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Application Note

Improved Accuracy of Scaling with OptiScale® 25 Devices

Scalable Process Filtration with OptiScale® 25 Devices

Abstract

Process development scale up tools should contain a minimum of membrane area to reduce required test volume of the valuable bioprocess fluid and should scale predictably to the corresponding large scale devices. However, performance differences may exist due to differences in flow geometries between the small and large scale devices, and variability in membrane and fluid properties. The effect of these differences is added risk and uncertainty in scaling estimations, necessitating the use of large safety factors that result in increased costs. In this study, key factors that impact scale up of OptiScale® devices were identified and quantified. Successful scale-up was realized by: **a)** proper small scale device design to maximize performance consistency; **b)** modeling the effect of device pleating on performance; **c)** instituting controls for membrane variability and; **d)** proper accounting of process hydraulic effects associated with fittings and elevation.

Introduction

Process development filtration evaluations are typically conducted using low volumes of process fluids using either discs or small devices to assess membrane performance. Measurements of flux and throughput per unit of membrane area can be used for initial estimates of filter requirements at full-process scale. Ideally, the process development tools contain a minimum of membrane area to conserve bioprocess test fluid requirements and scale linearly to their corresponding large scale devices. However, linear scale-up of small to large devices is sometimes not achieved in practice. Clean water flux in pleated cartridge devices has been shown to be up to about 50% lower than in small (47 mm) disc devices.[1] For some challenge stream conditions, where significant fouling occurs, even greater discrepancies between disc and cartridge performance have been observed.[2,3]

There are a number of factors that can confound scaling predictions if they are not carefully measured and controlled. These factors include: differences in flow geometries between small and large scale devices, fluid accessible filtration area, pressure losses associated with plumbing and elevation, and variability in fluid properties and membranes. Proper accounting of these factors has been shown to improve scaling performance. For example, a model that accounts for the hydraulic properties of porous pleat supports was shown to closely predict flux loss associated with pleating.[4] Careful accounting for fittings pressure losses, and modeling filtration performance based on membrane fouling mechanisms, have also been shown to increase the reliability of scaling calculations.[5] However, even taking into consideration these issues, large safety factors (typically between about 1.3 and 2) are commonly used to allow for variability in membrane performance and process conditions.[5,6,7]

To address process developer's need for reliable and consistent low volume filter sizing and scale up tools, we developed the OptiScale® 25 device. In this application note, the scalability of OptiScale® 25 devices to 10 inch cartridges was evaluated.

Materials and methods

Membranes and Challenge Streams

The filters evaluated included: Millipore Express® SHR 0.1 µm filters, Millipore Express® SHR with prefilter 0.5/0.1 µm filters, Millipore Express® SHF 0.2 µm filters and Millipore Express® SHC 0.5/0.2 µm filters. For the small scale tests, 25 mm membrane discs were installed into OptiScale® 25 devices, which contain 3.5 cm^2 of effective filtration area. All of the large scale tests were performed on commercially available 10 inch pleated cartridges. **Table 1** lists the cartridge types and relevant attributes.

Table 1. Properties of 10 inch cartridges evaluated in this study.

Device Code	Membrane Description	Pleat Support Material	Effective Filtration Area (m^2)
SHF-A	0.2 µm PES	Polypropylene	0.49
SHF-G	0.2 µm PES	Polyester	0.57
SHC-A	0.5/0.2 µm PES	Polypropylene	0.50
SHC-G	0.5/0.2 µm PES	Polyester	0.54
SHR-A	0.1 µm PES	Polypropylene	0.60
SHR-G	0.1 µm PES	Polyester	0.69
SHRP-A	0.5/0.1 µm PES	Polypropylene	0.49
SHRP-G	0.5/0.1 µm PES	Polyester	0.54

For all water permeability tests, small and large scale devices, reverse osmosis purified water was used. For throughput testing, three challenge streams were used as listed in **Table 2**. All solutions were prepared in 200-500 L quantities.

Table 2. List of challenge streams for throughput tests.

Filter	Challenge Stream
Millipore Express® SHC 0.5/0.2 µm PES	0.3 g/L soy T in Hyclone® DMEM with 3.7 g/L sodium bicarbonate and 1 g/L Pluronic® F-68 surfactant
Millipore Express® SHR 0.1 µm PES	5 g/L Bacto tryptic soy broth in Hyclone DMEM, 3.7 g/L sodium bicarbonate, 1 g/L Pluronic® F-68 surfactant
Millipore Express® SHR with prefilter 0.5/0.1 µm PES	2.0 g/L EMD soy in Gibco® DMEM with 3.7 g/L sodium bicarbonate and 1 g/L Pluronic® F-68 surfactant

OptiScale® 25 Design

The OptiScale® 25 device configuration is illustrated in **Figure 1**. The device contains a 25 mm membrane disc and a non-woven porous support that allows for unimpeded flow of filtrate to the underdrain and outlet. The underdrain structure was designed to provide good mechanical support for the membrane without restricting liquid flow.

Test Method

Both OptiScale® 25 devices and 10 inch cartridges were tested for clean water permeability at 10 psid and 21–25 ºC. Following the water permeability test, throughput tests using one of the challenge streams were run at 10 psid. Throughput testing was run until the membrane permeability was reduced by at least 95% compared to the clean water permeability.

Figure 1. Device design for evaluating 25 mm membrane discs. The membrane frontal area is 3.5 cm^2.

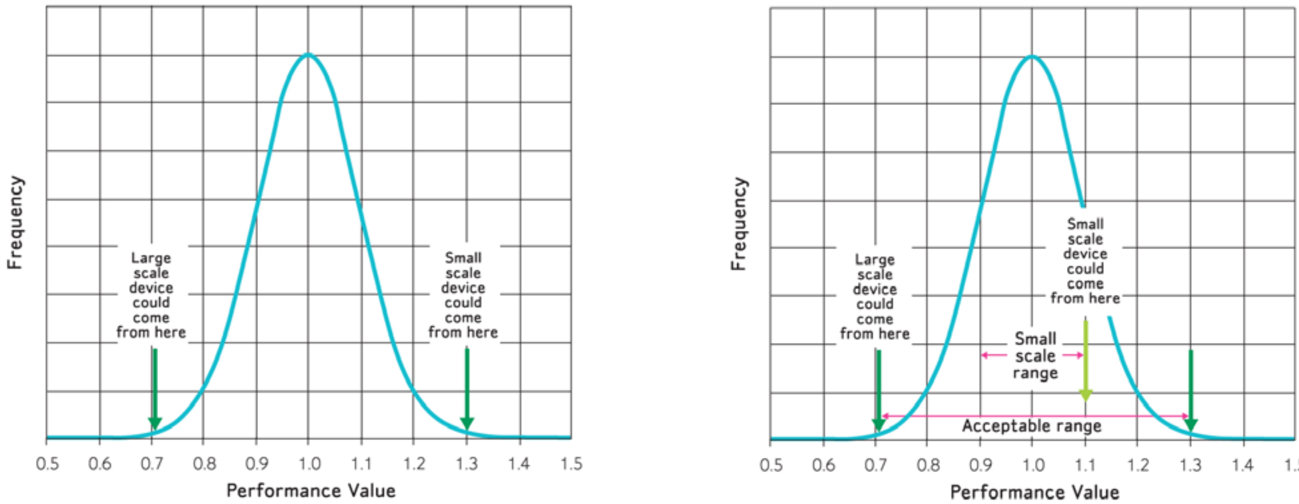

Figure 2. **a)** Hypothetical distribution of membrane performance (permeability or throughput capacity). **b)** Method for reducing scaling uncertainty.

Minimizing Membrane Variability

Estimates of process scale filter sizing that are extrapolated from small scale data should account for the possible range of membrane performance. Using a small scale device made with membrane from a well defined portion of the known manufactured membrane distribution can significantly reduce scaling uncertainties associated with membrane variability, as is illustrated in **Figure 2**. By design, all OptiScale® 25 devices contain only membrane that represents the center of the membrane performance distribution, which provides greater consistency and reliability in scale up and can allow for the scale-up safety factor to be substantially reduced.

Results and analysis

To demonstrate scaling accuracy, OptiScale® 25 devices and three 10 inch devices of each type listed in **Table 1** were tested for water permeability. The OptiScale® 25 devices and the corresponding 10 inch devices contained membrane originating from the same membrane lot. As shown in **Figure 3**, within lot permeabilities, the OptiScale® 25 devices closely tracked their corresponding 10 inch filter devices.

Water permeability

Figure 3 shows that there was good agreement (within 10%) between the predicted and measured permeate water flow rates for each of the membrane/cartridge types tested. The predicted values account for pleating effects[4], which will impact flow rates by 5–15% depending on cartridge type, and housing pressure losses.

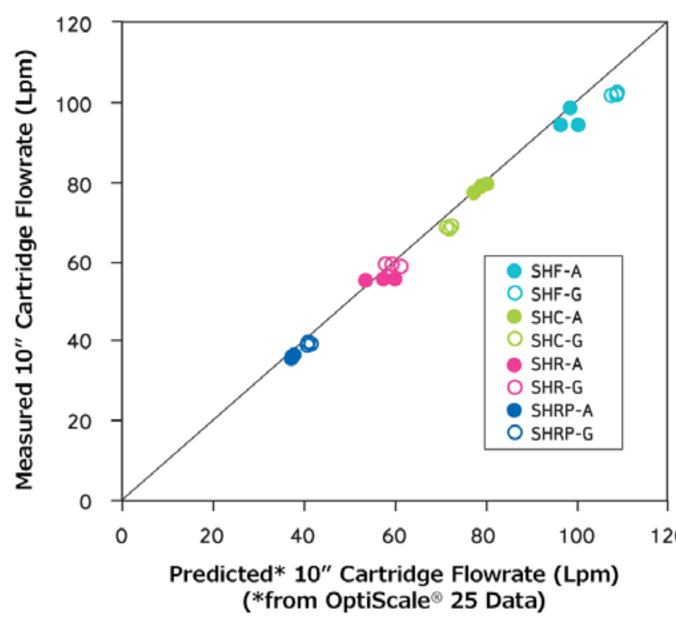

Figure 3. Water flow rate scaling predictions, accounting for housing pressure losses and pleating effects.

Throughput

Bioprocess fluids representing high fouling applications were also evaluated for all filter types listed in **Table 1**, except for the single layer Millipore Express® SHF 0.2 µm filter, which is typically utilized in low fouling applications. **Figure 4** shows measured vs predicted throughput after approximately 30 minutes of filtration time and a minimum 95% flux decay. Here again, there was excellent agreement between predicted and measured values.

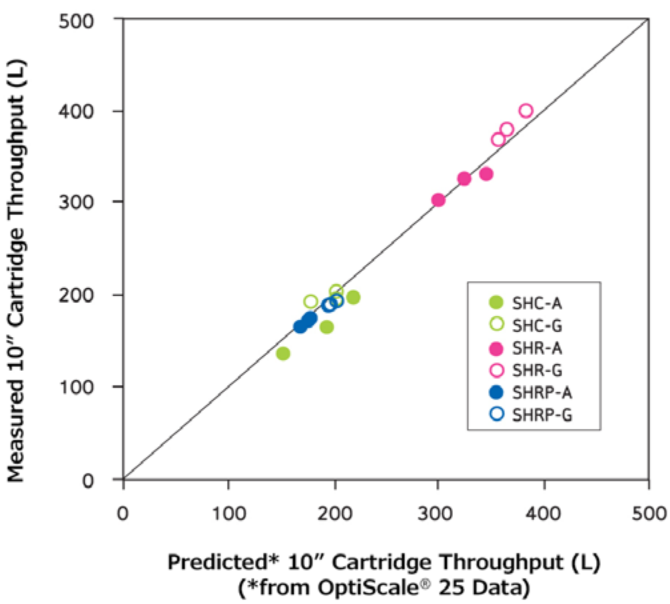

Figure 4. Measured vs. predicted throughput at a minimum 95% flux decay.

Conclusions

Scaling predictions of large-scale membrane filtration device performance from small scale devices must account for a number of factors, including differences in flow geometries between small and large scale devices, extramembrane flow resistances, and fluid accessible membrane area. Variability in membrane and fluid properties can also add uncertainty in scaling estimations.

It was found that successful scale-up could be realized by: **a)** proper small scale device design; **b)** employing models that simulate the effect of pleating on device performance; **c)** defining a narrow performance range for membranes installed into small scale devices; and **d)** proper accounting of hydraulic effects associated with fittings and elevation. Excellent agreement was found between measured and predicted 10 inch cartridge performance using OptiScale® 25 devices which enables lower scale-up safety factors and translates directly into savings in system size and cost.

References

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