Prefiltration and Process Improvements: Enhancing Virus Filter Performance with the Use of Adsorptive Depth or Surface Modified Prefilters

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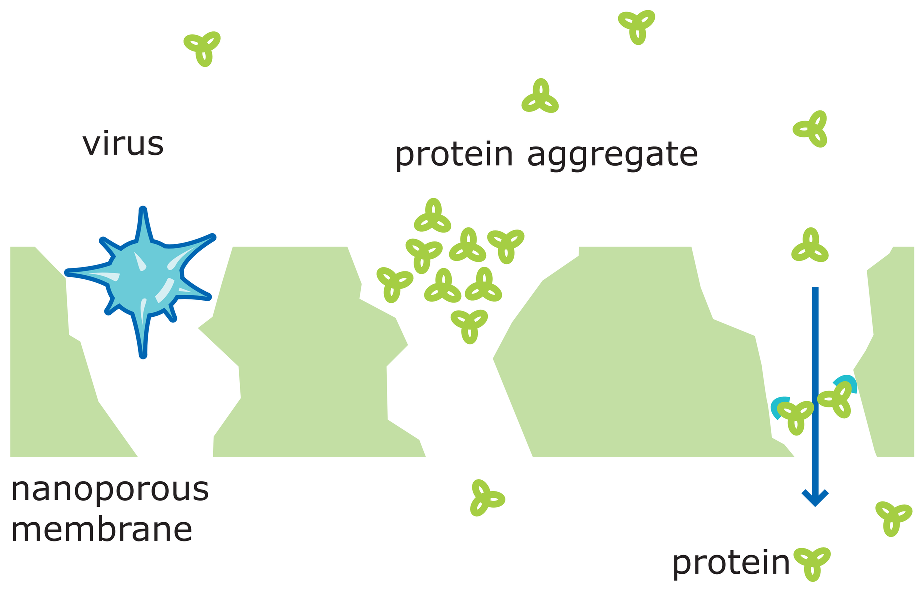
Abstract

Improvements in upstream process development often generate complex, high titer process streams, placing considerable demands on downstream processing steps. Protein aggregates in these feeds influence hydraulic performance of virus filters resulting in over-sized platforms and a significant impact on process economics. Virus filters from a broad range of manufactures provide robust viral clearance but the impact of aggregates on flux is dependent on the filter. The impact of conditioning protein solutions using prefiltration was assessed with several monoclonal antibody feed streams. Adsorptive depth or surface modified membrane prefilters upstream of the virus filter were shown to remove foulants from protein solutions, enhancing performance of the virus filter.

Why Do Virus Filters Plug?

- Pores of virus filters are sized to pass most proteins and exclude viruses
- Therapeutic protein feed streams may contain low levels of aggregates or other foulants that gradually plug the virus filter. Virus filter fouling may become more pronounced as the feed stream titer increases.
- Adsorption of monomer variants or fragments may also contribute to membrane plugging

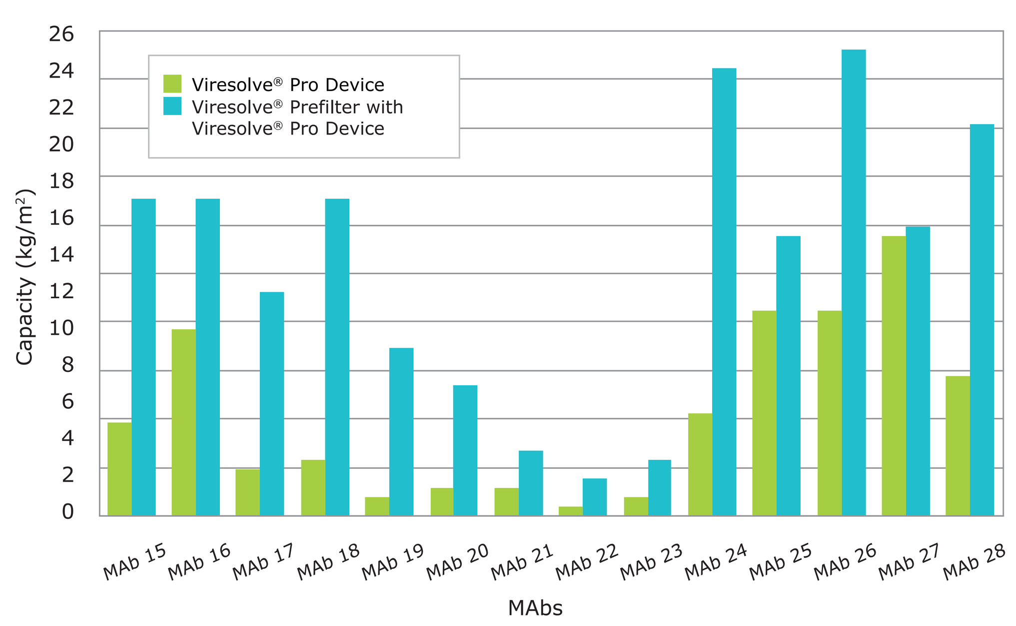


Viresolve® Prefilter

Adsorptive depth prefilter

- Composed of diatomaceous earth (DE), cellulose fibers and a binder containing cationic imine groups
- Regenerated cellulose membrane layer added downstream to reduce potential fiber shedding and serve as a flow distributor.
- Small, negatively charged or hydrophobic moieties from the feed stream are adsorbed by the depth media
- Effective operational range: pH 4 - 8 and conductivity 5 - 45 mS/cm

Figure 1 Viresolve® Prefilter Test Summary



In the absence of a prefilter, average mass capacity = 5 kg/m², ~50% of MAbs tested reached 5 kg/m².

Using the Viresolve® Prefilter, average mass capacity = 13 kg/m²

Lit No PS6336EN00 Rev. 3.0

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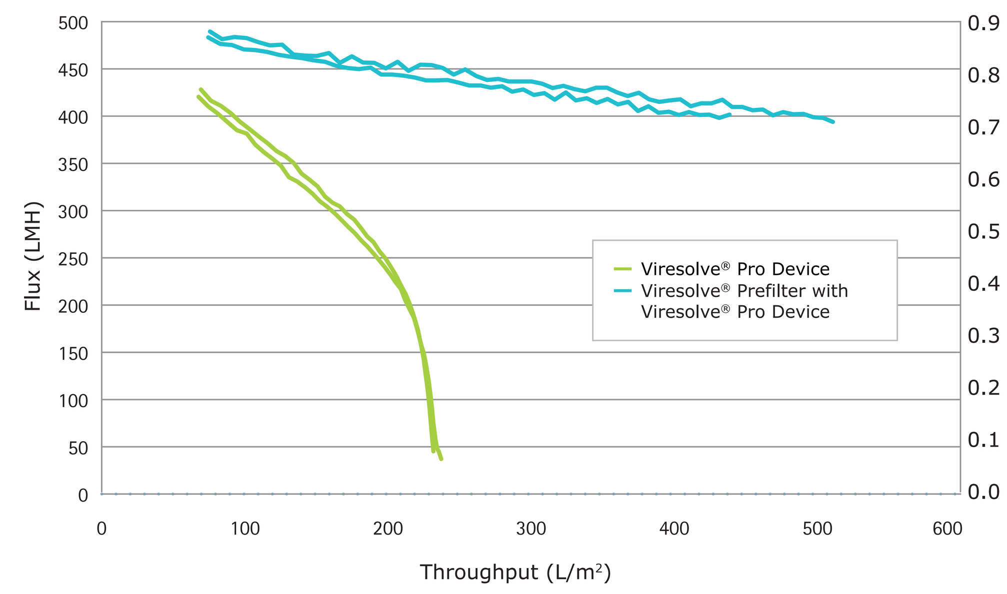
Figure 2 Viresolve® Prefilter Conditioned Feed (15 g/L)



Viresolve® Pro Shield

Surface modified membrane prefilter

- Support membrane: 0.2 µm PES
- PES membrane surface modified via cross-linked polymeric sulfonic acid cation exchange chemistry
- Surface chemistry binds to aggregates and other foulants
- Effective operational range: pH < 6 **and** conductivity < 30 mS/cm (see Figure 7)

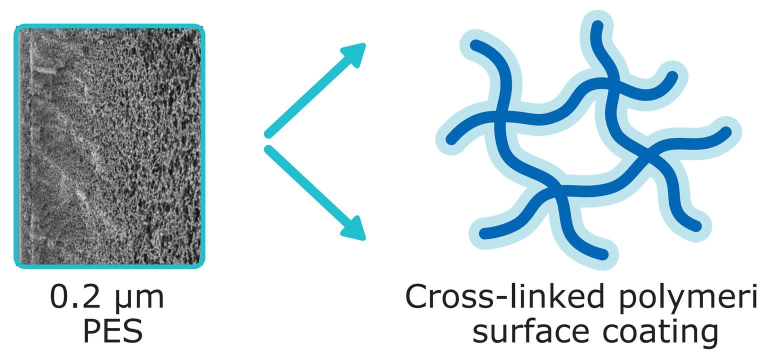
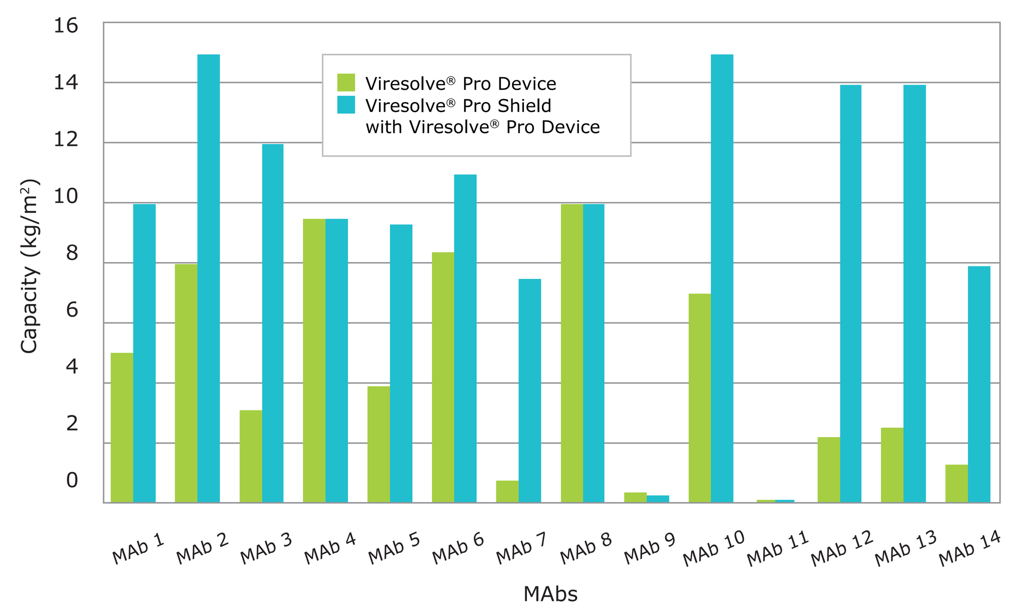


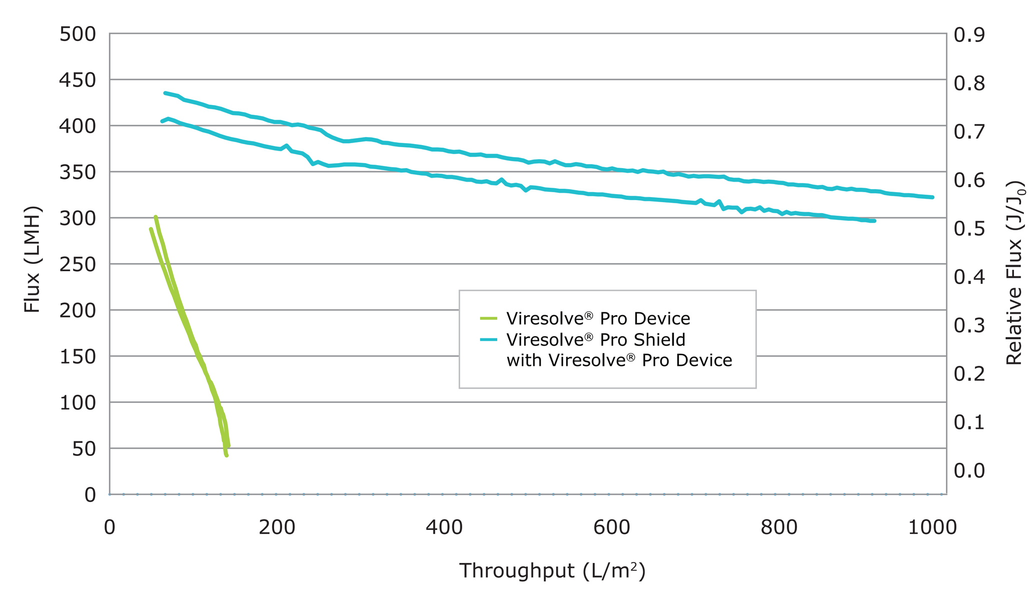
Figure 3 Viresolve® Pro Shield Test Summary



In the absence of a prefilter, average mass capacity = 4 kg/m², ~40% of MAbs tested reached 5 kg/m².

Using the Viresolve® Pro Shield prefilter, average mass capacity = 10 kg/m²

Figure 4 Viresolve® Pro Shield Conditioned Feed (20 g/L)



Our Patents in Prefiltration Technologies

US Patent 7,118,675 B2 covers the use of adsorptive depth filters or charged or surface-modified microfiltration membranes in front of a viral filter to enhance the virus filter performance by removing aggregates from protein solutions.

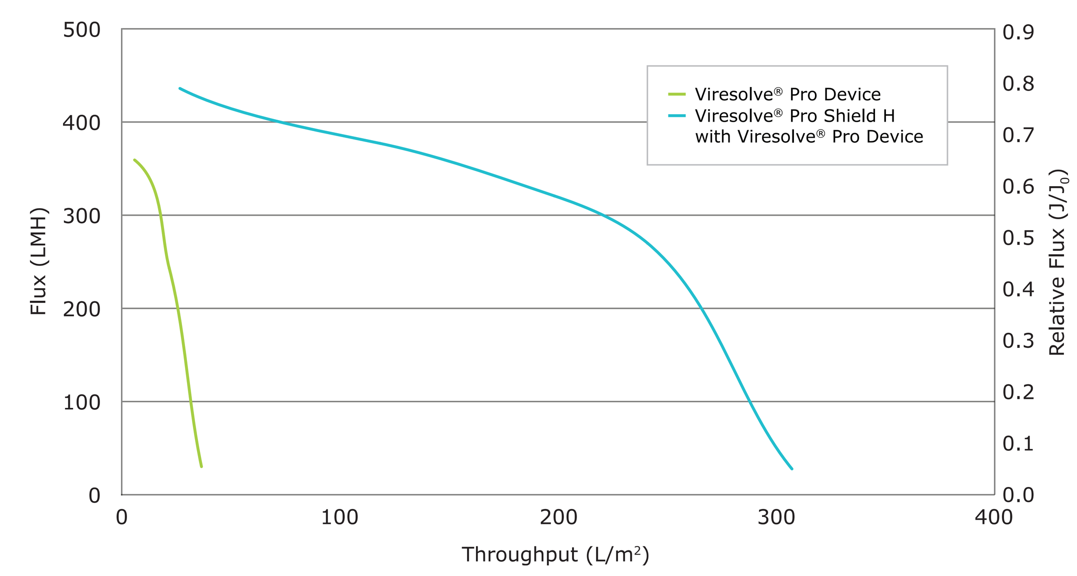
US Patent 7,465,397 B2 involves the process of removing aggregates and viruses using a depth filter upstream of a viral filter in either a constant pressure or pump system. Adsorptive depth filters and modified microfiltration filters that allow for increased capacity and robustness of our virus filters are part of our Viresolve® device offering.

Viresolve® Pro Shield H

Surface modified membrane prefilter

- Support membrane: 0.2 µm PES
- PES membrane surface modified via cross-linked mixed-mode chemistry
- Surface chemistry binds to aggregates and other foulants
- Effective operational range: pH > 5.5 **or** conductivity > 25 mS/cm (see Figure 7)

Figure 5 Viresolve® Pro Shield H Test Summary



In the absence of a prefilter, average mass capacity = 0.7 kg/m².

Using the Viresolve® Pro Shield H prefilter, average mass capacity = 5 kg/m²

Figure 6 Viresolve® Pro Shield H Conditioned Feed (13 g/L)

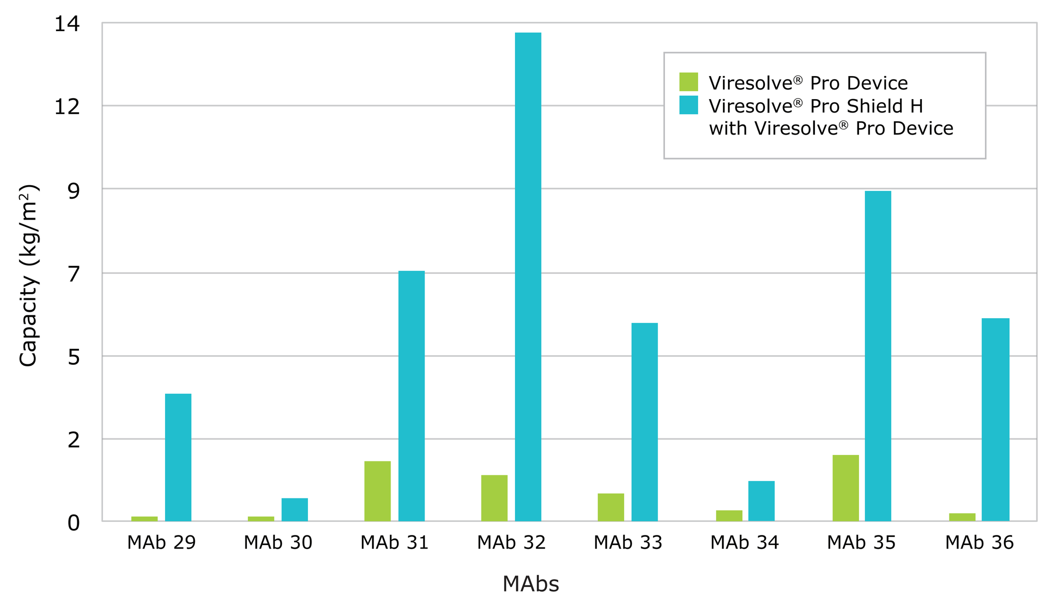
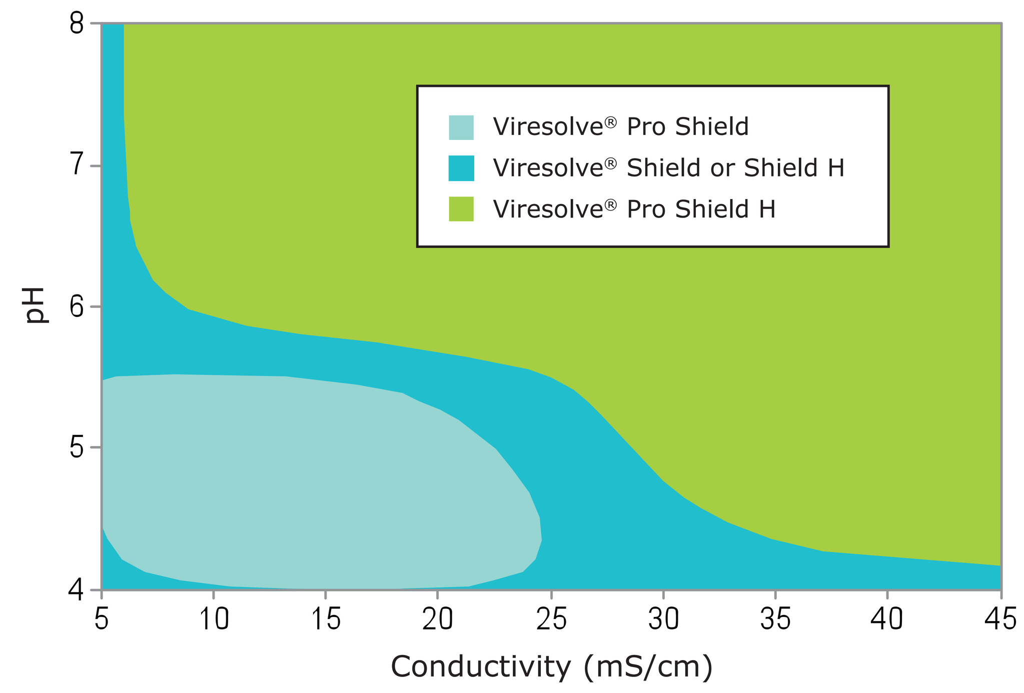


Figure 7 Selection Guide For Viresolve® Shield/Shield H Based On Feed Characteristics



Conclusion

Adsorptive prefiltration (membrane or depth filtration based) has been shown to effectively increase Viresolve® Pro Device capacity across multiple molecules and buffer pH/conductivity conditions. Efficacy of the prefiltration mechanism (cation exchange, etc.) is dependent on feed pH/conductivity. Adsorptive prefiltration provides an effective means to optimize the cost of a viral clearance operation using Viresolve® Pro Device and increases the robustness of the step by compensating for inherit variability in the aggregation profile and trace impurities within feed streams.