REAL-TIME MODEL-BASED CONTROL OF SINGLE PASS TANGENTIAL FLOW FILTRATION FOR PRODUCTION OF MONOCLONAL ANTIBODIES

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Single-pass tangential flow filtration (SPTFF) has emerged as an important alternative to batch ultrafiltration due to its potential in achieving high concentration factors of the target protein. To make it a continuous process, the target concentration must be reached in a single pass across the membrane without the need for recirculation. However, there are several challenges that must be overcome before SPTFF can be successfully integrated into the continuous biopharmaceutical process train. One of the main challenges is implementation of control strategies involving inline concentration, pressure, and flow sensors. This is challenging because most of the equipment are proprietary, and interfacing is difficult. The objective of the present work is to develop a system for the control of SPTFF using a distributed control system (DCS), programmable logic controllers (PLC), data historian and a central computer with capabilities of model simulation and robust & flexible control. We have developed a model-based control system incorporating a physics-based model, and sensors and control elements, which include near-infrared spectroscopy (NIRS) sensors for concentration monitoring, as well as weighing balances, pressure sensors, pumps, and valves. These elements were connected to the distributed control system (DCS) which was further linked to a central computer that is driven by dynamic control. Upon passing real-time process data to the physics-based model, the set points for operating conditions (flow rate and pressure) required to achieve a target protein concentration are determined through optimization. These operating conditions are passed onto the equipment *via* DCS. The execution of the controller decisions is implemented through the hardware-software integration of the controller computer with the SPTFF unit via OPC, LAN, Python, I/O modules, or other hardware-software communication protocols. The control system was implemented in a laboratory scale experimental facility and the control logic was validated by comparing the targeted protein concentration with the achieved protein concentration in real-time.