Scientific & Technical Report

# Introduction to Tangential Flow Filtration for Laboratory and Process Development Applications

## Introduction

Tangential flow filtration (TFF) is a rapid and efficient method for separation and purification of biomolecules. It can be applied to a wide range of biological fields such as immunology, protein chemistry, molecular biology, biochemistry, and microbiology. TFF can be used to concentrate and desalt sample solutions ranging in volume from 10 mL to thousands of liters. It can be used to fractionate large from small biomolecules, harvest cell suspensions, and clarify fermentation broths and cell lysates. This report describes the basic principles that govern TFF and the use of TFF capsules and cassettes in laboratory and process development applications.

## Why Use Tangential Flow Filtration?

1) TFF is easy to set up and use – Simply connect the TFF device to a pump and pressure gauge(s) with tubing and a few fittings, add your sample to the reservoir and you're ready to go. An example set-up is shown in Figure 1.
2) TFF is fast and efficient – It is easier to set up and much faster than dialysis. You can achieve higher concentrations in less time than with centrifugal devices or stirred cells.
3) Perform two steps with one system – You can concentrate and diafilter a sample on the same system, saving time and avoiding product loss.
4) TFF can be scaled-up or scaled-down – Materials of construction and cassette path length allow conditions established during pilot-scale trials to be applied to process- scale applications. TFF devices are available that can process sample volumes as small as 10 mL or as large as thousands of liters.
5) TFF is economical – TFF devices and cassettes can be cleaned and reused, or disposed of after single use. A simple integrity test can be performed to confirm that membrane and seals are intact.

## What Can Tangential Flow Filtration Do?

1) Concentrate and desalt proteins[3,6,9] and peptides
2) Concentrate and desalt nucleic acids [DNA/RNA/oligonucleotides[11]].
3) Recover and purify antibodies[4,7] or recombinant pro- teins from cell culture media.
4) Recover and purify plasmid DNA from cell lysates[5] or chromosomal DNA from whole blood.
5) Fractionate dilute protein mixtures[9].
6) Clarify cell lysates or tissue homogenates.
7) Depyrogenate (remove endotoxin from) water, buffers, and media solutions[8].
8) Prepare samples prior to column chromatography[3,7].
9) Harvest cells[1].
10) Recover or remove viruses[2,10].

**Figure 1**
*Minimate™ EVO TFF System with Minimate TFF Capsule*

*Minimate TFF capsule installed on a Minimate EVO TFF system with dual pressure gauges. The specially designed reservoir and system components allow samples to be concentrated to less than 10 mL.*

## Tangential Flow Filtration Overview

### What is Tangential Flow Filtration?

Membrane filtration is a separation technique widely used in the life science laboratory. Depending on membrane porosity, it can be classified as a microfiltration or ultrafiltration (UF) process. Microfiltration membranes, with pore sizes typically between 0.1 µm and 10 µm, are generally used for clarification, sterilization, and removal of microparticulates or for cell harvesting. Ultrafiltration membranes, with much smaller pore sizes between 0.001 and 0.1 µm, are used for concentrating and desalting dissolved molecules (protein, peptides, nucleic acids, carbohydrates, and other biomolecules), exchanging buffers, and gross fractionation. Ultrafiltration membranes are typically classified by molecular weight cutoff (MWCO) rather than pore size.

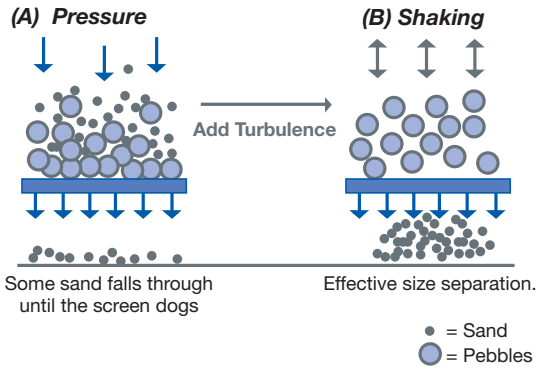
There are two main membrane filtration modes which can use either microfiltration or ultrafiltration membranes: 1) Direct Flow Filtration (DFF), also known as ”dead-end” filtration, applies the feed stream perpendicular to the membrane face and attempts to pass 100% of the fluid through the membrane, and 2) Tangential Flow Filtration (TFF), also known as crossflow filtration, where the feed stream passes parallel to the membrane face as one portion passes through the membrane (permeate) while the remainder (retentate) is recirculated back to the feed reservoir.

An analogy for understanding the theory behind TFF can be seen in trying to separate sand from pebbles using a sifting screen. The holes in the screen represent the pores in the membrane while the sand and pebbles represent the molecules to be separated. In DFF, the sand and pebble mixture is forced toward the holes in the screen. The smaller sand grains fall through the pores in the screen, but the larger pebbles form a layer on the surface of the screen.

This prevents sand grains at the top of the mixture from moving to and through the holes (Figure 2A). With DFF, increasing the pressure simply compresses the mixture with- out increasing the separation. In contrast, operating in a TFF mode prevents the formation of a restrictive layer by re-circulating the mixture. The process acts like a shaking sifter to remove the pebbles that block the holes in the screen, allowing the sand grains at the top of the mixture to fall toward and through the holes in the screen (Figure 2B).

**Figure 2**

*Separation of sand and pebbles using a sifting screen*

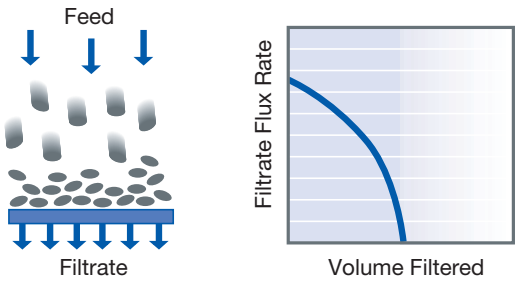



*(A) Applying direct pressure to the mixture allows the sand grains at the bottom to fall through. A layer of pebbles builds up at the screen surface preventing sand grains at the top from moving to and through the screen. (B) Shaking the screen breaks up the aggregated pebble layer at the bottom of the mixture and allows for complete fractionation. The crossflow dynamic of the feed stream in tangential flow filtration serves the same purpose as shaking in this example.*

In solution, the same effect is encountered for DFF (Figure 3). The flow of sample solution across the membrane surface sweeps away aggregating molecules that form a membrane-clogging gel (gel polarization), allowing molecules smaller than the membrane pores to move toward and through the membrane. Thus, TFF can be faster and more efficient than DFF for size separation.

**Figure 3**

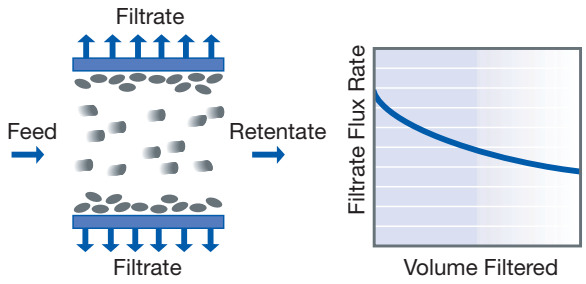
*Direct flow filtration process*




*(A) The feed is directed into the membrane. Molecules larger than the pores accumulate at the membrane surface to form a gel, which fouls the surface, blocking the flow of liquid through the membrane. (B) As the volume filtered increases, fouling increases and the flux rate decreases rapidly.*

**Figure 4**

Tangential flow filtration process




*(A) Sample solution flows through the feed channel and along (tangent to) the surface of the membrane as well as through the membrane. The crossflow prevents build up of molecules at the surface that can cause fouling. (B) The TFF process prevents the rapid decline in flux rate seen in direct flow filtration allowing a greater volume to be processed per unit area of membrane surface.*

## Applications

The primary applications for TFF are concentration, diafiltration (desalting and buffer exchange), and fractionation of large from small biomolecules. In addition, it can be used for clarification and removal of cells as well as cellular debris from fermentation or cell culture broths.

## Concentration

Concentration is a simple process that involves removing fluid from a solution while retaining the solute molecules. The concentration of the solute increases in direct proportion to the decrease in solution volume, i.e. halving the volume effectively doubles the concentration.

To concentrate a sample, choose a UF membrane with a MWCO that is substantially lower than the molecular weight (MW) of the molecules to be retained. This is important in order to assure complete retention and high recovery of the target molecule. A good general rule is to select a membrane with a MWCO that is 3 to 6 times lower than the MW of the molecules to be retained. If the sample will only be concentrated, then 3 times lower is sufficient. If significant diafiltration will also be applied to the sample, then an even lower MWCO (i.e. to 6 times lower) may be advisable.

The membrane is installed (or a disposable TFF capsule selected), and the TFF system is initialized (typically flushed with water and tested for water filtrate flow rate and integrity). Sample is added, a crossflow is established, feed and retentate pressures are set, then filtrate is collected. When the desired concentration is reached, the process is stopped, and sample recovery or diafiltration may begin.

## Diafiltration

Diafiltration is the fractionation process that washes smaller molecules through a membrane and leaves larger molecules in the retentate without ultimately changing concentration. It can be used to remove salts or exchange buffers. It can remove ethanol or other small solvents or additives.

There are several ways to perform diafiltration. In continuous diafiltration, the diafiltration solution (water or buffer) is added to the sample feed reservoir at the same rate as filtrate is generated. In this way the volume in the sample reservoir remains constant, but the small molecules (e.g. salts) that can freely permeate through the membrane are washed away. Using salt removal as an example, each additional diafiltration volume (DV) reduces the salt concentration further. (A diafiltration volume is the volume of sample before the diafiltration solution is added.) Using 5 diafiltration volumes will reduce the ionic strength by ~99% with continuous diafiltration.

In discontinuous diafiltration, the solution is first diluted and then concentrated back to the starting volume. This process is then repeated until the required concentration of small molecules (e.g. salts) remaining in the reservoir is reached. Each additional diafiltration volume (DV) reduces the salt concentration further. A diafiltration volume is the volume of sample before the diluting solution is added. Using 5 diafiltration volumes will reduce the ionic strength by ~96% with discontinuous diafiltration.

Continuous diafiltration requires less filtrate volume to achieve the same degree of salt reduction as discontinuous diafiltration, as illustrated in Table 1.

**Table 1**

*Comparison of continuous vs. discontinuous diafiltration*

| Volumes | Continuous | Discontinuous |
|---|---|---|
| 1 | 63.2 | 50.0 |
| 2 | 86.5 | 75.0 |
| 3 | 95.0 | 87.5 |
| 4 | 98.2 | 93.8 |
| 5 | 99.3 | 96.9 |
| 6 | 99.8 | 98.4 |
| 7 | 99.9 | 99.2 |

By first concentrating a sample, the amount of diafiltration solution required to achieve a specified ionic strength can be substantially reduced. To reduce the ionic strength of a 1 liter sample by 96% using discontinuous diafiltration requires 5 DV's or, in this case, 5 liters. If the sample is first concentrated ten fold to 100 mL, then 5 DV's is now only 500 mL. This represents a substantial savings in buffer and possibly time. Concentrating the sample increases the viscosity, which reduces the filtrate flux rate (rate of liquid flow through the membrane). If the viscosity increase is great, the flux rate may be sufficiently reduced to require more time to process the reduced volume sample. Additional information on the diafiltration process can be found in the article Diafiltration: A Fast, Efficient Method for Desalting, or Buffer Exchange of Biological Samples Scientific & Technical Report.

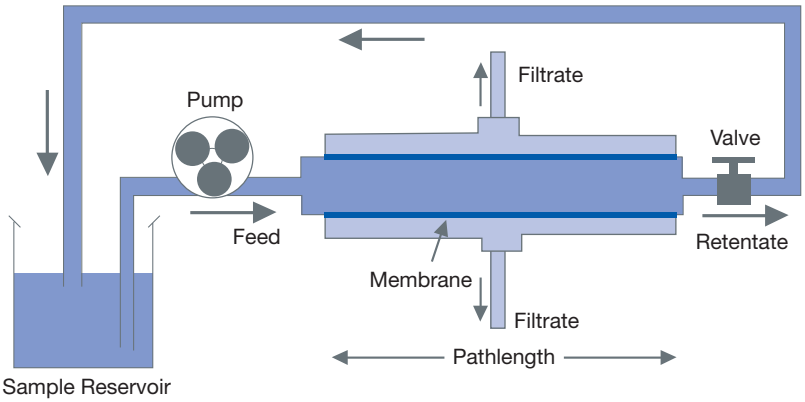
## Process Variables in Tangential Flow Filtration

Two of the important variables involved in all tangential flow devices are transmembrane pressure (TMP) and crossflow velocity (CF).

1) The transmembrane pressure is the force that drives fluid through the membrane, carrying along the permeable molecules
2) The crossflow velocity is the rate of the solution flow through the feed channel and across the membrane. It provides the force that sweeps away molecules that can foul the membrane and restrict filtrate flow.

**Figure 5**

*Flow path through a simple TFF device*




Fluid is pumped from the sample reservoir into the feed port, across the membrane surface (crossflow), out the retentate port and back into the sample reservoir (Figure 5). The crossflow sweeps away larger molecules and aggregates that are retained on the surface of the membrane, preventing gel polarization (the formation of a concentrated biomolecule layer on the membrane surface that can foul or plug the membrane). Liquid flowing through the narrow feed channel creates a pressure drop between the feed and retentate ports. This pressure, which is applied to the membrane, can be further increased by increasing the crossflow rate or by restricting the tubing at the retentate port. This transmembrane pressure (TMP) is the force that drives liquid through the membrane.

Liquid that flows through the membrane (filtrate or permeate) carries molecules smaller than the membrane pores through the filter. The trick to using TFF effectively is to regulate both the TMP and crossflow rate to prevent membrane fouling, thus allowing a greater volume of product to be processed in the least possible time.

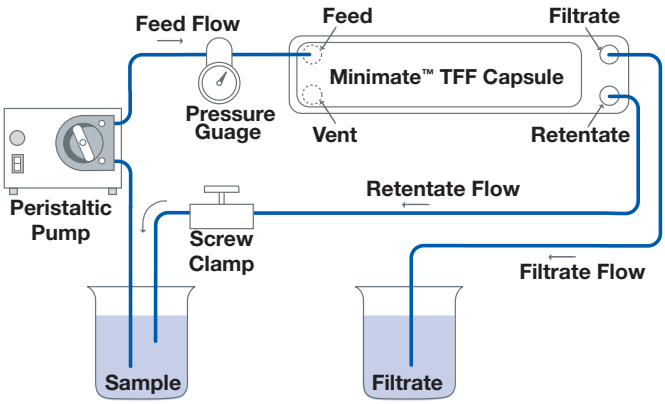
## Tangential Flow Device Assembly

Tangential flow filtration systems typically require a TFF device (capsule, cassette and holder, hollow fiber module, etc) with a pump (peristaltic or equivalent), tubing, valves or clamps, one or more pressure gauges, and a sample reservoir (Figure 6 and 7). Pressure gauges are typically installed at the feed, retentate, and filtrate ports in development and process TFF systems.

While it is possible to run a TFF system without pressure gauges, the use of at least one pressure gauge on the feed side (between pump and TFF unit) is strongly recommended. Pressure is an important variable in the TFF process. The ability to monitor and control the pressure leads to more consistent results, and can be very helpful for troubleshooting system problems.

Figure 6

*Diagram of a Minimate TFF Capsule system with pump, pressure gauge, retentate screw clamp, reservoirs and tubing connections*




Operation of a TFF system consists of the following steps:

1) Rinse the TFF device before use to remove the storage agent.
2) Establish the normalized water permeability (NWP, see glossary) of the membrane to establish a baseline for the device performance. (This step is not necessary but strongly recommended if the device will be cleaned and reused.)
3) Condition system with the sample buffer. (Conditioning helps remove air from the system, adjust system temperature and prevent possible precipitation or denaturation of biomolecules resulting from contact with flushing solution.)
4) Process the sample (concentration and/or diafiltration, or fractionation).
5) Clean; determine cleaning efficiency
6) Store TFF Device

## How to Choose the Proper TFF System for Your Application

To choose the proper TFF system, consider the following three steps:

**Step 1: Define the purpose of the TFF process.**

The biomolecule of interest in your sample is called a product. Separation can occur by choosing a membrane that retains the product while passing any low molecular weight contaminants. Alternatively, a membrane can be chosen that passes the product while retaining higher molecular weight components in the sample. It is also possible to combine both separations in a two-stage process that will fractionate out the product from both higher and lower molecular weight components. In the first stage, a membrane is chosen that passes the product and retains the higher molecular weight components. The filtrate from the first stage then becomes the sample for the second stage. For the second stage, the membrane is chosen to concentrate the product and remove lower molecular weight substances.

You will need to define your separation goals – Concentration, Diafiltration, or Fractionation. You must also consider the process volumes that you have to work with and any scale up requirements. It is important to know the concentration factor or the level of salt reduction required in order to choose the most appropriate membrane and system for the process.

**Step 2: Choose the membrane molecular weight cutoff**

The molecular weight cutoff (MWCO) of a membrane is defined by its ability to retain a given percent of a molecule in solution (typically 90% retention). As discussed earlier, to retain a product, select a membrane with a MWCO that is 3 to 6 times lower than the MW of the target protein. For fractionation, select a membrane MWCO that is lower than the MW of the molecule to be retained but higher than the MW of the molecule you are trying to pass.

**Step 3: Choose the flow channel configuration.**

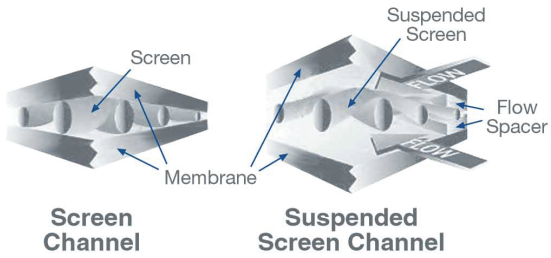
The sample concentration and solution characteristics (viscosity, particulates, etc.) determine the type of channel configuration required for the application. There are three different configurations available (Figure 8). Not all configurations are available with different TFF devices.

A) Screen channel configuration is used with a clean, filtered (0.2 µm) solution (no particles or aggregates that can get trapped in the screen). A woven separator in the channel creates gentle turbulence along the membrane surface, minimizing membrane fouling.

B) Suspended screen channel configuration has a more open structure in the retentate channel that provides better performance when highly viscous fluids (for example, serum) or particle-laden solutions are being used. It can also be used to concentrate cells or clarify cell or fermentation broths.

**Figure 8**

*TFF System Configuration*




Step 4: Determine the required membrane area for the application.

Choosing an appropriate cassette depends on the total sample volume, required process time, and desired final sample volume.

Use the following equation to calculate the membrane area required for processing a sample in a specified time:

$$A = \frac{V}{J \times T}$$

Where:

A = Membrane area ($m^2$)

V = Volume of Filtrate generated (liters)

J = Filtrate flux rate [liters/$m^2$/hour (LMH)]

T = Process Time (hours)

**Examples**

Example 1: What TFF system should I use to concentrate 10 liters to 200 mL in 2.5 hours?

Assume the average filtrate flux rate of 50 liters/$m^2$/hour (L/$m^2$/h, LMH).

Volumetric throughput (volume of filtrate) = 10 liters – 0.2 liters = 9.8 liters

$$A = \frac{9.8}{50\ L/m^2/h \times 2.5\ h} = \frac{9.8}{125} = 0.08\ m^2$$

Recommended System: Centramate holder with 1 membrane cassette, area of 0.093 $m^2$ (1 $ft^2$).

Example 2: You have 50 mL of sample (MW = 54KD) collected from a Mustang™ Q membrane chromatography module that was eluted in a buffer solution (0.05 M Tris, 0.5 M NaCl). You need to reduce the salt concentration below 0.05 M and then concentrate to 10 mL. Using a Minimate TFF capsule with a 10KD membrane on a Minimate EVO TFF system, how long will it take you if the average filtrate flux rate is 40 LMH and 3 diafiltration volumes (constant volume diafiltration) are required to get the salt concentration below 0.05 M.

Minimate Area = 50 $cm^2$ = 0.005 $m^2$

Sample Volume = 50 mL

Diafiltration Volume (1DV) = 50 mL

Average Filtrate Flux Rate = 40 LMH

Total filtrate volume (VT)= VD+ VC

Where

$V_D$ = Filtrate volume from diafiltration step

$V_C$ = Filtrate volume from concentration step

$V_T$ = VD + VC = (3 DV x 50 mL) + (50 mL – 10 mL)

$V_T$ = VD + VC = 150 mL + 40 mL = 190 mL = 0.19 L

A = V/(JxT)

Rewrite equation to solve for T

T = V/(JxA)

T = 0.19 L / (40 L/$m^2$/h x 0.005 $m^2$)

T = 0.19 / 0.2 = 1 h

When diafiltration is performed, the total volumetric throughput (filtrate volume) equals the initial sample volume multiplied by the number of diafiltration volumes. To save on buffer volume and processing time, very often sample is first concentrated and then subjected to diafiltration.

Example 3: You have a 1.0-liter sample (0.1 mg/mL) that you need to concentrate 10 times and diafilter to remove at least 99% of the salts. You have a Centramate cassette holder with one cassette 0.093 $m^2$ (1 $ft^2$). How much time will it take to process your sample?

The average filtrate flux rate for the process if you concentrate first and then diafilter is 40 LMH. If you do the diafiltration first and then concentrate, the average flux rate is 50 LMH.

Scenario A: Sample is first concentrated 10X (from 1.0 liters to 0.1 liters) followed by continuous diafiltration for 6 DV's to remove salt (Table 1)

Total filtrate volume ($V_T$) = $V_C + V_D$

Where:

$V_C$ = Filtrate volume in concentration step

$V_D$ = Total diafiltration volume (1 DV = 0.1 liters)

$V_T$ = (1.0 - 0.1) + (6 x 0.1) = 0.9 + 0.6 = 1.5 liters

Average filtrate flux rate = 40 LMH.

$$\text{Area (A)} = \frac{\text{Filtrate Volume (V)}}{\text{Average Filtrate Flux (J) x Process Time (T)}}$$

Rewrite to solve for T

$$T = \frac{V}{J \times A}$$

$$T = \frac{1.5 \text{ liters}}{40 \text{ L/m}^2\text{/h} \times 0.093 \text{ m}^2} = 0.4 \text{ h}$$

Scenario B: Sample is diafiltered first by continuous diafiltration for 6 DV's to remove salt (Table 1) and then concentrated 10X (from 1.0 liter to 0.1 liter),

Total filtrate volume ($V_T$) = $V_D$ + VC

Where:

$V_D$ = Total diafiltration volume (1 DV = 1 liter)

$V_C$ = Filtrate volume in concentration step

$V_T$ = (6 x 1.0) + (1.0 - 0.1) = 6 + 0.9 = 6.9 liters

Average filtrate flux rate = 50 LMH.

$$T = \frac{6.9 \text{ liters}}{50 \text{ L/m}^2\text{/h} \times 0.093 \text{ m}^2} = 1.48 \text{ h}$$

In this example, concentrating the sample first followed by diafiltration takes 0.4 hours. Reversing the process and doing diafiltration first takes 1.5 hours. Therefore, concentrating first has saved about 1 hour of process time. If the sample had been fairly concentrated to start, the results may have been very different.

In designing a process it is important to look at the total process and evaluate how filtrate flux rate changes may affect the process requirements.

**Table 2**

*General Product Selection Based on Starting Sample Volume*

| TFF Capsule or Cassette[1] | Membrane Area/ Capsule or Cassette | Typical Filtrate Flow Rate[2] at 50 LMH 20 °C | Recommended Retentate Flow Rate/ Capsule or Cassette for Screen Channel | Starting Sample Volume Range | Minimum Concentrated Volume[3] |
|---|---|---|---|---|---|
| | | LAB SCALE/SCALE-UP | | | |
| Minimate | 50 $cm^2$ | 4 mL/min | 30 – 40 mL/min | 25 – 500 mL | <10 mL |
| LV Centramate | 0.01 $m^2$ (0.1 $ft^2$)<br>0.02 $m^2$ (0.2 $ft^2$) | 8 mL/min<br>15 mL/min | 60 – 80 mL/min<br>120 – 160 mL/min | 40 – 2000 mL<br>60 – 4000 mL | 10 mL<br>15 mL |
| | | PROCESS DEVELOPMENT AND SMALL SCALE PRODUCTION | | | |
| Centramate | 0.093 $m^2$ (1.0 $ft^2$) | 4.6 L/hr | 600 – 800 mL/min | 0.2 – 20 L | 100 mL |

*1) Data is per unit or cassette. Centramate holder can hold 5 cassettes. Other column data can be calculated by multiplying table values by the number of cassettes installed in the holder.*

*2) Typical filtrate flow rate is based on an average filtrate flow rate of 50 LMH and a process time of about 4 hours. Actual value may be higher or lower depending on the MWCO of membrane, sample composition and viscosity, operating conditions i.e. TMP, cross flow rate, temperature, etc.*

*3) Minimum concentrate volume depends on system hold-up volume, reservoir design and pump type and speed. Smaller volumes can be achieved by minimizing tubing lengths and use of properly sized components, tubing, fittings, etc.*

## Tangential Flow Filtration Products

Table 2 lists TFF products for lab and process development. The table allows you to select a product based on starting sample volume. It gives recommended retentate flow rates and an estimate of filtrate flux rate. Many additional products (not shown) are available for larger scale applications. Table 3 recommends the retentate flow rate for Pall capsules and cassettes.

**Table 3**

*Recommended Retentate Flow Rate for Pall Capsules and Cassettes**

| Capsule/Cassette | Screen Channel | Suspended Screen Open Channel |
|---|---|---|
| Minimate | 30 – 40 mL/min | N/A |
| Centramate | 6 – 8 L/min/$m^2$<br>0.6 – 0.8 L/min/$ft^2$ | 10 – 15 L/min/$m^2$<br>1 – 1.5 L/min/$ft^2$ |

**Higher or lower flow rates may be used if required to process sample. Optimal values should be determined through trials on actual sample.*

For additional information, please contact Pall Corporation, or your local Pall Distributor, or visit our website at www.pall.com/lab.

## Summary

Tangential flow filtration is an easy, fast, and efficient method for separation and purification of biomolecules. TFF can be used to concentrate and desalt sample solutions ranging in volume from a few milliliters up to thousands of liters. It can be used to fractionate large from small biomolecules, remove endotoxins and virus particles from solutions, harvest cell suspensions and clarify fermentation broths and cell lysates. Selection of the appropriate TFF equipment and operating conditions requires a thorough understanding of the process requirements and parameters. Once established, a broad range of membranes, formats and equipment are available to handle almost any application.

## Glossary

**Concentration Polarization:** The accumulation of the retained molecules (gel layer) on the surface of the membrane caused by a combination of the following factors: trans-membrane pressure, crossflow velocity, sample viscosity, and solute concentration.

**Crossflow Rate (CF):** The retentate flow rate; Units in L/min. Provides the "sweeping" effect to reduce concentration polarization. The pressure drop, P ($P_{FEED} - P_{RETENTATE}$), is directly related to the CF.

**Crossflow Flux Rate (CFF):** Crossflow rate per unit area of membrane; Units L/min/$ft^2$ or L/min/$m^2$.

**Diafiltration:** The fractionation process that washes smaller molecules through a membrane and leaves larger molecules in the retentate (concentrate). It can be used to remove salts or exchange buffers, remove ethanol or other small molecules such as detergents, small peptides or nucleic acids.

**Filtrate:** The solution that passes through the membrane.

**Filtrate Flux Rate:** Filtrate flow rate per unit area: unit L/$m^2$/h (LMH). Filtrate flux rate is affected by crossflow rate, TMP and viscosity.

**Gel Layer:** The microscopically thin layer of molecules that forms on the top of the membrane. It causes a reduction in the filtrate flow rate and may increase the retention of molecules that would normally cross into the filtrate.

**Molecular Weight Cut Off (MWCO):** The molecular weight cutoff of a membrane sometimes called Nominal Molecular Weight Limit (NMWL) is defined by its ability to retain a given percent of a molecule in solution (typically 90% retention).

**Normalized Water Permeability (NWP):** Membrane water permeability corrected to a temperature of 20 ºC.

**Membrane Water Permeability:** Filtrate flux rate for water per unit of applied TMP. The water permeability is related to the membrane hydraulic resistance. It is significantly affected by temperature.

**Membrane Recovery:** Measure of the water permeability of the membrane after processing and cleaning compared to the water permeability of the "original" membrane.

% Membrane Recovery = ($NWP_{CLEAN}$ / $NWP_{ORIGINAL}$) x 100%

**Product Recovery:** The amount of product (mass or activity) recovered after processing compared to the amount in the starting sample. Usually expressed as a percentage of starting material.

**Retentate:** The sample that passes through the feed chan- nel (does not pass through the membrane). Also known as the concentrate.

**Tangential Flow Filtration (TFF) or Crossflow Filtration:** A process where the feed stream flows parallel to the membrane face. Applied pressure causes one portion of the flow stream to pass through the membrane (filtrate) while the remainder (retentate) is recirculated back to the feed reservoir.

**Transmembrane Pressure (TMP):** It is the driving force for liquid transport through the ultrafiltration membrane. Calculated as the average pressure applied to the membrane minus any filtrate pressure.

$TMP = (P_{FEED} - P_{RETENTATE}) / 2 - P_{PERMEATE}$

In most cases, pressure at filtrate port equals zero.

## Additional Literature

- Diafiltration: A Fast, Efficient Method for Desalting, or Buffer Exchange of Biological Samples
- Desalting and Buffer Exchange by Dialysis, Gel Filtration or Diafiltration
- Minimate TFF Capsule Data Sheet
- LV Centramate™ Data Sheet
- Centramate™ Cassette Data Sheet
- Omega™ Ultrafiltration Membrane

## References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