

An Update on the Advantages of Fibra-Cel® Disks for Cell Culture

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Abstract

With a renewed acceptance of perfusion processes in cell culture, both in the laboratory and for production applications [1], New Brunswick™ packed-bed bioreactors using Fibra-Cel disks are seeing an upsurge in interest.

This application note examines Fibra-Cel technology and its many advantages, from increased secreted protein yields to labor savings in applications including rabies vaccine production.

What Is Fibra-Cel?

Eppendorf Fibra-Cel is a solid-support growth matrix (Figure 1) for anchorage-dependent and suspension cell cultures. It is used predominantly in perfusion processes for the production of secreted products—such as recombinant proteins and viruses—and it is currently being evaluated for stem cell research [2].

Since the 1980s, scientists around the globe have been using Fibra-Cel to grow a wide range of cell types (see inset, right), including hybridomas and insect cultures. Originally used in New Brunswick™ CelliGen® autoclavable cell culture bioreactors, Fibra-Cel technology has now been successfully scaled up for commercial production in sterilizable-in-place systems as large as 150 liters. BioBLU® packed-bed, single-use vessels containing Fibra-Cel are also available for those who prefer the advantages of a disposable system.

Manufactured according to cGMP guidelines, Fibra-Cel is composed of two layers of nonwoven material—polyester and polypropylene—which are sonicated together, cut into disks, and electrostatically treated to attract cells and facilitate their attachment to the disks. Normally it takes about six hours for cells to attach to microcarriers (with a normal inoculum of 1×10^6 cells/mL), whereas cells can attach within 15 – 60 minutes on Fibra-Cel disks.

Cells successfully used on Fibra-Cel disks

Hybridoma: 123A, 127A, GAMMA, 67-9-B, DA4-4

Anchorage-dependent: 3T3, MRC-5 and other human fibroblasts, HEK 293, BHK, COS, CHO, stroma cells, hepatocytes

Insect cells: Tn-368, Sf9, rSf9, Hi-5

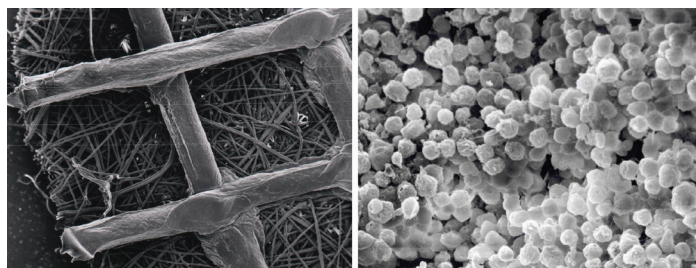


Figure 1. Scanning electron micrograph of Fibra-Cel disks (left); mouse-mouse hybridoma DA4.4 immobilized on Fibra-Cel disks during production at 1×10^8 cells/cm³ of packed-bed volume (right)

Moreover, the growth process for microcarrier cultures can require extended delays for periodic stoppage of stirring to allow time for cells to become attached. By comparison, the Fibra-Cel bed is inoculated (3×10^5 cells/mL of bed volume) in a single step.

Fibra-Cel in a New Brunswick bioreactor is also advantageous over microcarriers because it enables sustained long-term periods of high-density growth in perfusion mode, without danger of clogging because there are no filters. Perfusion is a mode of cell culture in which a fresh nutrient medium is continuously added to the culture while simultaneously removing the spent medium that contains the product of interest. In a New Brunswick bioreactor, cells growing on or in the Fibra-Cel disk bed are retained within the vessel, inside the packed bed, where they continue the production of the desired product.

The packed bed comprises two horizontally positioned screens that extend to the bioreactor vessel walls. Enclosed between the screens, a bed of Fibra-Cel disks serves as solid support for the growing cells (Figure 2). Cells growing in the disk bed become immobilized on or between the disks, where they remain throughout the culture run, protected from external shear forces. The process is favored for manufacturing because product yields can be increased by as much as tenfold over comparable processes [3]. Once the bioreactor is set up and inoculated, the culture can be maintained to produce proteins for long periods of time thus saving labor, time, and money.

Like the proprietary Eppendorf Cell Lift impeller, rotation of the discharge ports in the proprietary packed-bed impeller creates a low differential pressure at the base of the impeller tube, which circulates the medium throughout the system. The medium receives gases through a sparger located at the bottom of the inner tube, protecting the cells from being exposed to the gas liquid interface. This results in low turbulence and low shear stress on the culture. Exceptionally high cell densities are achievable due to the high surface-to-volume ratio provided by the disk bed, coupled with the ability to use perfusion. In comparison with other cell support systems, it was found that higher titers and cell densities were achieved in trials using Fibra-Cel disks [4].



Figure 2. Basket impeller with Fibra-Cel disks

Other benefits

Because higher yields are possible, smaller bioreactors can be used to substantially reduce the initial capital expenditure as well as reduce the utilities required for operation (such as electricity, water, and steam if required). In addition, because the cells remain entrapped, the packed bed eliminates the need for cell filtration to separate cells from the end product, thus simplifying harvesting. Last, product recovery and downstream processing can be more easily controlled because users can determine the volume of harvest material that is to be processed at any given time.

Commercial production

Bioreactors using Fibracel have been used in the production of a variety of commercial products. One example of commercial production includes end products such as EPO, which can now be commercially produced on the bench using Fibracel technology, eliminating the need for labor-intensive and space-consuming roller bottles. A substantial portion of the world's human rabies vaccine is also produced using Eppendorf Fibracel technology. Additionally, many of our customers are currently using Fibracel in their proprietary processes to produce interferons, monoclonal antibodies, and hormones.

In summary, Fibracel provides benefits in research laboratories as well as in commercial production. Our customers have found that because yields are high, bioreactors containing Fibracel packed beds can outperform much larger-sized bioreactors, thereby achieving commercial-scale production in a bioreactor with a far smaller footprint. Production space requirements are reduced, as are costs associated with labor, start-up, and operations.

For protocols on other cell lines, or for additional information on the Fibracel, see eppendorf.com.

References

- [1] Perfusion Bioreactors Are Making a Comeback but Industry Misconceptions Persist. Langer ES. *Bioprocessing J.* 9, Winter 2010–2011: 49–52.
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- [4] High Vero Cell Density and Rabies Proliferation on Fibracel Disks Versus Cytodex-1 in Spinner Flask. Hassanzadeh S, et al. *Pakistan J. Biol. Sci.* 2011: 1–8.

Ordering information

Description	Order No.
Fibracel® disks , a solid support growth matrix for mammalian, animal, and insect cells	
50 g	M1292-9984
250 g	M1292-9988

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