PROCESS DESIGN OF A FULLY INTEGRATED CONTINUOUS BIOPHARMACEUTICAL PROCESS USING ECONOMIC AND ECOLOGICAL IMPACT ASSESSMENT

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The majority of commercial-scale production of biological products is currently carried out in batch operation, that leads to low productivity, low yield, batch-to-batch variation in product quality, and high capital and operating cost. With the rapid expansion of market demand, competition from biosimilars, and market pressure for lower drug prices, pharmaceutical industry is investigating different production alternatives such as continuous manufacturing. Continuous biomanufacturing is a more cost-effective and flexible platform with higher productivity and yield, more consistent and better product quality, and smaller footprints. To facilitate the commercialization of continuous manufacturing, demonstration of economic and environmental viability is important. Many research groups have shown that there are tremendous economic benefits when the operation is transitioned from batch to continuous. Continuous platforms with different unit procedures, including perfusion techniques, capture scenarios, and membrane chromatography, have been systematically assessed. The ecological and operational robustness benefits of continuous biomanufacturing have been illustrated. However, to the best of our knowledge, few papers have considered the media and buffer preparation when constructing continuous platforms, although studies have shown that buffer preparation can be significant in the overall operational and scheduling activities. The study of the bottleneck shifting with respect to the increase of upstream production is also limited. Furthermore, most papers only examine the effects of process variables on the economics when conducting scenario analysis, but few investigates the impacts on the environmental footprints.

This work aims to establish an in-silico fully integrated continuous platform for the production of monoclonal antibody (mAb). This developed platform incorporates media and buffer preparation steps and combine innovative technologies such as intensified seed expansion and continuous high cell density perfusion bioreactors, single-pass tangential flow filtration, and single-use technologies. After process design and development, scheduling is performed to achieve the continuous operation and real-time media and buffer addition, followed by economic and environmental analysis based on environmental indicators (E-factors). Scenario analysis is carried out to assess the effect of upstream titer and bioreactor scale on process economics and environment. The shift of process bottlenecks with the increase of the upstream production capacity is explored and analyzed. Membrane chromatography, as an emerging technology, can help eliminate pore diffusion, enhance the bio-separation efficiency, and lower buffer consumption. As those benefits are of interest to the industry, membrane chromatography is incorporated into the process design and its impact on the overall process performance is investigated in terms of economic and ecological benefits. The results provide insights into the feasibility of transitioning from batch to continuous biomanufacturing considering cost and environmental metrics.

References

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