Evaluation of the BIOSTAT® CultiBag STR family in terms of scalability

Ute Noack¹, Sophie Brandt¹, Davy de Wilde², Gerhard Greller¹

¹Sartorius Stedim Biotech GmbH, D-37079 Göttingen, Germany
²Sartorius Stedim Belgium NV, Vilvoorde, Belgium

Introduction

Re-usable bioreactors have been the gold standard for many decades resulting in a large knowledge base on process control. However, recently a trend is observed in the industry where single-use bioreactors are being implemented in modern upstream processes. As many of these bioreactors show discrepancies from the traditional design a strong need has been expressed for new single-use bioreactors resembling on a classical design. Such design enables the user to improve the scale-up process based on experience and well-established guidelines. During this process, variables such as tip speed, mixing time, oxygen transfer and specific power input have to be considered.

In order to meet this demand of improved scalability Sartorius Stedim Biotech recently developed a new stirred single-use bioreactor up to 1000 L, the BIOSTAT® CultiBag STR. This poster characterizes the BIOSTAT® CultiBag STR family in terms of all relevant scale-up parameters linked to this specific bioreactor design.

Design

The BIOSTAT® CultiBag STR is comprised of a stainless steel support housing, a control system utilizing single-use sensors and a single-use bioreactor chamber. The CultiBag STR is a flexible cultivation chamber offering a broad range of connectors, tubings, impellers and sparger designs. The bag has a cylindrical shape and a height to diameter ratio of about 2:1, which is similar to conventional re-usable vessels.

Tip speed

Shear rate is an agitation-related parameter which is often evaluated, especially for cell culture applications. Impeller tip speeds can be correlated to maximum impeller shear rates.

<table>
<thead>
<tr>
<th>( \nu_{tip} ) [m/s]</th>
<th>STR 50 L agitation [rpm]</th>
<th>STR 200 L agitation [rpm]</th>
<th>STR 1000 L agitation [rpm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.6</td>
<td>80</td>
<td>50</td>
<td>30</td>
</tr>
<tr>
<td>1.2</td>
<td>160</td>
<td>100</td>
<td>60</td>
</tr>
<tr>
<td>1.8</td>
<td>240</td>
<td>150</td>
<td>90</td>
</tr>
</tbody>
</table>

Mixing time

Mixing is one of the most important operations in bioprocessing. Bulk liquid mixing is a critical factor for the scale-up of a cell culture process. Poor mixing can result in pH, temperature and nutrient gradients in large-scale bioreactors. An indicator of homogenous mixing e.g. during media feeds or pH correction, is the mixing time.

The determination of the mixing time using the concentration method was investigated by measuring at different positions the conductivity of distilled water following an addition of phosphate buffer at different agitation rates.

Specific Power Input

The specific power input is a parameter which is more commonly used for scaling agitation across sites or scales. The specific power input was calculated by measurement of the torque at maximum filling volume of tap water and at different agitation rates.

The Newton Number for the impeller configuration 2x3-blade segment impeller is 1.3.

Conclusions

- Complete scalability single-use bioreactor family
- Condition for a successful scale-up: same ratios are implemented in the BIOSTAT® CultiBag STR family
- Same \( k_{La} \)-values in all BIOSTAT® CultiBag STR sizes (scale-up criteria)
- Excellent mixing times

References
