**Power consumption and mixing dynamics for Newtonian and non-Newtonian across different single-use mini bioreactor configurations**

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**Highlights**

* Accurate power consumption measurements by the use of a dynamometer
* Detailed mixing dynamics assessment by means of the pH dual colorimetric technique
* Characterization of the impact of rotating speed and viscosity on Newtonian and non-Newtonian fluids
* Evaluation of the influence of baffles and internals on axial- and radial-flow configurations

**1. Introduction**

The biopharmaceutical manufacturing industry has created a pull for advancing high‐throughput, automated technologies for process development and optimisation such as disposable multi-parallel miniature bioreactor platform. Actually, the latter are increasingly used within the industry, not only as screening tools but also as scale-down models. Among the current commercially available small-scale bioreactor systems, the stirred-tank design has again become prevailing. In stirred-tank bioreactors, hydrodynamics governs bulk fluid mixing. The understanding of these two key physical aspects and of their interactions are required within the framework of scale-translation models. The selection of agitation configuration and operating conditions has then to meet two objectives. On the one hand, the influence of process variables on bioreactor performance has to be properly understood. On the other hand, hydrodynamics and mixing, as well as their coupling, need to be assessed in relation to the bioreactor design and scale. In this context, engineering characterisation is required to understand and quantify these multiscale transport phenomena for better bioreactor design. This work aims at gaining a better understanding of the mixing effectiveness within different single-use mini bioreactor configurations for both Newtonian and non-Newtonian fluids.

**2. Methods**

Measurements are performed in the mini bioreactor systems ambr® 250 (Sartorius Stedim Biotech). The reactor with a working volume of 250 mL has been fitted with either two Rushton turbines (20 mm diameter, 30 mm spacing), or two pitched-blade impellers (26 mm diameter, 30 mm spacing, up- and down-pumping) with or without four equally-spaced baffles. The internals (pH probe and gas sparger) are also used to study their influence on mixing and power characteristics. The working fluids are water and aqueous solutions of glycerol (viscous), sodium alginate (low shear-thinning) and xanthan gum (highly shear-thinning) of different concentrations. Rheological measurements are carried out using a Kinexus Lab+ rheometer (Malvern Panalytical).

The power draw in the different ambr® 250 configurations is measured by the use of a dynamometer based on a pneumatic bearing allowing rotation without friction. More information about the technique is provided in [1].

The Dual Indicator System for Mixing Time (DISMT) technique, based on a fast acid–base reaction in presence of pH indicators [2], is used to assess the mixing dynamics by using a camera. A description of the DISMT methodology and of the image-processing algorithm used to evaluate the mixing time can be found in [3].

**3. Results and discussion**

Power consumptions experiments with Newtonian fluids are carried out for providing the common thread of this work, and for characterizing the power curve of shear-thinning fluids within ambr® 250 configurations by means of the Metzner-Otto [4] and Rieger-Novak [5] methods.

The DISMT experiments are used to identify the main structures in the flow within ambr® 250 configurations, and to determine the macro-mixing time, the mixing time of segregated regions in the flow and the rate of reduction in size of the slow mixing regions for fluids with separate rheological behaviour [6].

The influence of Reynolds numbers on power consumption and mixing characteristics of baffled and unbaffled bioreactors is presented for operating conditions corresponding to non-aerated regime (no gas entrainment from the free surface). The impact of impeller type and of internals presence is investigated to assess the functional dependence of the power and mixing numbers on geometrical features under any fluid dynamic regime.

Finally, the mixing and power datasets are combined to determine and compare the mixing effectiveness of the agitation systems in relation with the operating conditions (rotating speed, working fluid).

**4. Conclusions**

The coupled analysis of power and bulk mixing characteristics of fluids with distinct rheological properties in different single-use mini bioreactor configurations, allows a first step towards a more systematic approach toward scale-down models development. An improved understanding of fluid dynamics and flow properties enables a more adequate application of key engineering parameters, in particular the power input.

**References**

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