Improve Process Efficiency in Bioprocess Streams by Prefiltration Optimization and Bioburden Reduction

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Introduction

Membrane-based prefilters are an important component of many downstream operations. They are used to limit the variability of process streams by removing plugging contaminants thereby protecting sterilizing-grade filters and other unit operations. Some prefilters contribute to process safety by reducing bioburden in intermediate process steps where sterilizing grade filters are not required.

Milligard® PES filters contain polyethersulfone (PES) membranes of different pore sizes for efficient particle removal from a broad range of process streams. These prefilters are compatible with caustic sanitization, gamma irradiation, autoclave and steam in place (SIP) sterilization methods. Table 1 lists the different pore sizes of Milligard® PES filters.

This poster summarizes throughput and bacterial retention performance of Milligard® PES membranes in OptiScale® capsules challenged with different streams. Throughput capacity was determined either alone or with a downstream sterilizing-grade filter.

Table 1. Milligard® PES Filters

Application	Milligard® PES Filter	Bioburden Reduction
Particle & Bioburden Reduction	1.2/0.2 µm nominal	≥6 LRV *Brevundimonas diminuta*
	1.2/0.45 µm	≥6 LRV *Serratia marcescens*
Particle Reduction	1.2/0.8 µm	NA

Methods

Throughput capacity studies

The streams used in these studies were selected to represent a wide range of particle sizes and particle size distributions (Figure 1); they were concentrated to achieve a high degree of plugging (> 90% flux decay at < 1000 L/m² of filtrate).

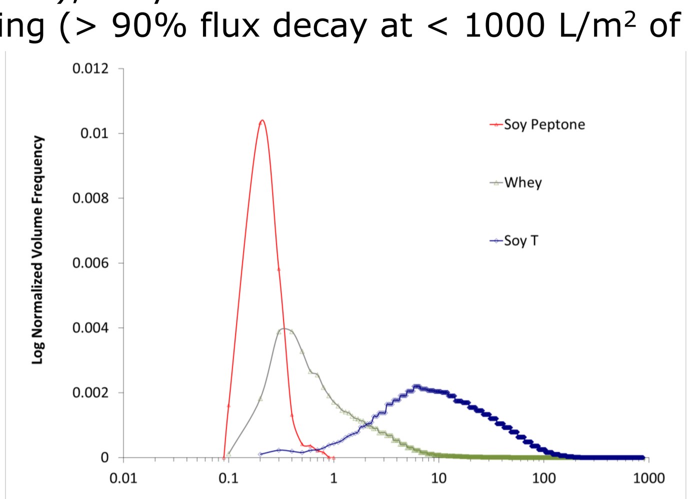

Figure 1. Particle size distributions of model streams

Throughput capacity of final sterilizing grade filters was measured both with and without Milligard® PES prefilter protection. The effect of different prefilter to final filter area ratios on throughput capacity was explored at area ratios ranging from 0.5:1 to 3:1. Tests were performed at both constant pressure (10 psi) and constant flow (500 LMH final filter) operating conditions. The experimental setup is illustrated in Figure 2.

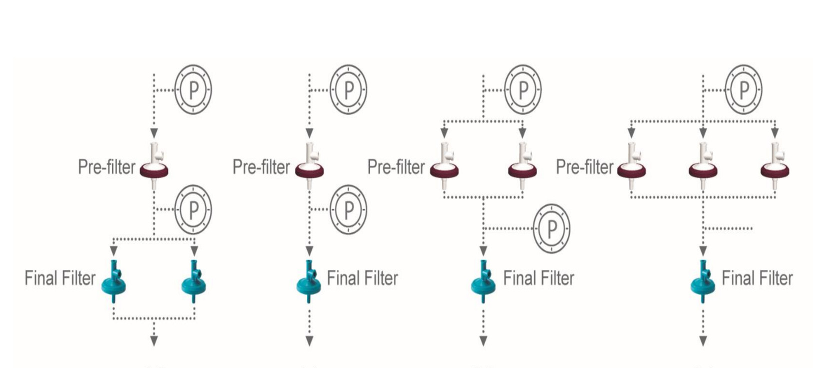

Figure 2. Experimental setup for throughput capacity tests

To quantify the particle removal capability of the prefilters, particle concentrations and size distributions of the challenge stream feeds and filtrates were measured using an optical particle counter (Liquilaz SO2).

Bioburden reduction studies

Bioburden reduction was evaluated using Milligard® PES 1.2/0.2 µm nominal and 1.2/0.45 µm membrane in OptiScale® capsules challenged at 2 psi with Soy peptone spiked with *Brevundimonas diminuta* or *Serratia marcescens.* Retention of these microorganisms was evaluated at different points of filter plugging.

Results

Final filter protection and throughput

Figure 3 illustrates the throughput capacity of a Durapore® 0.22 µm filter alone, and paired with a Milligard ® PES 1.2/0.2 µm nominal prefilter. The capacity of the combined prefilter/final filter train was almost 10 fold higher than that of the sterilizing filter alone.

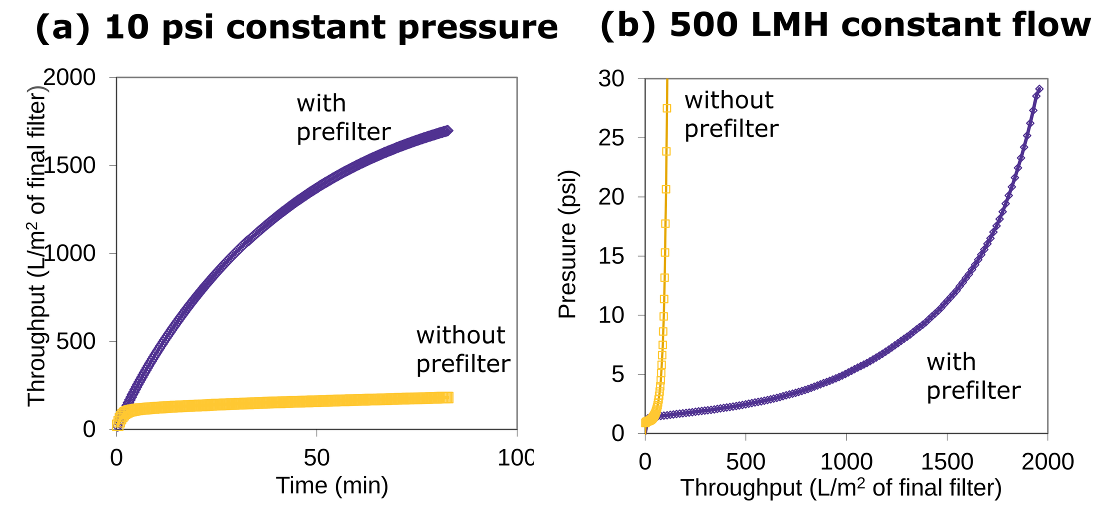

Figure 3. Effect of Milligard® PES 1.2/0.2 µm nominal filters on capacity of Durapore® 0.22 µm filter: (a) 10 psi constant pressure (b) 500 LMH (final filter) constant flow.

The impact of prefiltration on final filter throughput capacity for the 3 pore sizes of Milligard® PES filters, with 3 different particle size distribution streams, and 2 types of final filters (PVDF and PES) is summarized in Figure 4. These studies were performed at constant pressure of 10 psi.

The magnitude of final filter throughput improvements was dependent on the filter pore size, challenge feed, and the type of sterilizing filter. As prefilters have lower unit costs than sterilizing filters, any improvement in capacity due to prefilters can result in dramatic improvements in filtration economics.

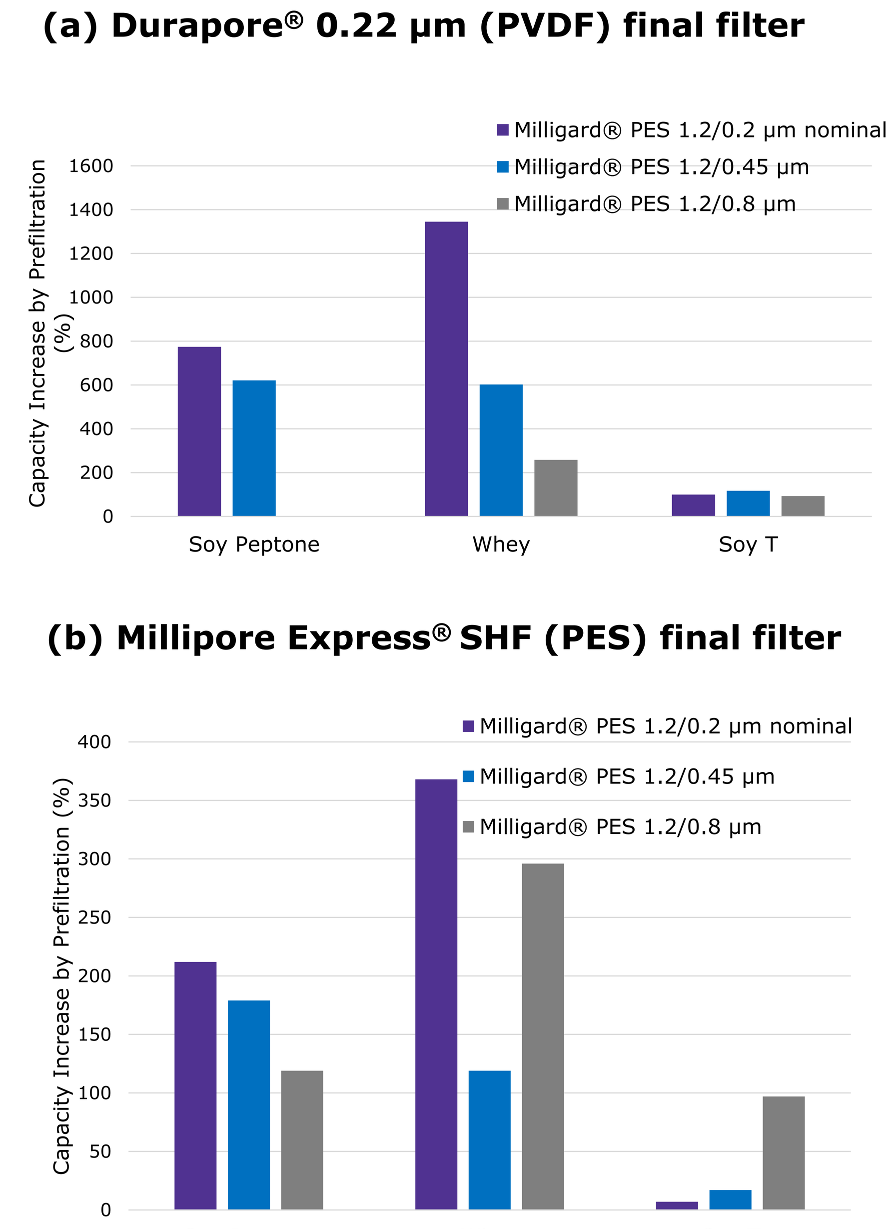

Figure 4. Final filter capacity improvement by prefiltration. % improvement is compared to stand-alone final sterilizing filter: (a) Durapore® 0.22 µm (PVDF) final filter; (b) Millipore Express® SHF (PES) final filter.

Optimization of area ratio

Increasing prefilter area will often improve final filter capacity. Optimizing the prefilter to final filter area ratio can result in a cost-effective filtration solution. Figure 5 shows an example of the capacity benefit of different area ratios. A theoretical model is available for efficient system sizing and optimization.

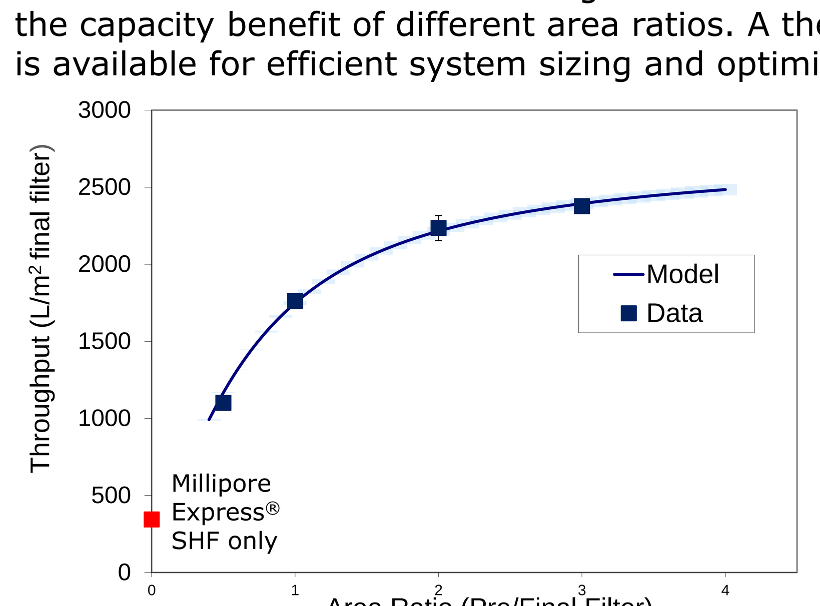

Figure 5. Effect of prefilter (Milligard® PES 1.2/0.2 µm nominal) to final filter (Millipore Express® SHF) area ratio on throughput capacity in Soy peptone at 10 psi constant pressure.

Particle removal by prefilters

Prefilters protect final filters and other unit operations by removing particles that would otherwise plug or contaminate downstream unit operations. Particle removal capability was quantified by measuring cumulative concentration of particles of different sizes in the Soy peptone challenge and filtrate solutions after processing through Milligard® PES filters. Most particles in this solution are smaller than 1.0 µm in size, with the highest concentration being at approximately 0.2 µm in diameter (Figure 1). Figure 6 shows that all Milligard® PES filters retained over 90% of the particles between 0.2 µm and 1.0 µm.

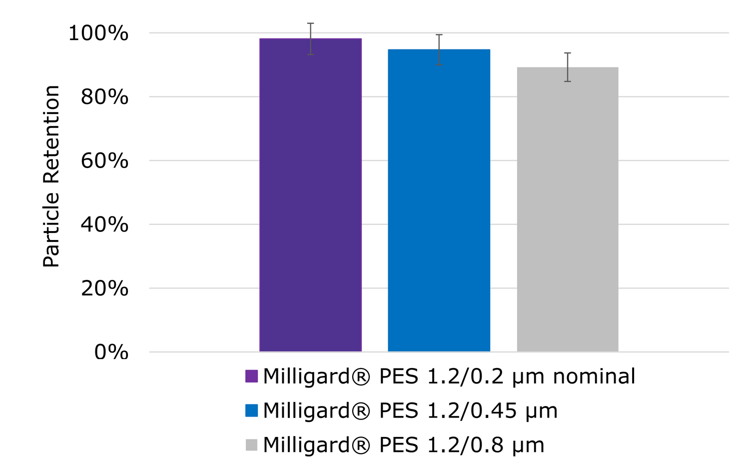

Figure 6. Soy peptone particle retention by Milligard® PES filters.

Bioburden reduction

Prefilters can provide an increased level of process safety by reducing bioburden. Milligard® PES 1.2/0.2 µm nominal filters have been validated to demonstrate ≥6 log *B. diminuta* retention while the Milligard® PES 1.2/0.45 µm filters have been validated to demonstrate ≥6 log retention of S. *marcescens*.

Figure 7 shows microorganism retention by 'stand alone' Milligard® PES 1.2/0.2 µm nominal and Milligard® PES 1.2/0.45 µm filters in the absence of a final sterilizing filter. The microorganism challenge level was > 10^7 cfu/cm² and filtrate grab samples were collected at different points of filter plugging. As would be expected based on a retention mechanism based on size exclusion, microorganism retention was robust (no breakthrough) under all conditions.

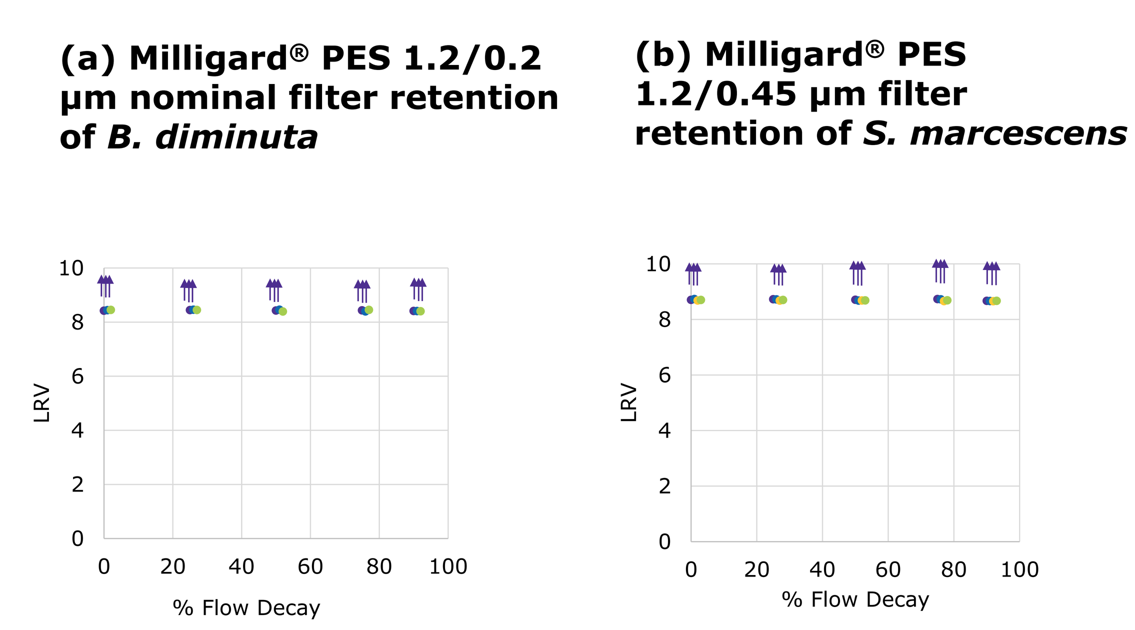

Figure 7. Log reduction values (LRV) as a function of filter plugging. (a) Milligard® PES 1.2/0.2 µm nominal filters challenged with *B. diminuta*; (b) Milligard® PES 1.2/0.45 µm filters challenged with *S. marcescens.* Data points indicate results from individual OptiScale® 25 devices; arrows indicate complete retention.

Summary

Milligard® PES filters are available in a range of pore sizes for processing different streams, are compatible with multiple sterilization methods, and have been validated to reduce bioburden. These filters:

- Dramatically improve the throughput capacity of both PVDF and PES sterilizing-grade filters, significantly improving filtration economics.
- Efficiently remove particulates from process streams.
- Can be used 'stand-alone' to provide sustained bioburden reduction even under conditions of extreme filter plugging.

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