The Effect of Retentate Vessel Mixing Homogeneity on Diafiltration Performance

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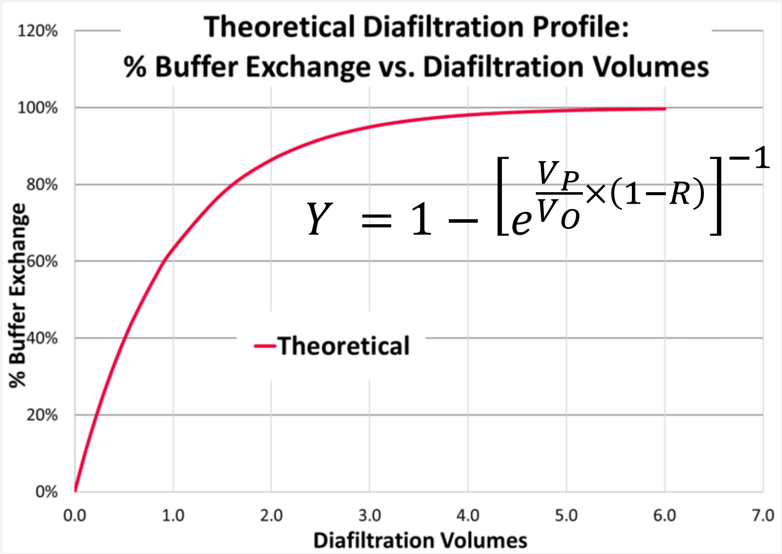
Introduction

A method of analysis for the interpretation of TFF diafiltration performance profiles is shown to connect back to the fluid dynamics and concentration gradients in the retentate vessel.

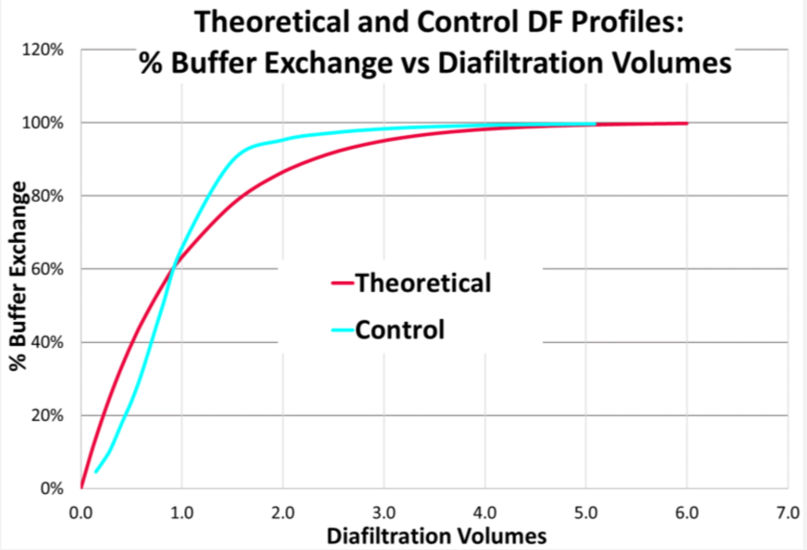
This method aids in the development of a UF/DF step that is consistent from bench-scale to manufacturing, reducing scale-up risks caused by differences in the feed properties. Under ideal conditions, a DF profile would closely match the theoretical profile.



Conventional Retentate Vessel

A control run simulating a conventional retentate vessel included one impeller and one retentate return in the lower part of the vessel. The chart below presents the actual diafiltration profile results by the membrane compared to the theoretical showing a deviation stemming from a variation in solution consistency in the feed.

This deviation from the theoretical is a result of a lower exchange rate through the first diavolume and a higher rate after.

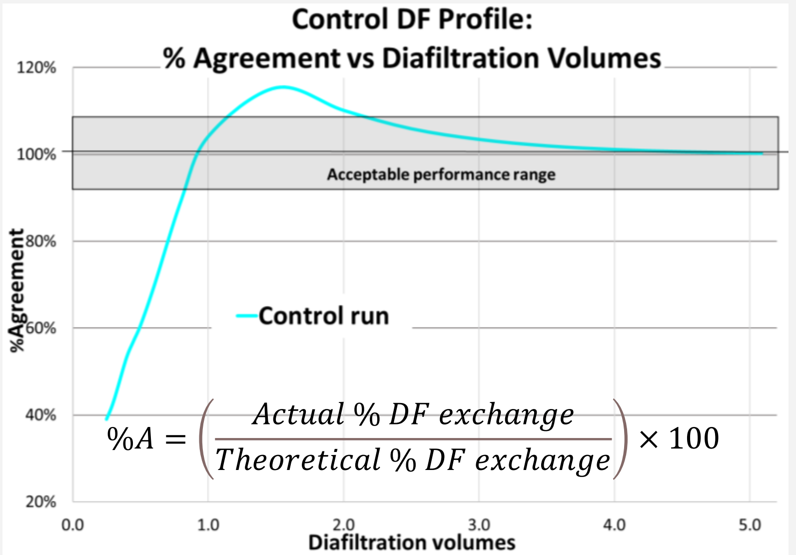


The Method

A plot of the agreement ratio (%A) of a UF/DF profile against the theoretical profile provides further insight.

Under ideal conditions the percent agreement would be 100%. A specification range of ±10% (gray box) from the theoretical profile was adopted to establish a target.

The control run %A profile shows significant deviation from the accepted performance range prior to 2 DV. This is due to a lack of consistency in the feed solution caused by poor mixing dynamics in the retentate vessel.



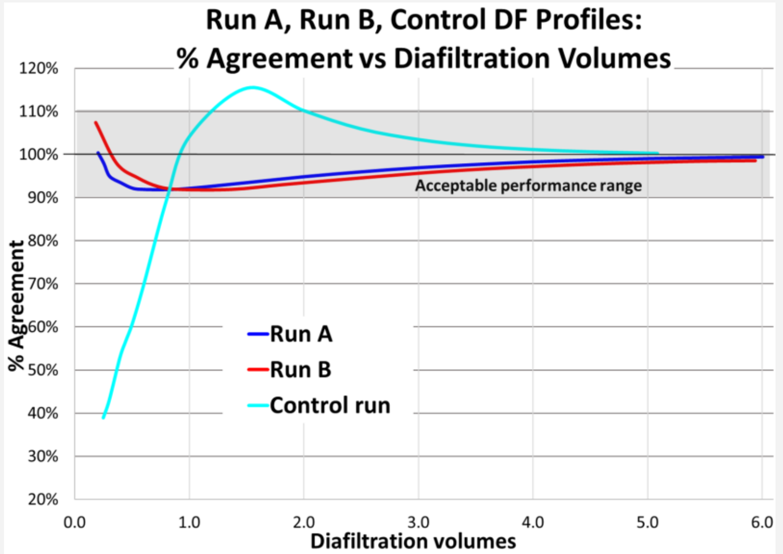
Case Study & Conclusion

Runs A and B were performed under different process conditions on a Repligen KrosFlo® RS 30 TFF system. Key features of this system include dual impellers, in-line buffer addition, and two retentate return ports.

Run ID	Retentate Volume (L)	Crossflow flux (LMH)	Upper Mixer (RPM)	Low Mixer (RPM)	Retentate Return
A	40	120	100	100	Low- & mid
B	10	300	NA	100	Low-level

The %A shows that Runs A and B were within 10% of ideal performance throughout the entire run, in stark contrast to the conventional vessel.

These superior DF performance results are attributed to the unique design features of the KrosFlo® RS 30 that created greater feed consistency by improving retentate vessel homogeneity.



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