

# PROCESS ANALYTICAL TECHNOLOGY (PAT) FOR AUTOMATED, REAL-TIME CONTROL OF CONTINUOUS MANUFACTURING OF MONOCLONAL ANTIBODIES (MABS)

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Real-time in-process quality control is critical to ensure consistent product quality in continuous manufacturing of biotherapeutics. The key challenges include dealing with feed variability, equipment breakdown or process errors without needing to stop the process or compromising on output product quality. We showcase the deployment of control strategies for downstream unit operations in an automated continuous train for mAbs including capture, viral inactivation, polishing and formulation at lab scale. Several control strategies are automated and deployed for real-time control of the continuous train, including spectroscopy-based models for control of concentration variations in capture chromatography, mechanistic models for pH control in viral inactivation, pressure-based control of dead-end filtration, at-line HPLC for pooling decisions in polishing chromatography, and integrated flux controllers for maintaining retentate concentration in single-pass tangential flow ultrafiltration. The controls are facilitated by a system of surge tanks integrated with a distributed control system (DCS) and a Python-based control script for continuous monitoring and automated control.

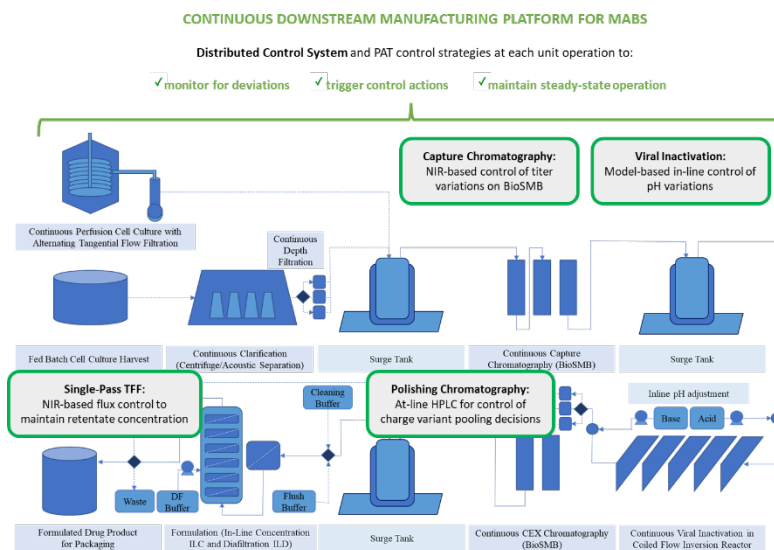


Figure 1: Continuous downstream platform used in case studies showing the location of the PAT control tools

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