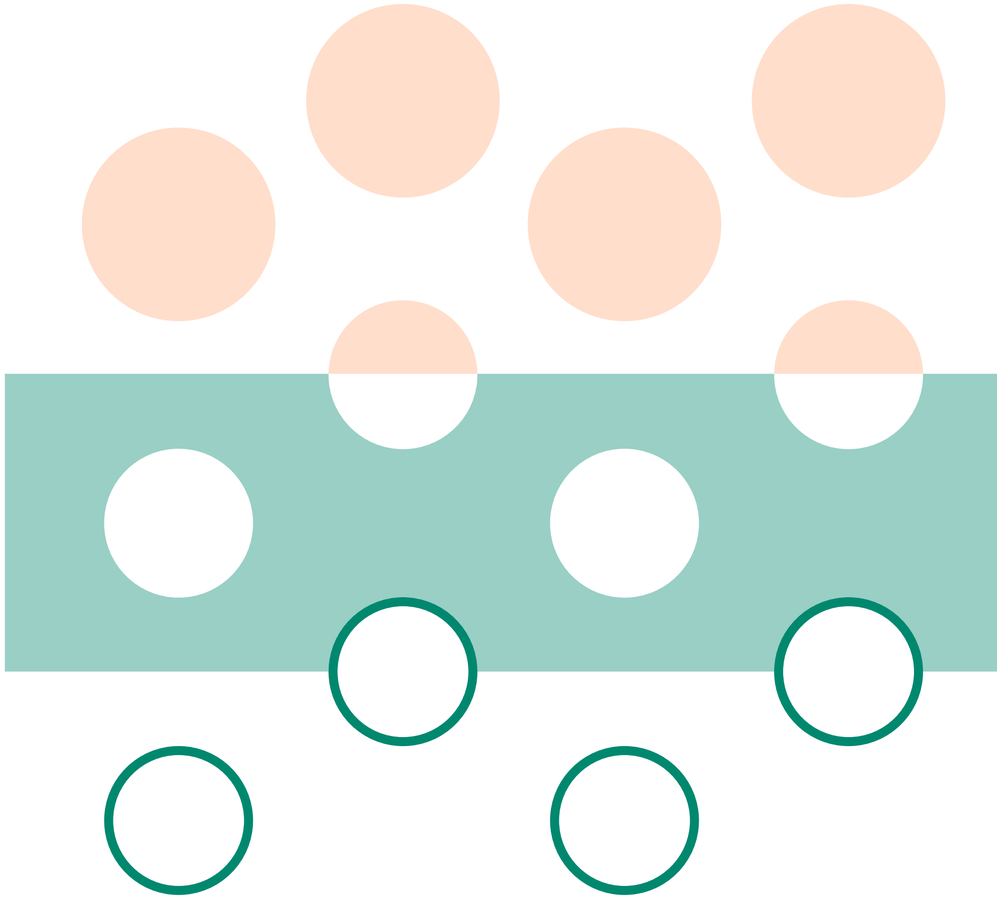
Membrane separations

Selecting a cross flow cartridge



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Four key questions

To ensure your separations process operates successfully and efficiently, you must select the proper cartridge. Selecting the proper cartridge, however, requires some technical preparation. For example, which of the 500 Cytiva cartridge filters should you select? How does the multitude of process variables influence cartridge selection? To understand the cartridge selection process, you must be able to answer these four questions:

1. **Process considerations** — How do process variables influence cartridge selection?
2. **Membrane performance** — What size molecules or bacteria will a cartridge retain?
3. **Cartridge specifications** — What fiber diameter and membrane surface area can you use?
4. **Cartridge model numbers** — How do you identify and order the right cartridge?

01

How do process variables influence cartridge selection?

Process variables influence cartridge selection. While understanding the magnitude of the influences requires experience and technical knowledge, the basic relationship between process variables and cartridge selection remain similar (Table 1).

Table 1. The influences of process variables in selecting a cross flow cartridge

Process variables	Selection consideration
Cell concentration Cell protein separation	Use microfiltration or open ultrafiltration cartridges for bacteria removal and cell concentration. Select membrane pore size based on the specific application.
Virus removal Protein concentration Desalting	Use ultrafiltration cartridges for molecular-scale applications such as desalting and protein concentration.
Solutions variables	**Selection consideration**
Solids loading Viscosity Shear sensitivity	High solids loading and high viscosity fluids work best with larger hollow fibers and longer lengths. With fluids that are not shear sensitive, you can use small diameter fibers.
Volume	As volumes increase, you typically increase the cartridge housing size and membrane surface area to shorten production time. You can consider multiple cartridges in series or parallel configuration.
Temperature	As temperature decreases, the efficiency of filtration often decreases, and larger cartridges might be appropriate. For example, cold-room processing at 4°C can take twice as long as room temperature processing.
Other variables	**Selection consideration**
Time constraints	Increased membrane area and larger housing size shorten production time.
Pump constraints	Larger diameter (large surface area) cartridges with many large fibers require pumps with high flow rate capacities.
Heat sterilization	Choose autoclavable or steam-in-place models.
Retrofit	To retrofit an existing system, cartridge dimensions and connection hardware must be compatible with the existing system.

02

What size molecules or bacteria will a cartridge retain?

To match a cross flow cartridge to an application, you must know how the membrane in the cartridge performs under standard conditions. For example, if the goal of the application is to retain *E. coli*, what membrane pore size should you consider? To answer such questions, you can use membrane performance data (Table 2 and Table 3). Table 4 puts the membrane performance numbers into perspective by providing you with practical pore size recommendations for common applications. Normally, you would test the selection with a small scale trial. Table 5 lists the membrane pore sizes available in ultrafiltration and microfiltration cartridges.

Table 2. Membrane performance data for retaining bacteria

Membrane pore size	Organism	Challenge (organisms/mL)	Organism concentration in permeate
0.45 µm	*Saccharomyces cerevisiae*	5.0 × 10E+7	Undetectable
0.45 µm	*E. coli*	6.0 × 10E+9	Undetectable
0.2 µm	*Serratia marcesens*	3.1 × 10E+7	Undetectable
0.2 µm	*E. coli*	6.0 × 10E+9	Undetectable
0.2 µm	*Brevundimonas diminuta ATCC 19146*	2.5 × 10E+7	Undetectable
0.1 µm	*E. coli*	6.0 × 10E+9	Undetectable
500 000 NMWC*	*E. coli*	6.0 × 10E+9	Undetectable
500 000 NMWC	*Giardia muris*	1.5 × 10E+5	Undetectable
500 000 NMWC	*Cryptosporidium paryum*	8.2 × 10E+4	Undetectable

* Nominal molecular weight cutoff

Table 3. Membrane performance data for retaining molecules

		Percent solute rejection at nominal molecular weight cutoff*								
Solute	**Solute molecular weight**	**1000**	**3000**	**5000**	**10 000**	**30 000**	**100 000**	**300 000**	**500 000**	**750 000**
$MgSO_4$	n/a	6	1							
PVP K15	10 000			80	75					
PVP K30	40 000				90	70				
PVP K90	630 000						95	90	80	60

* Percent rejection = 1 – (permeate concentration ÷ feed concentration) × 100

In practical terms, for product concentration, choose a nominal molecular weight cutoff (NMWC) pore size that is three to five times smaller than the target protein or molecule you want to concentrate on the retentate side. For product clarification and contaminant removal, choose a NMWC pore size that is ten times greater than the target protein or molecule you want to collect in the permeate.

Table 4. Recommended membrane pore size for select application

Application	Ultrafiltration (NMWC)	Microfiltration (µm)
Bacterial/pyrogen removal	10 000	
Protein concentration	3000, 5000, 10 000, 30 000	
Enzyme concentration	10 000, 30 000, 50 000	
Virus concentration/purification/removal	100 000, 300 000, 500 000, 750 000	
Protein/antigen recovery from fermentation broth	500 000, 750 000	0.1, 0.2, 0.45, 0.65
Bacterial cell concentration	500 000	0.1, 0.2
Insect cell concentration		0.1, 0.2
Mammalian cell concentration		0.2, 0.45, 0.65
Yeast concentration		0.1, 0.2, 0.45
Continuous cell culture perfusion		0.1, 0.2, 0.45
Red blood cell washing		0.45, 0.65
Red blood cell stroma removal	500 000	0.1
Hemoglobin concentration	5000, 10 000	
Peptide concentration	1000, 3000	

Table 5. Membrane pore size availability

Ultrafiltration (NMWC)	Microfiltration (µm)
1000	0.1
3000	0.2
5000	0.45
10 000	0.65
30 000	
50 000	
100 000	
300 000	
500 000	
750 000	

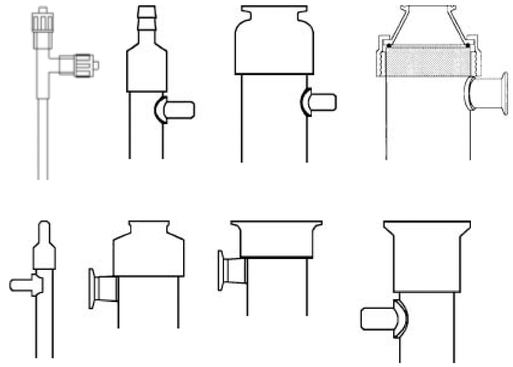


Figure 1. A partial selection of the fittings available on Cytiva cartridge filters.

03

What fiber diameter and membrane surface area can you use?

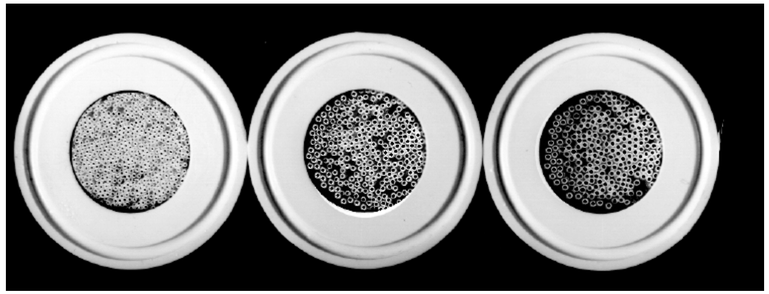
The inside diameter of the fibers in Cytiva cartridges range from 0.25 to 1.75 mm. Use larger diameter fibers for solutions with high suspended solids, high cell densities, and high viscosity (Table 6 and Fig 2).

The membrane surface area inside Cytiva cartridges ranges from 16 cm^2 to 28 m^2. Use larger surface area cartridges with larger process volumes or to shorten processing time (Table 7).

You can order Cytiva cartridges with various fittings and in various configurations (Figure 1). See the user manual *Selection handbook, hollow fiber cartridges and systems for membrane separations* for additional information about fittings and physical dimensions.

Table 6. Selecting the proper fiber diameter

Solution characteristics			Membrane	
Type	**Suspended solids**	**Viscosity**	**Lumen ID (mm)**	**Fiber diameter code**
Clarified feed streams (proteins and viral preps) Pyrogen-free water	None	Low	0.25, 0.5	B, C
E. coli Mammalian cells Yeast cells Blood products	Moderate	Moderate	O.75, 1	D, E
Yeast cells Fungal cells Mycelial cells	High	High	1.75	G



0.5 mm, code C 0.75 mm, code D 1 mm, code E

Figure 2. Cross-sectional view of cartridges showing fiber.

Table 7. Nominal cartridge specifications

MidGee™ Cartridges

Housing identifier	ID (mm)	Membrane area (cm^2)
MM	0.25	25
	0.5	26
	0.75	24
	1	16
H22	0.75	29
	1	38
H24	0.5	42
H42	0.5	41
	1	73

Lab and pilot scale cartridges

Housing identifier	ID (mm)	Membrane area (ft)	(m)
3M	0.25	0.4	0.037
	0.5	0.15	0.014
	0.75	0.13	0.012
	1	0.12	0.011
3X2M	0.5	0.31	0.029
	1	0.24	0.023
4, 4M	0.25	1.29	0.12
	0.5	0.7	0.065
	0.75	0.5	0.046
	1	0.45	0.042
4X2M	0.5	1.5	0.14
	1	0.9	0.085
5	0.25	4	0.375
	0.5	2.1	0.2
	0.75	1.7	0.16
	1	1.3	0.12
6	0.5	5.2	0.48
	0.75	4	0.37
	1	3	0.28
8	0.25	9.7	0.9
	0.5	5.7	0.53
	0.75	4.4	0.41
	1	3.9	0.36
9	0.5	12.5	1.15
	0.75	10	0.93
	1	9	0.84

Pilot and process scale cartridges

Housing identifier	ID (mm)	Membrane area (ft)	(m)
35	0.25	29	2.7
35SMO	0.5	14.5	1.35
35STM	0.75	10.8	1
	1	9.9	0.92
37	1	10.2	0.95
45	0.5	37	3.5
	0.75	28.5	2.65
	1	27	2.5
45MSM	1	25	2.3
55	0.5	35	3.25
55SMO	0.75	27	2.5
55STM	1	23	2.1
65	0.5	66	6.1
	1	47	4.4
65MSM	0.5	60	5.6
	1	45	4.2
75	0.5	60	6
	1	40	3.7
85	0.5	140	13
	1	97	9
85MSM	1	95	9
152M	0.5	140	18
	1	102	9.5
154M	0.5	300	28
	1	205	19

04

How do you identify and order the right cartridge?

To identify and order the proper cross flow cartridge, you must understand the model numbering convention. Each group of numbers or letters in the model number represents information about the cartridge.

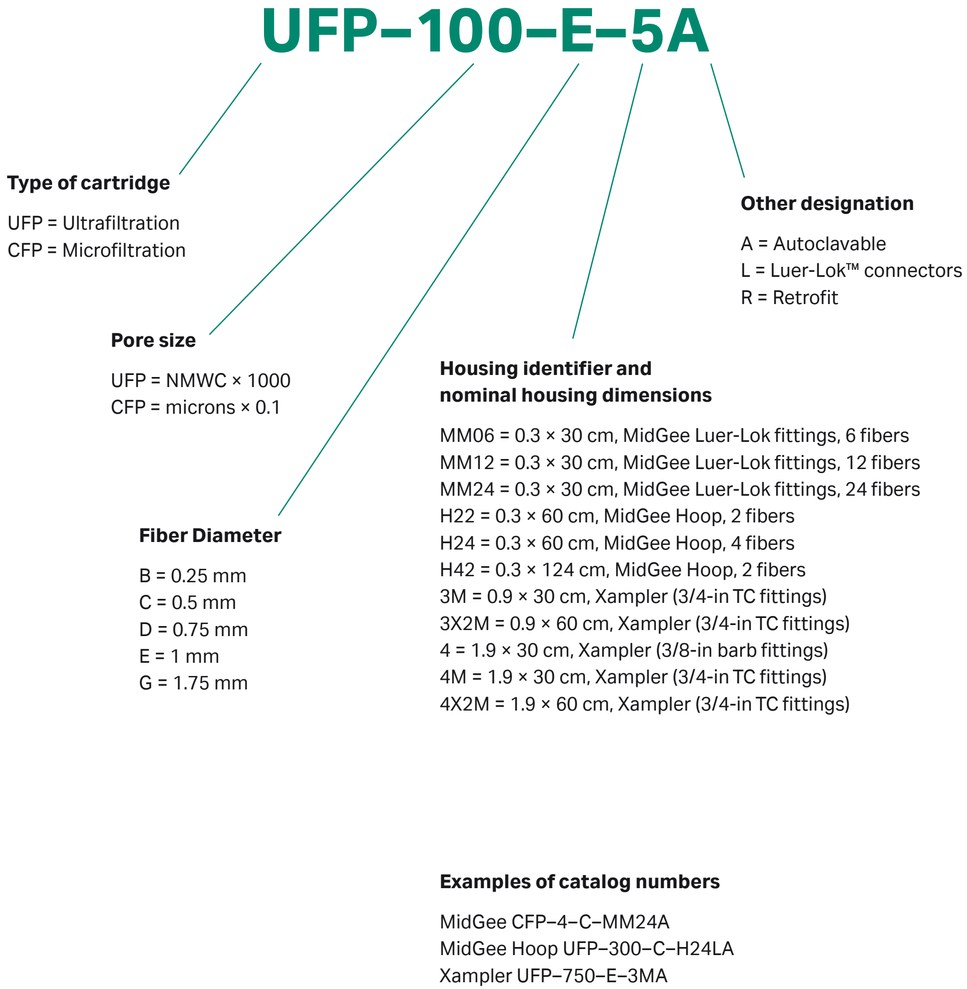


Figure 3. Key to cartridge model number conventions.

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