ENGINEERING CHARACTERISATION OF A CUBIC SINGLE-USE BIOREACTOR GEOMETRY

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Single-use technologies have played a key role in rapid vaccine development in response to the COVID-19 pandemic, with reduced costs, improved process flexibility, and higher production rates when compared to their traditional stainless steel counterparts. The growing development of single-use bioreactors has however led to other deviations from conventional STRs, with design opportunities allowing for the emergence of novel bioreactor configurations. One such single-use bioreactor (SUB) with a unique cubic geometry is Pall Corporation's Allegro™ STR bioreactor range, which was utilised in scale-up studies associated with COVID-19 vaccine development [1]. Improvements in mixing and higher specific power input are some of the advantages offered by this novel design [1]. However, despite inherent advantages in emerging novel SUB configurations, extensive engineering characterisation of such designs is necessary in the development of robust processes, to maximise product yields and quality. This work focuses on the characterisation of the Allegro STR bioreactor by experimental and computational studies on a scale-down 1 L mimic. Force gauge measurements indicated that the turbulent impeller power number was 2.17 ± 0.05 in up-pumping mode, in agreement with that of the 200 L STR. Mixing time was assessed using the Dual Indicator System for Mixing Time (DISMT) technique where recorded images were processed by an in-house developed MATLAB code to objectively determine mixing homogeneity across the global flow field. The number of impeller revolutions to achieve 95% homogeneity (Nt_m) was 24.6 ± 1.1, in agreement with that of the industrial 50-2000L range [(2)]. The aforementioned results indicate suitability of the scale-down geometry for further characterisation of the Allegro STR. Transparency of the scale-down mimic allowed for particle image velocimetry (PIV) measurements for characterisation of hydrodynamic conditions across the agitation range. Such data was also used in the validation of a computational fluid dynamics (CFD) model developed on Ansys, which was subsequently used for simulation of cell shear stress exposure over time.

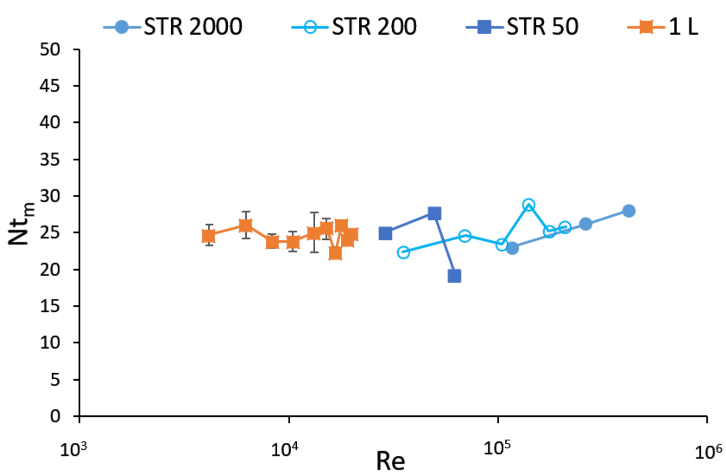

Figure 1 – Scalability of Allegro STR range mixing characteristics demonstrated by comparison of 1 L mixing number with industry scale data.

Ultimately, simulated data of particle shear exposure throughout circulation time in the vessel is aimed for use in the design of an ultra scale-down (USD) device mimicking cell culture shear exposure in the industrial STR range. A 1 L Allegro STR prototype suitable for cell culture is currently being produced, where future work will involve comparison of cell and product characteristics cultivated in the SUB geometry to that of the USD device, for validation purposes. If successfully validated as an appropriate mimic of shear conditions in the Allegro STR bioreactor, such a device would provide a mL scale process environment suitable for rapidly and inexpensively informing optimal industrial scale agitation conditions for applications such as vaccine production.

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