IMPROVED METHOD OF CHARACTERIZING ULTRAFILTRATION MEMBRANES FOR BIOPROCESSING

ABSTRACT

The porosity of an ultrafiltration (UF) membrane is typically characterized by the passage of molecular weight markers, being proteins or polymers. However, these methods have not been well-standardized in the industry. In this application note, we highlight a novel method and apply it to characterize SepraPor® hollow fiber ultrafiltration membranes manufactured by Meissner. This new characterization method provides for a more precise and comprehensive performance profile of UF membranes as compared to other characterization methods used in industry. Improvements in UF membrane characterization methods translate directly into more predictable purification processes with enhanced and more consistent batch-to-batch filtration performance.

INTRODUCTION

Ultrafiltration (UF) membranes are typically used in downstream processes such as purification and concentration for antibodies, mRNA vaccines, and virus-like particles (VLPs). Ultrafiltration also remains a critical purification tool in emerging cell and gene therapies (CGT) involving viral vectors and lipid-based vectors. Particularly, hollow fiber form factors are preferred over plate-and-frame cassettes in the CGT space due to their low shear, low fouling, and reliable performance. On the other hand, microfiltration (MF) membranes are more appropriately applied for micron-sized particles such as retention of cells in cell culture perfusion processes. Figure 1 shows the pore size distribution of UF membranes ranging from 5-50 nm and MF membranes with sub-micron pores illustrating the wide spectrum of pore sizes used in bioprocess filtration applications. The data shown come from typical results obtained from different types of membranes in the industry in order to highlight the contrast between both pore size denominations.

Figure 1: Pore size distribution of ultrafiltration and microfiltration membranes.
UF MEMBRANE CHARACTERIZATION

Permeability is a straightforward measurement involving water flow rates at fixed pressures. Porosity determination is however more ambiguous, as it depends on the supplier, as well as the membrane material and structure, as summarized in Table 1.

Table 1: Summary of parameters used to characterize ultrafiltration membranes.

<table>
<thead>
<tr>
<th>Ultrafiltration Membrane Characterization</th>
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<tr>
<td>Permeability</td>
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<tr>
<td>Clean water flux (LMH/bar)</td>
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<tr>
<td>Porosity</td>
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<tr>
<td>MWCO:</td>
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<td>Molecular weight cut-off (kDa)</td>
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Advanced Molecular Weight Cut-Off Assignment Method

SepraPor® uses a minimum of three molecular weight (Mw) markers to characterize the molecular weight cut-off (MWCO) of a UF membrane. MWCO characterization is performed on each UF membrane lot manufactured. Figure 2 compares the passage profiles of a SepraPor® 300 kDa MWCO membrane manufactured by Meissner and a 300 kDa MWCO membrane from another manufacturer (Supplier A). SepraPor® follows an advanced method of characterization comprising of multiple Mw markers. The Mw markers used for MWCO characterization are assigned numbers from 1 to 4. Marker 1 has the lowest Mw, while the Mw of the other markers progressively increases with increasing numbers up to 4. For each Mw marker tested (1 through 4), a validated filtration process and calibrated scientific instrumentation were used to determine the degree of passage of each marker.

Figure 2: Comparative MWCO membrane passage of a 300 kDa UF SepraPor® membrane (Meissner) and a 300 kDa UF membrane by another manufacturer (Supplier A).
As depicted in Figure 2, Supplier A specifies only the maximum passage percentage of a single Mw marker to characterize the filtration performance of its 300 kDa UF membrane. In comparison, the passage profile of a 300 kDa SepraPor® (Meissner) UF membrane specifies a more comprehensive set of attributes. It is evident that by using a minimum of 3 Mw markers and providing minimum and maximum value passage boundaries for each Mw marker, a UF membrane is not only better characterized, but will also impart significantly more process understanding when deployed in purification processes.

The advantage of using 3 Mw markers following the new advanced method is most evident when comparing additional porosities. As depicted in Figure 3a, the specifications of 100 and 300 kDa SepraPor® (Meissner) UF membranes are clearly defined and distinct. In contrast, as depicted in Figure 3b, Supplier A uses the same Mw marker to characterize both its 300 kDa UF membrane and its 100 kDa UF membrane. Since the product specifications of Supplier A only reference a maximum passage percentage for each porosity, there is a clear overlap of the supplier’s product specifications, making the distinction between two different MWCO’s ambiguous.

SepraPor® UF membranes have tighter passage ranges, use multiple Mw markers and have minimal overlap between MWCO bands. Each MWCO assignment has its own allocated passage band, i.e., a unique passage vs Mw marker relationship. Under the new advanced MWCO assignment method, the passage bands emerge as the critical attribute to assign a MWCO. SepraPor® UF hollow fibers are manufactured to have their retention profile at each Mw marker match a pre-allocated MWCO passage band.

In Figure 4 we show the passage profile of three separate 300 kDa SepraPor® UF membrane lots. SepraPor® UF membranes are well-characterized by their specified passage bands. As a lot release criterion, each lot of SepraPor® UF membranes manufactured must fall within all three Mw passage ranges. This constitutes a significantly more comprehensive and scientifically rigorous characterization process than current accepted industry practices for UF membrane lot release. Any singular Mw marker practice for UF membrane characterization may lead to undesirable overlapping product specifications.
A three Mw marker characterization MWCO assignment method directly improves the lot-to-lot consistency of UF membranes manufactured which translates into lower process variability for end users.

**Improved Flux Performance**

SepraPor® UF membranes exhibit high flux performance. Figure 5 shows flux on the y-axis and MWCO on the x-axis for multiple SepraPor® UF membranes. Higher membrane permeability and more predictable performance afforded by lower and upper boundaries ensure more efficient and more reproducible purification processes for demanding bioprocess applications.

Figure 4: MWCO passage bands of three different lots of 300 kDa SepraPor® (Meissner) UF membranes

**Figure 5:** Flux vs MWCO data for SepraPor® UF membranes depicting tight ranges for enhanced process repeatability. (Data shown based on minimum 10 lots per MWCO.)
CONCLUSION

SepraPor® UF hollow fibers are characterized following a novel 3 Mw marker MWCO assignment method surpassing current industry practices for improved lot-to-lot consistency and more predictable flow rate performance. The scientifically more rigorous characterization of MWCO of SepraPor® UF membranes using multiple Mw markers will not only reduce process development time, but will also allow manufacturing processes to operate at peak performance, consistently.

CHOOSE SEPRAPOR® FOR YOUR DEMANDING APPLICATIONS

SepraPor® UF hollow fibers are developed with higher industry standards:

- Better flow rate performance
- Scientifically rigorous characterization of MWCO, using multiple Mw markers
- Accurate and precise MWCO assignment
- Improved lot-to-lot consistency

LEARN HOW SEPRAPOR® CAN HELP YOU

With SepraPor® ultrafiltration membranes, we are committed to achieving a higher level of material characterization to help our customers develop processes that run at peak performance, consistently.

Well-characterized membranes with enhanced consistency can improve the performance of your purification process. Learn how you can streamline your processes with SepraPor®.

INNOVATE WITH US FOR YOUR NEXT GENERATION PROCESSES

We welcome customer collaborations to continuously develop the best products and membranes in the industry.

For further information and to discuss how SepraPor® ultrafiltration membranes can help you in your application, please contact us at innovations@meissner.com.