

# Streamline Laboratory-Scale Concentration, Desalting, And Buffer Exchange Processes

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## Key Words

- Peristaltic Pumps
- Tubing Pump
- Tangential Flow Filtration
- Cross Contamination
- Transmembrane Pressure
- Crossflow Velocity

In Tangential Flow Filtration (TFF), the majority of the feed flow travels tangentially across the surface of the filter, rather than into the filter as with dead-end filtration. In protein purification, the term Tangential Flow Filtration is used to describe cross-flow filtration with membranes. The process can be used at different stages during purification, depending on the type of membrane selected.

The principle advantage of TFF is that the filter cake (which can blind the filter) is substantially washed away during the filtration process, increasing the length of time that a filter unit can be operational. It can be a continuous process, unlike batch-wise dead-end filtration.

Tangential Flow Filtration is typically selected for feeds containing a high proportion of small particle size solids (where the permeate is of most value) because solid material can quickly block (blind) the filter surface with dead-end filtration. Examples of this include the extraction of soluble antibiotics from fermentation liquors.

## Peristaltic pumps improve performance of TFF systems

The use of peristaltic pumps as an essential part of a complete separation technology solution provides several advantages. The fluid path is simple, with only one wetted part. With proper tubing selection very high purity can be achieved with very little spallation and all wetted parts meet US and European Pharmacopeia Biological Reactivity Test standards, *In Vivo*.

The fluid path is disposable and can be sterilized, which eliminates sources of cross contamination. The low shear, gentle pumping action provides gently processing of biomolecules helping improve yield

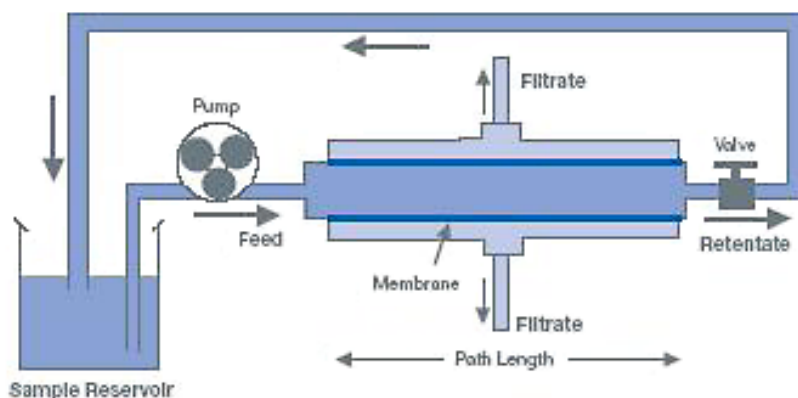


Figure 1. Flow Path through a Simple TFF Device.

and efficiency. Finally, net tubing materials provide long term, reliable use for pressure up to 100 PSIG. This capability provides a wide safety margin when processing high value biomolecular materials.

Thermo Scientific peristaltic pumps provide solutions from research to pilot plant scale up. This enables consistency of materials and performance while developing your critical production processes.

## 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.

## 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 1). 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).

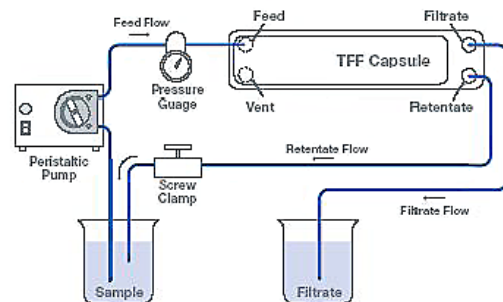


Figure 2. Diagram of a system with pump, pressure gauge, retentate screw clamp, reservoirs and tubing connections.

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 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 2). Pressure gauges are typically installed at the feed, retentate, and filtrate

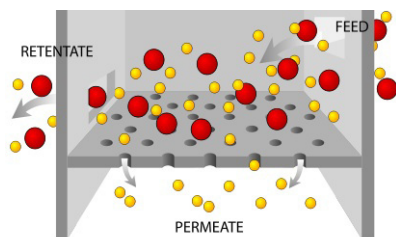


Diagram of cross-flow filtration

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.

### Alternative pump selections for Tangential Flow Filtration

TFF typically recommends a pressure monitoring gauge that has a maximum range up to 4.1 BARg (60 PSIG). This is the maximum TMP (Transmembrane pressure) recommended for a TFF system before damage to the membrane can occur. Pump performance for use in TFF application should meet the specifications outlined in Table 1.

	Low pressure	High Pressure
Flow	Up to 300 ml/min	Up to 300 ml/min
Pump Pressure Capability	Up to 30 PSIG	Up to 60 PSIG
Suitable Tubing Materials	Pharmed BPT	Style 100 Reinforced Silicone
Recommended Thermo Scientific FH Series Pump	72-320-000	72-320-100
Recommended Tubing Size	Size 16	Size 16

Table 1. Specifications for pump performance in TFF applications.

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