

MILLIPORE

pure bioprocessing



**Void-free tangential flow
UF membranes for robust,
reliable protein purification**

What does it take to make the world's most trusted UF

If you're trusting your process to a UF membrane, don't you want to know what goes into making it?

We recognize that Millipore membranes play a mission-critical role in your purification process. By giving you an "inside" look at the science, the advanced manufacturing technology and the stringent quality procedures that go into every Millipore UF membrane, we hope you'll see that the trust you place in our products is well-founded.

Choosing the right membrane

What makes one membrane better than another for a given application? What technical factors should guide your decision process? Let's take a look at some important elements to review when evaluating a particular membrane for your process.

The new era of TFF membranes

Biomax[®] and Ultracel[™] PLC UF membranes represent a whole new generation of TFF solutions. They deliver the most robust, consistent ultrafiltration performance ever. A unique, void-free structure makes the difference. We'll show you why.



A 45-year reputation for real world results

For over 45 years, Millipore has been synonymous with membranes. A charter member of the biopharmaceutical community, we also play the role of scientific partner. In fact, many industry-accepted membrane purification techniques including plasma fractionation, cell harvesting and virus removal originated in Millipore development laboratories.

An important part of our own development effort is understanding the specific needs of our customers, from the benchtop to the pilot plant to the manufacturing floor. That way, every time we advance our membranes or devices, you'll see a direct improvement in your process. Real results in the real world, that's what counts. And that's where the reputation comes from.

membrane?



Unmatched breadth of technology platforms

In order to develop process-ready membrane solutions for an entire spectrum of applications, we've had to develop a substantial knowledge base and a high level of technical versatility. Compared to other manufacturers who focus on only one or two processes, Millipore has become adept at all of them. So, to solve your particular application problem, we can draw on expertise and experience across literally all membrane manufacturing technologies.

Scientific partnerships that extend our scope of discovery

As scientists, we realize the importance of staying ahead of the technology curve. Our collaboration with leading academic institutions and research centers around the world broadens our intellectual horizon and adds depth to our talent pool, giving us an important window into the future. So when emerging technology becomes robust enough for commercialization, we can quickly deliver these new tools to our customers.

Outstanding scientists from diverse disciplines come together to produce unique, value-added solutions to real world separation problems.

Void-free UF membranes deliver unprecedented process

Millipore's innovative design approach, combined with patented manufacturing techniques, has produced a new generation of TFF membranes with superior surface chemistry, robust construction and a reproducible, void-free structure.

Delivering better retention and higher yields

Whether you choose Millipore's Biomax® or Ultracel™ PLC membrane, you will see significant process improvements.

- Sharper retention cutoffs, for improved processing specificity
- Higher process flux, for maximum throughput, reduced processing costs and higher yields
- Greater strength and durability, for enhanced process reliability

10X higher resistance

Rigorous tests show that when compared to conventional membranes, Void-free membranes offer 10X higher resistance to undesirable pressure conditions. The combination of the void-free structure and increased mechanical strength deliver superior retention and robust performance ideally suited for today's bioprocessing applications.

Biomax.® Pure speed.

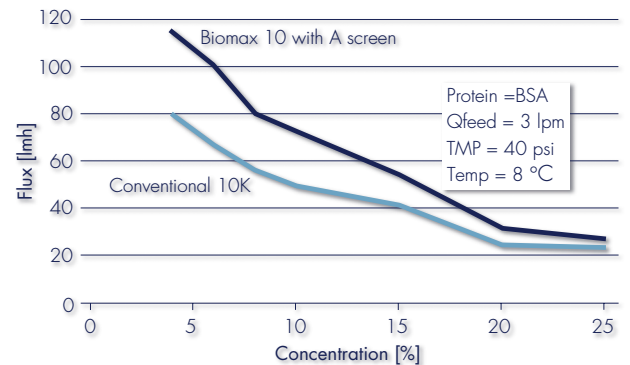
Fast processing, exceptional chemical resistance

Biomax void-free membranes are composed of a polyethersulfone (PES) layer backed by non-woven polypropylene for optimal performance and strength. Extremely rugged, they are ideally suited to applications requiring harsh cleaning and biological decontamination regimens. They withstand all standard cleaning chemicals with no degradation in separation performance.

Unlike conventional PES membranes that exhibit excessive protein binding, Biomax delivers excellent retention as well as a high yield of your valuable product. The void-free structure assures greater mechanical strength and superior integrity. These properties plus the membrane's inherently higher working flux allow fast, economical processing.

High Flux in Pellicon® 2 Cassettes: Biomax 10 with BSA

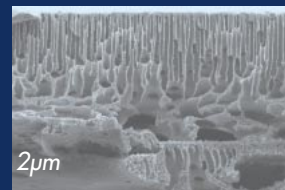
Comparison of Biomax 10 in Pellicon 2 cassettes with conventional cassettes Flux vs Concentration



Millipore Void-Free UF Membrane

In the Millipore UF membrane shown above, the void structure has been eliminated. Instead, there is a uniform, highly integral pore structure across the membrane's entire separation layer.

Because of this, void-free membranes can be made with a more "open" average pore size that retains your biomolecule while passing unwanted contaminants. This gives them 30-40% greater permeability and higher working flux than conventional membranes designed for the same application. You get a more retentive membrane, smaller, more efficient systems and higher yields.



Conventional UF Membrane

Conventional UF membranes have a thin, dense skin supported by a structure with cavern-like voids.

Voids can cause surface defects and reduce strength. To maintain high retention, manufacturers compensate by tightening the porosity of the overall membrane; unfortunately, this adversely impacts flow performance and process economics.

ss performance.

Ultrasel™ PLC. Pure recovery.

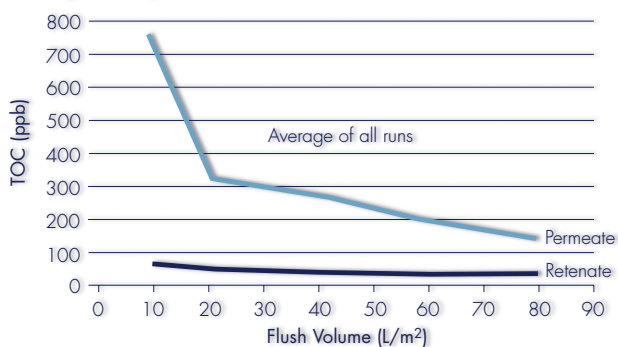
Ultra-low protein binding, robust process performance

Ultrasel void-free membranes combine the ultra-low protein binding, low fouling and solvent resistance of cellulosic membranes with excellent mechanical strength and robust process performance. Casting the regenerated cellulose onto our own polyethylene microporous substrate provides a robust structure that is resistant to backpressure and able to maintain integrity despite process upsets.

Ultrasel membranes are extremely hydrophilic. They resist fouling, are easy to clean, and are ideal in process streams that include lipids, DNA, RNA, antifoaming agents and organic solvents. In addition, the void-free structure enhances retention and allows fast, efficient processing while maintaining maximum recovery of high value proteins.



Flushing Efficiency of Ultrasel PLCGC Cassettes



Did you know...
Void-Free membranes
improve process yields
by 2-3%



PROPERTY	BIOMAX MEMBRANES	ULTRACEL PLC MEMBRANES
MEMBRANE	Polyethersulfone with void-free structure	Composite regenerated cellulose with void-free structure
MOLECULAR WEIGHT CUT-OFF	5 kD-1,000 kD	5 kD-1,000 kD
RELATIVE PROTEIN BINDING	Low to medium – use with > 0.1 mg/mL solutions	Ultra low – far superior for use with dilute protein solutions
pH RANGE	1-14	2-13
KEY BENEFIT	<ul style="list-style-type: none"> Highest flux Exceptional chemical compatibility 	<ul style="list-style-type: none"> Ultra-low protein binding Low fouling Solvent resistant Use with defoamers

Translating knowledge, experience and advanced tec



All the science in the world can't do your process any good unless it can be translated into consistent, reliable products. To make sure we deliver the reliability you need lot to lot and batch to batch, we've become as zealous about quality as we are about membrane science. In fact, at Millipore, the two are inseparable.

The most rigorous quality program in the industry

Millipore TFF membranes are designed, developed and manufactured in a cGMP-compliant facility, to ISO[®]9000 Quality Systems Standard.

Our membranes are cast using rigorous, validated protocols. Each lot of membrane is subjected to a battery of quality control tests to ensure that retention, flux and integrity characteristics consistently meet exacting process requirements.



For most of our biopharmaceutical customers, membranes are at the heart of their processes. Membrane consistency and reliability directly impact yields and overall results.



Did you know...
Void-Free membranes are more integral than conventional membranes



Technology into consistent, reliable products.

Building a more robust TFF membrane

Advanced manufacturing capabilities, plus patented materials technology and innovative chemistry allow Millipore to offer a broad range of UF membranes for bioprocessing applications.

While a variety of materials and techniques may be employed in Millipore's leading edge cGMP manufacturing operation, the basic steps we take in producing, or "casting" a UF membrane remain essentially the same:

Step 1. Raw Materials Matched to the Intended Application

Membrane material (typically an organic polymer) and solvents are carefully selected for the intended application. The choice of material and chemistry directly impacts the temperature range, solvent compatibility, pH range and protein binding characteristics of the final product.

The substrate or base upon which the membrane is cast is also critical. The proper

substrates assure integrity and robustness, resulting in higher yields and better process reliability.

Step 2. Controlled Mixing for a Consistent, Reproducible Process

In this step, raw materials and solvents used in the manufacturing process are measured and mixed under carefully controlled conditions. Homogeneous solvent/polymer mixtures are required to assure membrane consistency.

Step 3. Precise Casting Shapes the Final Product

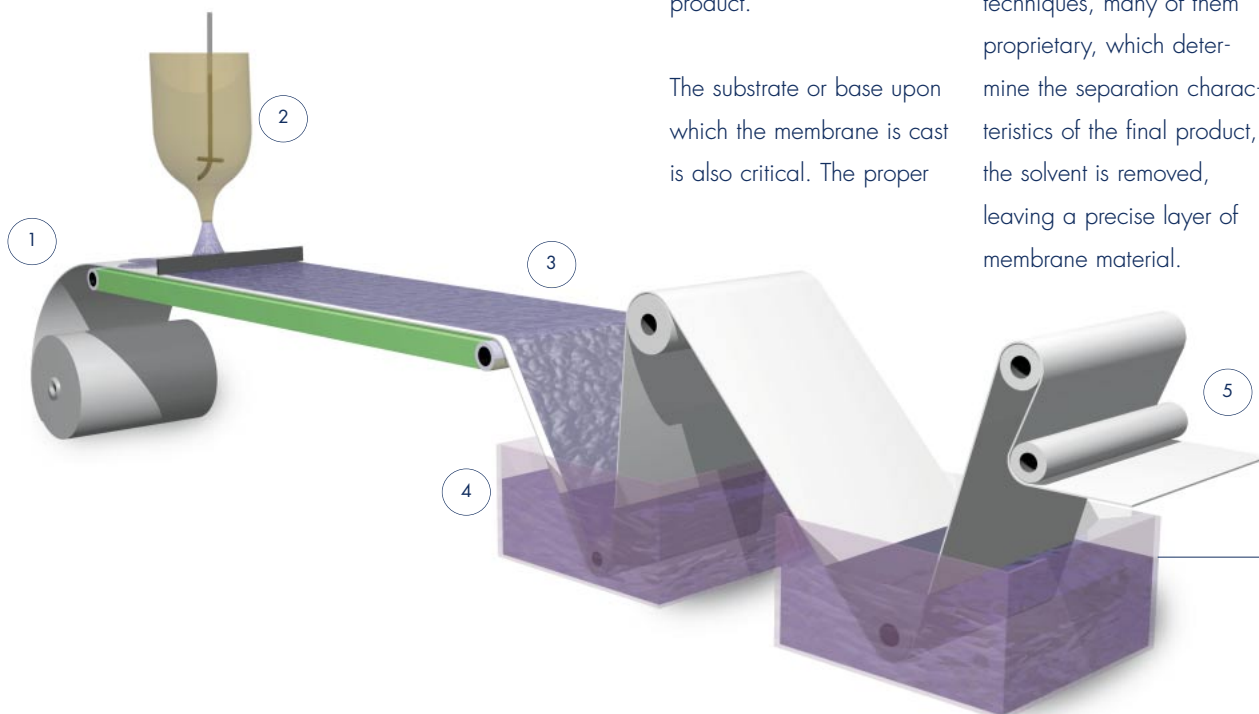
The solvent/polymer mixture is spread out, or "cast" in a thin layer on a moving conveyor. Using a number of techniques, many of them proprietary, which determine the separation characteristics of the final product, the solvent is removed, leaving a precise layer of membrane material.

Step 4. Chemical Modifications Fine-Tune Application Performance

A high percentage of membranes used today are made from hydrophobic polymers, which must be chemically modified to allow their use in aqueous separations. A number of proprietary surface chemistries may be applied to give the final membrane desired performance characteristics for an intended application.

Step 5. Unmatched Quality Assurance

Rigorous control of raw materials and management of process variables is required to assure membrane consistency. Millipore's sophisticated ISO9000 registered Total Quality Management system also includes product release tests for thickness, permeability, retention, integrity and strength.



Every process presents its own u



Every UF protein purification train involves a complex series of steps. Not only the separation itself, but prefiltration, cleaning, integrity testing, system equilibration, concentration and product recovery—plus, of course, validation.



Did you know...
Void-Free membranes
deliver better retention
and higher yield



nique challenges.

Pick the right TFF membrane for your process

While there may be many variables to consider when you're evaluating membranes and suppliers, in-process TFF performance is likely to be a composite of a few key parameters. Here they are, along with why they're important.

Retention	First, the membrane must be sized for your particular separation. Optimizing retention, which is the major factor in optimizing yield, is a function not only of the pore size distribution, but also of the consistency and structural integrity of the membrane.
Flux	The closer the actual pore size approximates the desired cut-off, the greater the flux. Maximizing the pore size allows process fluids to pass more readily; at larger scales, this results in faster, more cost-effective processing. As with retention, flux is also a function of pore size distribution and structural integrity.
Reproducibility	Consistent membranes keep your process predictable. How the membrane performs, day-to-day and year-to-year, reflects the technology, process design and the quality control expertise of the membrane manufacturer.
Protein Binding	The protein binding characteristics of a TFF membrane can be particularly important when processing high value therapeutic biomolecules. Low protein binding membranes are less prone to fouling during processing, and hold up a minimum of valuable product.
Service Life	The actual service life of a membrane is closely linked to several factors, including robustness of membrane materials, chemical compatibility of the membrane with process and sanitization streams, as well as overall quality and consistency of the micro-structure.

It's our job to understand all of the steps, how they work together, and how to keep them in control. We'll work closely with you to design and optimize your process and speed your time to market, and can help you select the right membrane and device for your specific application. We can also offer advice about scale-up, cleaning, validation and anything and everything else related to your TFF membrane process.

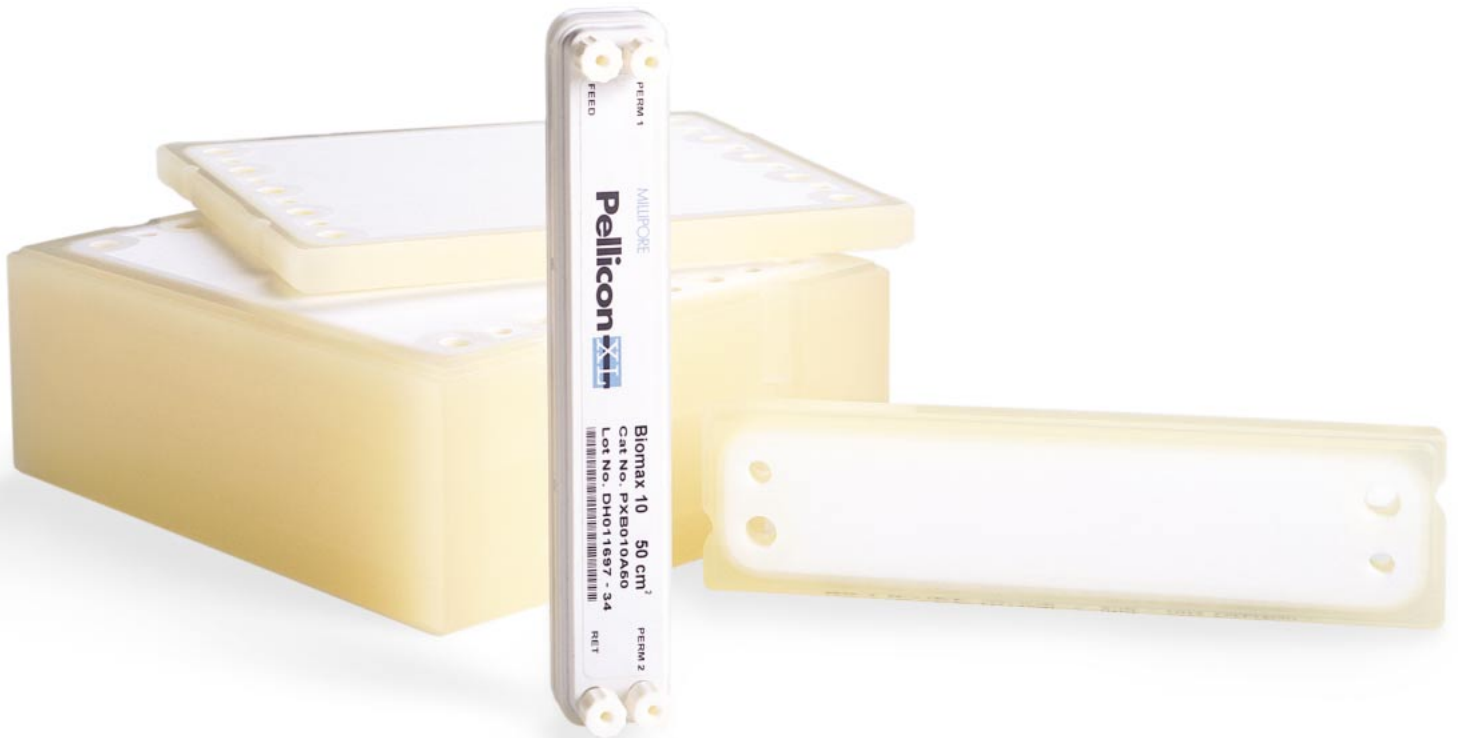


Access Pharmaceutical Services, a Unique Business Advantage

Millipore offers a comprehensive program of applications engineering support, at our own extensive facilities as well as at customer locations. These services include:

- Applications engineering to help integrate and optimize the use of advanced TFF technology in your facility
- Installation and operational qualification services, with complete documentation and testing packages
- Training on TFF process scale-up, optimization, validation and development

TFF bioprocessing from benchtop through manufacturing



Millipore TFF membranes are playing an important role in the biopharmaceutical industry at every scale, from discovery through full commercialization.



Biomax, Ultracel PLC and other TFF membranes are available in a wide variety of devices, to meet every process need from benchtop R&D through full-scale manufacturing.

Laboratory and Pilot scale systems are available to meet your process development and Pilot production needs. ▶

Millipore also provides custom-engineered TFF systems optimized to take full advantage of our high performance TFF membranes. Systems are available in every volume range, from milliliters through thousands of liters.



- Concentration, clarification and desalting of proteins and other biomolecules
- Buffer exchange
- Pre-chromatographic clarification to remove colloidal particles
- Depyrogenation
- Cell harvest, washing and clarification
- Harvest of virus particles for vaccine manufacture

To Place an Order or Receive Technical Assistance

For additional information call your nearest Millipore office:

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1-800-MILLIPORE (1-800-645-5476)

In the U.S., Canada and Puerto Rico, fax orders to
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You'll also find a wealth of information on our web site at
www.millipore.com

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