STRATEGIES FOR SMALL-SCALE PERFUSION CULTURES IN AMBR®250 HT BIOREACTOR SYSTEM

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Perfusion cell cultures have continuous fresh media addition and spent media removal using a cell retention device. Due to the cell retention and media exchange, perfusion cultures have higher viable cell densities (VCD) and overall productivity than fed-batch cultures. Despite these advantages, perfusion cultures are seldom used to produce licensed biotherapeutics. A significant barrier to implementation is the limited availability of small-scale perfusion models that can be used for process design. The current study evaluated two small-scale perfusion culture models using a CHO cell line expressing an IgG, in an ambr® 250 HT system without the perfusion modification. The first model system used centrifugation, while the second model system used *in-situ* gravity settling to retain cells. At low perfusion rates (<1VVD), the centrifugation perfusion model achieved a VCD >50 million cells/mL, while the gravity settling model achieved ~20 million cells/mL. The gravity settling model observed an average cell bleed of 18% due to incomplete clarification of cells during the media exchange. Yet, the gravity settling model had very stable VCD, cell viability, and productivity profiles over 39 days. The centrifugation model was also able to achieve stable VCD, cell viability, and productivity profiles over 39 days. Due to the lower cell bleed, the centrifugation model had higher VCDs and productivities, resulting in a cumulative titer of 6.9 g, while the *in-situ* gravity-settling model achieved a 2.2 g cumulative titer. In contrast, the parallel fed-batch cultures only produced 0.4 g in 14 days. Interestingly, both perfusion models had similar cell specific productivities (Q_p) of approximately 27 pg/cell·day. The higher VCD centrifugation model could be used to evaluate media compositions and feeding strategies, while the more stable gravity model can be used to evaluate product stability and cell line stability. Potential sources for process failures and process control complexities also could be evaluated in the ambr® 250 HT system without a cell retention device.

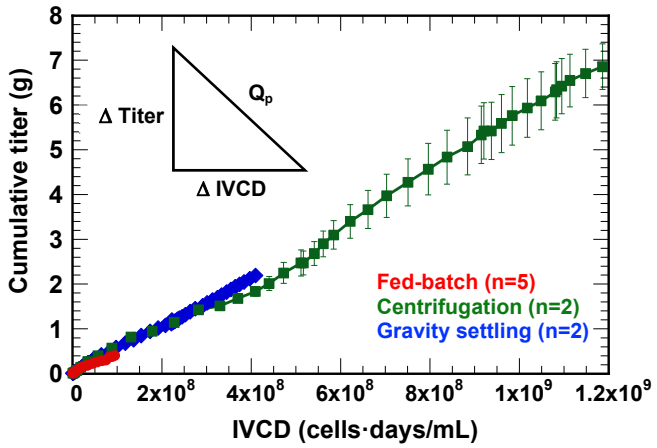

Figure 1 – Cumulative titers versus the integrated viable cell density (IVCD). The slope of these curves is the cell specific productivity (Q_p) which was similar for the three modes of operation