Sterile filter membrane selection for cell culture media filtration

Introduction

Sterile filtration is a critical step in bioprocessing because it is used to help ensure that fluids entering a manufacturing process are free of microorganisms. Filtration is a key part of a broader contamination control strategy (CCS), helping protect product quality and process integrity. In practice, sterile filters are commonly used in applications such as cell culture media preparation, where maintaining sterility before fluid enters the bioreactor is essential. Sterilizing-grade filters must balance microbial retention with process efficiency. Their performance, especially in terms of capacity and throughput, can significantly impact process reliability, cost, and overall system design.

While mycoplasma-retentive (0.1 µm) filters are employed as enhanced barrier solutions in some bioprocesses, their reduced pore size inherently increases flow resistance, typically resulting in lower filtration flux. Consequently, implementation of these higher-retention filters requires careful consideration of process throughput, pressure limitations, and overall filtration economics. High-fouling fluid streams often require a prefilter upstream of the sterilizing-grade filter, increasing cost and complexity.

Thermo Scientific™ LifeASSURE™ PDA Series Filters with a 0.2-µm pore rating and a built-in upstream prefilter layer are designed to process high-fouling streams. These filtration devices have been verified to be retentive, in accordance with American Society for Testing and Materials (ASTM) F838 standards, demonstrating complete retention of *Brevundimonas diminuta* (*B. diminuta*). The objective was to evaluate the LifeASSURE PDA filter under challenging filtration conditions and compare its performance with commercially available alternatives.

This study evaluated the performance capacity of common sterile filter membranes used in bioprocessing applications. Trypticase soy broth (TSB), a cell culture media component and common plugging stream model and surrogate, was used to evaluate the Thermo Scientific™ LifeASSURE™ PDA020 filter alongside four other double-layer polyether sulfone (PES) filters from leading suppliers.

Materials and methods

Model cell culture media

BD™ Bacto™ TSB (Soybean-Casein Digest Medium) was purchased from Waters Corporation. Fresh media were prepared for each experiment. All media batches were prepared from the same lot to 30 g/L by stirring the powder at 900 rpm in type II reverse osmosis deionized (RODI) water from PTI Process Chemicals at 55°C for 20 minutes. All media were cooled to 25°C prior to experiments. To ensure media quality, all media were prescreened using a Sper Scientific turbidity meter (Model 860040) to quantify turbidity. As a media prescreening tool, all experiments were run only when the turbidity values were below 1 nephelometric turbidity unit (NTU).

Filter membrane

All membranes evaluated in this study have a pore rating of 0.2 µm and are designed to handle high-capacity streams. The membranes were placed in a Millipore™ Swinnex™ 25 mm filter holder with a back pressure screen and a polypropylene non-woven fabric, Typar™ style, with 316L support from Fiberweb LLC. The filter holder was thoroughly wetted by static soak in a solution of 50% water and 50% isopropyl alcohol for ten minutes. This ensured that the filtration device does not have air locking or phobic spots, which artificially reduces the effective filtration area (EFA). Prior to each trial, pure water permeability was measured to ensure the membrane wetting process was adequate and the EFA was accurate.

Equipment and testing

A constant-volume experiment was run using the FilterTec™ II NFF Lab System. The Masterflex™ Easy-Load™ II pump head pumped water or TSB from a reservoir using a 1/8-inch tubing set. The fluid passed through a Parker SciPres II™ pressure sensor positioned immediately upstream of the filter holder, with a stated accuracy of ±3% over a range of 0 to 55 psi (0–3.79 bar). An OHAUS™ Adventurer™ Balance was used to measure the filtered broth exiting the outlet of the tubing set. Figure 1 shows the experimental setup for these lab-scale filterability studies.

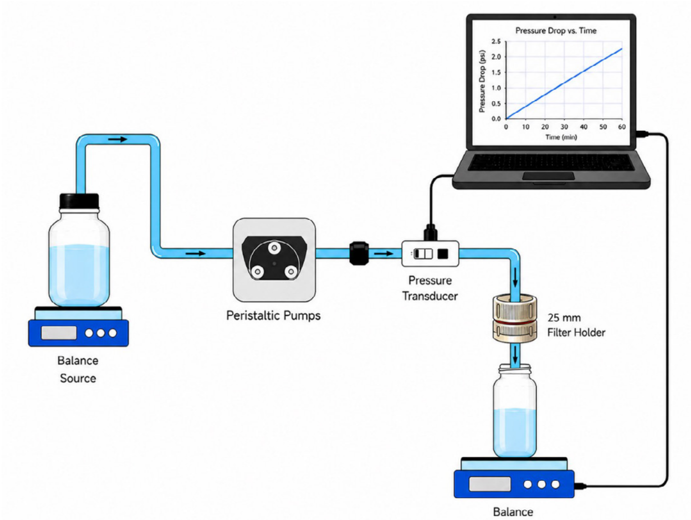

Figure 1. Experimental setup for constant volume filterability studies. Filterability studies were performed using a peristaltic pump to deliver media at a constant rate through a 25 mm filter holder. Data was recorded electronically on a pressure sensor located immediately upstream of the filter and an analytical balance measuring filtrate mass.

An initial pure water flow test was performed, with RODI water pumped at a rate of 35 mL/min for 10 minutes onto the scale through the filter holder. After that, the prepared TSB was sent at a rate of 8 mL/min (~1,250 L/m² per hour (or LMH), which is in the high range for typical constant volume filtration in bioprocesses) through the filter holder until the pressure at the filter holder reached 17 psi (1.17 bar). At 15 psi (1.03 bar) the pressure increase inside the filter was exponential. As additional data may introduce variability, 15 psi was set as the upper cutoff for data collection.

Results and discussion

This section describes how filter performance was evaluated between LifeASSURE PDA filters versus those from leading suppliers using 25 mm samples. To mimic the filtration process at the manufacturing scale, TSB was filtered through the membranes at a constant rate, enabling the observation of filter behavior up until the filter fouls or pressure buildup in the system would require a filter changeover. This method is also more accurate for plugging streams than experiments where the transmembrane pressure is kept constant.

Filter throughput and capacity

Figure 2 presents TSB capacity measurements. Pressure is shown as a function of throughput, defined as the volume of TSB filtered per unit of EFA. The LifeASSURE PDA filter demonstrated higher capacity under the evaluated conditions. The overall upstream pressure remained lower than that of other filters evaluated.

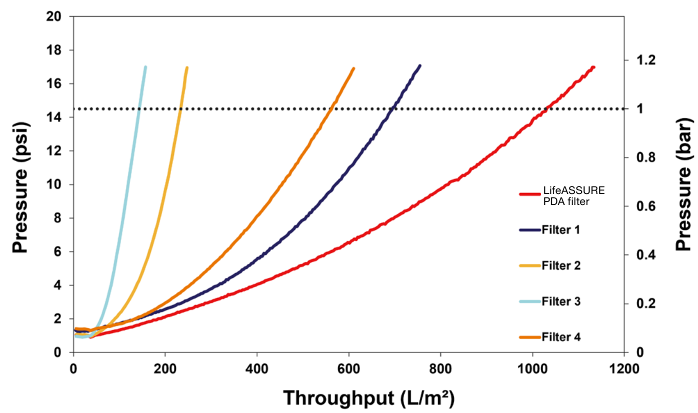

Figure 2. Filter capacity comparison. The capacity of the LifeASSURE PDA filter and four other filters was observed by flowing TSB at a constant rate and observing the pressure as a function of throughput.

Constant volume processes are often terminated when filter fouling causes the pressure to reach a defined threshold of 14.5 psi (1 bar), prior to the exponential increase that occurs in pressure across the membrane at 15 psi (1.03 bar). The LifeASSURE PDA filter maintained lower operating pressure throughout the experiment and demonstrated the highest capacity.

Figure 3 compares filter membrane TSB capacity at the 14.5 psi endpoint. The LifeASSURE PDA filter processed 1,051 L/m². Since all experiments were carried out using a similar methodology, the LifeASSURE PDA filter demonstrated a 34% higher capacity than other membranes tested. This was calculated by taking the difference in throughputs between the LifeASSURE PDA filter and the next-highest performing filter and dividing by the LifeASSURE PDA filter's throughput.

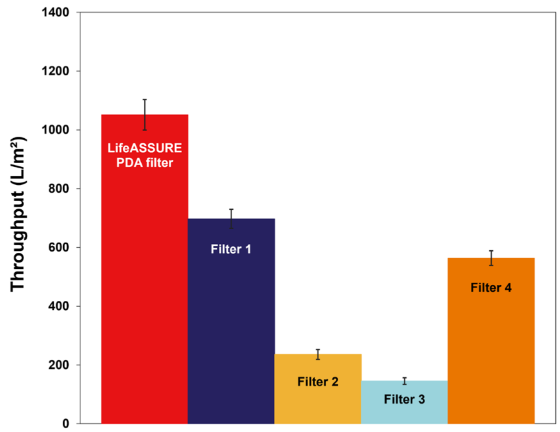

Figure 3: Throughput of TSB through the filter membrane at 14.5 psi (1 bar).

Thermo Scientific™ polyethersulfone (PES) membranes incorporate an advanced dual-layer retention design engineered to deliver superior filtration performance and process reliability. This innovative architecture combines a controlled upstream capture layer with a highly retentive downstream layer, enabling efficient depth filtration while maintaining precise retention.

The upstream membrane layer features a graded pore structure optimized for progressive particle capture. This architecture promotes low fouling behavior, high contaminant-holding capacity, and consistent throughput. Its robust mechanical strength and tailored pore distribution make it ideally suited for demanding applications such as bioprocessing, buffer preparation, and critical clarification.

The downstream membrane layer is fully retentive in accordance with ASTM F838 standards, demonstrating complete retention of *B. diminuta*. Designed with a slightly less asymmetric structure and an expanded retention zone, this layer features a gradual pore size transition across the membrane. This controlled distribution enhances bacterial retention assurance and adds a high level of process security.

Together, the upstream and downstream layers create a synergistic filtration system that captures particles throughout the membrane depth while maintaining stringent retention performance. The result is a membrane that facilitates high throughput, low differential pressure, and extended service life—making it a strong choice for filtration applications requiring both efficiency and reliability.

Case study: Process economy at 2,000 L

Small-scale filterability studies are the first step in scaling to larger processes. The measured capacity can be translated into the amount of EFA needed to filter 2,000 L of TSB under the tested conditions. The number and size of consumable filtration capsules can be derived from the theoretical EFA. Equations 1 and 2 demonstrate how the small-scale filterability trials were used to predict the minimum number of capsules required for a 2,000 L bioprocess.

$$\left(\frac{2{,}000\ \mathrm{L}}{1{,}051\ \frac{\mathrm{L}}{\mathrm{m}^2}}\right) = 1.90\ \mathrm{m}^2$$

Equation 1. Calculation of the minimum surface area of filter membrane required for a theoretical 2,000 L process of TSB by dividing the desired process volume by the throughput 1,051 L/m² observed at the small scale.

$$\frac{1.90\ \mathrm{m}^2}{2.34\ \frac{\mathrm{m}^2}{\text{30-inch capsule}}} = \text{one 30-inch capsule}$$

Equation 2: Calculation of the minimum number of capsules required for a theoretical 2,000 L process, by dividing the minimum surface area required by the surface area offered per capsule.

Figure 4 shows the predicted minimum number of filter capsules needed to process a theoretical 2,000 L batch of TSB for all filter suppliers.

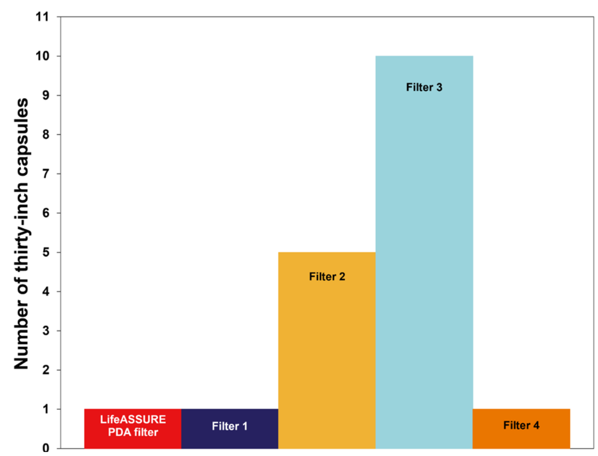

Figure 4. Minimum number of 30-inch capsules to filter 2,000 L of TSB.

Due to the LifeASSURE PDA filter's high capacity under the evaluated conditions, less membrane area is needed in a large-scale process. The LifeASSURE PDA filter's 30-inch capsule has an effective filtration area of 2.34 m². Therefore, to filter the 2,000 L of TSB, the process would require a single 30-inch LifeASSURE PDA capsule.

Conclusions

This study demonstrates that the LifeASSURE PDA020 filter enables consistently strong performance when compared to other 0.2 µm multilayer sterile filters evaluated under identical test conditions.

During TSB filtration, the LifeASSURE PDA filter maintained lower upstream pressure and achieved the highest throughput capacity, offering up to 34% greater capacity than the nearest competitor. This performance supports longer run times before pressure limits are reached and may reduce premature filter changeout.

Based on internal testing across five different products, Thermo Scientific's filter demonstrated comparable capacity to leading alternatives. In these evaluations, Thermo Scientific's filter was able to process 2,000 L using a single 30-inch capsule. Other leading vendors' products may require one or more 30-inch capsules to achieve the same volume.

These results suggest the potential for using a reduced membrane area and therefore fewer filter capsules in certain applications, which may help lower consumable usage, simplify installation and validation, and reduce handling time. Collectively, these factors can contribute to improved process efficiency and more favorable filtration economics, depending on the specific use case.

Overall, the Thermo Scientific LifeASSURE PDA filter demonstrates a balanced advantage in capacity and scalability, supporting efficient sterile filtration performance without increasing system complexity.

Authors

Cameron Butler, Engineer II, R&D

Sap Chattopadhyay PhD, Sr Manager, Purification

Matt Daley, Sr Product Manager

LP Raman, Sr. Manager, Bioprocessing Filtration

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