PLUG-AND-PLAY SOFTWARE FOR MECHANISTIC MODELLING OF END-TO-END CONTINUOUS MANUFACTURING OF MONOCLONAL ANTIBODIES

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Monoclonal antibodies (mAbs) are the highest selling class of biopharmaceuticals. With continued growth in sales of existing mAb products and a growing pipeline of mAb product candidates being developed, the total sales of mAb products and all biopharmaceuticals will continue to increase in the coming years [1].

Biomanufacturing unit operations are largely designed and controlled through the use of data-driven models fit to experimental data. It is well-established that the use of mechanistic models can accelerate process development, simplify scaleup, and optimize manufacturing operations, but the available software tools have been limited. Mechanistic models for continuous biomanufacturing have been of increasing interest in recent years, as the industry strives to increase productivity and lower costs. Integrated mechanistic models for a continuous biomanufacturing plant need to account for the effects of changes in any unit operation on processes further downstream.

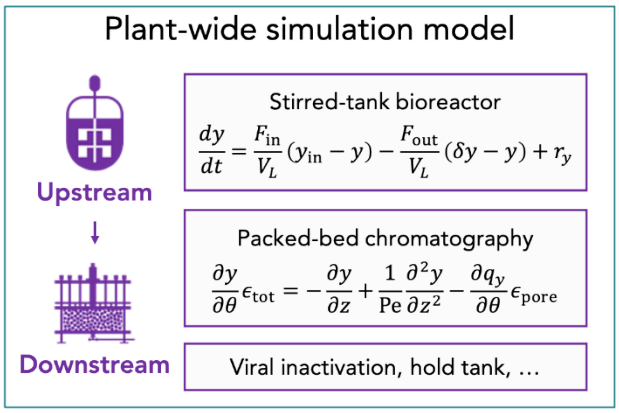

Figure 1 – Mechanistic modeling software for integrated continuous manufacturing

This presentation describes a software tool for carrying out high-fidelity dynamic simulations of integrated continuous mAb manufacturing plants. The simulations include mechanistic models of individual unit operations, including bioreactors, chromatography columns, viral inactivation units, and filtration units. The software implements the best mechanistic models available in the literature which are validated using experimental data. These validated individual units are then combined into a plant-wide dynamic model that includes the effects of model parameter uncertainties and disturbances, which is then used to validate the integration of the individual models and to map changes in operating conditions to the critical quality attributes and other variables of interest anywhere in the system.

In addition to design of the integrate c ontinuous manufacturing plant, plant-wide mechanistic predictive models can be used to design, compare, and evaluate various control and real-time release testing strategies [2]. The plant-wide simulation software is designed to make the replacement of individual models and unit operations seamless. This plug-and-play ability enables the simulation-based evaluation of multiple process options before equipment is swapped in and out of the real physical manufacturing plant, including for less-established technology such as protein capture and purification via crystallization [3,4].

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