scaling from Process Development to Production
with a High Density Adherent Cell Growth Platform

CORNING

A major challenge in manufacturing adherent cells for advanced therapies is producing the large quantities of cells needed in a cost-effective manner. Corning has developed a novel fixed bed bioreactor (FBR) platform that is designed to deliver significant surface area intensification and high-yield bioproduction capability.

The Corning Ascent FBR System is designed to enable process development and production scale cell culture for cell and gene therapy workflows with high yields and viable cell harvest capability that may result in substantial cost savings when compared to existing commercial FBR systems. The Ascent FBR platform enables linear scalability from 1 m² to 1,000 m² with efficient process transfer during scale-up.

Advances in cell and gene therapy, biotherapeutics, and more, require technology innovation

Recent advances in biotherapeutics and cell and gene therapy may hold unprecedented promise for difficult-to-treat health conditions. From oncology to diabetes to rare diseases, innovative and rapidly evolving technologies continue to pave the way for potential treatment options once thought impossible.

For example, in gene therapy, recombinant adeno-associated (AAV) and lentiviral vectors (LVV) have emerged as leading gene delivery tools for *in vivo* and *ex vivo* gene therapies, respectively. Similarly, advances in cell therapy and regenerative medicine have forced the industry to evaluate new methods for automated and scalable cell manufacturing. However, most existing manufacturing technologies for these modalities do not provide the true scalability and automation the industry requires. Now more than ever the industry needs a scalable, cost-efficient and automated cell manufacturing option.



Corning Ascent FBR System 5



Corning Ascent FBR System 100

Actual instrument component appearance may differ from images.

An improved system for cell and gene therapy workflows

To address the need for a more efficient solution, Corning developed the Ascent FBR System, designed to combine the benefits of adherent bioproduction platforms with the scale and automation of suspension manufacturing systems.

The innovative Ascent bioreactor was designed to enable uniform media flow to enhance cell health and drive high-density uniform cell growth for a more homogeneous cell population. These design attributes enable >90% transfection efficiencies for gene therapy applications resulting in high AAV vector yield/m². Higher yields can lead to fewer required runs, an overall reduction in media and lower operational costs.

The design of the Ascent bioreactor also enables efficient harvest and collection of viable cells, expanding its utility to a broad range of cell therapy applications. The ability to harvest cells allows the Ascent platform to be used for seed train and production workflows where the cell is the product. This versatility simplifies the overall upstream process, reducing the need for multiple technologies and offering true scalability across capacities ranging from 1 m² to 1,000 m². Collectively, these benefits may help drive faster development time to production and significant savings in manufacturing costs.

True scalability

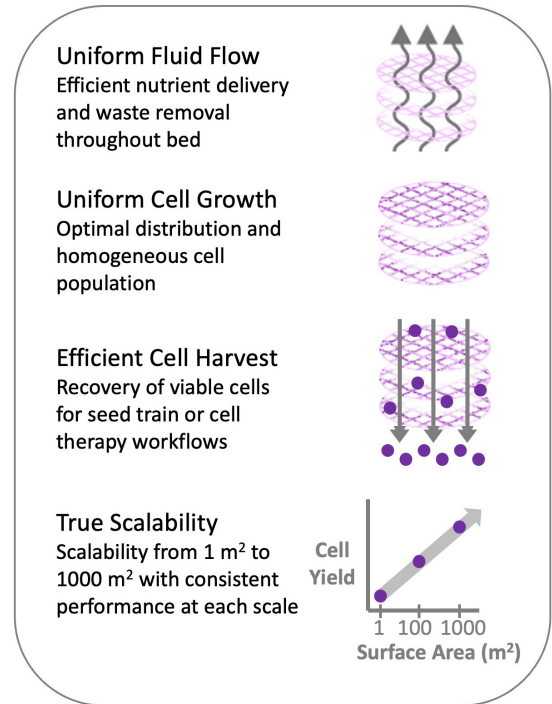
Corning's Ascent FBR System is designed to enable efficient transition from process development to production while maintaining consistent performance at each scale.

How it Works

The Ascent FBR System is designed around a single-use bioreactor supported by a media conditioning vessel and other accessory consumables, monitored and controlled by an innovative biocontroller.

The Bioreactor

The Ascent FBR System's bioreactor features a specially treated and packed polymer mesh that enables uniform, low-shear fluid flow through the bioreactor bed, which promotes evenly distributed cell growth and enhances exposure of cells to nutrients and reagents. Bioreactors will be available in multiple surface area sizes to provide scalability from 1 m² to 1,000 m².



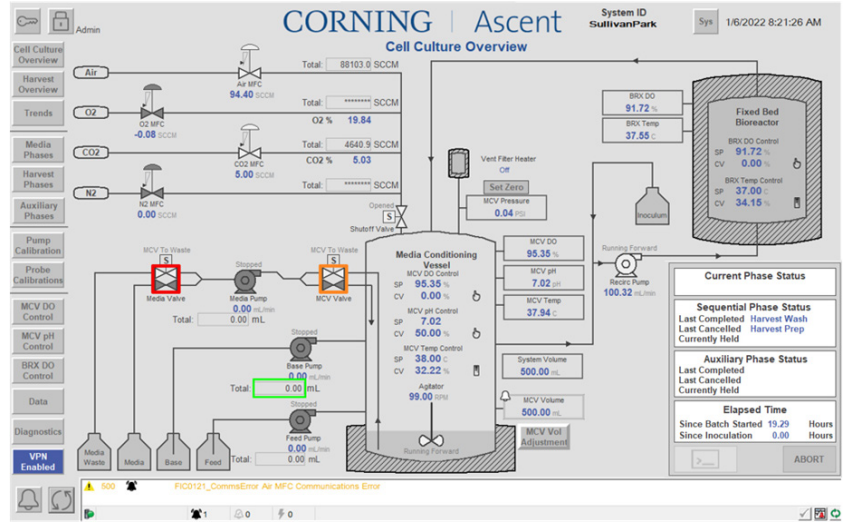
Bed Height	Surface Area		
	Ascent FBR System 5	Ascent FBR System 100	Ascent FBR System 1000
4 cm	1 m ²	20 m ²	200 m ²
10 cm	2.5 m ²	50 m ²	500 m ²
20 cm	5 m ²	100 m ²	1,000 m ²

The Media Conditioning Vessel

The Ascent FBR System utilizes a separate conditioning vessel, which enables flexibility in managing media conditions and developing optimal processes within the platform. The system's consumable set is equipped with disposable sensors for key process parameters (pH, dissolved oxygen, temperature). All fluid-contacting components are pre-assembled and irradiated; no autoclaving is required.

The Automated Controller

The system controller with Human-Machine Interface (HMI) touchscreen display allows the user flexibility to operate the system in manual or automated modes. During cell culture, a recirculation pump circulates media from the MCV through the bioreactor. A separate pump aids in removing depleted media from the MCV and replacing it with fresh media during media maintenance. Cell culture pH and nutrient levels are monitored and maintained via feed and base pumps while temperature is kept constant. At harvest, cells can be released or lysed in situ from the bioreactor.



Features and Benefits

Features	Benefits
Specially treated woven mesh polymer substrate	<ul style="list-style-type: none"> Uniform fluid flow – efficient nutrient delivery and waste removal Uniform cell growth – beneficial cell distribution and confluence at transfection Improves cell health and product yield
FBR designed to harvest viable cells with >90% recovery	<ul style="list-style-type: none"> Enables its use in other application workflows that require cell recovery for downstream use Enables the bioreactor to be used for seed train, streamlining vessel-to-vessel cell transfer
Bioreactors scale from 1 m ² to 1,000 m ²	<ul style="list-style-type: none"> Consistent platform performance from process development to production size can save process development time/cost (reduced time to market)
Separate media condition vessel (MCV)	<ul style="list-style-type: none"> Provides flexibility in media volume and dilution strategy for transfection reagents prior to addition
Automated control, including disposable sensors monitor DO, pH, temperature	<ul style="list-style-type: none"> Reduced labor costs, hands-off operation, reduced risk of human error
Closed system, ready to use, irradiated consumables	<ul style="list-style-type: none"> No autoclaving necessary; minimal set-up and probe calibration required, which can save hours of valuable time

Uniform Fluid Flow

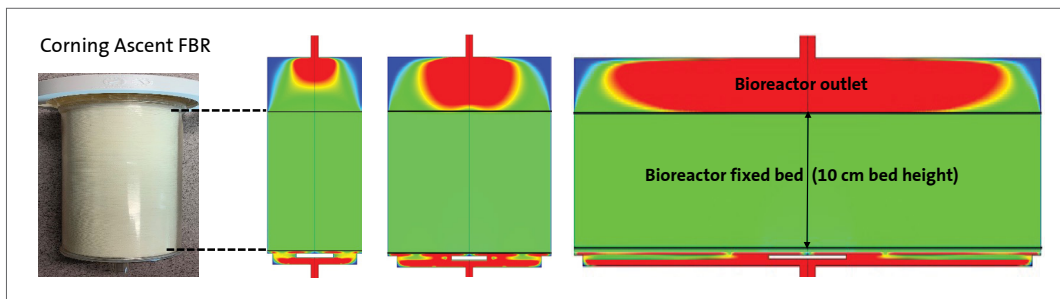


Figure 1. Computational Fluid Dynamics (CFD) modeling for different scale prototype vessels with 10 cm packed bed height shows low shear and uniform flow across a large variation of packed bed diameters.

Residence Time Distribution (RTD) Test Confirms Uniform Fluid Flow through the Corning® Ascent® FBR System

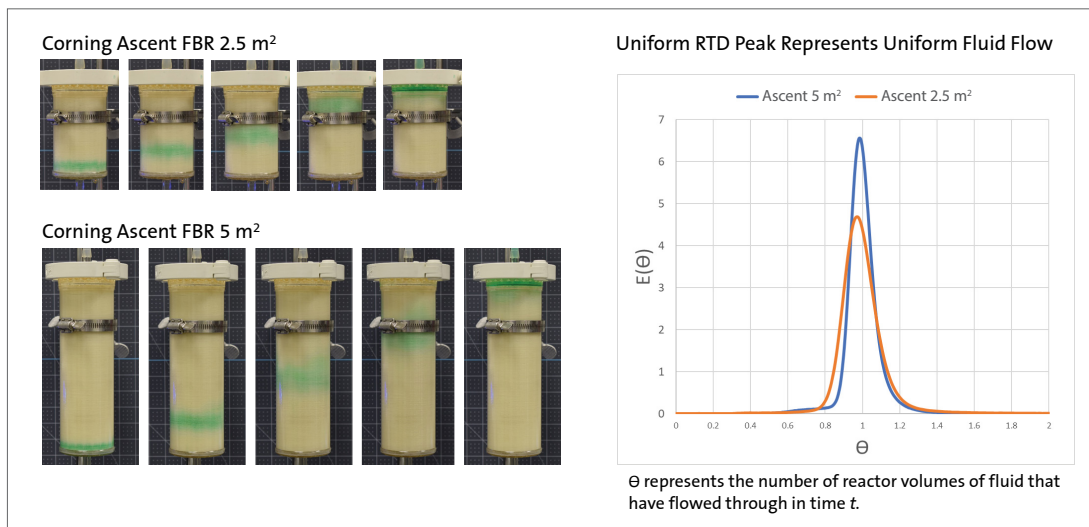


Figure 2. Left panel: Timelapse images showing the pattern of a tracer dye solution flowing through 2.5 m² and 5 m² bioreactors over time (flow rate = 100 mL/min.). Right panel: A tracer dye solution was injected into a flow of Milli-Q® water at the FBR inlet and the absorbance of the solution was measured every 2 seconds at the FBR outlet using a UV-Vis spectrophotometer (Thermo Scientific, 630 nm). The final calculated $E(\Theta)$ or Θ are dimensionless (normalized parameters) which are independent of bioreactor volumes or flow rates. Flow rate = 100 mL/min. $\Theta = 1$ and t corresponds to approximately 2.4 min. for the 2.5 m² FBR and approximately 4.6 min. for the 5 m² FBR.

Uniform Cell Attachment and Growth

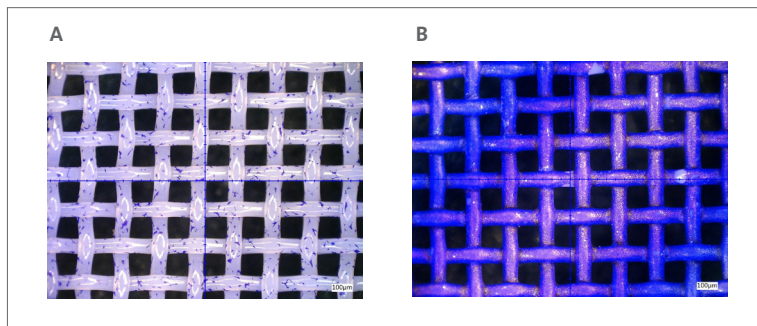


Figure 3. The woven mesh that makes up the substrate in the Corning Ascent FBR enables uniform cell adhesion and growth of cells. In these images (magnification = 100X), crystal violet staining of HEK293T cells reveals uniform cell seeding after three hours (A) and subsequent uniform cell growth after 3 days (B).

Efficient Cell Harvest

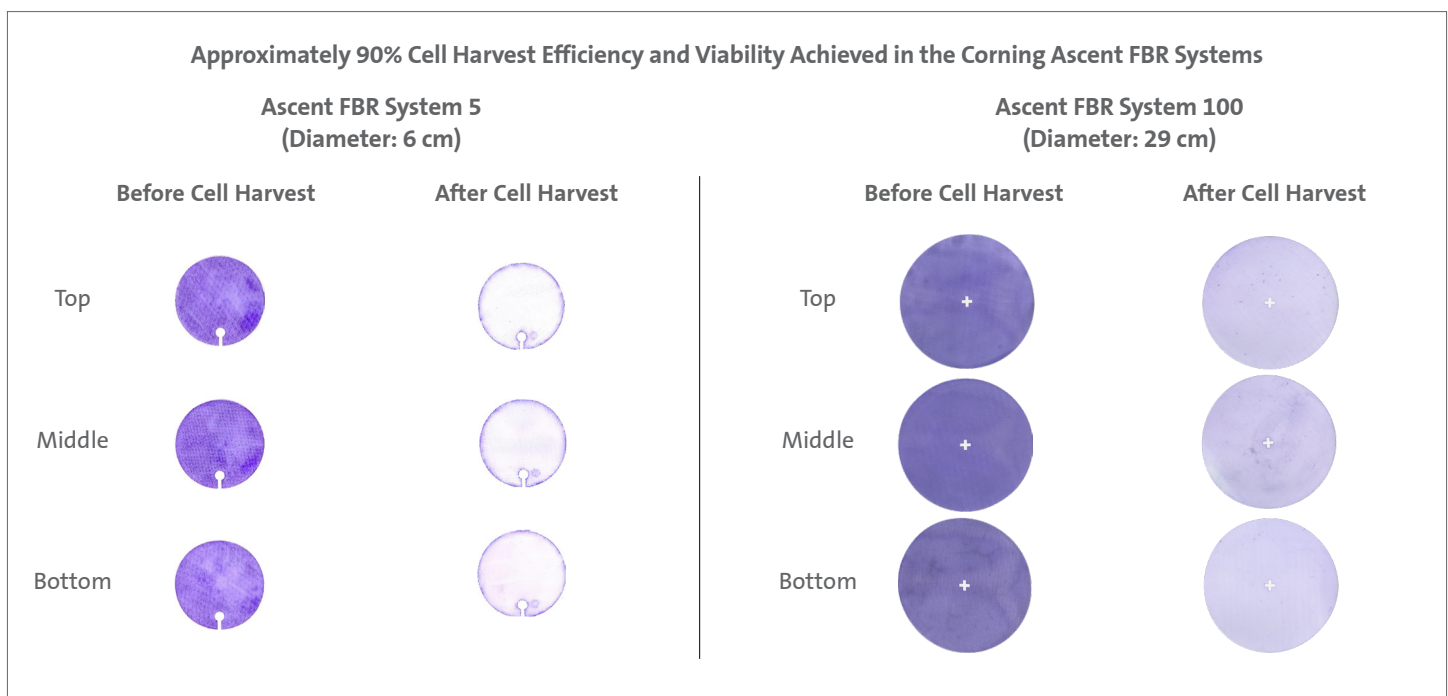


Figure 4. Crystal violet staining shows that cell distribution is uniform across each disk as well as throughout the top, middle, and bottom of the bioreactor in both Ascent FBR Systems 5 and 100. Efficient cell harvest is also shown. Images are not to scale.

Uniform Transfection Across the Bioreactor

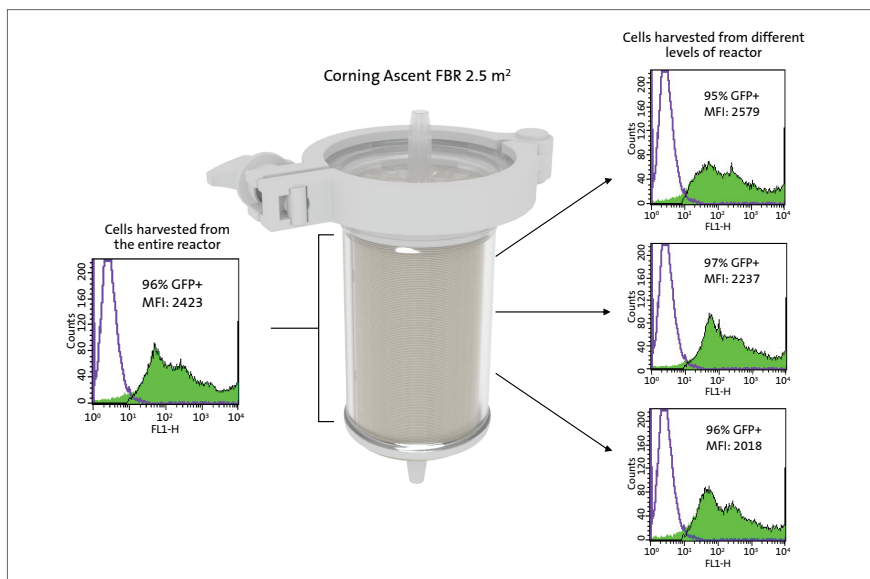


Figure 5. The Corning Ascent FBR has achieved uniform transfection efficiency across a 2.5 m² bioreactor transfected with AAV2-GFP plasmids. Average % of GFP+ cells was 90.9. (Flow cytometry data are 72 hrs. post-transfection).

Improve your Production Process with the Corning® Ascent® FBR System

From process development to manufacturing, you can scale-up production of adherent cells and cell products (e.g., viral vectors) in a single, automated technology platform. The Ascent FBR System is designed to deliver:

- ▶ Potential cost savings: With high yield per cm², production will require fewer runs to achieve the same quantity of product which may result in additional savings from lower consumption of media and serum/m² as well as reduced downstream processing time and waste
- ▶ Viable Cell Harvest: Recover cells for capture of cell-associated viruses, seeding into larger reactors, and a path to cell therapy workflows
- ▶ Reduced CapEx and labor costs: Easy set up, self-contained closed system with irradiated consumables—laminar flow hood not required for operation
- ▶ Uniformity and Scalability: Bioreactors range from 1 m² to 1,000 m², designed for uniform cell growth and process scalability.

For additional information or to request a demonstration, visit www.corning.com/AscentFBR or contact your local Corning Account Representative.

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