The Science of Selection:
Choosing the Right Hollow Fiber Filter

Article

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Introduction

Tangential flow filtration (TFF) with hollow fibers (HF) is a cornerstone of bioprocessing and biopharmaceutical manufacturing, particularly in downstream operations. It plays a critical role in ultrafiltration/diafiltration (UF/DF), enabling fast, gentle concentration and buffer exchange of liquid feed stock. Unlike its normal flow filtration (NFF) counterpart, downstream processing using HF TFF reduces membrane fouling, enhances throughput, and ensures batch-to-batch consistency across scales.

Key Considerations in Selecting an HF Filter

Determining the optimal HF filter is essential for a successful experiment or manufacturing campaign and depends on several key factors, including pore size selection, membrane chemistry, scalability, and processing parameters such as flux and time. Investing time and effort in selecting the best HF filter for downstream TFF operations enables scalability, process consistency, and optimal yields. The following factors, listed below without specific order, present key considerations that bioprocessing manufacturers should evaluate when assessing an HF TFF process. Use this online calculator to get started.

Pore Size Selection

Pore size, or molecular weight cut-off (MWCO), determines if a molecule is retained or passes through. Choose a HF membrane with a MWCO smaller than your target product to retain it, or a larger MWCO to let it pass into the permeate stream. For optimal retention, the MWCO should be **3–6 times smaller** than the target molecule; conversely, for efficient passage, the MWCO should be **3–6 times larger**.

Common MWCO selections and their applications:

- **30 kDa**: Suitable for retaining monoclonal antibodies (mAb, ~150 kDa)
- **100 kDa**: Ideal for capturing Adeno-associated virus (AAV, ~25 nm)
- **500 kDa**: Designed for retaining Lentiviral vectors (LVV, ~100 nm)

Membrane Chemistry

The choice of membrane chemistry directly affects filtration performance. Hydrophilic membranes, such as Repligen's modified polyethersulfone (mPES), offer higher flux and lower protein binding, making them ideal for aqueous-based processes. They also resist fouling from lipids and antifoams, ensuring a more stable filtration process. In contrast, hydrophobic membranes like polyvinylidene fluoride (PVDF) and polysulfone (PS) repel water and exhibit lower flux, making them more suitable for organic solvents, venting, and air filtration applications. Additionally, chemical compatibility plays a crucial role— polytetrafluoroethylene (PTFE), for instance, provides excellent resistance across a wide range of chemicals, making it a versatile option for challenging applications [1,2].

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Processing Parameters

Selecting the right filter configuration goes beyond pore size — it requires careful consideration of factors such as surface area, shear rate, flux, and operating pressure and their scaling implications. **Surface area**, determined by the number of hollow fibers within a module, their length, and the fiber inner diameter, significantly influences filtration capacity and process time. A larger surface area allows for higher throughput and reduces fouling, but excessive sizing can introduce inefficiencies, such as increased pump requirements and hold-up volume.

When designing a **scalable process**, it is not only valuable to scale the surface area of the module to the processing volume, but to also linearly scale the **shear rate.** Shear rate (s^{-1}) refers to the rate at which the layers of the liquid feed stream move relative to each other within a hollow fiber module[3]. Shear rate is dictated by the inner diameter of each hollow fiber and the number of hollow fibers within the module and can be modulated by controlling the feed and retentate flow rate. Shear-sensitive materials, such as cells and certain proteins, can be damaged by high shear forces. Conducting small-scale shear rate scouting experiments helps ensure product integrity before scaling up.

Processing flux can be determined through scouting experiments at the bench scale and will help determine the processing time and required surface area for scale-up.

- **Ultrafiltration (UF; MWCO < 750 kDa):** Typically operated without permeate flow control, where flux may decrease over time due to pressure buildup. The right filter size ensures maximum processing flux and prevents prolonged process duration.
- **Microfiltration (MF; MWCO > 750 kDa):** Often run with controlled permeate flow, allowing for more predictable processing and better flux stability.

Balancing surface area, flux and other processing parameters is key to optimizing filtration performance and ensuring smooth scale-up transitions.

Conclusion

Selecting the right hollow fiber module requires a thoughtful approach, balancing application-specific requirements with key process parameters. Establishing the correct pore size and surface area lays the foundation for success, while screening studies help fine-tune factors such as membrane chemistry, shear rate, pressure, and flux. With the right selection strategy, manufacturers can achieve process consistency, efficiency, and scalability. The Repligen team is available to assist with membrane selection and provide expert guidance for optimizing TFF operations. Contact us today.

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References

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