PERFUSION MICROBIOREACTOR WITH INTEGRATED CELL RETENTION DEVICE

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Intensified perfusion processes are a key component in Integrated Continuous Biomanufacturing that still faces many challenges. For example, delivering the right amount of nutrients for extremely high cell densities at economically feasible perfusion rates need the right cell culture media and process development. To this end, data sets are generated using high-throughput small-scale models. In the absence of a cell retention device that can work with those small working volumes, strategies that mimic perfusion are being used. For example, a common technique is to use either high density batch or simulation of perfusion in spin tubes or ambr®15 using discrete media exchanges. However, the applicability of the data generated in these small-scale models is limited and process development must be supplemented with perfusion bioreactors at benchtop scale. The key point that these small-scale models miss to accurately predict perfusion processes is a cell retention device that enables continuous media exchange while retaining cells in the bioreactor. In this work we will present the evaluation of a perfusion microbioreactor system. This 2mL perfusion microbioreactor has all the requirements to accurately control DO, pH and temperature; it is equipped with a filtration-based cell retention device and optical density sensors that enable the performance of continuous perfusion with automated cell bleed (Figure 1). We will show cell performance in the perfusion microbioreactor system at 2vvd using a CHOZN®-GS producing a fusion protein (n=3) and a CHO-S producing an IgG (n=2) in steady state with a target viable cell density of 50x10^6vc/mL and dynamic perfusion. We will then compare cell growth, metabolites and production to steady state and dynamic 3L perfusion bioreactors and we will review process modifications made during the evaluation, including gas and mixing strategies. Lastly, we will present two case studies using the perfusion microbioreactor system: 1) Evaluation of cell performance in three different media. 2) Determination of minimum CSPR.

References

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