CONTINUOUS COUNTER-CURRENT DIALYSIS (C3D) - THE FUTURE OF DIAFILTRATION

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Next-Generation Manufacturing aims to develop practical solutions for the continuous bioprocessing platform, thus providing significant improvements in efficiency, productivity, and sustainability over current batch processes. Diafiltration (DF) is a pivotal buffer exchange step to attain desired ionic strength and pH prior to final formulation into drug product. Typically DF is operated in batch-mode, comprised of several recirculation cycles performed using a sizable skid and expends buffer that is 6-7 times the product volume. The inherent batch mode of operation makes DF inconducive to continuous processing. In this work, we report the development of an intensified continuous buffer exchange technology based on counter-current hollow fiber dialysis that reduces buffer consumption by 80%. We evaluated the performance of bioprocess and medical-grade hollow-fiber units towards buffer exchange (pH), removal of salt (conductivity) and spiked tracers (spectrophotometry).

The intensified dialysis platform provided a significant (~8x) reduction in membrane area and footprint of the setup. We successfully evaluated scale-out approaches for nominal productivities from 0.5 kg/day to 14 kg/day of a mAb product representative of anticipated productivity for 500L to 3000L perfusion processes. In addition, we demonstrated continuous 5 kg/day processing of 120 g/L mAb product for 5 days with overall buffer consumption of 470L (0.018 L/g, mAb), which is significantly lower than (estimated) 2500L for batch DF (0.1 L/g, mAb). Since the volume of water is the major factor for process size, efficiency and environmental sustainability metrics, this decrease in water consumption is a major advantage for downstream processing. The turndown ratios afforded by the dialysis platform make it tunable towards continuous and fed-batch processes while providing unparalleled simplicity in automation and hardware compared to other state-of-the-art technologies.