TWO SMALL-SCALE PERFUSION MODELS FOR THE AMBR250 TO ENABLE THE STUDY OF PRODUCTION STABILITY

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Key Words: Small-scale, Perfusion, gravity settling, centrifugation

Perfusion cell cultures typically have higher volumetric productivity compared to batch and fed-batch cell cultures. Despite all the advantages of perfusion, perfusion cultures are still only rarely used to produce any licensed products. Barriers to usage for production include, limited small-scale perfusion models, more complex process control, and higher process failure risk. Yet, perfusion cultures are preferred for hard to express and unstable molecules. This project evaluated the use of the ambr250 HT bioreactor system for two small-scale perfusion models for a CHO cell lines expressing an IgG. One model used *in situ* gravity settling, while the other model used centrifugation to achieve cell retention. In this proof of concept project, the gravity settling model achieved a cumulative titer of just over 2 g in 39 days, compared to approximately 0.5 g for the 14-day fed-batch controls (Figure 1). The centrifugation model achieved a cumulative titer of over 6.5 g in 39 days. Interestingly, the cell specific productivities were the same for the fed-batch and the two perfusion models at approximately 26 pg/cell·day. The gravity settling model was simpler to operate and could be used as a small-scale model to assess genome and product stability. The centrifugation model was more complex to operate due to daily manual operations. Nevertheless, the centrifugation model reached higher cell densities, and thus could be used for media and feeding optimization studies. Additionally, several process control complexities could be modeled and studied using the ambr250 which cannot be simulated with spin tube perfusion models. Potential sources for process failure could also be investigated. The capability to use the ambr250 for small-scale models in gravity settling or centrifugation mode opens up the study of long-term cultures where pH and DO profiles are maintained, which could be used to gain information on product and process stability.

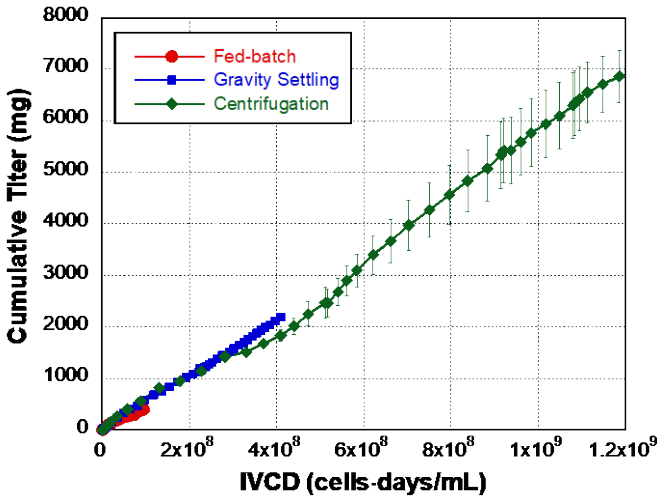

Figure 1 – Cumulative titers versus the integrated viable cell density (IVCD) for three modes of operation in the ambr250 HT bioreactor system. The slope of these curves represents the cell specific productivity, which was similar for the three modes of operation.