

Challenges and solutions for obtaining high titer therapeutic protein formulations

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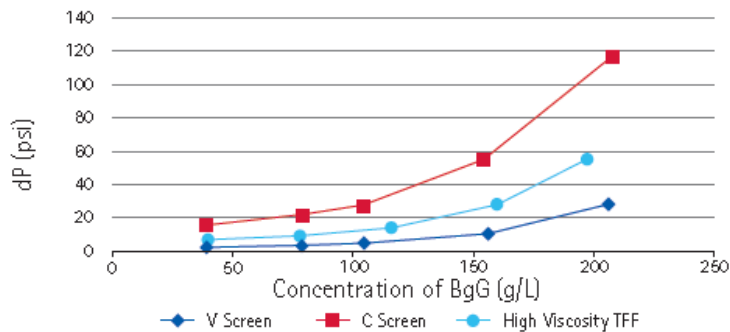
Formulating proteins at > 150 g/L with 25-30 cP viscosities using Tangential Flow Filtration (TFF) is challenging but



1. But handling high viscosity solution is possible if the correct feed channel or operation mode is selected
2. Selecting the right buffer increases protein stability (conformational and interfacial) and titer
3. Mitigation strategies can be implement to overcome excipient depletion or enrichment due to Donnan Effect

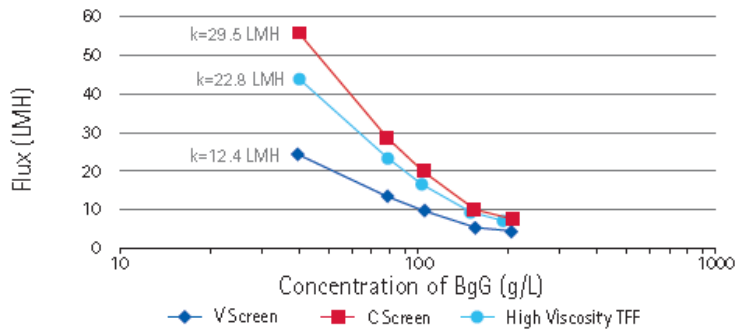
1. Handling highly viscous solutions by TFF

A/ Select suitable Feed Screen channel



Graph 1: Pressure drop vs concentration of BgG

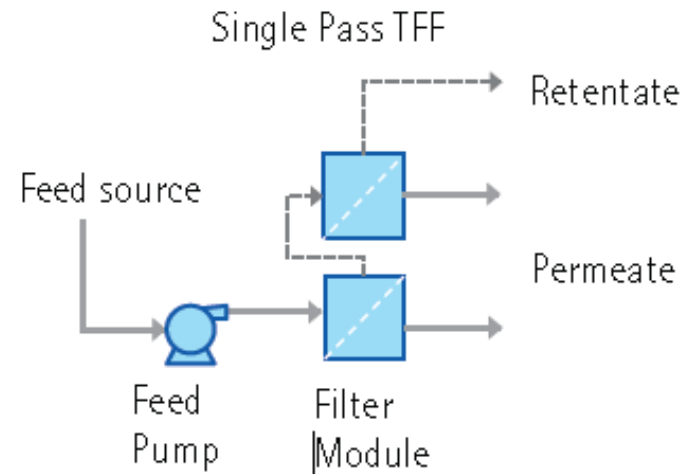
Pressure drop vs concentration curve of C screen, V screen and high viscosity TFF devices. All devices were tested at 8LMM cross flow rate.



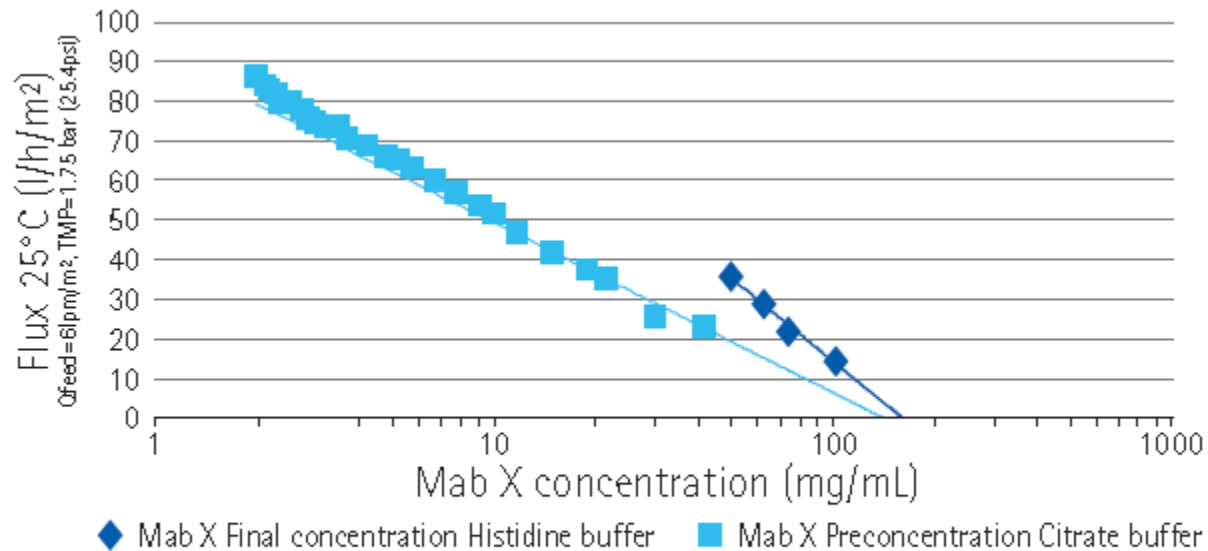
Graph 2: Flux vs concentration of BgG

All devices were tested at 8LMM cross flow rate.

B/ Think Single-pass TFF



2. Selecting the right buffers... for stability and high titer



Graph 4: Flux vs Mab X concentration

On a 0.11 m² Pellicon[®] cassette with Ultracel[®] 30 kD C screen membrane

3. Mitigate the Donnan effect leading to excipient depletion or enrichment

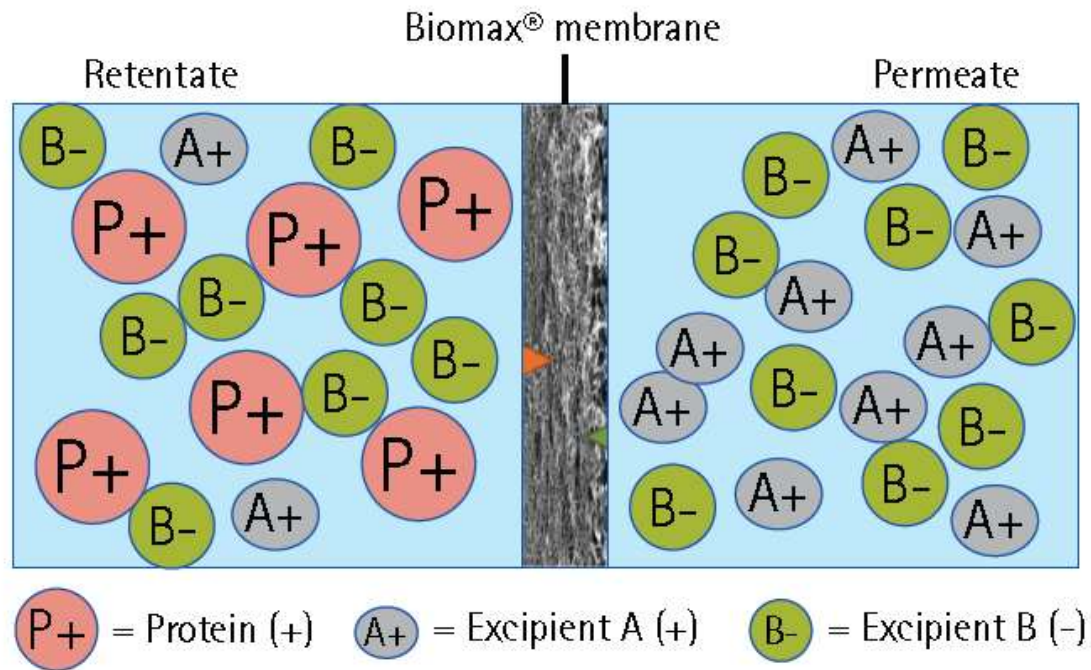


Figure 3: Illustration of the Donnan Effect: Unequal distribution of solutes across the membrane

Here a positively charged protein (in pink) attracts the negatively charged solute (in green) on the retentate side, leading to a solute concentration enrichment on the retentate side.

