Spring 5-12-2016

Modeling perfusion for medium component optimization using ambr15TM

Deila Lyons
SAFC

Modeling perfusion for medium component optimization using ambr15™

An increasing number of biopharmaceutical companies are employing intensified perfusion as a means to increase volumetric productivity. Traditional perfusion systems have successfully used media developed for fed-batch cultures when target cell densities are relatively low (e.g., $20x10^6$vc/mL) and perfusion rates are relatively high (e.g., 5 vvd). High perfusion rates can be desirable when producing labile proteins in order to reduce the effective retention time of the protein in the bioreactor. Commonly, intensified perfusion processes applied in the production of stable proteins reach cell densities greater than $50x10^6$vc/mL with perfusion rates below 2vvd. In intensified perfusion, the minimum perfusion rate is determined by the consumption rate of nutrients or the accumulation of detrimental by-products in the bioreactor. The reduced cell specific perfusion rates (CSPR) used in intensified perfusion requires rebalancing the concentrations of specific medium components for optimal performance. The efficient optimization of critical medium components requires sufficient data to allow the use of statistical tools such as multivariate analysis (MVA), and as such needs the use of scale-down systems. A major limitation in moving forward in the development of perfusion media for intensified perfusion is the lack of commercially available perfusion devices for small scale modeling. Traditional perfusion scale down models such as repeated batch or simulated perfusion processes can have severe limitations that would affect component utilization along with equivalent cellular responses. In this work, we evaluate small scale models employing automation and process control and we assess their suitability for modeling the performance of high cell densities perfusion cultures in bioreactors. In addition, we will show its application for media development.