Spectrum®
MicroKros and MidiKros
Hollow Fiber Filters

User Guide

Spectrum® MicroKros Hollow Fiber Filters

Spectrum® MidiKros Hollow Fiber Filters

Spectrum® MidiKros TC Hollow Fiber Filters

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Abbreviations

CE	Cellulose Ester
GMP	Good Manufacturing Practice
HF	Hollow fiber
kD	Kilodalton
L	Limited exposure
ME	Mixed Cellulose Ester
mPES	Modified Polyethersulfone
NR	Not Recommended
PES	Polyethersulfone
PS	Polysulfone
R	Recommended
TC	Tri-clamp
TFF	Tangential Flow Filtration
U	Unknown

1. Introduction

Spectrum® MicroKros and MidiKros Hollow Fiber Filter Modules from Repligen are designed for crossflow membrane separation of small volumes and tangential flow laboratory separations. These are the first tangential flow devices for processing volumes as small as 2 ml. They are an ideal alternative to centrifugation for applications where pellet formation is undesirable. Flow can be supplied using either syringes or peristaltic pumps like the KrosFlo® KR2i or KrosFlo® KR1. Spectrum MicroKros Hollow Fiber Filter Modules have a total membrane surface area ranging from 13 - 92 cm^2 to process volume ranging from 2 ml - 50 ml. Spectrum MidiKros Hollow Fiber Filter Modules have a total membrane surface area of 75 - 610 cm^2 to process volumes from 20 ml - 200 ml.

Tangential Flow Filtration (TFF) membrane technology from Repligen is ideal for microfiltration and ultrafiltration. Repligen utilizes advanced hollow fiber flow geometry in which every fluid path is identical in length and dimension. The membrane module housing is constructed of polysulfone with inlet and outlet ports for retentate. Either a syringe or a peristaltic pump drives the process fluid through the fiber lumen via the inlet port and out the outlet port. The retained solutes (retentate) are progressively concentrated and recirculated tangentially through the lumens. Solvent and small solutes (permeate) pass through the hollow fiber pores into the extra capillary side and out the filtrate port on the side. Uniform flow distribution makes it practical to process difficult streams such as those containing suspended solids, fibers, particles, and cells.

1.1 Features and Benefits

Features

- Ready to use
- Large surface area in compact housings
- Non-pyrogenic by LAL
- Animal-free

Benefits

- Reduces concentration polarization
- Enhances filtration rate
- Gently washes protein, cells, and particles
- Washes without pellet formation
- Manufactured in an ISO Class 7 clean room under GMPs
- Meets USP class VI standard for biocompatibility

1.2 Applications

- Concentration of protein, antibodies, and microbial cells
- Diafiltration of proteins or uniform latex particles and other diagnostic particles
- Clarification of lysates to remove cell debris from soluble proteins
- Recovery of serum from whole blood
- Media clarification for hollow fiber bioreactors
- Virus separation

2. Specifications

Figure 1. Spectrum MicroKros Hollow Fiber Filter Modules

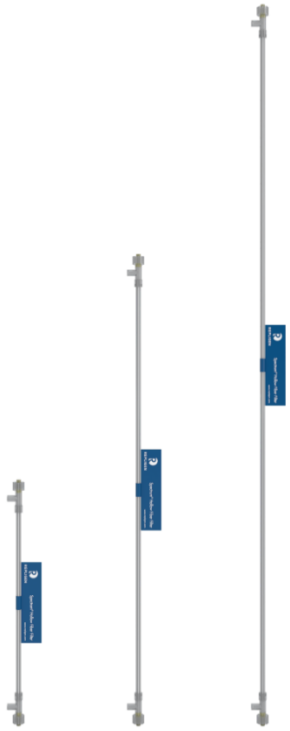


Table 1. Spectrum MicroKros Hollow Fiber Filter Module Materials and Volumes

Description	Materials and Volumes
Housing	Polysulfone
Connections	Male Luer Lok (MLL) inlet and outlet, Female Luer Lok (FLL) filtrate
Potting	Epoxy
Process Volume	2 - 50 ml
Surface Area	13 - 92 cm^2

Table 2. Spectrum MiniKros Hollow Fiber Filter Module Specifications

Membrane	Fiber	MWCO
Modified Polyethersulfone (mPES)	0.5 mm 1.0 mm	3 kD, 5 kD, 10 kD, 30 kD, 50 kD, 70 kD, 100 kD, 300 kD, 500 kD, 750 kD 3 kD, 5 kD, 10 kD, 30 kD, 50 kD, 70 kD, 100 kD, 300 kD, 500 kD, 75 kD
Mixed Cellulose Ester (ME)	0.6 mm 1.0 mm	0.1 µm, 0.2 µm 0.2 µm
Polyethersulfone (PES)	0.5 mm 1.0 mm	0.2 µm 0.2 µm, 0.5 µm
Polysulfone (PS)	0.5 mm	10 kD, 50 kD, 500 kD, 0.05 µm

Figure 2. Spectrum MidiKros and MidiKros TC Hollow Fiber Filter Modules

Spectrum MidiKros Hollow Fiber Filters

Spectrum MidiKros TC Hollow Fiber Filters

Table 3. Spectrum MidiKros Hollow Fiber Filter Module Materials and Volumes

Description	Materials and Volumes
Housing	Polysulfone
Connections	Female Luer Lok (FLL) inlet and outlet, Female Luer Lok (FLL) filtrate
Connections (TC Filter)	1/2” Tri-clamp (TC) inlet and outlet, Female Luer Lok (FLL) filtrate
Potting	Urethane
Process volume	20 - 200 ml
Surface area	75 - 610 cm^2

Table 4. Spectrum MidiKros Hollow Fiber Filter Module Specifications

Membrane	Fiber	MWCO
Modified Polyethersulfone (mPES)	0.5 mm 1.0 mm	3 kD, 5 kD, 10 kD, 30 kD, 50 kD, 70 kD, 100 kD, 300 kD, 500 kD, 750 kD 3 kD, 5 kD, 10 kD, 30 kD, 50 kD, 70 kD, 100 kD, 300 kD, 500 kD, 75 kD
Mixed Cellulose Ester (ME)	0.6 mm 1.00 mm	0.1 µm, 0.2 µm 0.2 µm
Polyethersulfone (PES)	0.5 mm 1.0 mm	0.2 µm 0.2 µm, 0.5 µm
Polysulfone (PS)	0.5 mm	10 kD, 50 kD, 500 kD, 0.05 µm

Spectrum MicroKros and MidiKros Hollow Fiber Filter Modules are available wet or dry. Mixed CE ME, PES and mPES modules are packaged dry because the fibers are hydrophilic and do not need pre-flushing. However, the PS filters are hydrophobic and require pre-flushing. They are available wet in hydrogen peroxide to add convenience by eliminating the pre-flushing procedure.

3. Filter Preparation

3.1 Dry Membrane Preparation

For mixed CE and mPES fibers, flush with 2 mL of water per cm^2 of surface area to remove trace levels of glycerin. For PES flush with 1 mL of water of 20% alcohol (Isopropanol, Ethanol or Methanol) per cm^2 of surface area and follow by flushing with 2 mL of water per cm^2 of surface area to remove all alcohol.

3.2 Pre-flushed Membrane (Wet) Preparation

Flush module with 2 mL per cm^2 of surface area with water or preferred buffer to remove hydrogen peroxide.

3.3 Storage and Shelf Life

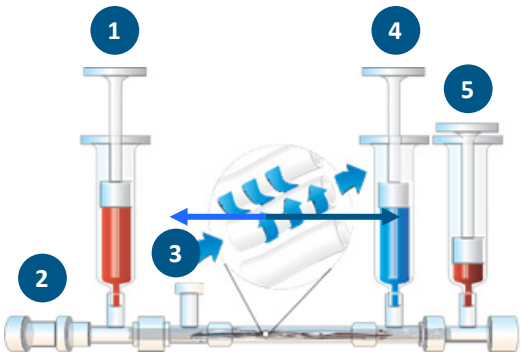
Both wet and dry Spectrum Hollow Fiber Filters should be stored at room temperature. If they are stored in a dry (50% R.H.) and cool (< 95° F/35° C) environment, they will have a shelf life of three years.

3.4 Set-up Using Syringes

To operate the Spectrum MicroKros Hollow Fiber Filter Modules using syringes:

1. Connect an arm of each female luer tee to both male luer retentate ports of the module.
2. Connect to the two remaining luer tee arms, a male luer cap and a male luer check valve.
3. Connect a second male luer cap to the female end of the check valve.
4. Connect luer syringes to the two open stems of the luer tees. One syringe contains the product to be processed, the second is empty. A third luer syringe and a male luer cap are connected to the two filtrate ports (Figure 3).

Figure 3. Spectrum MicroKros Hollow Fiber Filter Module Hand Operation Mode



1. Sample flow
2. Check valve for diafiltration mode/Topped off batch mmode
3. Luer cap
4. Filtrate collection syringe
5. Retentate flow collection syringe

3.5 Crossflow Filtration

Tangential flow or crossflow filtration is initiated by:

1. Apply pressure to the retentive syringe containing the process fluid.
2. Allow the other syringes to move freely. Fluid will flow through the lumen of the fibers from the full syringe downstream to the empty retentate syringe.
3. Apply pressure to the receiving syringe to change the direction of flow back to the originating syringe.
4. Continue this process by applying pressure first to one syringe then to the other, repeatedly. Cell or particle-free filtrate is forced into the filtrate syringe.
5. Only apply pressure to only one retentate syringe at a time. Applying pressure to both syringes will induce backpressure and reduce the efficiency of crossflow filtration. Typical filtration rate varies from 1 ml/min - 5 ml/min depending on the membrane type.

3.6 Diafiltration

For washing cells or particles to remove unbound free protein, diafiltration can be performed as follows:

1. Introduce 1 ml of the product to be washed (the volume will show as 0.5 ml on the syringes, as 0.5 ml is the hold-up volume of the module with the syringes attached.
2. Add 4.5 ml of particle free buffer via the check valve. This step dilutes all components by 5.5-fold.
3. Concentrate the cells or particles back to 1 mL (0.5 ml on the syringe) by the concentration techniques above. This step restores the original concentration of cells or particles while not concentrating surfactants, proteins or other solutes that freely permeate the membrane. Unwanted solutes are reduced in concentration by a factor of 5.5.
4. Additional purification can be achieved by repeating the process. Final purification will be 5.5 * n, where n is the number of times that the process is repeated.

3.7 Pump Operation

Spectrum MicroKros Hollow Fiber Filter Modules can also be operated using a peristaltic pump. Spectrum® MidiKros Hollow Fiber Filters can only be operated with a pump. This technique requires that either Spectrum® MicroKros or MidiKros Hollow Fiber Filters be installed with tubing connecting the module inlet to the retentate outlet. The tubing must have a tee connecting the feed/buffer reservoir to the pump suction, and a capped connection for removing air in the pump discharge. Fluid is pumped in a closed loop across the membrane surface. As filtrate is generated, more fluid is automatically drawn into the loop. Overall processing volume is equal to the holdup volume of the tubing plus the module retentate volume. It is possible to achieve retentate volumes as low as 2 ml by using short tubing.

4. Membrane Compatibility

This chemical resistance chart is intended for use as a guide, not as a guarantee of chemical compatibility. Variables in temperature, concentrations, durations of exposure and other factors may affect the use of the product. It is recommended to test under your own conditions.

Chemical Compatibility Chart

Ordering Information

To order Spectrum MicroKros and MidiKros Hollow Fiber Filter Modules please visit the Repligen e-store.

To find the specific Spectrum Hollow Fiber Filter for your application, use the Repligen Hollow Fiber Filter Configurator.

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