

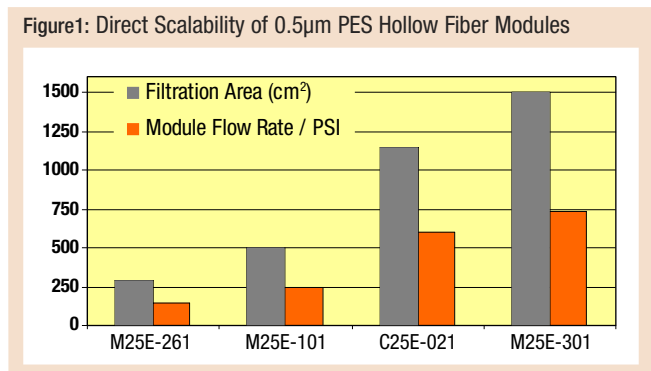
# Hollow Fiber Membrane Separations: Gentle Process Filtration and Counter-Current Dialysis



The biopharmaceutical industry is becoming more dependent upon gentle processing for isolating and purifying shear-sensitive biologicals. Spectrum's hollow fiber (HF) membrane technology provides the low pressure and low stress environment required for the downstream processing of whole cells, proteins, virus and other labile products. Typically, operating parameters for flat sheet separations have to be established or redeveloped at the production scale. Hollow fiber membrane offers the unique benefit of optimization for R&D volumes that can be directly scaled up to production without having to reoptimize process parameters. Process optimization with smaller volumes saves time, money, and valuable product. Lastly, the disposability of Spectrum's HF membrane modules and flow paths make FDA validation much easier.

## GENTLE PROCESS FILTRATION: MAMMALIAN CELL WASHING AND PERFUSION

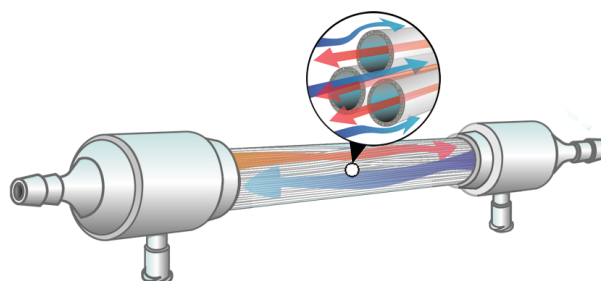
Due to the increasing demand for separating shear-sensitive or viable cells, Spectrum has advanced the direct scalability of hollow fiber filtration by developing the KrosFlo Research II TFF System (KRII) for the optimization of small volume separations. While Spectrum's disposable HF module retains the labile cells, the KRII completely monitors and displays all operating pressures and the retentate flow rate to assure efficient separation and product preservation. Operating Spectrum's PES hollow fiber irradiated module (part no. M55E-301-01S, 0.2 m<sup>2</sup>, 0.5 μm MWCO), the KRII is programmed to provide a 5 mL/min/fiber retentate flow rate and maintain a low TMP (< 2 psig) required for mammalian cell processing. A permeate flux rate of 50–75 LMH is fixed by utilizing a secondary permeate pump. A 1-mm fiber lumen is also essential to minimize the shear stress imposed on the cell line and maintain a high viability of > 95%. Pressure alarms and pump shut-off set points are programmed into the KRII upfront to prevent cell lysis caused by over pressurization or pump suction. All process parameters are fed live into Spectrum's KF Comm Software for data retention and plotting.



The hollow fiber filtration can then be directly scaled up to production by simply increasing the process volume, module fiber count, and flux rate while maintaining the operating pressures, fiber flow rate (mL/min/fiber), and process duration already established for the smaller batch volume.

## COUNTER-CURRENT DIALYSIS

There is an increasing demand for hollow fiber counter-current dialysis for the purification of delicate biologicals and substances with molecular characteristics not conducive for other separation techniques. Conventional dialysis involves smaller volume "samples" in a flat-sheet device or tubular membrane dialyzed overnight against a limited volume buffer. Pressurized filtration can cause product damage or precipitation as a result of forced concentration. Chromatography typically requires drastic changes in buffer conditions that can result in reduced product recovery. Counter-current dialysis can purify liters of sample in a relatively short amount of time without compromising product integrity or yield. While the sample is circulated through the lumen of the hollow fibers, the buffer is pumped through the extra-capillary side generating minimal TMP. This "dynamic dialysis" effectively increases the concentration gradient causing a passive and gentle product purification to occur in a matter minutes to hours. The entire process is directly scalable to larger sample volumes.



## 3 MAJOR ADVANTAGES OF COUNTER-CURRENT DIALYSIS:

- Purification of delicate or difficult substances
- Dialysis of larger volumes
- Dialysis in less time
- Directly scalable

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