High Protein Concentration Case Study

Albumin is a blood plasma protein that can be produced by a fractionation / purification process of human blood plasma or through recombinant technology using a compatible host cell organism. Purification of albumin produced from either upstream process requires a concentration step to prepare the protein solution for formulation or final bulk unit operations. Current concentration methods utilize ultrafiltration (UF) membranes that retain the desired albumin protein. However, current UF filters often become fouled during processing resulting in increased process times and shortened membrane life.

Novel modules manufactured by SmartFlow Technologies alleviate this common process hurdle during albumin concentration. The patented design of the SmartFlow Technologies OPTISEP® modules utilizing *SmartFlow*™ TFF promotes optimal permeate flux and eliminates fouling and clogging during UF processing. Figure 1 illustrates the flow path of material through the OPTISEP module, where the processing stream utilizes the full area of the membrane. In addition, the variable channel heights and open channels within the modules permit high concentrations of protein, such as albumin concentrations of 30%, to be processed without clogging the membrane.

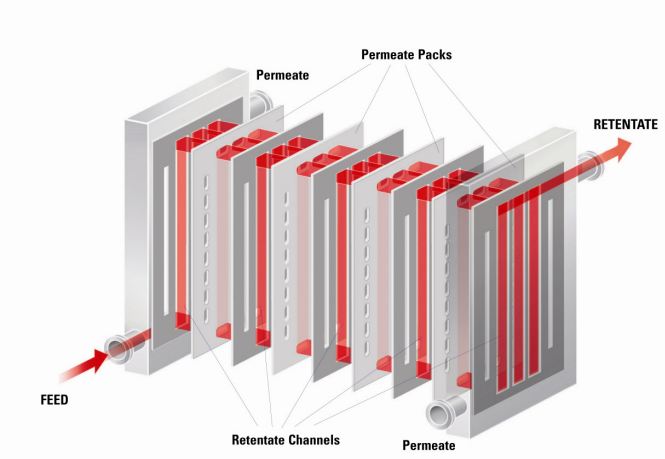

Figure 1: Process Fluid Flow through OPTISEP Module

A leading biotechnology company working with SmartFlow Technologies installed an OPTISEP module in their downstream process to concentrate albumin following initial separation from a host cell. For installation testing, the customer provided material to perform both optimization and a demonstration of the module's ability to concentrate the albumin protein. A total 81L of an albumin (65kDa) solution was processed across an OPTISEP 7000 $1m^2$ module with a 0.5mm channel height. The membrane used was regenerated cellulose (RC) with a 10kDa molecular weight cut off (MWCO). At the initiation of testing, the transmembrane pressure (TMP) and shear rate were optimized. This optimization was followed by a 40X concentration of the material.

The first step of optimization was identifying the TMP for operation. Testing was performed with the albumin solution recirculating through the system while the TMP is adjusted and corresponding permeate flux rate is recorded. The optimal TMP is reached when the permeate flux rate reaches a peak and plateaus or decreases. Figure 2 illustrates the permeate flux rate reaching a peak at 56psig. For further testing, this is identified as the optimal TMP for processing.

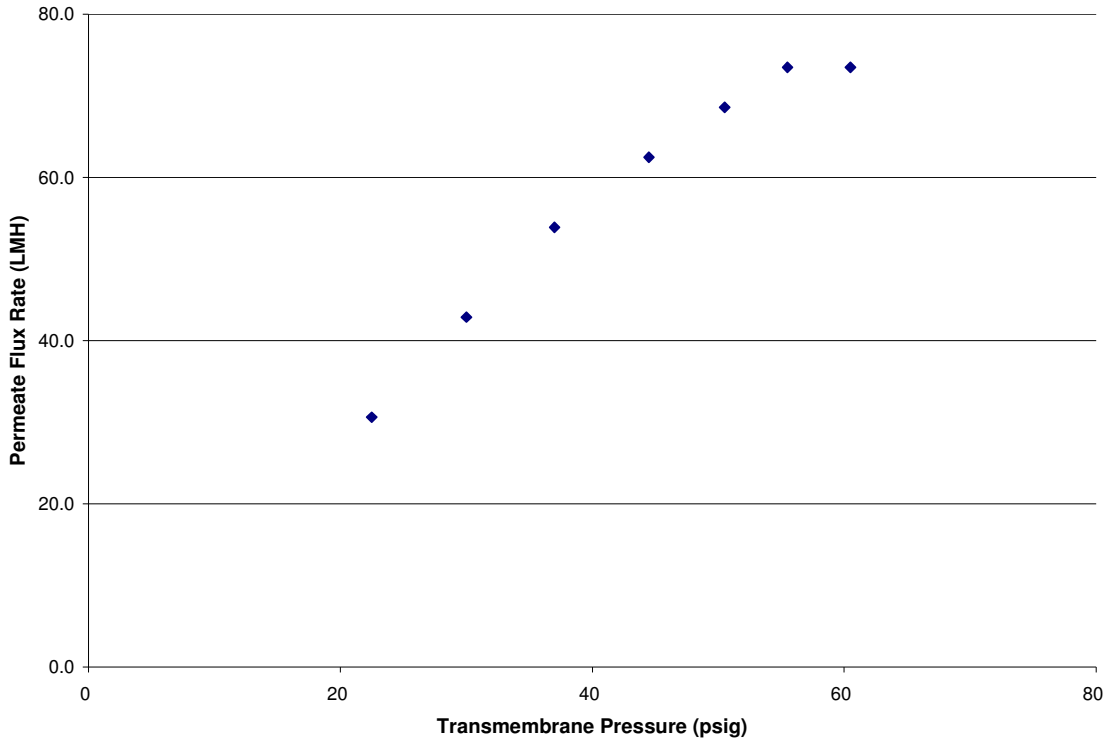

Figure 2: Permeate Flux Rate versus TMP for Optimization Testing

After completing this step, the optimal shear rate was investigated by starting initial concentration while keeping the TMP constant and adjusting the shear rate via the recirculation rate. Figure 3 shows a linear relation between the shear rate and the permeate flux rate such that as the shear rate was decreased, the permeate flux rate showed a similar step decrease. The optimal shear rate was identified as 30,000s^{-1} based on the increased permeate flux rate noted during testing.

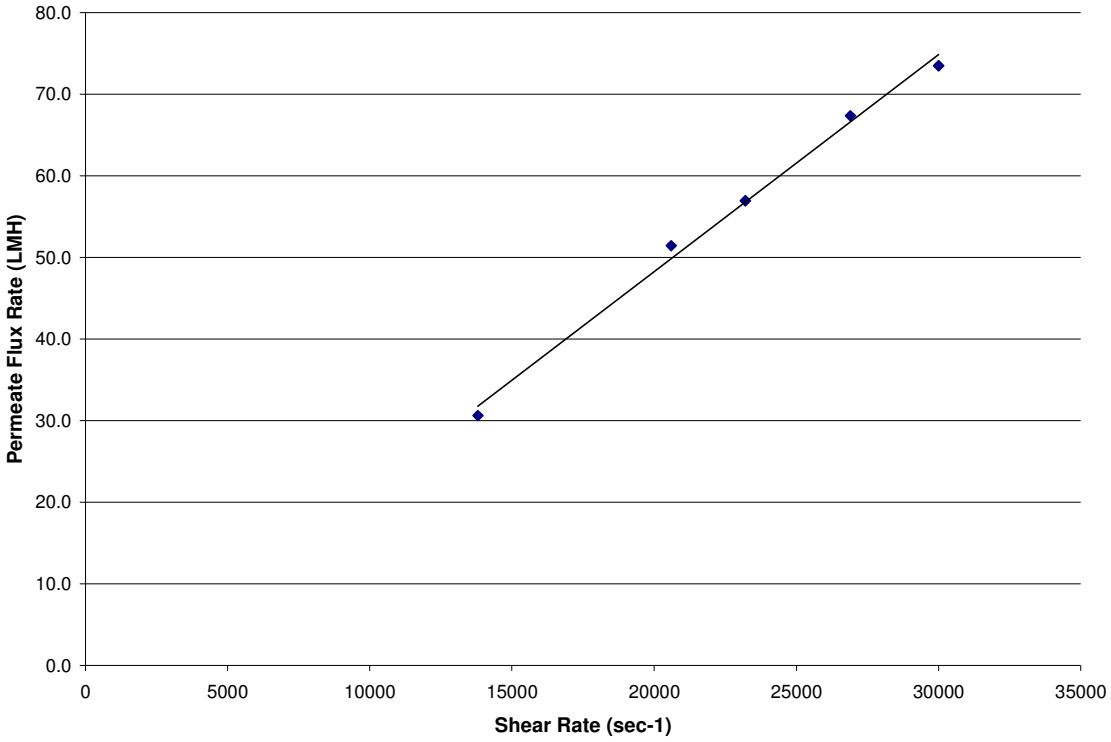

Figure 3: Permeate Flux Rate versus Shear Rate for Optimization Testing

Upon optimization completion, the demonstration of the module's operation capabilities was performed. Figure 4 shows the instantaneous flux rates versus concentration factor for the entire concentration process. Because the module completed a 17X concentration in approximately 30 minutes, an additional 31L of pre-filtered albumin solution was added and the entire batch (81 L) was concentrated to a final concentration of 40X. As shown in the figure, the OPTISEP 7000 operated with a high permeate flux rate and decreased only 8% by the 2X concentration point. The overall average permeate flux rate to reach 17X concentration was 62 LMH, and as evidenced in the figure, when the process reached 17X concentration, the permeate flux rate remained near constant at 48 LMH with a drop to only 40LMH by 40X. This maintenance of permeate flux rate during a 40X concentration demonstrates that the design of the OPTISEP module eliminates fouling and membrane clogging to permit a consistent operation even at high protein concentration.

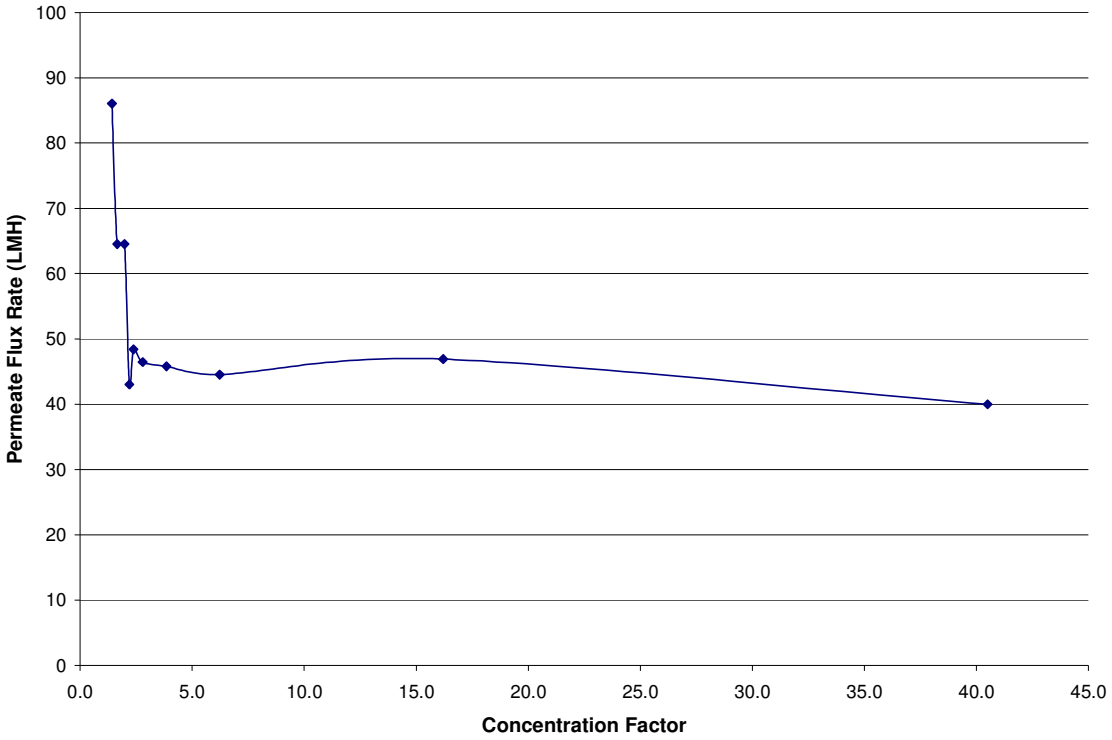

Figure 4: Permeate Flux Rate vs. Concentration Factor during Albumin Concentration

Because the membrane does not foul, a greater permeate flux rate is achieved, which permits more batches to be processed utilizing the same footprint. Additionally, because the OPTISEP modules can reach concentrations exceeding 30% albumin, the flexibility for formulation is greatly expanded. Using the OPTISEP filter modules for albumin production eliminates a common bottleneck in albumin purification, which increases the overall efficiency of the manufacturing operation.