SARTORIUS

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Evaluation of Feed Flow Geometry in Hydrosart® Cassettes With Protein Solutions

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Introduction

Sartorius Sartocon® cassettes are available with the option of two internal flow geometries. Sartocon® cassettes with "E" type spacers are designed for high- protein concentration applications and for viscous products; while the cassettes with "ECO" screens are designed for protein concentrations less than 15% (150 g/L) and for other products with low viscosity [<3cp (3mPas)]. With current mAb harvest targets of ≥5 g/L and increased use of subcutaneous dosages, protein concentrations often approach 200 g/L or more. It is therefore important to understand when to use each type of cassette and the implications. This evaluation demonstrates that "ECO" channel cassettes can achieve twice the flux at one-third the feed flow rate of the "E" channel cassette. The "ECO" cassettes feature up to 26% more surface area per standard cassette width, making it possible to install more filter area in the cassette holder.

Find out more: www.sartorius.com/tff-cassettes

Methods

The effects of recirculation rate, pressure, and protein concentration on permeate flux were evaluated with Sartocon® Slice 200 "E" channel and "ECO" channel cassettes. All testing was conducted using a Sartorius Sartoflow® Slice 200 Benchtop Crossflow (TFF) system. All pressures, flow rates, and weights were measured by the system and transmitted to a spreadsheet.

Testing was conducted using 30 kDa Hydrosart® Ultrafilter cassettes; and the test solutions were either a 5 g/L mAb solution or 1% milk.

Cassettes were cleaned between tests with (0.1 N) NaOH.

During the diafiltration steps, the feed reservoir remains vacuum sealed and the diafiltration is performed at constant volume. The diafiltration buffer is suctioned into the reservoir under vacuum created by the rate of permeation. Post diafiltration, the mAb solution was further concentrated to the desired end-point.

Figure 2: Sartocon® Slice 200 cassettes represent Sartorius smallest scale-down device in the Sartocon® cassette product family.

Figure 1: Sartoflow® Slice 200 Benchtop System with a Sartocon® Slice 200 cassette holder, feed vessel and balance for permeate measurement.

Figure 3: The Sartocon® Slice 200 cassette has the same flow geometry as the larger cassettes and allows for linear and predictable scaling. The cassette requires a Sartocon® Slice stainless steel holder for use.

Results

Temperature and protein concentration have a profound influence on permeate flux. As shown in Figure 4, flux increases as both temperature increases and protein concentration decreases. Regardless of the temperature or the protein concentration, one can see in Figure 4, that the influence of increasing recirculation rate is also increasing permeate flux. Furthermore, the slope of each line is the same, which means that one is able to accurately predict the performance of the cassette with the protein solution based on the process variables.

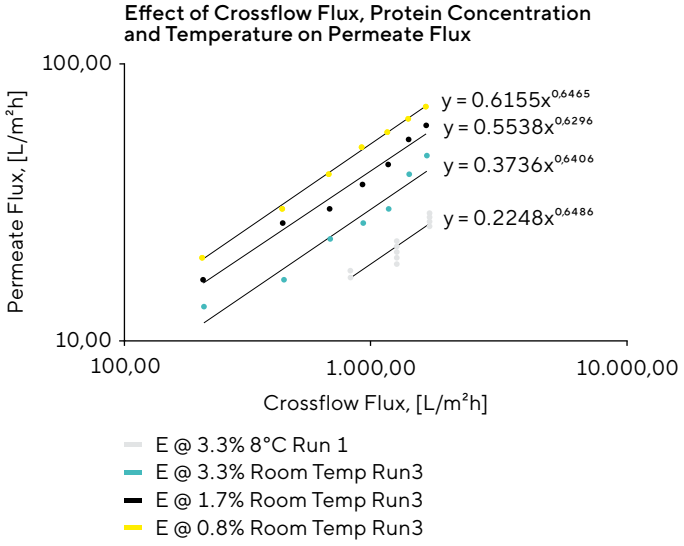

Figure 4: Permeate flux was measured at different recirculation rates between 200 to 1800 L/m²h, at 8 and 20 °C using 1% milk at protein concentrations from 0.8- 3.3%, using a 30 kDa "E" channel Slice 200 cassette.

Flow channel geometry also has a profound influence on permeate flux. In Figures 5 and 6, the thinner "ECO" channel cassettes achieve flux values equivalent to the "E" channel cassette at approximately one-third the recirculation rate of the higher "E" channel cassette.

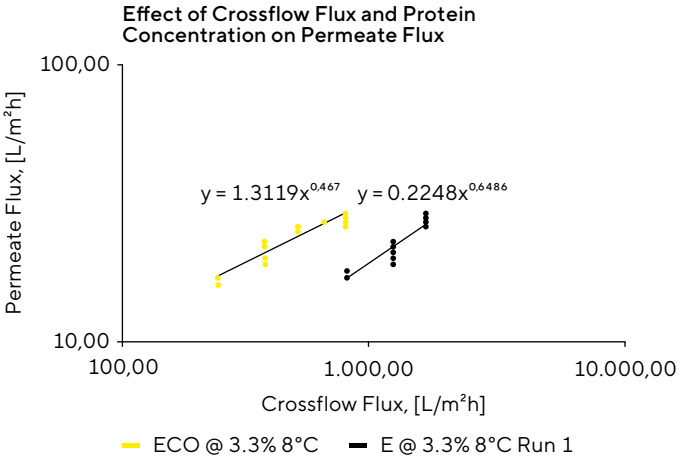

Figure 5: 30 kDa "ECO" and "E" channel Sartocon® Slice 200 permeate flux was measured at different recirculation rates between 200 to 1800 (L/m²h) at 8 °C using 1% milk.

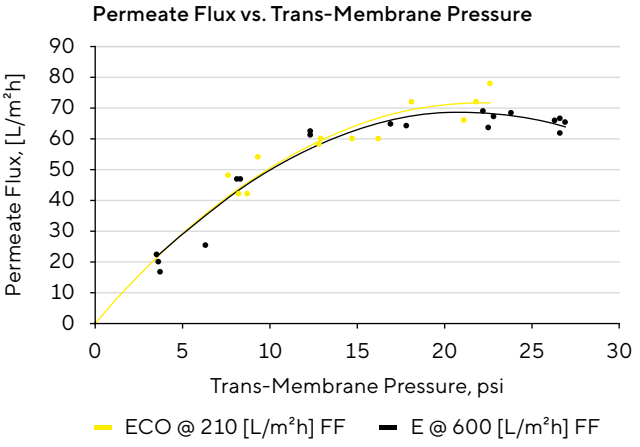

Figure 6: Permeate flux was measured at different TMP values at recirculation rates of 210 (L/m²h) and 600 (L/m²h) for 30 kDa "ECO" and "E" channel cassettes respectively using a mAb solution at 5 g/L.

There are instances where the "E" channel cassettes fail to approach the flux values of the "ECO" cassette even at three times the recirculation flow rate. In Figure 7, the "ECO" cassette has 60% higher flux than the "E" channel cassette. This is typically the case when both the protein concentration and viscosity are low.

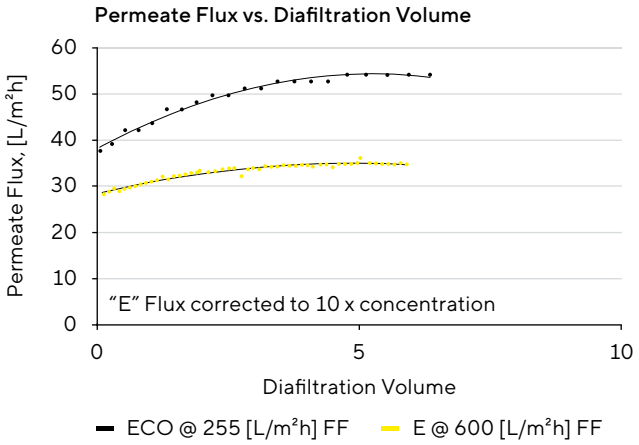

Figure 7: 30 kDa "ECO" and "E" channel Sartocon® Slice 200 cassette permeate flux was measured at feed flow rates (FF) of 255 and 600 (L/m²h) respectively during the diafiltration of a mAb at 5 g/L against citrate buffer.

In the permeate flux versus TMP plot (Figure 8), the effect of the channel height difference between the "E" and "ECO" cassettes is further illustrated. When approaching the pressure-independent region of the plot, which is typically close to where one achieves optimal performance from an ultrafilter, the "ECO" channel is equal to or better than the "E" channel cassette at one-third the crossflow rate.

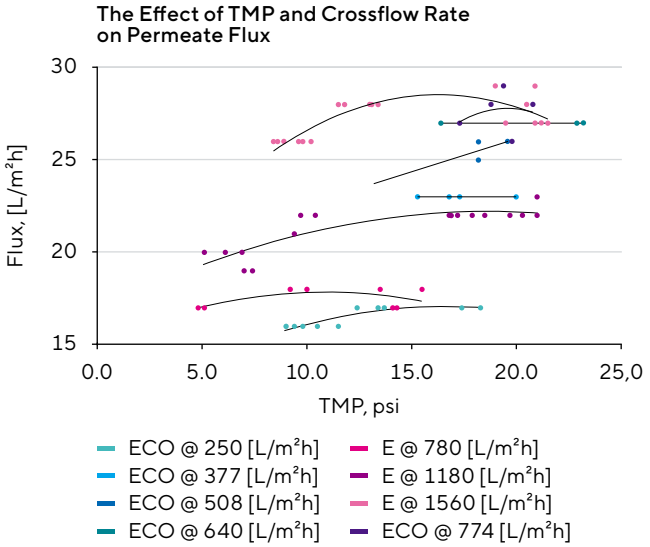

Figure 8: 30 kDa "ECO" and "E" channel Sartocon® Slice 200 cassette permeate flux was measured at different recirculation rates from ~250 to 1600 L/m²h at different TMP values using 1% milk.

In the concentration plot (Figure 9), 1% milk is concentrated from 3.3% protein to 15% protein. Though the two plots are virtually superimposable, the difference between them is that the "E" channel cassette crossflow feed rate in this experiment is 2.6 times higher than that of the "ECO" channel cassette.

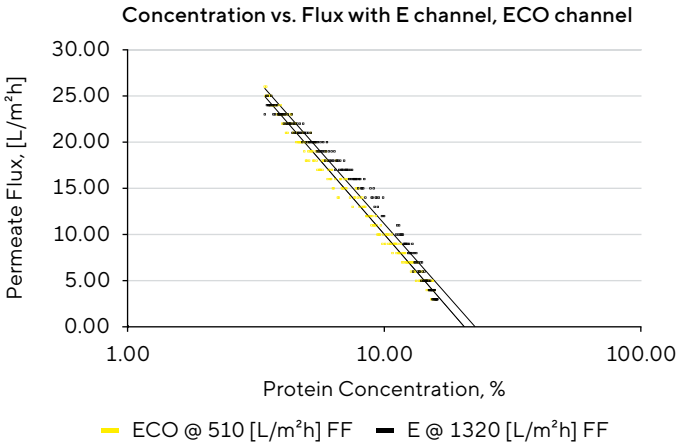

Figure 9: 30 kDa "ECO" and "E" channel Sartocon® Slice 200 cassette permeate flux was measured at feed flow rates of 510 and 1320 (L/m²h) respectively during the concentration of milk five-fold from a protein concentration of 3.3% to 15%.

Hydrosart® cassettes are easy to clean regardless of the format. The low-protein binding and non-fouling characteristics of Hydrosart® are the properties that ensure high yields and easy cleaning. A 15-minute CIP cycle with (0.1 N) NaOH at room temperature effectively recovered membrane flux to its out-of-the box value. In each instance, the post-use permeate flux was the same as the pre-use flux, (Table 1).

Water flux	Initial [L/m²h]	Final [L/m²h]
Hydrosart® "E"	68 @ 10.8 psi	70 @ 11.1 psi
Hydrosart® "ECO"	54 @ 9 psi	54 @ 9 psi

Table 1: Water flux before use and after cleaning.

Summary

Cassette feed and retentate channel height influences the required recirculation rates for optimal TFF performance. In order to achieve equivalent flux between wide channel "E" cassettes and narrow "ECO" channel cassettes, the wide channel "E" cassette requires about three times higher flow rate than "ECO" channel cassettes.

Permeate flux is a function of both pressure and shear generated by the rate of recirculation. At lower protein concentrations, "E" channel cassettes with recirculation rates three times that of "ECO" channel cassette can have protein flux values 20-40% lower than "ECO" channel cassettes.

At higher protein concentrations as viscosity increases, "E" channel cassette flux values rise to values equal to "ECO" channel cassettes. At high protein concentrations (>15%), "ECO" channel cassettes become impractical because of the resultant extreme pressure drop within the channel, therefore making the "E" channel cassette the appropriate choice.

Appropriate cassette channel height selection can profoundly influence a process skid design. Pump, valve, piping, surface area, and cost can vary by a factor of two-to-three fold – based on the cassette selection.

For applications where the final protein concentration remains ≤15-18%, the Sartorius "ECO" channel is recommended. Operation at a much lower differential pressure allows one to achieve much higher protein concentrations with the "E" channel cassette.

For questions please contact your application specialist.

Example Scale-Up Difference
Process: Five times concentration of 500 liters of a 5 g/L mAb followed by a five volume diafiltration and then a final 20x concentration. Total permeate volume for a 500 L process as described above is 975 liters.

Process time = Two hours total
Average flux: "E" Channel = 35 (L/m²h),
"ECO" channel = 55 (L/m²h)
Resultant system sizing requirements; is 14 m² with a recirculation pump of 140 L/min for the "E" channel cassette and 9 m² and a 40 LPM recirculation pump for the "ECO" channel cassette.

For a cost comparison for different size processes see Table 2 below:

Scale	"E" Cassette	"ECO" Cassette
50 L capital	$85,000	$85,000
Cassettes	$4,500	$2,500
500 L capital	$300,000	$200,000
Cassettes	$50,000	$36,000
1000 L capital	$500,000	$350,000
Cassettes	$100,000	$75,000

Product Information

Sartocon® ECO Hydrosart® Cassettes
Available types and order numbers

Cut Off	Sartocon® Slice 200 Cassettes 0.02 m² Filter Area	Sartocon® Slice Cassettes 0.14 m² Filter Area	Sartocon® Cassettes 0.7 m² Filter Area	Sartocube® Cassettes 3.5 m² Filter Area
10 kDa	3M81443902E--SW	3M51443901E--SW	3M21443907E--SW	3M21443935E-BSW
30 kDa	3M81445902E--SW	3M51445901E--SW	3M21445907E--SW	3M21445935E-BSW
100 kDa	3M81446802E--SW	3M51446801E--SW	3M21446807E--SW	M21446835E-BSW
300 kDa	3M81447902E--SW	3M51447901E--SW	3M21447907E--SW	3M21447935E-BSW

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