THE CHALLENGES OF PERFORMING HIGH DENSITY PERFUSION PROCESSES IN SINGLE USE BIOREACTORS

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Single use technologies (SUT) have become embedded in the biopharmaceutical industry over the last 20 years. An important recent trend in the industry is a pivot towards continuous processing. SUT are being deployed for continuous perfusion cultures where expected viable cell concentrations are higher than 1 x 10^8 /mL. Although SUT provides many advantages, there are also some challenges associated with its application to intensified perfusion processes. In particular, the single use bioreactor has to provide enough oxygen to the culture to maintain aerobic respiration. The main challenges of adapting single use systems for perfusion culture are limited power dissipation (P/V) and limited gas flow rates. These problems arise because plastic is a weak material of construction limiting torque on the simpler shaft and back pressure on the gas outlet filters. These problems are compounded at larger scales due to unfavourable cross-sectional area to volume ratios.

Lonza have characterised a number of single use bioreactor systems for their ability to achieve sufficient mass transfer to support perfusion culture. In this poster we will present results from one such system. Oxygen mass transfer was characterised for different sparger and impeller configurations over a range of power dissipations and superficial gas velocities at various levels of oxygen enrichment. A DoE approach was used to characterise the design space for oxygen mass transfer in two different bioreactor scales. Response surface models were used to quantify the contributions of different factors on the overall oxygen mass transfer. Whilst the response of oxygen mass transfer was broadly in line with expectations certain interesting observations were made. For example, an interaction between impeller type and power dissipation was observed. This caused us to look more closely at the impact of impeller design on the distribution of the gas phase. The experiments we have carried out so far enabled us to design a new approach to manipulate the oxygen transfer rate via multiple spargers.

It was concluded that the single use bioreactor system under evaluation was capable of supporting between 0.4 and 1 x 10^8 viable cells/mL depending on the cell specific oxygen consumption rate.