PAT strategies for modelling and control of single-pass tangential flow ultrafiltration (SPTFF) in continuous manufacturing of monoclonal antibodies

ABSTRACT

Formulation of biotherapeutics using single pass tangential-flow filtration (SPTFF) is a critical step in continuous manufacturing processes for many drugs including monoclonal antibodies (mAbs). The concentration of the mAb in the final formulation is a critical quality attribute which affects safety and efficacy. The final concentration of the drug is determined by the flux across the module in a single pass, with no scope for repeated recirculation. Therefore, it is critical to design the membrane configuration and select the operating parameters such that the concentration target is met in a single pass. We develop a hybrid model for flux across a single membrane and use it as a building block to model complex SPTFF configurations and facilitate in-silico design of customized SPTFF configurations resulting in up to 40% savings in membrane area. We also propose an empirical control strategy to control the output concentration of a continuous ultrafiltration step. The control strategy leverages in-line concentration, flowrate and pressure sensors, including near infrared spectroscopy (NIRS) flow cells to measure the concentration of mAb in the feed and retentate streams in the range 0.5-200 g/L. The proposed system is the first approach that consistently achieve concentration targets over long continuous campaigns in spite of feed variability.

PUBLICATIONS

[1] Thakur, G., Thori, S., & Rathore, A. S. (2020). Implementing PAT for single-pass tangential flow ultrafiltration for continuous manufacturing of mAbs. Journal of Membrane Science, 613, 118492.

[2] Thakur, G., & Rathore, A. S. (2021). Modelling and optimization of single-pass tangential flow ultrafiltration for continuous manufacturing of monoclonal antibodies. In Separation and Purification Technology (Vol. 276, p. 119341). Elsevier BV. https://doi.org/10.1016/j.seppur.2021.119341