EXPERIMENTAL AND COMPUTATIONAL FLUID DYNAMICS STUDIES OF ADHERENT CELLS ON MICROCARRIERS IN AN AMBR® 250 BIOREACTOR

Marco C. Rotondi, Aston Medical Research Institute & Sartorius Stedim Biotech
m.rotondi@aston.ac.uk
Alvin W. Nienow, Aston Medical Research Institute & University of Birmingham
John P. J. Betts, Sartorius Stedim Biotech
A. Neil Bargh, Sartorius Stedim Biotech
Ned Grace, Sartorius Stedim Biotech
Barney Zoro, Sartorius Stedim Biotech
Mariana P. Hanga, Aston Medical Research Institute
Christopher J. Hewitt, Aston Medical Research Institute
Qasim A. Rafiq, Aston Medical Research Institute & University College London

Key words: high-throughput process development, microcarrier-based cell culture, fluid dynamics, Vero cells

Interest for microcarrier-based processes for the large-scale culture of adherent cells has recently grow, due to possible application in vaccine and cell therapy. This opportunity drives the need for effective, high-throughput, single-use, process development tools that can be translated successfully into industrial-scale systems. The automated ambr® 250 platform is one such technology, operating at a volume between 100 – 250mL, both high-throughput and single-use. The ambr250 has demonstrated significant success for suspension-based mammalian cell culture applications. However, additional investigations need to be performed on microcarrier-based processes for the culture of adherent cells. The fluid dynamics characteristics of the bioreactor must be sufficiently well understood to enable successful scale-up to larger scale bioreactors. Physical parameters such as fluid velocity, power number and shear stress are important for any cell culture. With microcarriers, there is an additional challenge as the fluid dynamics must take into account the presence of the particulate solid phase. A critical aspect for cell cultivation on microcarriers is the minimum agitator speed required to achieve complete microcarrier suspension, NJS. Under these conditions, the surface area of the attached cells is available for transfer of nutrients (including oxygen) to the cells and metabolites from them, whilst higher speeds hardly increase these transport processes and may lead to damaging fluid dynamic stresses being generated. It is also extremely beneficial to predict the flow dynamics of the stirred tank based on computational fluid dynamics (CFD). Once validated, CFD modelling is a very useful tool for analysing flow patterns, mixing time, mean and local specific energy dissipation rates, shear stress, and other parameters important for scale up in order to optimise the overall bioreactor geometry. In addition to the above fluid dynamic aspects, cell culture studies was also performed in parallel to analyse the cell growth at and around the minimum speed for microcarrier suspension, NJS. The CFD and experimental results with the single-use ambr250 bioreactor will be discussed in detail during the final presentation.