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# Scale Up of Direct Flow Membrane Filters

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## ABSTRACT

The costs associated with biological solutions dictate the need to develop scale-down devices that can be reliably used for equipment selection and process optimization. For direct flow filtration, a linear relation between the performance of discs and pleated structures has traditionally been assumed. However experimental results show that this assumption does not hold in all cases[1-3]. An investigation was conducted to understand the dynamics underlying these results. Dye staining was used to visualize the membrane surface area utilization. Fluid dynamic simulations were conducted to characterize any transport differences among the different geometries. We investigated the effect of solution properties and operating parameters on scale up. Scaling factors and the guidelines on scale up of direct flow filters are presented.

## INTRODUCTION

Availability of scale down devices that accurately predict manufacturing scale performance is critical for rapid and low-cost process development and process characterization studies.

For direct flow filtration, the traditional scale up practice has been to maintain the same filtrate volume to membrane area ratio while operating at the same constant pressure or constant flux. Recent studies, however, point to some challenges on the assumptions of linear scalability between discs and pleated cartridges[1-3]. This study was designed to determine the performance relationship between disc and pleated configurations. As pleated cartridges come in two pleating configurations: traditional star pleat (standard fanpleat) and crescent (or 'laid-over' pleat), we included both pleat geometries in our analysis. In addition, the investigation examines the dynamics behind the observed differences.

## MATERIALS AND METHODS

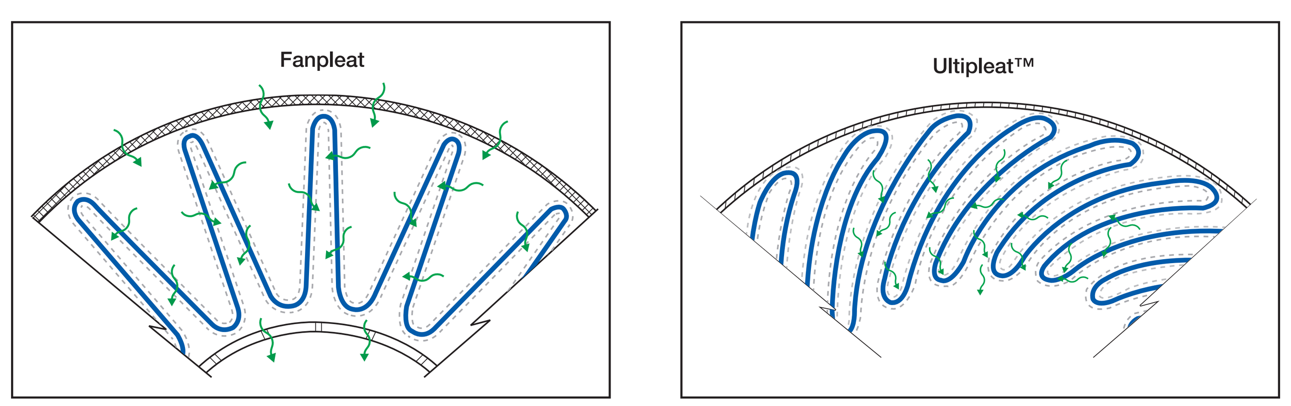
### Filters

47 mm diameter discs of Pall Fluorodyne® EX grade EDF 0.2 µm membrane were evaluated (filtration holder area = 11.1 cm²). The pleated Pall Fluorodyne EX membrane configurations evaluated were 5.1 cm (2 inch) nominal length "fanpleat" modules (filtration area = 0.075 m²) as well as 2.5 cm (1 inch) and 25.4 cm (10 inch) nominal length Ultipleat® construction cartridges (laid-over pleats, filtration areas = 0.11 m² and 1.1 m², respectively) (Figure 1).

Test work was also conducted with 47 mm diameter discs, 2.5 cm (1 in.), and 25.4 cm (10 in.) nominal length Ultipleat construction cartridges (filtration area = 0.095 m² and 0.95 m², respectively) for 0.1 µm Pall Fluorodyne EX EDT membrane.

**Figure 1.**

*Schematic showing pleat structure and flow direction in a traditional "fanpleat" or "starpleat" filter cartridge and a "crescent" or "laid-over" Ultipleat pleated filter cartridge.*




### *Challenge Solutions*

A range of challenge solutions were used for filtration studies. These include IgG with 0.85% NaCl prepared in pH 7.4 phosphate buffer, bovine whey in pH 7.4 phosphate buffer, pepsin in pH 7 phosphate buffer and cell culture media (Dulbecco's Modified Eagle Medium, DMEM) supplemented with peptones (Porcine Peptone 3 and HySoyT). The solutions were filtered under a range of operating conditions to assess the effect of operating conditions on scalability. Additionally, several concentrations of whey were filtered to assess the effect of solution concentration. The list of challenge solutions and operating conditions are summarized in Table 2.

### Methods

Water permeability of the filters was measured at a constant differential pressure of 10 psi prior to filtering the challenge solutions. A disc, a fanpleated capsule, and an Ultipleat cartridge were run in parallel.

For constant pressure trials, filtration was conducted in parallel through the three filter configurations to ensure a consistent challenge solution while applying the same differential pressure across all filters. Filtration was stopped after 90% flux decay was achieved.

For constant flow trials, filtration was stopped after a differential pressure of 20 psi was reached across all the filters. For both constant pressure and constant flux filtration, each solution was filtered multiple times using new filters each time.

## RESULTS AND DISCUSSION

### Water Flux Ratio

The water permeabilities obtained during the investigation for discs, fanpleat and Ultipleat cartridges are listed in Table 1. The permeabilities for the 1 in. and 10 in. Ultipleat cartridges are consistent and 50% lower than the permeability obtained for the discs with Fluorodyne EX EDF membrane. The permeability for fanpleat cartridges was 23% lower than that obtained for the discs.

**Table 1**

*Clean Water Permeabilities (temperature-corrected to 20 °C) and Water Flux Ratios. The Flux Ratio is Defined as the Ratio of the Water Permeability of a Pleated Device to that of a Flat Disc*

| 0.2 µm Pall Fluorodyne EX Grade EDF Membrane Filters | Mean Water Permeability (20 °C, LMH/psi) | Water Flux Ratios Relative to 47 mm Disc |
|---|---|---|
| 47 mm Disc (n = 21) | 624 ± 5% | 1 |
| Fanpleat 2 in. (n = 26) | 479 ± 8% | 0.77 |
| Ultipleat 1 in. (n = 21) | 305 ± 11% | 0.49 |
| Ultipleat 10 in. (n = 5) | 319 ± 17% | 0.51 |

### Capacity Ratio

In this study, capacity is defined as the throughput (filtered volume per unit membrane area) at which the fluid flow rate through a filter configuration drops by 90% (for constant pressure operation) or at which the differential pressure across the filter assembly reaches a particular pressure drop (usually 20 psi) (for constant flow operation). Capacity ratio is defined as the ratio of throughput for a pleated filter to that of disc. The throughput values and capacity ratios for solutions tested are shown in Figure 2 and tabulated in Table 2.

**Figure 2**

*Plot shows Capacities of the Filters Tested*

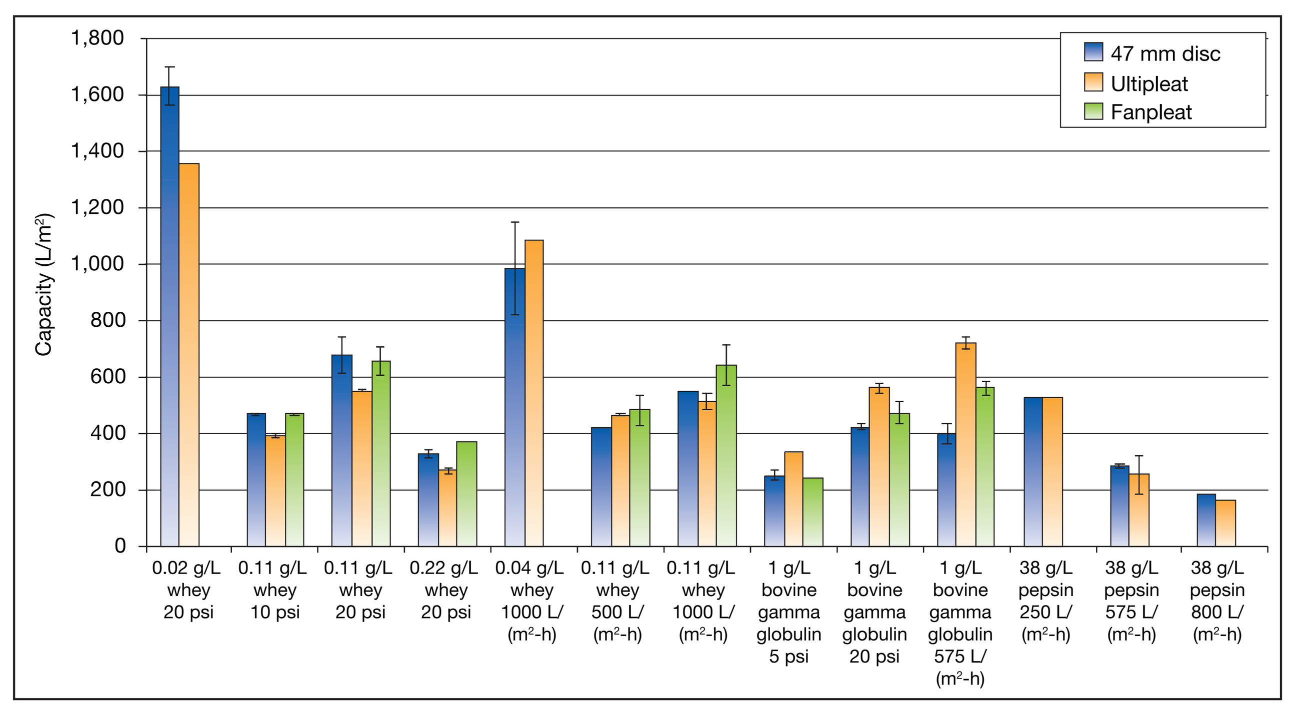



**Table 2**

*Summary of the Capacity and Capacity Ratios*

| Fluorodyne EX Grade EDF Membrane Filters | 47 mm Disc Mean Capacity [L/m²] | 2 in. Fanpleat Mean Capacity [L/m²] | 1 in. Ultipleat Mean Capacity [L/m²] | 2 in. Fanpleat Capacity Ratio | 1 in. Ultipleat Capacity Ratio |
|---|---|---|---|---|---|
| **Test Conditions** | | | | | |
| 0.02 g/L whey – 20 psi | 1627 | – | 1355 | – | 0.83 |
| 0.11 g/L whey – 10 psi | 469 | 469 | 392 | 1.00 | 0.84 |
| 0.11 g/L whey – 20 psi | 678 | 658 | 552 | 0.97 | 0.81 |
| 0.22 g/L whey – 20 psi | 330 | 373 | 268 | 1.13 | 0.81 |
| 0.04 g/L whey – 1000 L/(m².h) | 986 | – | 1082 | – | 1.10 |
| 0.11 g/L whey – 500 L/(m².h) | 420 | 483 | 467 | 1.15 | 1.11 |
| 0.11 g/L whey – 1000 L/(m².h) | 550 | 644 | 515 | 1.17 | 0.94 |
| 1 g/L IgG – 5 psi | 253 | 243 | 334 | 0.96 | 1.32 |
| 1 g/L IgG – 20 psi | 423 | 473 | 560 | 1.12 | 1.32 |
| 1 g/L IgG – 575 L/(m².h) | 400 | 560 | 720 | 1.40 | 1.80 |
| 38 g/L pepsin – 250 L/(m².h) | 530 | – | 529 | – | 1.00 |
| 38 g/L pepsin – 575 L/(m².h) | 288 | – | 255 | – | 0.89 |
| 38 g/L pepsin – 800 L/(m².h) | 183 | – | 162 | – | 0.89 |

The capacity ratios for the Fluorodyne EX grade EDF "fanpleat" capsule filters range from 0.96 – 1.4 and for the Ultipleat cartridge from 0.8 – 1.8 (Table 2). This strongly suggests that the lower water permeability values obtained in pleated cartridge has no correlation to the filtration performance characterized by filtration capacity.

## RESULTS AND DISCUSSION *(continued)*

The data was analyzed to understand how the capacity ratios for pleated filters and discs are influenced by:

1. Choice of feed solution
2. Mode of operation (constant pressure versus constant flow)
3. Operating pressure or flux magnitude, and
4. Concentration of fouling species present in the feed solution.

The data confirms the capacity ratio is independent of the level of the pressure or flux, as well as is insensitive to the degree of fouling for a given feed solution and mode of operation.

For certain solutions, the capacity ratio was greater than 1, suggesting the Ultipleat geometry improves filterability. Based on all the trials, the lowest capacity ratio for pleated filters to that of discs is 0.8. For practical design purposes, the capacity scaling factor from discs to Ultipleat configurations may conservatively be assumed to be 0.8.

With 0.1 µm-rated Fluorodyne EX EDT, the capacity ratio lies between 1.8 and 1.1, except for one particular solution, media supplemented with HySoyT mixture, for which a lower capacity ratio was observed with both Ultipleat and "fanpleat" filter configurations and with similar micron rated filters from other manufacturers[3]. This reinforces that the capacity ratio among different filter formats is solution properties dependent. Further tests conducted showed that, with this particular solution, use of a 10 µm pre-filtration improved the capacity ratios by 80% (from 0.40 to 0.72) specifically resulting from removal of large particulates from feed solution [4].

### Flux Dynamics

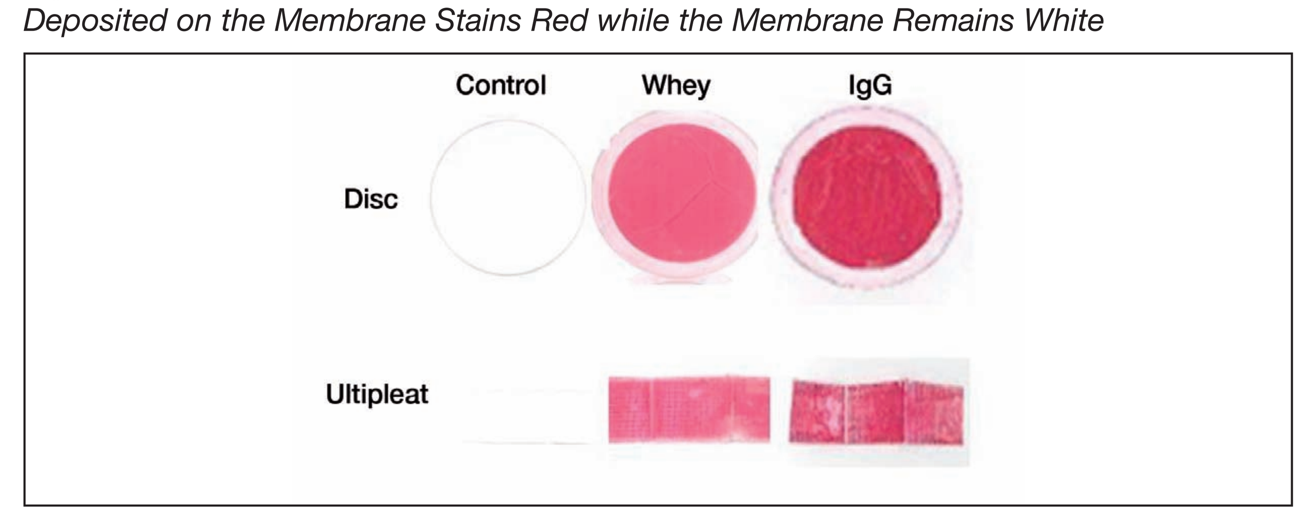
A series of investigations were conducted to understand why the flux and capacity do not scale up linearly. These include: (a) estimation of membrane area utilized for the filtration in pleated filter and disc by performing dye binding studies and (b) mathematical modeling to understand flux and transmembrane pressure distribution in a pleat.

### Dye Binding Studies

The utilization of membrane surface area during filtration was characterized through the use of a dye (Ponceau S) after filtering various protein solutions through the membrane. Figure 3 shows membranes that have been exposed to the dye after processing IgG and whey as well as a control wetted out with water. The red color in both the tip and the roots of the pleats (Figure 4a) demonstrate that 100% of the surface area of the membrane is used through the filtration process.

**Figure 3**

*Representative Samples of Membranes from Filters used to Filter 0.11 g/L Whey and 1 g/L IgG Solution. The Membranes were Immersed in a Protein-staining Dye, and Protein Deposited on the Membrane Stains Red while the Membrane Remains White*




### Modeling the Flow through the Pleated Structure

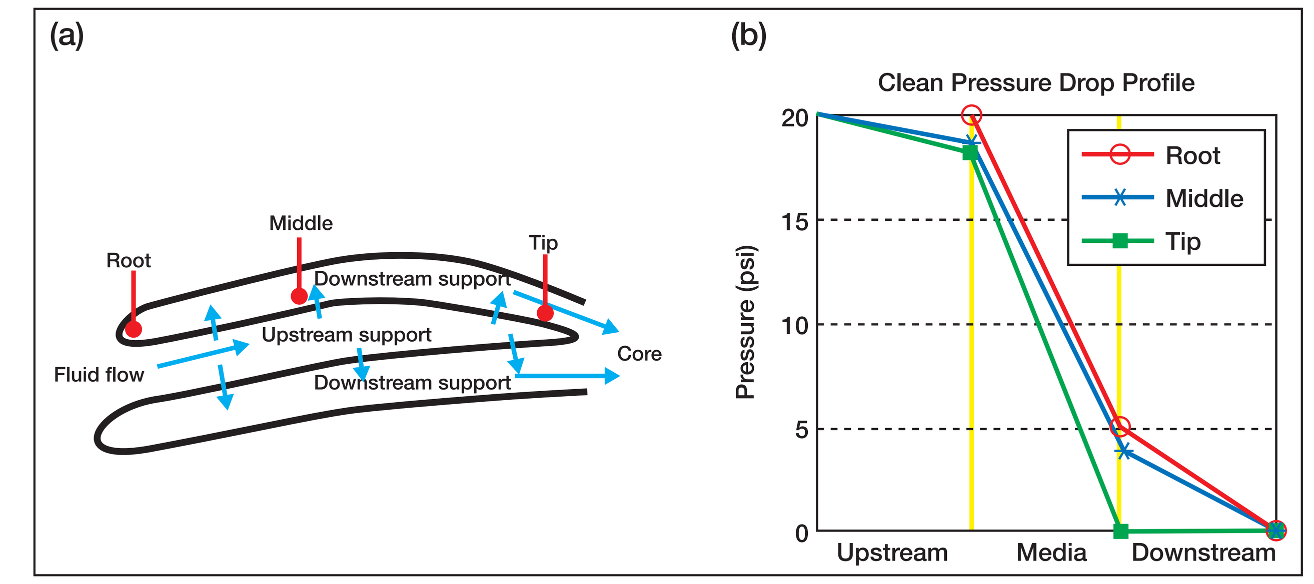
A mathematical model was used to characterize the pressure and flux profiles along the pleats. The model incorporated the lateral hydraulic resistances of the support layers upstream and downstream of the membrane together with the permeability of the membrane to compute the pressure and flux profiles. The results for a Fluorodyne EX grade EDF Ultipleat cartridge while filtering a non fouling liquid with a viscosity of 1 cp are shown in Figure 4.

The results of the model predict a lower average transmembrane pressure as well as a non-uniform pressure profile along the pleat length as a result of the additional hydraulic resistances of membrane support layers. Lower average transmembrane pressure explains the lower flux values observed in both pleated configurations ("fanpleat").

## CONCLUSIONS

**Figure 4**

*(a) Schematic showing flow direction and different sections of a pleat, and (b) shows transmembrane pressure profile at root, middle, and tip.*




## CONCLUSIONS

Dye binding studies demonstrated that all the membrane area in an Ultipleat configuration filter is utilized during the filtration and that lower values of flux and capacity is not related to the inaccessibility of the complete membrane area.

It was also observed that the clean water permeabilities for fanpleat capsules and Ultipleat cartridges were lower (23 and 50% respectively) than the permeabilities obtained for the disc. Mathematical modeling of flow through an Ultipleat filter predicted a lower average transmembrane pressure as well as a non-uniform transmembrane pressure profile along the pleat length resulting from the additional hydraulic resistances of membrane support layers in a pleated filter. Lower average transmembrane pressure explains the lower flux values observed in both pleated configurations. Furthermore, this study shows that lower clean water permeability values obtained in pleated cartridges has no correlation to the filtration performance characterized by filtration capacity.

For Fluorodyne EX grade EDF membrane, the capacity ratios of the pleated filters relative to discs depends upon the nature of the feed solution and has been shown to vary from 1.8 to 0.8 for Ultipleat configuration cartridges. This suggests that in the most conservative design case for these filters, the area calculation from disc to pleated cartridge could allow for a 0.8 scaling factor. In that case, the high area per unit cartridge in the Ultipleat configuration should still result in better overall process economics compared with other pleating options. Further studies may confirm that even more advantage may be taken in the case of feed solutions with capacity ratio greater than 1 or where the capacity ratio remains unaffected by the level of the pressure or flux, as well as by the degree of fouling for a given feed solution or mode of operation.

In conclusion, we recommend use of 47 mm discs for initial screening and process optimization, whereas 1 in. cartridge elements should be used for filter sizing.

## ACKNOWLEDGEMENTS

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