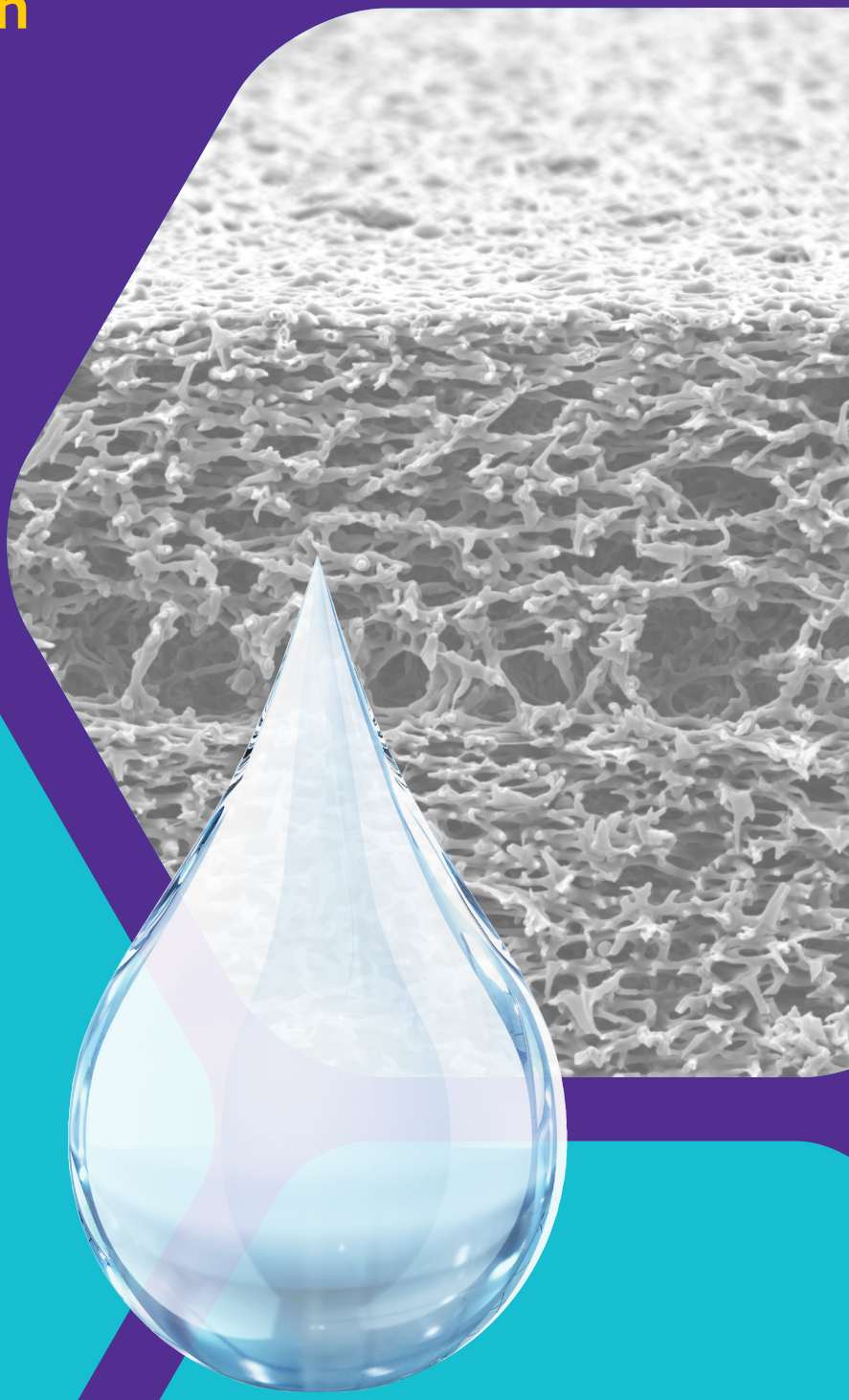
MilliporeSigma

A clarifying guide to

Membrane Filtration



The life science business of Merck KGaA, Darmstadt, Germany operates as MilliporeSigma in the U.S. and Canada.

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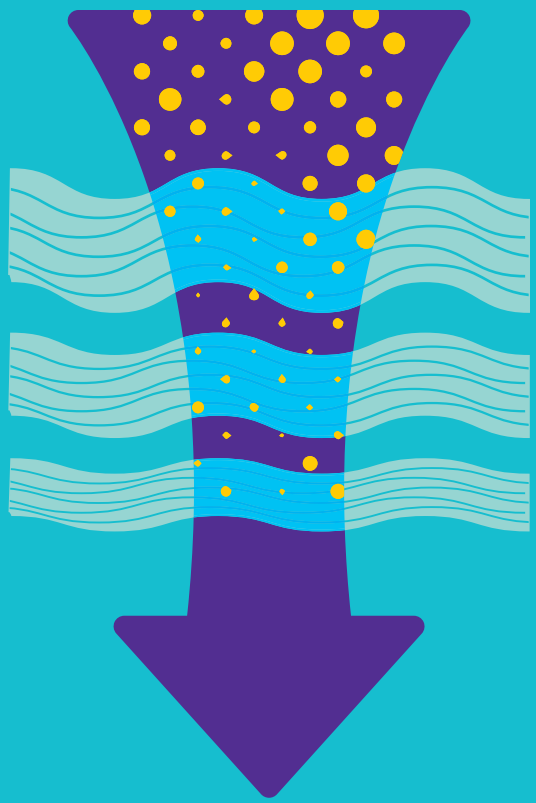
Table of Contents

More than 60 years of membranes—for filtration, and beyond

The history of filtration can be traced to the earliest civilizations for which there are written records, when materials like cloth were used in efforts to strain water and make it safer for human use. MilliporeSigma's role in the development of modern filtration dates to the early 1950s, when the Lovell Chemical Company, a small business located near Boston, Massachusetts, won a contract with the U.S. Army Chemical Corps to develop and manufacture membrane-based filtering devices that could be used for rapid and sensitive detection of microorganisms in drinking water. When this membrane technology was declassified in 1953, Jack Bush—a Lovell employee—acquired the rights and established the Millipore Filter Company.

In 1955, the Millipore Company filed its first patent for microporous nylon film, and went on to supply membranes used in the development of popular nucleic acid and protein blotting techniques. In a 1975 paper, Prof. Edwin Southern published the Southern blot technique for electrophoretic DNA detection using Millipore® nitrocellulose membranes. Prof. Harry Towbin's signature 1979 publication of the Western blot protein detection method (so named by W. Neal Burnette, a scientist who published on the technique from a different laboratory) also featured Millipore® nitrocellulose membranes. Both techniques were optimized in the 1980s on polyvinylidene fluoride (Durapore® PVDF) membranes, which were first introduced by Millipore Corporation.

Since its inception, Millipore Corporation (now MilliporeSigma) has pioneered the use of membrane technology in hundreds of diverse applications, and established itself as the industry leader in filtration with innovations like Millex® filters, the first disposable syringe filtering devices; the iconic Stericup® filter units; and Milli-Q® systems, the first lab-scale ultra-pure water solutions. Laboratories across academic, pharmaceutical, biotechnology and industrial sectors rely on MilliporeSigma as a trusted partner for high-performance, specialty membranes and filter devices. Today, our research and development scientists remain committed to membrane science—stay tuned for another six decades of innovation in filtration.



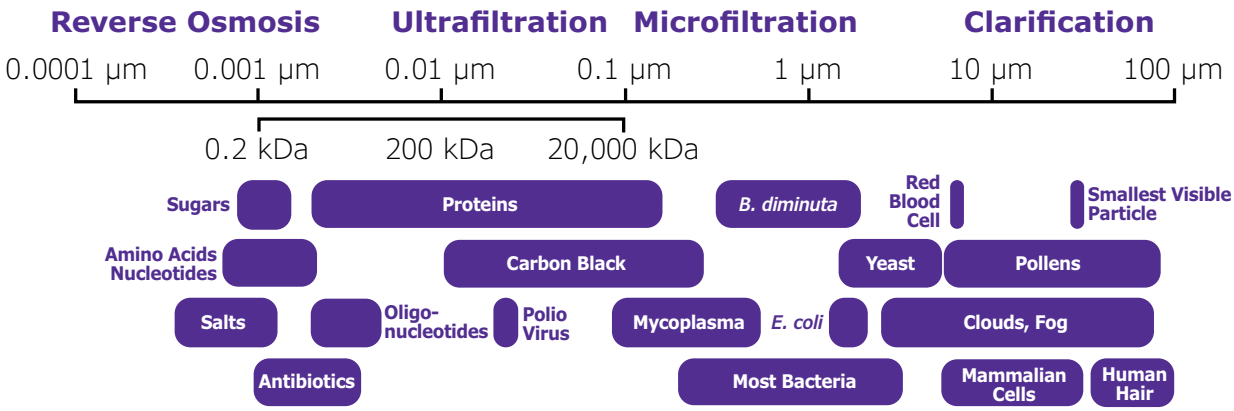
Why membrane performance matters

Filtration is the process of separating solids from fluid states of matter (liquids and gases), and serves a vital role not only in making water safe for human use, but in chemical, biological, and industrial applications. Filtering buffers, media and other reagents removes cells, cell debris, and other contaminants that can jeopardize experimental results or accelerate equipment wear.

True filtration is a physical process

Filtration involves passing a solution through a porous layer that retains undesirable particles, while allowing fluid to pass. It differs from sieving, which uses a single porous layer to trap particles larger than the barrier perforations. It is also unlike adsorption, where particles in the feed fluid bind to an adsorptive matrix based on their charge, and become trapped.

The process of filtration is deceptively simple, with much more to consider than coupling a selectively permeable membrane to a collection reservoir. The remarkable diversity of available filter devices is tied to the complex and distinct membrane technologies at work at the macro- and microscopic levels. Membranes remove impurities from sample that may affect critical biological and chemical determinations, downstream analysis, and assay performance. Because impurities may be ionic, molecular, or particulate, the right filter choice can make a significant difference in yields, reproducible results, and filtrate quality. This guide will help you navigate the intricate world of membranes used in filtration devices—and maybe, along the way, you'll become as fascinated with membrane design as we are.



Types of filtration

Filtration methods vary depending on the size of the particle to be removed from a solution. Four types of filtration by increasing target particle size are: reverse osmosis, ultrafiltration, microfiltration, and clarification (see preceding figure, and below).

Reverse osmosis
(ionic separation)

- Separates ions or molecules using a semipermeable membrane or barrier. Applied pressure overcomes osmotic pressure and forces solvent to move from a high solute concentration to a low solute concentration
- Rejects a high percentage of organic matter, other particulates, and >99% of salts
- Typical rating is based on sodium chloride retention: ≤ 0.001 µm (<100 Daltons)

Ultrafiltration
(macromolecule separation)

- Separates particles and dissolved molecules from fluids based on particle size
- Used for concentration, fractionation, desalting, and buffer exchange
- Carried out in pressure-driven, vacuum-driven or centrifugal devices
- Typical rating: 0.001–0.05 µm (1–1,000 kDa Nominal Molecular Weight Limit [NMWL])

Microfiltration
(particle retention/exclusion & sterilization)

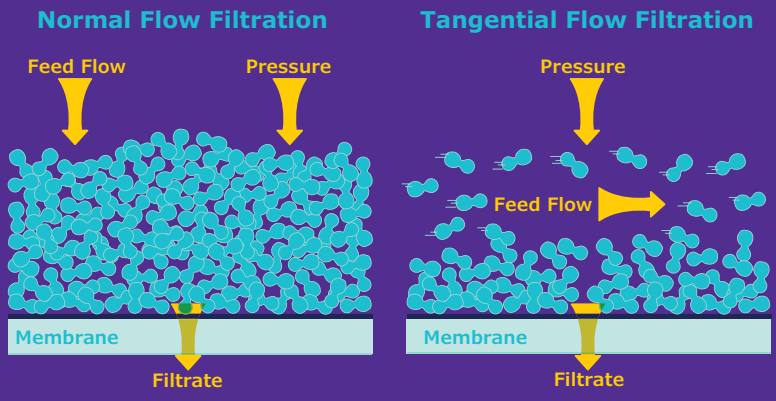
- Separates/removes particles (both rigid and deformable types) and biological entities—such as bacteria and cells—based on particle size
- Carried out in syringe, multi-well plates, filter units, or disc filters
- Typical rating: 0.025–10 µm; and rated as nominal (~98% retention) or absolute (100% retention of the size equal to the pore size rating)

Clarification filters
(pre-filtration, particle analysis)

- Retains/removes large particles, aggregates, and debris based on size
- May serve as a primary filtration step before microfiltration
- Carried out in syringe filters, multi-well plates, or disc filters
- Typical rating: > 5 µm

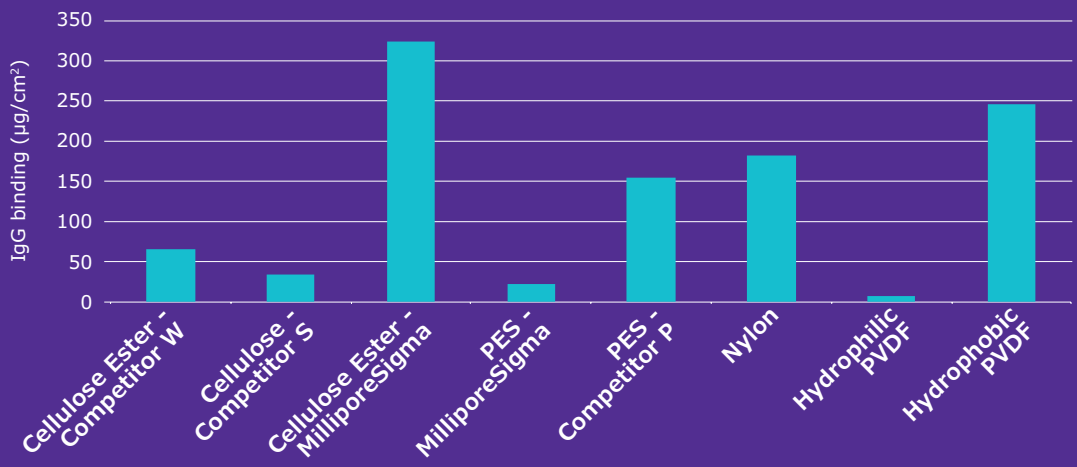
Directional flow in ultrafiltration

Ultrafiltration membranes are commonly used in the purification of precious biomolecules. During ultrafiltration, it is important to balance flow rate, or flux, with retention in order to ensure optimal performance. A membrane's flux is defined as flow divided by the membrane area. Flux is used with ultrafiltration membranes to enable scalability.



Protect your proteins

Microfiltration membranes are often used to filter cell culture media containing protein additives, such as those in serum supplements. Researchers must be confident that when cell culture solutions are filtered, whether to ensure sterility and/or to remove particulates, desirable proteins are not lost to adsorption onto the membrane. For example, concentrations of growth factors needed to maintain special cell types must remain constant before and after filtration. Membrane material selection is therefore critical for minimizing unintentional loss of proteins to the filtration process.

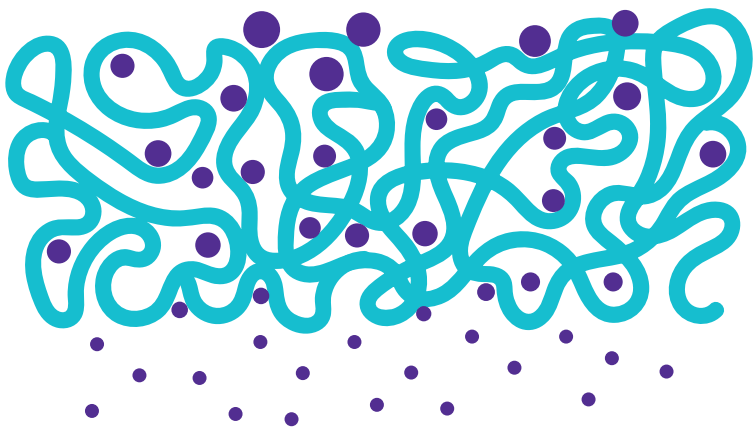


Factors to consider for microfiltration

Microfiltration removes particles or biological entities in the 0.025 µm to 10.0 µm range from fluids or gasses by passage through a microporous medium, such as a membrane filter. Although micron-sized particles can be removed by non-membrane or depth materials such as those found in fibrous media, only a membrane filter having a precisely defined pore size can ensure quantitative retention.

Sample characteristics: The choice of microfiltration membrane depends on sample characteristics, composition, and volume. Both the solute and the dissolved molecules or particles of the sample to be filtered must be chemically compatible with the filter membrane.

Throughput & flow rates: Flow rate refers to the time it takes for a particular flow stream to pass through the filter. Flow rate depends on membrane thickness, porosity, and pore architecture as well as sample viscosity and other physicochemical characteristics.



Depth filters randomly entrap particles, as shown in this cross-sectional schematic

Membrane pore size: Pore size determines the filter's ability to filter out particles of a certain size, measured by diameter. 0.1 and 0.2 or 0.22 µm pore size membranes are rated as sterilizing grade, whereas 0.45 µm membranes are considered general purpose filters.

Membrane wettability: For liquid filtration, a membrane must be wettable with the fluid being filtered. The wettability of a membrane is dependent on the chemical properties of the membrane surface. Most sterile filtration applications require hydrophilic membranes, which allow for direct filtration of aqueous samples.

Fouling characteristics: The susceptibility of a membrane to fouling, or becoming clogged, depends on characteristics like membrane composition and pore structure. For example, if an asymmetric membrane is used in the wrong orientation (with smaller pore openings at the top, or 'feed' side), this may cause fouling.

Prefiltration: Prefiltration with a depth filter (see membrane characterization, page 11) prior to microfiltration helps remove most particulates, and prolongs the life of downstream filter membranes. Prefiltration may also be carried out using a large pore (5 – 10 µm) membrane.

Membrane support: Optional support screens and discs can be used to provide added strength to thin membranes.

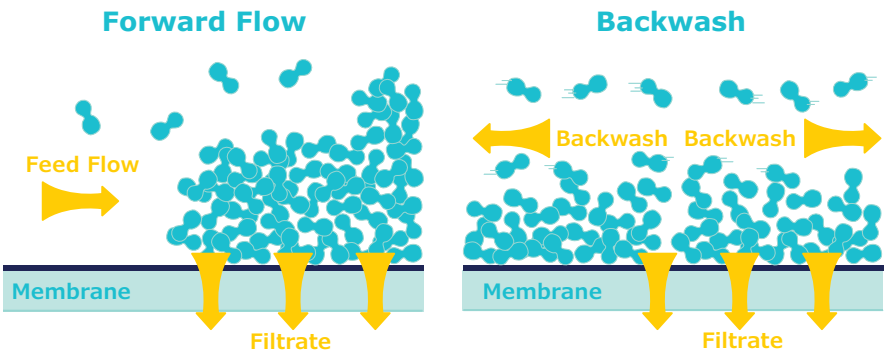
Backwashing: For some filtration applications, the particles that collect on the membrane must be removed. Symmetric membranes can be used in both directions and are more amenable to backwashing compared to asymmetrical membranes (learn more about membrane pore symmetry on page 13).

Cross flow: In a cross flow system, particulates are swept away from the membrane surface for improved throughput. By contrast, particulates collect on the membrane of a dead-end flow system and can cause fouling.

Agitation: Sample agitation (e.g., vibration, stirring, and ultrasonic agitation) improves throughput by preventing particulates from aggregating on the membrane surface.

Flow rate and filter life: Particulates can slowly build up on the membrane surface, forming a compacted filter cake layer that reduces flow rate. Adjusting the flow rate per unit area of filter surface can improve throughput. A larger filtration area allows particulate distribution, lending to increased throughput.

Scale of filtration system: A pressure drop in the filter media or holder/housing can occur in smaller filter systems. Scaling up the size of filter membranes, holders/housings, and filter devices will improve pressure.



Factors to consider for clarification

Bioburden and unwanted particles can affect downstream product quality and foul your membrane filter, reducing its effectiveness and service life. Clarification and prefiltration are critical steps that remove these contaminants early in the process, extending the life of downstream/terminal filters.

Sample input & composition:
An important consideration when choosing a membrane for any application is the chemical compatibility of the membrane material with the mobile phase of the solution. In order to minimize the risk of structure failure during filtration, the liquid being filtered must not be chemically reactive with the membrane. Although this is typically a concern for the liquid phase of the sample, dissolved solutes may also be reactive with the membrane chemistry.

Benefits of using prefiltration/ clarification filters:

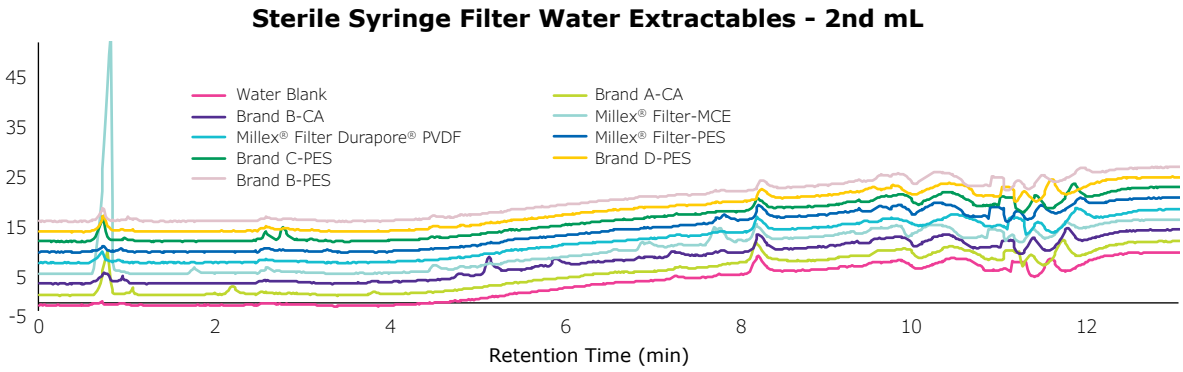
- Extend the lifespan and throughput of downstream filters
- Aids in the reduction of potential fouling or clogging of microfiltration membranes

Pre-filtration membrane structure and composition factors:

- Dirt or particle retention capacity
- Tendency of fiber materials (such as glass) to shed particles (see extractables, below)
- Predisposition for nonspecific adsorption of molecules

Device extractables: don't believe in ghost peaks

Clarified filtrates may contain extractables, which are contaminants that originate from the filter or device itself. Extractables can be produced by shedding of filter materials (for example, polymer particles from membranes or fibers from nonwovens), residual chemicals from the manufacturing process, or by secondary chemistries washed off the filter. Extractables may be responsible for unexpected traces in downstream HPLC analysis of filtrate.

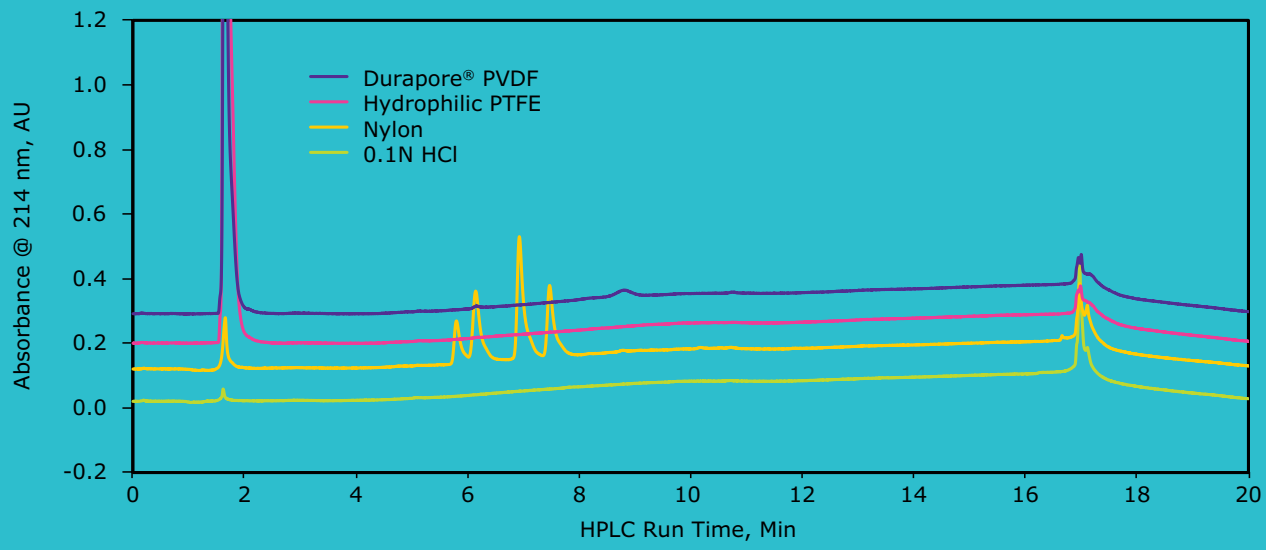


Comparison of extractables from syringe filters from various manufacturers. Water was used as the extraction solvent. All syringe filter devices show different levels of extractables which can impact the downstream analysis. Durapore® membrane-based syringe filter devices (MilliporeSigma) demonstrate the very low level of extractables that are desired for valid downstream analysis following filtration.

(CA=cellulose acetate; PVDF=polyvinylidene fluoride; PES=polyethersulfone; MCE=mixed cellulose esters)

Filtration prep tip:

In many cases, **extractables** can be significantly **reduced by preflushing** the syringe filter with a few milliliters of the sample to be filtered.



Nylon membrane-based syringe filter devices frequently demonstrate higher levels of extractables. Data above shows HPLC peaks due to extractables from syringe filter devices that use nylon membranes, with or without glass fiber pre-filtration.For more about extractables, see page 16.

Membrane manufacturing methods

Membrane diversity arises from composition, pore structure and morphology, which take form based on the specific manufacturing technique used (see below). Some of the processes used to create common membranes are as follows:

Solvent-cast method

- Membrane forms as a precipitate when a polymer solution comes in contact with a non-solvent
- Used to create polyvinylidene fluoride (PVDF), polyethersulfone (PES), and nylon membranes

Air-cast membranes

- Membrane forms as a precipitate when a polymer solution comes in contact with air as non-solvent
- Used to create mixed cellulose esters (MCE) membranes

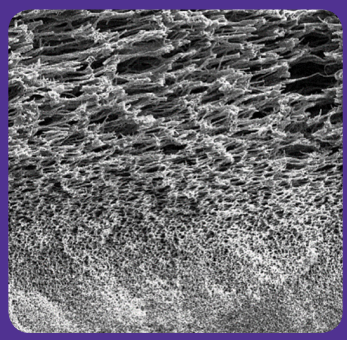
Expansion under heat & pressure

- Membrane forms when a thin polymer film is stretched under heat and pressure to create a porous structure
- Used to create polytetrafluoroethylene (PTFE) and polyolefin membranes

Track-etched membranes

- Membrane forms using a combination of charged particle bombardment followed by chemical etching to create uniform pores
- Used to create polycarbonate and polyester membranes

Other methods for manufacturing microporous membranes include melt phase inversion method (polyethylene membranes), electrospun nano fiber membranes (nylon), and sintering (PTFE).



Structure of a solvent-cast membrane

Scanning electron microscopy reveals the pore structure of a polyethersulfone membrane formed by the solvent cast technique.

Manufacturing expertise:

Equipment in our manufacturing clean rooms is engineered and maintained to exacting specifications to ensure membrane integrity and lot consistency.

How are membranes characterized?

Physical parameters:

- Thickness — Depending on the filter type, the thickness of membrane filters ranges from 10 to 170 µm. Depth filters can range between 100 and 500 µm in thickness.
- Mechanical properties — Membrane mechanical properties like tensile strength and elongation are generally not critical factors for basic filtration, but may be critical for manufacturing devices.
- Porosity — Porosity refers to the number of pores (as a percentage of the open area) in a membrane. It also indicates how much air content is present in the membrane, which is directly proportional to flow rate. The majority of solvent-, air-, and, heat-cast membranes (PVDF, PES, Nylon, MCE, and PTFE) have ~65–85% porosity, and hence 65–85% air content and higher flow rate. However, track-etched membranes (PC and PET) contain only ~5–15% porosity.

Pore Structure:

The majority of membranes have an irregular pore structure as visualized by SEM images (see photos on page 13), creating a tortuous flow path for particles or cells. However, the pores of track-etched membranes, which are created by high energy radiation, are uniform and cylindrical.

Pore size:

Pore size relates to the filter's ability to filter out particles of a certain size; for example, a 0.2 µm membrane will filter out particles with a diameter of 0.2 microns or larger. Pore size is a critical variable as it defines the membrane retention and flowrate properties.

Composition:

The chemical composition of a membrane determines its compatibility with solvents, binding properties, and wetting characteristics. Incompatible solutions or solvents can dissolve/damage the membrane, or reduce membrane performance by absorbing into or altering the polymer matrix.

Flow vs. flux (air vs. liquid):

Depending on the application and chemical composition of the membrane, air or water/solvent flow rate provides information about filtration capacity. With air flow, a critical factor to consider is pressure drop across a membrane as air flows through it.

Binding characteristics (non-specific adsorption of molecules to filter membranes):

Small molecules, proteins, and nucleic acids bind to various membranes differentially, depending on the physiochemical properties of the analyte, solvent, and membrane materials. Since a membrane disc has limited surface area, no further binding occurs once all the surface sites are saturated. This information is useful when trying to reduce or eliminate analyte binding to the membrane.

Chemical compatibility & extractables:

Extractables are impurities that leach out of a membrane when it is exposed to certain solvents/solutions, and that impact downstream analysis. Although most extractables are low molecular weight compounds, some can be polymeric in nature. Extractables are related to chemical compatibility; solutions that alter the membrane structure can cause leaching.

Transparency:

Membranes can become transparent when treated with special solvents that alter the refractive index of the membrane material. For instance mixed cellulose ester membranes become transparent when treated with acetone / triacetin or Polycarbonate membranes can be made transparent when treated with immersion fluids.Transparency is critical for microscopy applications.

Membrane Integrity Testing:

Integrity testing of filters is fundamental to process filtration applications in the pharmaceutical industry, and may be classified as destructive or non-destructive. Destructive challenge testing (in accordance with ASTM F838-83 methodology) is the best way to determine a sterilizing filter's bacterial retention capacity. The three types of non-destructive integrity tests are the bubble point test, the diffusion test, and the water flow integrity test for hydrophobic filters.

How is pore size measured?

Bubble point:

Bubble point is a practical, nondestructive test used for estimating the pore size of microporous filters. This test measures the minimum pressure required to force liquid out of the pores as an indirect survey of pore size. Bubble point is inversely proportional to pore size (i.e., a high bubble point is indicative of a small pore size). Importantly, this test provides information about the largest pore in a membrane, since the largest pore requires the lowest pressure to push liquid through.

Bacterial/Mycoplasma Challenge:

This test determines the minimum particle size that a filter can retain by challenging the membrane with micro-organisms of a defined size. Testing is carried out in accordance with the following criteria:

- **Bacterial Retention** (*Brevundimonas diminuta*, ATCC 19146 Health Industry Manufacturers Association [HIMA] challenge equal to or exceeding 1.0×10^7 cfu/cm^2 of effective filter area, Microbiological evaluation of filters for sterilizing liquids. No. 3, Vol. 4, April 1982. 34 pp)
- **Mycoplasma Retention** (*Acholeplasma laidlawii*, ATCC 23206, challenge equal to or exceeding 1.0×10^7 cfu/cm^2 of effective filter area)

Scanning Electron Microscopy (SEM):

A small section of the membrane is appropriately treated and evaluated by scanning electron microscope. This technique measures pore diameter of surface pores and pore size distribution.

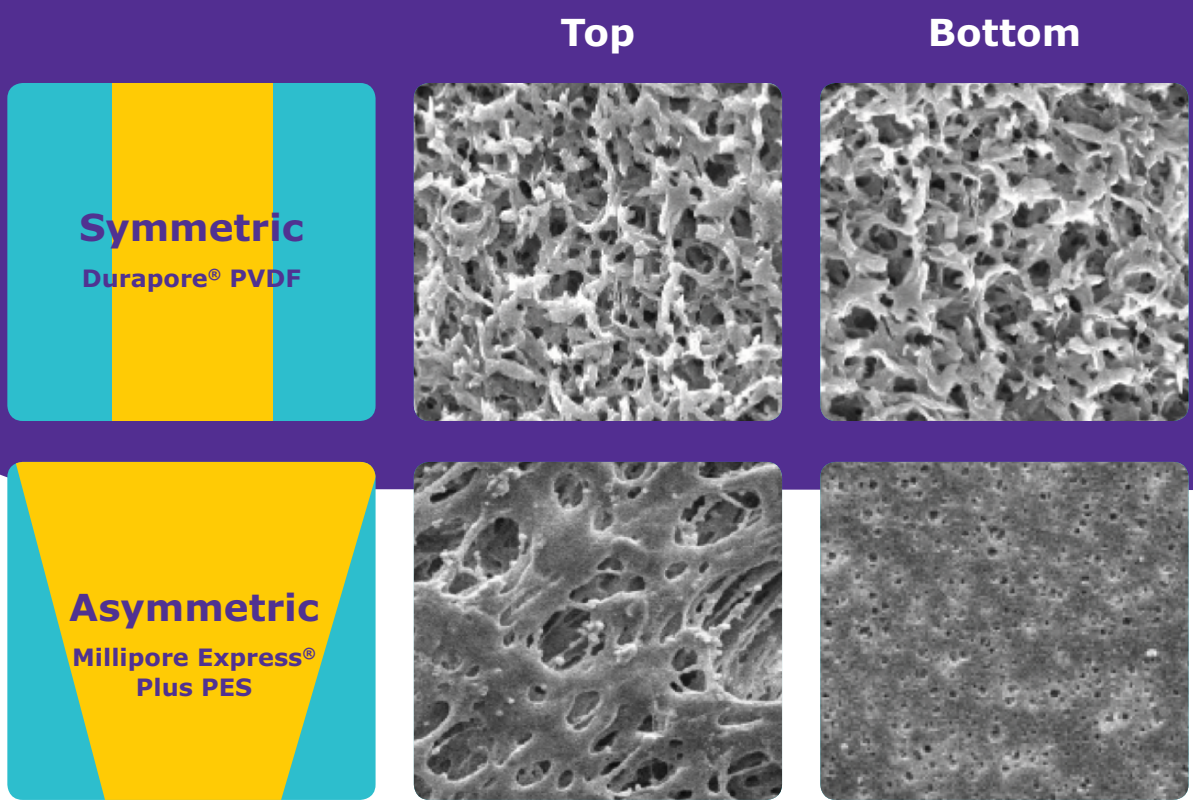
Porosimetry:

In this physical method, liquid is forced into the membrane under pressure and the penetration profile is analyzed mathematically to determine pore size. This technique measures pore volume and associated pore size distribution.

Instruments for testing bubble point include a simple bubble point test apparatus, left (Fisher Scientific Cat. No. XX6700L55), and the Integritest® 5, above, an easy-to-use, portable and fully automated integrity test system for verification of filters and processing equipment.

Membrane throughput: What's structure got to do with it?

Membrane design can significantly impact the filtration process with respect to flow rate, analyte binding, and volume retention. Depending on the manufacturing process, pore structure can be symmetric or asymmetric. In a traditional symmetric design (for example, Durapore® PVDF membrane, upper panel below) the membrane pores have a consistent throughout the thickness of the membrane. However, in an asymmetric structure (like Millipore Express® Plus PES, lower panel), membrane pores are wider at the top or feed surface of the membrane, where filtration starts, than at the bottom. Microscopy images of an asymmetric structure (below, top row) show that the mean pore diameter decreases from the pre- to the post-filtration side. In addition to yielding faster flow rates, membrane asymmetry increases filtration capacity and extends useful lifetime by permitting the membrane to tolerate higher particle loads and protein concentrations.



Architecture matters. Different membranes can vary with regard to pore structure across their thickness. In the SEM images shown above, Durapore® PVDF membrane shows symmetric pore structure across thickness of the membrane, so the top and bottom membrane surfaces appear similar. In contrast, the Millipore Express® Plus PES membrane (lower panel) is manufactured with an asymmetric pore structure. Larger pore openings at the feed surface increase flow rate, and pore diameter narrows toward the bottom surface of the membrane to exclude contaminants from the filtrate.

Characterization of membrane sterilizing grade

Bioburden

This test estimates the number of viable microorganisms in or on a medical product, device, or raw material before sterilization. It is performed by extraction using the immersion method, and by enumeration using the membrane filtration method. Bioburden is crucial to sterilization dosing and routine tracking of bioburden levels in a quality program.

Endotoxin level

- **Endotoxin (Gel Clot Method), a compendial method as per USP <85>**

  The limulus amoebocyte lysate (LAL) gel clot technique detects endotoxins based on clotting of the lysate reagent in the presence of endotoxin. This assay is derived from the biology of the horseshoe crab (*Limulus polyphemus*), which produces LAL enzymes in blood cells (amoebocytes) to bind and inactivate endotoxins from invading bacteria. This immune reaction produces clots, which are detected in the LAL test. The minimum concentration of endotoxin required to cause the lysate to clot under standard conditions is the labelled sensitivity of the lysate reagent (λ).

- **Endotoxin (Kinetic Turbidmetric Method), a compendial method as per USP <85>**

  The kinetic turbidimetric assay detects the presence of bacterial endotoxin over time by monitoring the increase in sample turbidity when sample is mixed with LAL reagent. The reaction time is inversely proportional to the amount of endotoxin present. The amount of endotoxin in an unknown sample is calculated by comparing its reaction time to the reaction time of standard solutions with known concentrations of endotoxin.

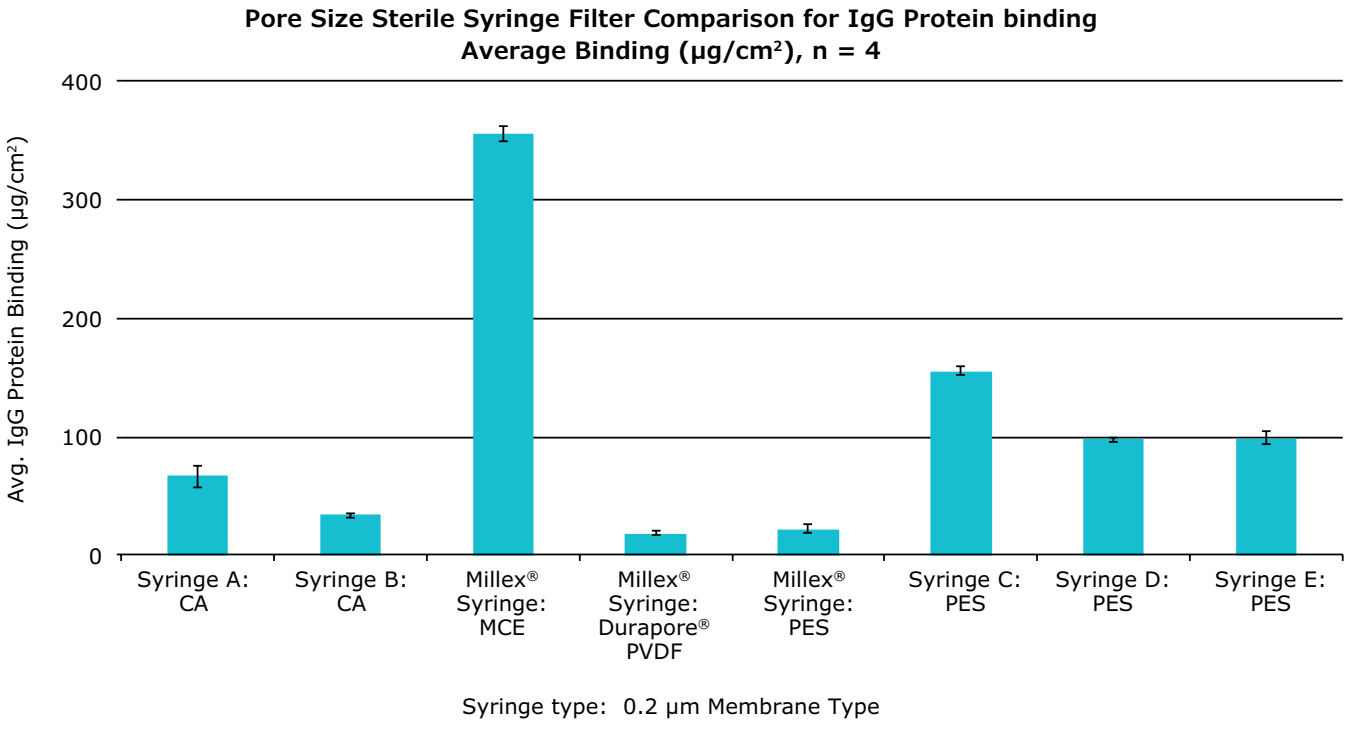
Sterile membranes: not born that way

Most membrane-based devices are supplied non-sterile or sterile. When an application requires sterile filtration, filter devices are typically sterilized by three common methods: Gamma radiation, ethylene oxide (EtO) exposure, or steam exposure (autoclaving). Of these, gamma radiation and ethylene oxide methods are used on an industrial scale so that the product received by the customer is already sterilized and ready for use. Steam sterilization (autoclaving) can easily be performed by the user, even if the devices are purchased non-sterile. In most cases, membrane composition and the device type dictate the method used for sterilization.

Protein binding characteristics

When filtering a sample containing analytes or other valuable components, it's important to be ensure that these analytes are not lost by binding to the filtration device, and that the molecular composition of the filtrate is not altered by the process of filtration.

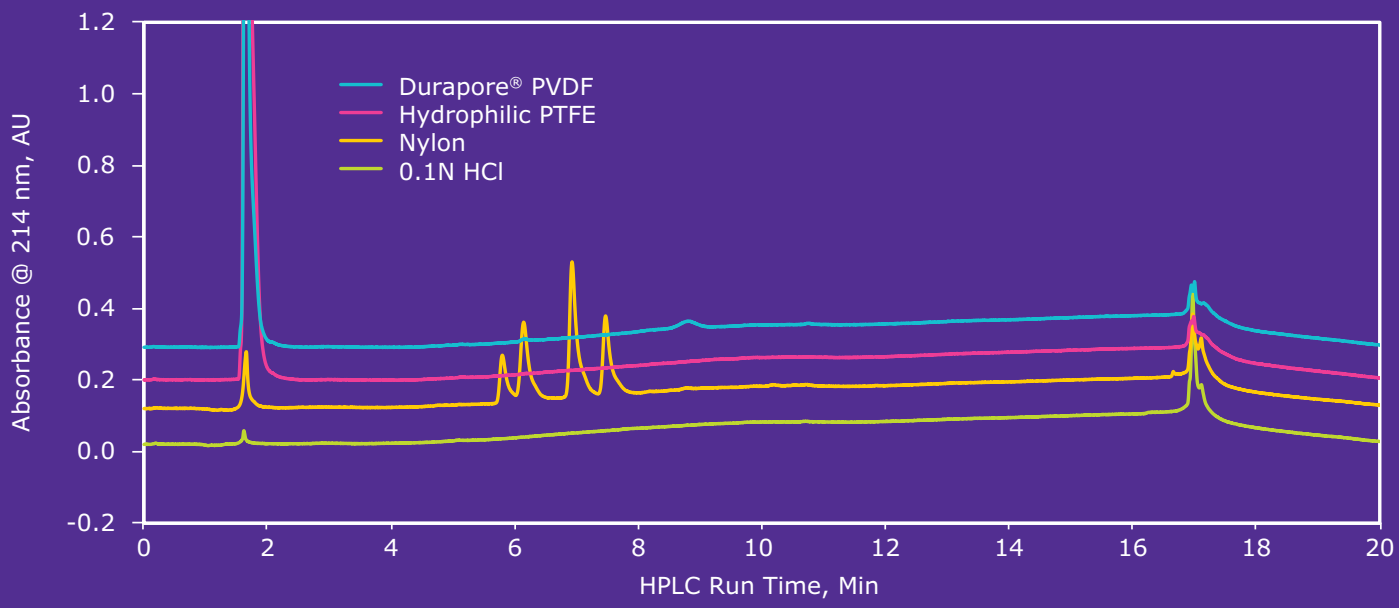
Because the internal surface area of polymeric microporous membranes is 100 to 600-fold greater than the frontal surface area, a vast surface area is available for nonspecific binding. Of all membranes evaluated, the hydrophilic PVDF microporous membrane was found to be extremely inert, with the lowest protein binding properties and the highest product recovery.



(CA=cellulose acetate; MCE=mixed cellulose esters; PVDF=polyvinylidene fluoride; PES=polyethersulfone)

Membrane selection tip

The binding of small molecules is dependent not only on the membrane, but on solution characteristics. Consider analyte properties when choosing a filter device to ensure compatibility of solution with the membrane and to ensure maximum yield.



Membranes may leach extractable impurities depending on the interaction of the membrane chemistry with the solution that passes through it during filtration. Here, chromatography reveals four extractable peaks resulting from the filtration of a given solution through a nylon membrane (yellow trace) that are not present following filtration with PTFE (magenta trace) or Durapore® PVDF (blue trace) membranes. For this filtration application, a membrane demonstrating few or no additional peaks compared with the control (green trace) may be the best choice.

Filtration device construction and characterization

Choosing a device for laboratory filtration tasks starts with selecting appropriate pore size and membrane composition. The need for sterile filtrate, as well as the volume of the buffer, media or other reagent to be filtered is used to determine the optimal device from amongst diverse formats such as syringe filters, vacuum filters with bottle receivers, filter tops for reusable labware, and more. Finally, chemical compatibility of the solution with the membrane informs selection of appropriate filtration device.

Housing and seal composition

Regardless of the scale of the filtration process, the filter is housed in a device so that the device can:

- provide mechanical support for the filter, without which most filters would rupture under the forces they endure during use
- incorporate a mechanism to seal the edge of the filter so that liquid flow is exclusively through the filter. If the liquid flows around the edge of the filter, the filtrate is contaminated.

Sealing

There are several ways to seal a filter into a housing. Reusable devices can be constructed of glass, plastic, or stainless steel. The filter is placed into the base of the unit with a gasket or o-ring that covers its perimeter. The top of the unit is screwed or clamped into place, and the pressure of the closure seals the edge of the membrane. Assembly of the unit needs to be done carefully to prevent movement or distortion of the filter.

For fabricated devices, the filter is most commonly sealed with adhesives, direct bonding, or overmolding.

Adhesives

Adhesive is applied to the perimeter of the filter to provide an impenetrable barrier between the housing and the filter, with some adhesive flowing of necessity into the porous structure of the filter. An advantage of an adhesive is that it allows the bonding of different types of filters into a single device.

Direct bonding

In direct bonding, ultrasonic welding or heat sealing is used to bond the filter directly to the plastic housing in a single step. Because this method involves localized melting of the housing and/or filter, it is best suited to membrane and thin, nonwoven filters. The polymer used in the filter and the housing have to be selected for compatibility with each other so that a strong, integral bond can be formed. The advantage of direct bonding is that the seal is formed immediately without any requirement for further processing. Thick filters and non-polymeric filters cannot be sealed by this technique.

Overmolding

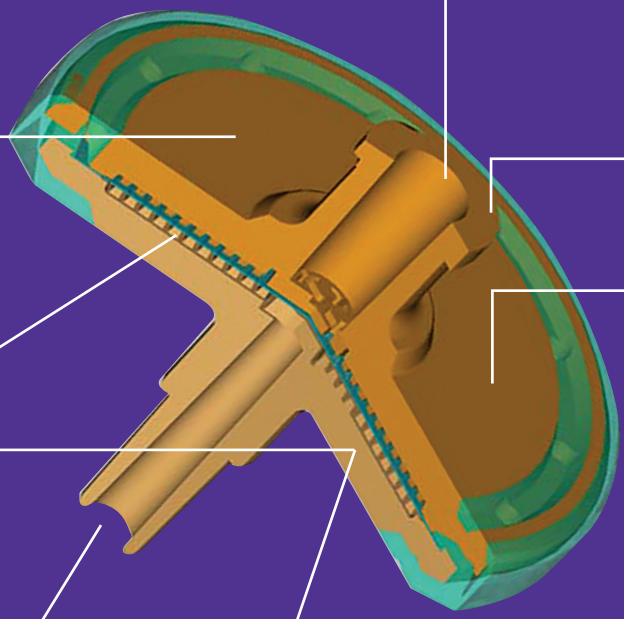
Overmolding is a simplified process for sealing a filter into a device. Plastic is molded around the filter and other parts of the housing to form an integral seal and a complete device in one step. As the liquid plastic fills in the air spaces between the parts of the housing, it also penetrates into the edge of the filter

Regardless of the method use to seal the filter into a device, the seal must be integral, meaning that nothing may pass through it—and the process cannot introduce holes in the filter. The efficacy of the sealing process can be assessed in an integrity test. This method involves pressurizing a finished device on one side of the filter and measuring the rate of liquid or air passage on the downstream side.

Anatomy of a Millex® filter

Reliable syringe filtration requires thoughtful device engineering that incorporates robust housing design features which will:

- **Prevent leakage**
- **Minimize holdup volume**
- **Ensure high particle retention**
- **Tolerate high operating pressures**
- **Reduce extractables**



Improving Throughput: Choose a Millex® Filter Based on Sample Volume

Sample Volume	Filter Size	Hold up Volume (after air purge)	Filtration Area
< 1 mL	4 mm	10 µL	0.1 cm^2
1–10 mL	13 mm	25 µL	0.65–0.8 cm^2
10–100 mL	25 mm	100 µL	3.9–4.0 cm^2
10–200 mL	33 mm	80 µL	4.5 cm^2

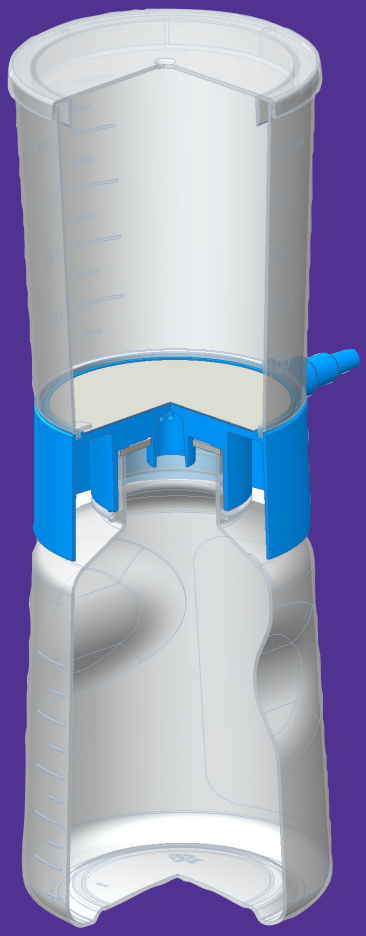
A closer look at Stericup® filters

Stericup® filters are known to research scientists worldwide for reliable, high-performance membranes and optimum sterile filtration.

The systems combine a Steritop® filter unit with a receiver bottle for filtering and storing volumes up to 1000 mL, and are ideal for sterilization and/or clarification of buffers, cell and tissue culture media and other aqueous solutions.

The recently introduced Stericup® Quick Release filters are the next generation of the original Stericup® systems, delivering ergonomic design updates to optimize user control and streamline the filtration process — all while safeguarding results with the proven performance of Millipore® membranes.

- **150 – 1000 mL capacity filter cup and receiver bottle offer the right volume for diverse buffer, media, and reagent solutions.**
- **Vacuum-aided filtration speeds flow rate and reduces holdup.**
- **A broad selection of filter compositions and pore sizes ensure fast flow, low protein binding, and appropriate exclusion of contaminants from filtrate.**



Factors to consider when choosing membrane filtration

Membrane surface area

Expanding the filter surface area increases filtration flow rate and throughput. Larger membrane surface area also facilitates processing of difficult-to-filter solutions, as it reduces the pressure required to pass the sample across the membrane. This can be particularly important for syringe filtration. When it is critical to retain protein and other biomolecule concentrations with no loss to the filtration process, it may be preferable to decrease surface area and to select very low-binding membrane materials such as PVDF.

Sample volume

Filter device selection must consider both the input and expected output volumes of feed and filtrate, respectively. Samples as small as few milliliters are typically filtered by pressure filtration using a syringe; larger volumes may be filtered by gravity, or aided by vacuum or pressure into receiver flasks, which may be supplied sterile, and may be single-use or resuable.

Chemical composition of sample and membrane compatibility

Filter material must be compatible with the chemical nature of the liquid being filtered, and for the conditions under which the filtration will be performed. This will minimize the risk of membrane and/or device structural failure during filtration.

Although chemical compatibility usually addresses the liquid phase of the sample, dissolved solutes may interact with the membrane in an undesirable manner. The solute of interest should not be adsorbed onto the surface of the filter. Most polymers used to make filters are highly adsorptive for biomolecules and will bind them out of the sample stream until the polymer surface is saturated. If a low binding surface is required, this property should be considered during the selection process.

In venting applications, hydrophobicity of a filter is used to allow release of air bubbles from a liquid stream. The sample stream should not contain detergents or solvents that will wet out the surface of the filter.

Filtration mode of operation

Depending on parameters of the filtration task such as volume and throughput, filtration may proceed via gravity, or may be aided by the application of positive pressure, as in manual syringe filtration. Vacuum filtration can speed the flow of sample across the filter, and this force applied from the filtrate side of the membrane may reduce holdup volumes and improve filtrate yield.

Normal Fluid Filtration [NFF] vs. Tangential Flow Filtration [TFF]

In tangential flow filtration (also known as cross-flow filtration), the direction of the feed solution flow is tangent to the filter surface, in contrast to normal fluid filtration (NFF), in which the feed flows perpendicular to the surface of the membrane. This redirecting of the feed flow prevents buildup of solids on the membrane which can form a filter cake. This method may be preferable for high throughput applications where the feed is high in particulate solids, as it can extend filter life.

Sterile Filtration on all scales

Centrifuge and Vacuum Driven

media volume

1 mL	10 mL	50 mL	100 – 200 mL	150 mL – 1 L	2 – 10 L

Ultrafree®-MC and Ultrafree®-CL sterile centrifugal filters

Steriflip® Filter

Stericup® Quick Release and Steritop® Filters

Stericap™ PLUS Filter

Pressure Driven

media volume

1 mL	10 mL	50 mL	100 – 200 mL	<2 L	2 –20 L

4 mm Millex® Filter

13 mm Millex® Filter

25 mm Millex® Filter

33 mm Millex® Filter

Sterivex™ Filter

Steripak™ Filter

Sterile filtration solutions for the range of requirements:

Device Type	Maximum Sample volume	Membrane surface area, cm^2
Ultrafree®-MC	0.5 mL	0.2
Ultrafree®-CL	2 mL	0.8
Sterile Millex® (4 – 50 mm)	< 1 mL – 4 L	0.1 – 19.6
Steriflip®	50 mL	7
Sterivex™	1 or 2 L	10
Stericup® & Steritop®	150, 250, 500 & 1000 mL	40
Stericap™ Plus	2 – 10 L	40
Steripak™	Up to 20 L	100 – 200

Fit-for-purpose filtration starts with our Membrane Selection Guide

Prefiltration/Clarification

Hydrophilic

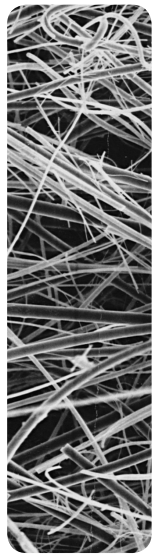
Hydrophobic

Particle size: 10 µm+

Examples: Large particles in environmental samples and industrial fluids, total suspended solids in wastewater, cell aggregates and multicellular organisms, pollen

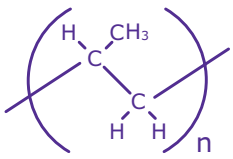
Filter type: Depth and net filters

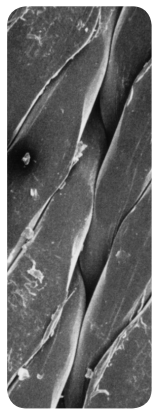
Glass Fiber Filters



Membrane Material	Borosilicate Glass or Quartz Microfibers
Pore Sizes (µm)	0.2 – 8.0
Thickness (µm)	230 – 1200
Water Flow Rate (mL/min/cm^2)	1.2 – 6.0
Air Flow (L/min/cm^2) @ 10 psi	10.6 – 139
Wettability	Hydrophilic
Temperature Limitations	500 – 950 °C max
Chemical Compatibility	Recommended for aqueous solvents
Sterilizability	Autoclave, EtO and gamma
Surface Option	White
Key Properties	Prefiltration down to 0.6 µm particles, high temperature-compatible and non-shedding options, pure and binderless materials
Key Applications	Toxic Characteristic Leaching Procedure (TCLP), Total Suspended Solids (TSS), heavy metals analysis, prefiltration, air monitoring
Devices	Millex® syringe filters, filter discs

Polypropylene Net Prefilters





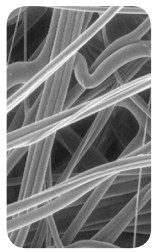
Membrane Material	Polypropylene
Pore Sizes (µm)	25 up to 80
Thickness (µm)	320 – 450
Wettability	Hydrophobic
Chemical Compatibility	Compatible with aqueous solvents
Sterilizability	Autoclave, EtO and gamma
Surface Option	White
Key Properties	Large pore size options, good solvent resistance
Key Applications	General prefiltration and clarification , suitable for organic solvents
Devices	Filter discs

Hydrophilic

Hydrophobic

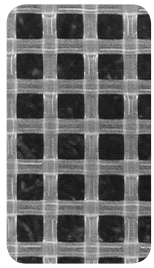
Polypropylene Prefilters

Membrane Material	Polypropylene
Pore Sizes (µm)	0.6 – 30
Thickness (µm)	95 – 145
Wettability	Hydrophobic
Temperature Limitations	90 °C max
Chemical Compatibility	Recommended for aqueous
Sterilizability	Autoclave, EtO and gamma
Surface Option	White
Key Properties	High particle retention and dirt-holding capacity, low pressure drop
Key Applications	General prefiltration and clarification, suitable for organic solvents
Devices	Filter discs



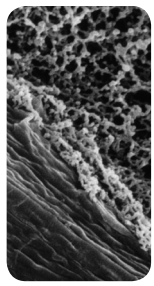
Nylon Net

Membrane Material	Nylon
Pore Sizes (µm)	10 – 180
Thickness (µm)	45 – 135
Porosity (%)	4 – 53
Wettability	Hydrophilic
Chemical Compatibility	Compatible with both aqueous and organic solvents
Sterilizability	Autoclave, EtO and gamma
Surface Option	White
Key Properties	Large pore size options, uniform pore structure
Key Applications	Cell collection, large particulate filtration, particle analysis, flow cytometry sample prep, toxicology and drug screening on *C. elegans* and zebrafish
Devices	Steriflip® filters, filter discs



Reinforced Prefilter Membrane

Membrane Material	Mixed Cellulose Esters around a polyester web
Pore Sizes (µm)	0.2 – 1.2
Thickness (µm)	150 – 270
Water Flow Rate (mL/min/cm^2)	12 – 260
Wettability	Hydrophilic
Temperature Limitations	70 °C max
Chemical Compatibility	Recommended for aqueous solvents
Sterilizability	Autoclave, EtO
Surface Option	White
Key Properties	Non-shedding, high dirt-loading capacity, low pressure drop
Key Applications	Prefiltration ahead of sterilizing grade filters
Devices	Filter discs



Microfiltration

Hydrophilic

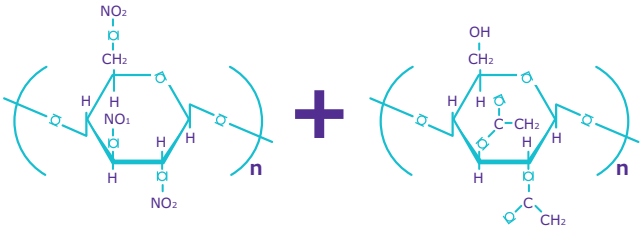
Hydrophobic

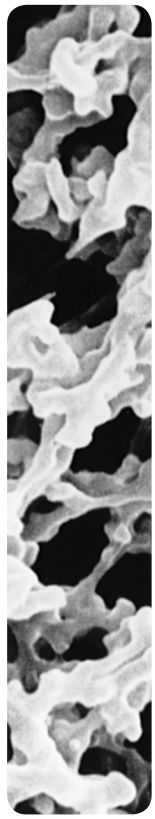
Particle size: 0.025 µm to 10 µm

Examples: Bacteria including *B. diminuta*, microorganisms, undissolved excipients, dust, asbestos, mycoplasma

Filter type: Screen filters

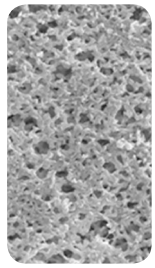
MF-Millipore™ Membrane





Brand Name	MF-Millipore™ Membrane
Membrane Material	Mixed Cellulose Esters (MCE)
Pore Sizes (µm)	0.025 – 8
Thickness (µm)	105 – 150
Water Flow (mL/min/cm²) @27.5 in. Hg	20.1 – 625
Air Flow (L/min/cm²) @ 10 psi	0.12 – 68.9 (typical values)
Porosity (%)	70 – 84
Wettability	Hydrophilic
Refractive Index	1.50 – 1.52
Temperature Limitations	55 °C max
Protein Binding Capacity	(IgG) 299 – 319 µg/cm²
Chemical Compatibility	Recommended for aqueous solvents
Sterilizability	Autoclave, EtO
Surface Option	Black, white, gridded
Key Properties	Versatile fast-flowing membrane, supports cell growth, high protein-binding
Key Applications	Sterilizing filtration, air monitoring, general clarification, bacteriological analysis, drop dialysis, particle analysis, colony hybridization, nucleic acid and protein blotting, ELISpot
Devices	Millex® syringe filters, Millicell® plates/inserts, Cathivex® filters, MultiScreen® plates, Stericup® filters, Steritest™ devices, Sterivex™ filters, Microfil® devices, filter discs

Nylon Membrane

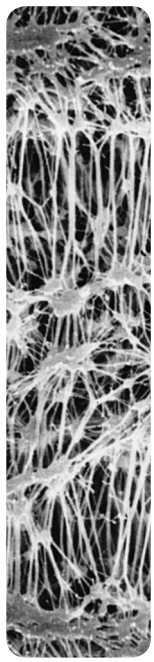


Membrane Material	Nylon
Pore Sizes (µm)	0.2 – 1.2
Thickness (µm)	150 – 190
Water Flow Rate (mL/min/cm²)@ 27.5 in. Hg	8.0 – 21.2 (typical value)
Wettability	Hydrophilic
Chemical Compatibility	Compatible with both aqueous and organic solvents
Sterilizability	Autoclave, EtO and gamma
Surface Option	White
Key Properties	General purpose, good solvent resistance
Key Applications	Particle removal and clarification of solvents, particle analysis
Devices	Millex® syringe filters, filter discs

Hydrophilic

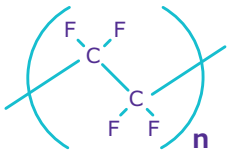
Hydrophobic

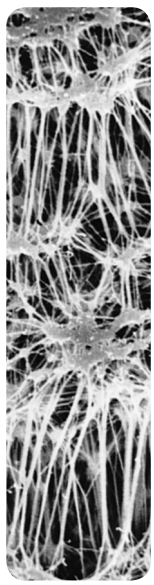
Fluoropore™ Membrane



Brand Name	Fluoropore™ Membrane
Membrane Material	Hydrophobic Polytetrafluoroethylene (PTFE)
Pore Sizes (µm)	0.2 – 3
Thickness (µm)	50 – 150
Porosity (%)	85
Liquid Flow (mL/min/cm²) @27.5 in. Hg	24 – 286 (methanol)
Air Flow specs (L/min/cm²) @ 10 psi	5 – 20
Wettability	Hydrophobic
Temperature Limitations	130 °C max
Chemical Compatibility	Compatible with both aqueous and organic solvents
Sterilizability	Autoclave, EtO
Surface Option	White
Key Properties	Solvent-resistant, fast-flowing, low pressure drop, low extractables, low binding
Key Applications	Clarifying acids, bases and solvents, air monitoring, filtering and venting gases, UV spectroscopy, radiation monitoring
Devices	Millex® syringe filters, filter discs

LCR Membrane





Brand Name	LCR Membrane
Membrane Material	Hydrophilic Polytetrafluoroethylene (PTFE)
Pore Sizes (µm)	0.45 only
Thickness (µm)	140
Porosity (%)	80
Water Flow Rate (mL/min/cm²) @27.5 in. Hg	28.4
Air Flow (L/min/cm²) @ 10 psi	1.1 (typical values)
Wettability	Hydrophilic
Temperature Limitations	130 °C max
Chemical Compatibility	Compatible with both aqueous and organic solvents
Sterilizability	Autoclave, EtO
Surface Option	White
Key Properties	Minimal extractable levels, broad chemical compatibility
Key Applications	HPLC mobile phase filtration, clarifying acids, bases and dilute protein solutions
Devices	Millex® syringe filters, Millex Samplicity® filters, filter discs

Microfiltration (continued)

Hydrophilic

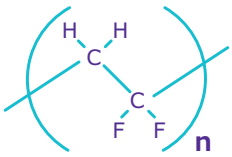
Hydrophobic

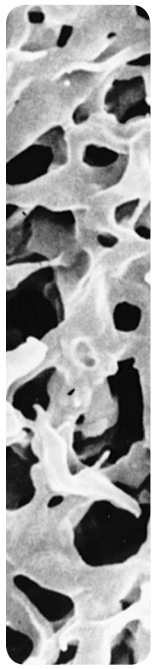
Particle size: 0.025 µm to 10 µm

Examples: Bacteria including *B. diminuta*, microorganisms, undissolved excipients, dust, asbestos, mycoplasma

Filter type: Screen filters

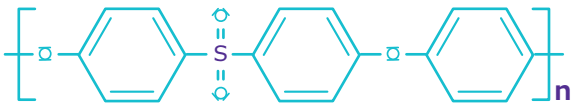
Durapore® Membrane

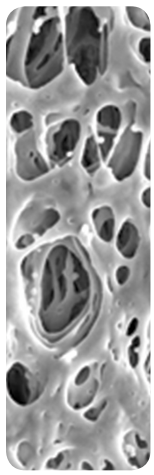




Brand Name	Durapore® Membrane
Membrane Material	Polyvinylidene fluoride (PVDF)
Pore Sizes (µm)	0.1 – 5
Thickness (µm)	80 – 140
Water Flow (mL/min/cm²) @ 27.5 in. Hg	(hydrophilic) 4 – 208
Air Flow (L/min/cm²) @ 10 psi	(hydrophobic) 0.9 – 4.9 (typical values)
Wettability	Hydrophilic and hydrophobic options
Refractive Index	1.42
Temperature Limitations	85 °C max
Protein Binding Capacity	(IgG) < 10 µg/cm²
Chemical Compatibility	Recommended for aqueous solvents
Sterilizability	Autoclave, EtO and gamma
Surface Option	White
Key Properties	Low protein-binding (hydrophilic), solvent-resistant (hydrophobic)
Key Applications	Clarifying filtration of protein-containing solutions, gas filtration and venting (hydrophobic), solvent filtration (hydrophobic)
Devices	Millex® syringe filters, Millipak® filters, MultiScreen® plates, Stericup® filters, Steritest™ devices, Sterivex™ filters, Ultrafree® filter units, filter discs

Millipore Express® PLUS Membrane



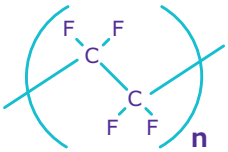


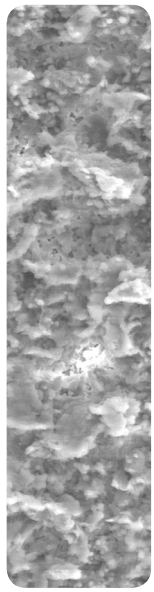
Brand Name	Millipore Express® PLUS Membrane
Membrane Material	Polyethersulfone (PES)
Pore Sizes (µm)	0.22, 0.45
Thickness (µm)	130 – 185
Water Flow Rate (mL/min/cm²) @27.5 in. Hg	27 to greater than 44
Wettability	Hydrophilic
Protein Binding Capacity	(IgG) 22 µg/cm²
Chemical Compatibility	Recommended for aqueous solvents
Sterilizability	Autoclave, EtO and gamma
Surface Option	White, plain or gridded
Key Properties	Fast flow, high throughput, low protein binding
Key Applications	Sterilizing filtration of biological solutions
Devices	Stericup® filters, Millex® syringe filters, MultiScreen® plates, filter discs

Hydrophilic

Hydrophobic

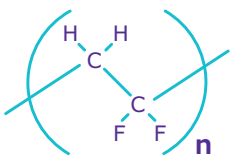
Mitex™ Membrane

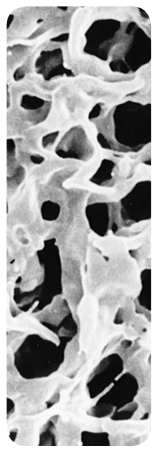




Brand Name	Mitex™ Membrane
Membrane Material	Hydrophobic Polytetrafluoroethylene (PTFE)
Pore Sizes (µm)	5 – 10
Thickness (µm)	125 – 200
Water Flow (mL/min/cm^2) @27.5 in. Hg	47 to greater than 125
Air Flow (L/min/cm^2) @ 10 psi	117 – 167
Wettability	Hydrophobic
Temperature Limitations	260 °C max
Chemical Compatibility	Compatible with both aqueous and organic solvents
Sterilizability	Autoclave, EtO
Surface Option	White, plain or gridded
Key Properties	Pure PTFE (unbacked), easy handling, solvent-resistant, fast-flowing, low extractables
Key Applications	Clarifying acids, bases, solvents and cryogenic fluids, hydraulic fluid analysis
Devices	Millex® syringe filters, filter discs

Immobilon® Membrane





Brand Name	Immobilon® Membrane
Membrane Material	Polyvinylidene fluoride (PVDF)
Pore Sizes (µm)	0.22 – 0.45
Wettability	Hydrophobic
Protein Binding Capacity	(IgG) Avg 333.4
Chemical Compatibility	Compatible with both aqueous and organic solvents
Sterilizability	Autoclave, EtO and gamma
Surface Option	White
Key Properties	High protein-binding, durable
Key Applications	Protein blotting (Western), ELISpot
Devices	Membrane roll stock and sheet, MultiScreen® plates

Microfiltration (continued)

Hydrophilic

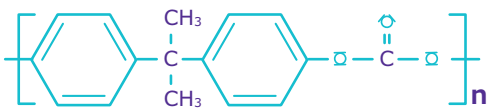
Hydrophobic

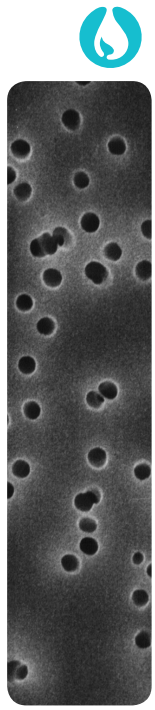
Particle size: 0.025 µm to 10 µm

Examples: Bacteria including *B. diminuta*, microorganisms, undissolved excipients, dust, asbestos, mycoplasma

Filter type: Screen filters

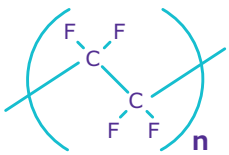
Isopore™ Membrane

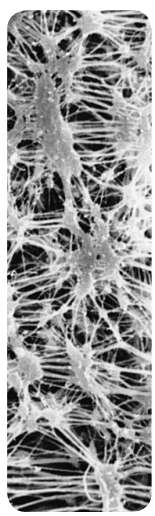




Brand Name	Isopore™ Membrane
Membrane Material	Polycarbonate
Pore Sizes (µm)	0.1 – 10
Thickness (µm)	21 – 27
Porosity (%)	5 – 10
Water Flow Rate (mL/min/cm²) @ 10 psi	0.5 – 250
Air Flow (L/min/cm²) @10 psi	1.3 – 72 (typical values)
Wettability	Hydrophilic
Refractive Index	1.6
Temperature Limitations	140 °C max
Chemical Compatibility	Compatible with both aqueous and organic solvent
Sterilizability	Autoclave, EtO and gamma
Surface Option	White, brown
Key Properties	Narrow pore size distribution, collects particles on surface for analysis
Key Applications	Particle analysis, air monitoring, microscopy, cell migration and chemotaxis assays, epifluorescence, size fractionation of cells and particulates
Devices	Millicell® plates/inserts, MultiScreen® plates, filter discs

Omnipore™ Membrane





Brand Name	Omnipore™ Membrane
Membrane Material	Hydrophilic Polytetrafluoroethylene (PTFE)
Pore Sizes (µm)	0.1 – 10
Thickness (µm)	30 – 85
Water Flow Rate (mL/min/cm²) @8.97 in. Hg	2 – 1250
Wettability	Hydrophilic
Chemical Compatibility	Compatible with both aqueous and organic solvents
Sterilizability	Autoclave, EtO
Surface Option	White
Key Properties	Compatible with both aqueous and organic solvents, broad chemical compatibility
Key Applications	Clarifying acids, bases and aqueous solutions
Devices	Membrane

Ultrafiltration

Hydrophilic

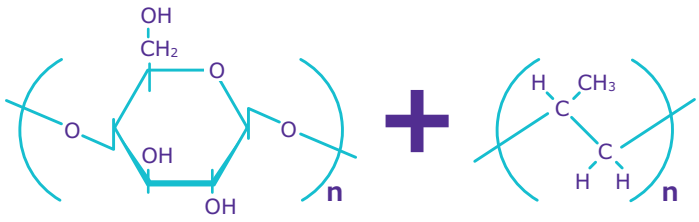
Hydrophobic

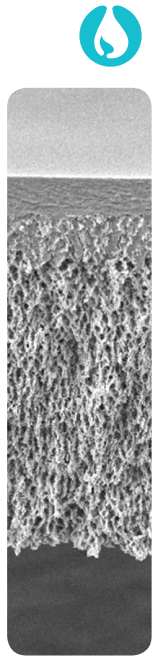
Particle size: 1 kDa to 500 kDa

Examples: Proteins, virus, nucleic acids and nanoparticles

Filter type: Ultrafilters

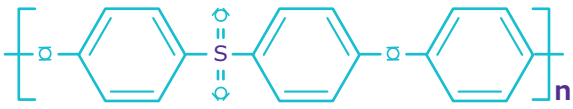
Ultracel®-PL Membrane

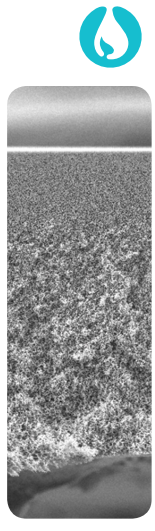




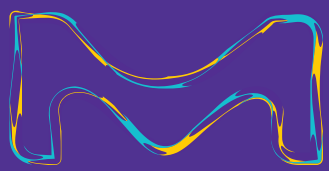
Brand Name	Ultracel®-PL Membrane
Membrane Material	Regenerated Cellulose
Pore Sizes (NMWL)	1 – 100 kDa
Wettability	Hydrophilic
Chemical Compatibility	Broad chemical compatibility, compatible with both aqueous and organic solvents
Sterilizability	Autoclave, EtO and solvent incubation
Surface Option	White
Key Properties	Low protein binding, polyolefin backing material provides support without impeding flow
Key Applications	Concentration of protein solutions, separation of low from high molecular weight molecules, protein binding studies, buffer exchange
Devices	Amicon® Ultra devices, Stirred cell membrane discs, Microcon® devices, Centrifree® devices

Biomax® Membrane





Brand Name	Biomax® Membrane
Membrane Material	Polyethersulfone (PES)
Pore Sizes (NMWL)	5 – 500
Thickness (µm)	300
Wettability	Hydrophilic
Temperature Limitations	50 °C max
Chemical Compatibility	Compatible with aqueous solvents and alcohols, Compatible with pH 1–14
Sterilizability	Autoclave, EtO and solvent incubation
Surface Option	White
Key Applications	Concentration of protein solutions, separation of low from high molecular weight molecules, buffer exchange
Key Properties	Low to moderate protein binding, high flow rate, Polyolefin backing material



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