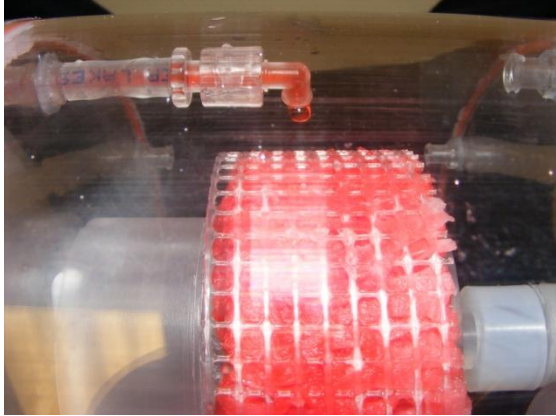




EXPRESS[®] BIOREACTOR

The Next Generation in High Performance Cell Culture



The patented Express[®] Bioreactor represents a Paradigm shift in culturing cells. Cells are grown on a bee-hive like spongy matrix which is suspended in a sterile chamber in an atmosphere of air/ CO₂. This provides a high surface area and high oxygen availability for growing both suspension and anchorage-dependent cells. The cells can be grown in a batch, fed-batch or perfusion mode. The Express[®] Bioreactor is disposable, comes pre-sterilized and can be easily set up in a standard air/ CO₂ incubator.

Unlike conventional bioreactors, the Express[®] Bioreactor requires no rocking or agitation whatsoever. By eliminating shear and the limitation of oxygen availability, 5- 30 fold higher cell densities and higher product yields are easily achieved.

Express[®] Bioreactor Highlights

- 5-30 X Higher Productivity
- High Cell Density
- Attachment or Suspension Cells
- Hybridomas, CHO, HEK 293, Fungal, Insect Cells
- Grow in Serum, Harvest Serum Free
- Low media usage
- High Oxygen Availability
- Zero shear
- Perfusion or Batch
- Easy, single-use, disposable
- Cost-effective
- Small Footprint

The Problem with traditional Culture Cell

All traditional bioreactors have one thing in common. Cells grow in the liquid nutrient medium which is also the means by which dissolved oxygen is transported to the cell surface. Air/ CO₂ is dissolved in the medium by bubbling the gas into it followed by stirring or rocking of the medium to aid in its diffusion to the cells. The oxygen which is known to have a poor solubility in the medium is rapidly depleted as the cell density rises, resulting in apoptosis, an eventual “crash” or death of the culture. To prevent this, the bubbling, stirring or rocking rates are all increased over time to increase oxygen delivery. Unfortunately, these actions cause an increase in shear rates that fragile mammalian cells cannot handle. In perfusion systems like hollow fibers rate of media exchange is increased to enhance oxygen transport. This leads to direct increase in media consumption, and increased cost of goods.



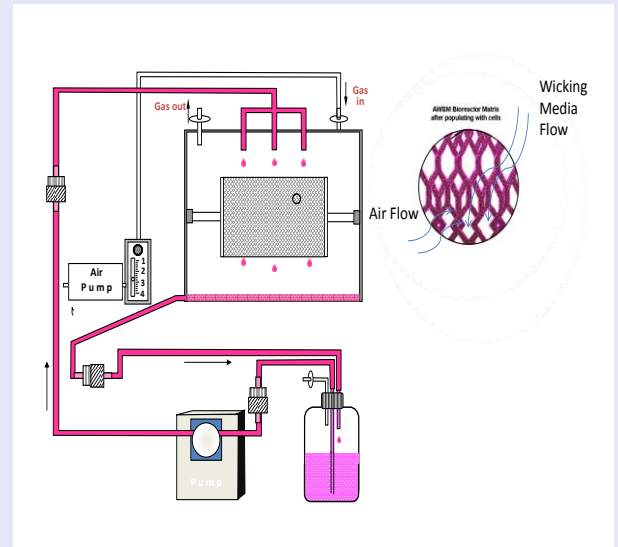
The Breakthrough Solution

In the Express® Bioreactor, the feeding and the oxygen transport are decoupled. The very porous honey-combed matrix is constantly exposed to air/ CO₂ and provides a large surface area for a large population of cells to grow on mimicking a “lung” with superior gas exchange abilities. Fresh media is constantly dripped on to the matrix and allowed to wick through the matrix to the cell surface. Product and waste metabolites are constantly removed while the cells are growing only a thin layer of medium away from O₂. This unique design can thus support high cell density, high oxygen availability and nutrient exchange while continuously removing product and deleterious waste metabolites from the cells with zero shear. Surface treatment of this biocompatible matrix assures growth of conventional suspension cells as well as difficult to grow attachment cells. Hybridomas, HEK 293, CHO fungal, yeast and insect cells have all been grown in the Express® Bioreactor.

How it Works

Culture media is continually dripped very slowly onto the top of the “lung”-like matrix and allowed to wick by capillary action, as a very thin film over the entire growth surface. Circulating air flows freely throughout the large pores integral to the matrix. Cells are never submerged, but continually bathed by the thin film of culture media, thus allowing every growing cell equal access to highly efficient gas-exchange.

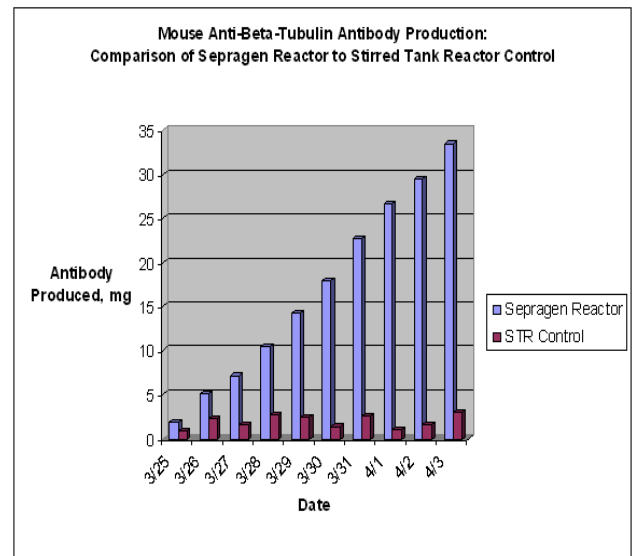
Innoculation, feeding and harvesting are all completed in a simple media exchange procedure. To date a variety of cell lines including hybridomas, CHO, human embryonic kidney (HEK), fungal and insect cells have all been successfully grown to high densities.



Case Study 1: Up to 15X Higher Productivity

Comparison of the Express® Bioreactor vs. Standard Stirred Tank

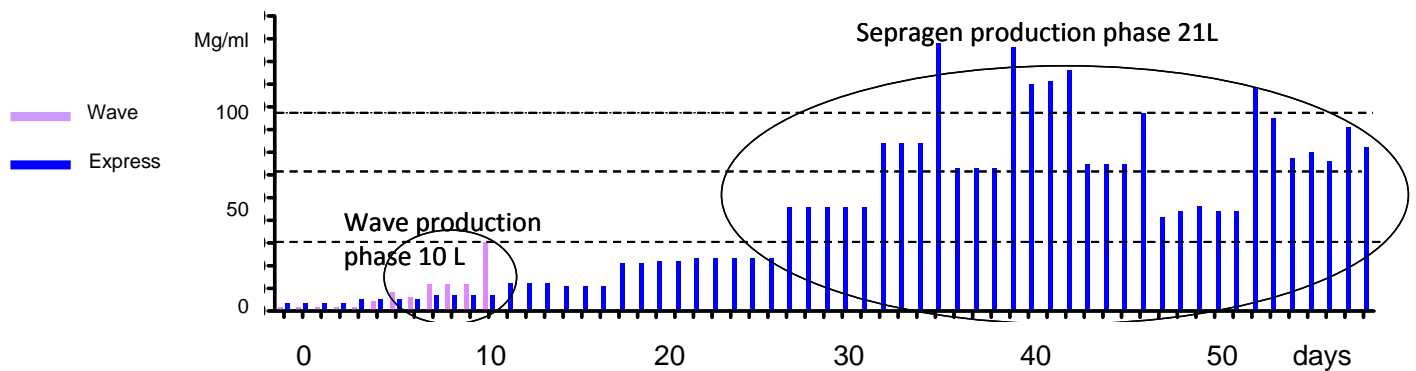
This experiment was designed to compare the productivity of a standard 1 liter stirred tank bioreactor with a similar sized Express® Bioreactor. Hybridoma cells were grown in both bioreactors and the cumulative output of antibody produced was measured. The data shows a 15-fold higher antibody production in the Sepragen Express® Bioreactor.



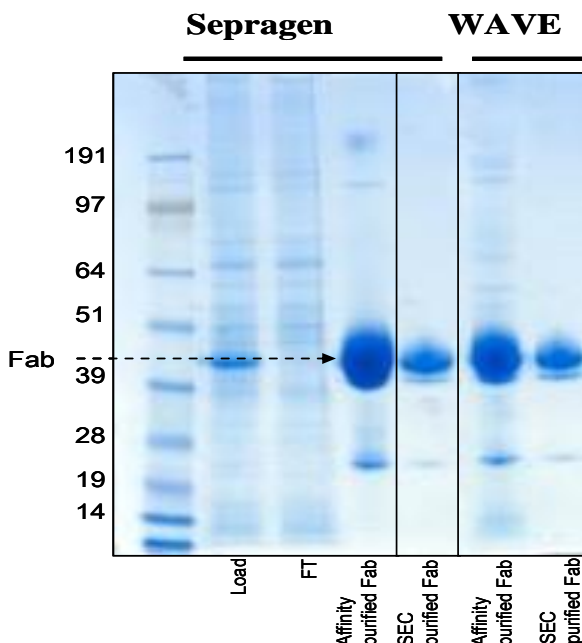
Case Study 2: Up to 25X Higher Productivity with CHO Cells

Comparison of the Express® Bioreactor vs. Wave® Bioreactor

CHO K1 cells expressing a FAb were grown in both a Sepragen Express® Bioreactor as well as a conventional Wave® Bioreactor. Both bioreactors were seeded with the same number of cells. The Express® Bioreactor was run in a perfusion mode for 110 days. The Wave® was run to terminal harvest and taken down after 14 days. The significantly higher productivity of the Express® Bioreactor, along with the ease of use and the long-term viability of the cells, demonstrates the Express® as a robust and superior platform for mammalian cell culture.



	Production phase Wave® 10 liter bag	Express® 1 Liter system (total 21 Liters harvested)
Total Product	900mgs/12 days	2216 mgs/28.5 days
Mean mgs/day	75.0 mgs/day	78.0 mgs/day
Mean mgs/liter	900/10L = 90 mgs/liter	2216/21L= 105.5 mgs/liter
Mean mgs/L/day	(90 (day 12) -60 (day 11) = 30) 30 mgs/L/day (day 12)	78.0 mgs/L/day



	Fab Qty	Yield	MW (Mass Spec)	K _d (Forte BIO)
Express®	108 mgs	55 mgs	48028	3.1 nM
Wave®	90 mgs	40 mgs	48029	4.7 nM

The above data shows the Express® Bioreactor's ability to dramatically increase productivity and continuous production for several months, while maintaining a high density viable culture. Yields were superior, and product purity and quality attributes were comparable.

Technology Comparison

The Express® Bioreactor offers the most versatile platform for High Performance Cell Culture. A comparison chart of the advantages of the Express® Bioreactor versus other commonly used systems is shown below:

	Attachment Cells	Suspension Cells	Perfusion	Footprint	Productivity per Liter Media	Flexibility	Scalability
Sepragen Express®	+++	+++	+++	+++	+++	+++	+++
Bags	+	+++	++	+	++	+	++
Stirred Tank	+	++	++	+	+	+	+++
Rollers/Cell Factories	++	+	-	+	++	++	+
Hollow Fibers	+	+	+	++	+	++	+

Ordering Information

The ordering information and part numbers are listed below:

Model	Part#	Description
Express- 500	41-0500-00	Pre-sterilized 500 ml bioreactor with matrix, filters, fittings, tubing and media bottle connector
Express- 1000	41-1000-00	Pre-sterilized 1000 ml bioreactor with matrix, filters, fittings, tubing and media bottle connector
Accessories		
Media Recirculation Pump	41-1000-10	Low flow, Low heat, small footprint peristaltic pump
Air Pump	41-1000-12	Pumping air/ CO ₂ through bioreactor
Air Flow Controller	41-1000-11	Regulate air/ CO ₂ flow

Sepragen Has What It Takes

Sepragen's pioneering spirit of innovation brings to you the Express® Bioreactor. You can now use this high performance cell culture tool to enable making antibodies and other proteins from a number of different expression systems easily and cost effectively. Call 510-475-0650 to discuss your needs today!



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