BIOPROCESS IMPROVEMENT BY DESIGN-MODIFIED BIOREACTOR FLOW PROPERTIES

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ABSTRACT
The aim of this study was to achieve bioprocess intensification by bioreactor flow field improvement. Two component properties of the flow field, namely, flow and shear are represented by two macroscopic mixing characteristics – impeller pumping capacity, Fl, and rate of kinetic energy dissipation, ε. Mixing rates are affected by impeller design and may be the result of a design-imposed flow modification of characteristics, e.g. higher or lower bioreactor circulation and/or turbulence properties can be achieved. The results illustrated that two basic impeller types – a modified flat-blade and modified inclined blade, could tailor a stirred bioreactor flow field in a pre-selected style. The design modification was aimed at higher oxygen transfer via increased ε or improved ε-distribution in the bioreactor bulk. Zones of different ε were revealed, implying different oxygen tension and bioreaction intensity. For the sake of prognostic evaluation, the mass transfer coefficient k_L was determined. The designs of slotted flat and inclined blades were found to be prospective in terms of energy efficiency and can be recommended for design retrofitting of existing bioreactors.

Keywords: bioreactor equipment, mixing, impeller design, flow modeling
Abbreviations: FB: flat blade impeller; MRF: multiple reference frame model; OTR: oxygen transfer rate; PBT: pitched blade turbine impeller; PFB: perforated blade impeller; SB2: slotted blade impeller; STB: slotted trapezoidal blade impeller
Symbols: D: impeller diameter [m]; D_L: oxygen diffusivity [m²/s]; Fl: flow number [Q/ND²]; k: turbulence kinetic energy [m²/s²]; k_L: liquid (biofluid)-based mass transfer coefficient [m/s]; N: impeller angular velocity [s⁻¹]; P: power [W]; P_0: power number [N²D²p/µ]; Q: flow rate produced by the impeller (indices axial-a/radial-r) [m³/s]; u, v, w: turbulence component velocities [m/s]; U: fluid mean velocity [m/s]; V: bioreactor/biofluid volume [m³]; ε: rate of kinetic energy dissipation [m²/s³]; ρ: bioreactor/biofluid volume [m³]; ρ_L: biofluid density [kg/m³]; η_L: biofluid viscosity [Pa·s]

Introduction
Bioprocess intensification is a major source of improvement of the present potentials of biotechnology and fermentation industry. Recent literature on biotechnology reveals numerous cases of bioreactions that require high dissolved oxygen tension in order to obtain higher yields in shorter fermentation time (1, 13). Our own measurements of bioproduction rates of exopolysaccharides have shown an increase of up to 40% in the bioproduction by the species Aerobacillus palidus depending on the oxygen transfer rate (OTR) and stagnancy elimination (15). The latter properties depend on the quality of mixing. It has been widely accepted that high OTR and low flow stagnancy can be ensured by a specific arrangement of the flow field generated by the mixer, these properties being prevalingly related to specific impeller designs.

Mixing techniques have always been targeted at better balance between shear and flow. The latter are well represented by circulation rates (e.g. Fl) and by the local rate of kinetic energy dissipation, ε. The circulation number, Fl, can be expressed by the volumetric flow rate in three flow dimensions, i.e. axial, radial and tangential one, being related to the axial, radial and tangential velocities. The parameter ε [m²/s³] is defined, as rate of kinetic energy (k) decay per second due to dissipation, with k = (u² + v² + w²)/2 [m²/s²] based on the turbulent velocity components u, v and w [m/s]. These parameters depend locally on the bioreactor geometry and more specifically on the impeller design. Velocity distribution of various mixing devices is covered well by recent research (13). Data on turbulence variables has been neglected. Reference to recent literature shows an increasing trend towards computational identification of flows introduced by various impellers. Recalling previous fundamental studies by Van’t Riet and Smith (14), Oldshue (12) and Nienow (11), one can find further detailed recent analyses by Kumaresan and Joshi (8), Moilanan et al. (9, 10), and Zhao et al. (16). Analyzing these authors’ results, one could infer the potentials of computational flow modeling for providing clear and detailed flow field image of mixing and for extending the development of local impeller analysis. Both these features motivated the present study.

The objective of this study was to present new prospective data for enhancement of the energy effectiveness of bioreactor performance based on flow modification by impeller design.
Materials and Methods

Our previous studies on flat (4, 5) and inclined (6) blade impellers revealed two basic geometries appearing superior compared to conventional flat and pitched blade turbines. Out of ten possible modifications, we have selected three designs of good performance to introduce oxygen transfer and circulation improvements. The designs considered are shown in Fig. 1. Fig. 1a represents flat blade (FB) modifications PfB (perforated blade) and SB2 (slotted blade), and Fig. 1b exhibits conventional inclined blade (PBT) modification abbreviated as slotted trapezoidal blade (STB). These impellers have been classified as prospective mixing devices in previous studies and they were selected to be analyzed further related to bioprocess intensification.

In all cases, a stirred vessel of ID 0.4 m, and impeller configuration D/T = 0.33, H = T, C = T/2 were used. The working volume was 50 dm$^3$. The working liquid was water at 20 °C. The vessel schematic is shown in Fig. 1c.

The method of computational flow modeling (2, 13) was employed in the analysis. The quasi-homogeneous physical model was assumed with emphasis on the liquid phase effects on the performance parameters. The realizable “k-ε” model (3) was found to be an appropriate tool at the particular Reynolds number (Re > 10$^4$) corresponding to impeller speeds exceeding 7 rps in most cases.

The MRF (multiple reference frames) solution approach (3) was used and a structural mesh was elaborated, as illustrated in Fig. 2. Visualizations of the flow field were generated by introducing multiple planes shown in the figure, as well as by generation of iso-surfaces. Runs were carried out with various cell number but the results shown are representative for 0.3 10$^6$ cells.
The algorithm of calculation comprised the following steps: 1) computation in the domain of the moving frame attached to the rotor to yield values on the frame boundary, 2) acceptance of velocity at the frame boundary as starting values for computations in the stationary frame, 3) computations in the domain of the stationary frame, 4) check-up of residuals, 5) continuation of the iterative steps, when residuals do not match the criteria $<10^{-4}$, and 6) end of calculation when residuals become less than $10^{-4}$.

Model validation was done based on power number $P_o$ ($P_o = \frac{P}{N^3 D^5 \rho_L}$, where $P$ is power in W, $N$ is impeller angular speed in rps and $\rho_L$ stands for liquid density in kg/m$^3$). Predicted versus measured parameters are shown in Table 1.

### TABLE 1
Predicted vs. measured power numbers of PfB and SBT

<table>
<thead>
<tr>
<th>$N$, rpm</th>
<th>PfB meas./pred.</th>
<th>SBT meas./pred.</th>
</tr>
</thead>
<tbody>
<tr>
<td>300</td>
<td>4.22/3.62</td>
<td>0.3/0.24</td>
</tr>
<tr>
<td>400</td>
<td>3.73/3.49</td>
<td>0.17/0.27</td>
</tr>
<tr>
<td>500</td>
<td>3.47/3.52</td>
<td>0.21/0.26</td>
</tr>
<tr>
<td>600</td>
<td>3.24/3.54</td>
<td>0.22/0.24</td>
</tr>
</tbody>
</table>

A total of 5 runs were carried out for each setup of a starting geometry at variable speed of rotation. The relevant parameters’ values were selected for the analysis.

**Results and Discussion**

The convective mixing is illustrated by circulation flow numbers $F_l$, e.g. axial (a), radial (r) and average (av.) corresponding to mixing time, in Table 2. They present the estimate for the convective capacity of the impeller. $F_l$ was determined by integrating the axial ($U_a$) and radial ($U_r$) velocities crossing the impeller discharge surface $F$- circular for $Q_a$ and cylindrical for $Q_r$, i.e.

$$Q = \int_0^F U_F dF$$

According to these data, the slotted impeller designs, namely, PfB, SB2 and STB were found to be compatible with the conventional designs (FB, PBT), meaning that the decrease introduced by reduced solidity does not change the circulation markedly.

In order to reveal the complete mixing performance of the agitators for bioreaction engineering purposes, estimate of mixing by turbulent diffusion is required. Thus, also a measure for the turbulence rate was obtained. A representative estimate of turbulence has been found recently based on the work of Kawase et al. (7). These authors recommend evaluation of the superficial oxygen transfer coefficient, $k_L$, relative to the rate of turbulent kinetic energy dissipation $\varepsilon$, as follows from the equation:

$$k_L = C_1 \sqrt{D_L \left( \frac{\varepsilon \rho_L}{\eta_L} \right)^{0.25}}$$

In this equation, the parameter $D_L = 1.98 \times 10^{-9}$ m$^2$/s is oxygen diffusivity at 20 °C in water, $\varepsilon$ [W/kg] or [m$^2$/s$^3$] is the rate of turbulent kinetic energy dissipation related to the continuous phase, $\rho_L$ [kg/m$^3$] and $\eta_L$ [Pa·s] are the density and the viscosity of the continuous aqueous phase, $L$. These parameters impose the effect of motion by $\varepsilon$ and $\eta_L$ and allow the study of the effect of fluid flow on the mass transfer during bioreaction. Based on broth similar conditions, coefficient $C_1 = 0.3$ was assumed from reference (9).

Using this equation, one could map the bioreactor volume by benchmarking the oxygen transfer coefficient $k_L$ based on energy dissipation rate, the latter being illustrated in Fig. 3 and Fig. 4, e.g. bearing in mind that according to Equation 1, $\varepsilon = 0.1$ m$^2$/s$^3$ corresponds to $k_L = 2.35 \times 10^{-4}$ m/s, 0.2 m$^2$/s$^3$ corresponds to $2.79 \times 10^{-4}$ m/s, 0.3 m$^2$/s$^3$ to $3.1 \times 10^{-4}$ m/s, and 0.4 m$^2$/s$^3$ to $3.22 \times 10^{-4}$ m/s. Related to impeller design, turbulence was represented by local kinetic energy dissipation rate $\varepsilon$, as shown in Fig. 3 for impellers FB, PfB and SB2, and in Fig. 4 for PFB and STB. Accordingly, zones of low $\varepsilon \sim 0.1-0.2$ would correspond to hindered oxygen transfer and low bioreaction rate while zones of high $\varepsilon \sim 0.6-0.7$ would represent intensive oxygen transfer and high rate of bioreaction.

**Fig. 3.** $\varepsilon$-contour plots (m$^2$/s$^3$) at equal input power: PBT (600 rpm), STB (1000 rpm).

**Fig. 4.** $\varepsilon$-distribution at various height.

**Fig. 5.** $\varepsilon$-distribution at various height.
The integrated parameters of Fig. 3 and Fig. 4 are plotted in Fig. 5, Fig. 6 and Fig. 7. Fig. 5 illustrates the height distribution of $\varepsilon$ corresponding to Fig. 3. Fig. 6 indicates the volume-average values of $\varepsilon$ related to the bioreactor bulk. Fig. 7a and Fig. 7b present the areas corresponding to iso-surfaces of constant $\varepsilon$ as illustrated in Fig. 7c for $\varepsilon \approx 0.2$ m$^2$/s$^3$ of the case of PBT in Fig. 4.

### TABLE 2

<table>
<thead>
<tr>
<th>Impeller type</th>
<th>$F_{\text{I}} = Q_a/ND^3$</th>
<th>$F_{\text{I}} = Q_r/ND^3$</th>
<th>$F_{\text{av}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>FB</td>
<td>0.47</td>
<td>0.86</td>
<td>0.66</td>
</tr>
<tr>
<td>PfB</td>
<td>0.51</td>
<td>0.74</td>
<td>0.63</td>
</tr>
<tr>
<td>SB2</td>
<td>0.45</td>
<td>0.71</td>
<td>0.58</td>
</tr>
<tr>
<td>PBT</td>
<td>0.71</td>
<td>0.23</td>
<td>0.47</td>
</tr>
<tr>
<td>STB</td>
<td>0.65</td>
<td>0.21</td>
<td>0.43</td>
</tr>
</tbody>
</table>

The figures show increased area of the $\varepsilon$-contours that correspond to the slotted flat blade cases. The results for the slotted inclined blades are not so convincing but are still compatible. Consequently, such designs might be considered to be favorable for improvement of bioreactor performance.

In a further step of the analysis, assuming quasi-homogeneous approximation of two-phase flow and negligible effect of gas presence upon turbulence, the turbulence parameter $\varepsilon$ was transformed into prognostic oxygen transfer coefficient $k_L$ according to Equation 1. In order to compare the power efficiency, also the input power per unit volume was added from previous studies (4, 5, 6). The $k_L$ values corresponding to the bulk averages of $\varepsilon$ are compared in Table 3 versus the power input per unit bioreactor volume imposed by the impellers.

### TABLE 3

<table>
<thead>
<tr>
<th>Impeller type</th>
<th>$P/V$, W/dm$^3$</th>
<th>$k_L$, m/s ×10$^4$</th>
</tr>
</thead>
<tbody>
<tr>
<td>FB (450 rpm)</td>
<td>1.9</td>
<td>3.80</td>
</tr>
<tr>
<td>PfB (500 rpm)</td>
<td>1.7</td>
<td>3.82</td>
</tr>
<tr>
<td>SB2 (500 rpm)</td>
<td>1.7</td>
<td>3.85</td>
</tr>
<tr>
<td>PBT (600 rpm)</td>
<td>1.2</td>
<td>3.60</td>
</tr>
<tr>
<td>STB (1000 rpm)</td>
<td>1.0</td>
<td>3.30</td>
</tr>
</tbody>
</table>

Compared to conventional design FB and PBT, the SB2 and PfB impellers might exhibit increased efficiency of oxygen transfer in terms of input power and the STB impeller is fully compatible. Consequently, the use of slotted blade impellers for retrofitting of existing bioreactors is possible and might be recommended as a prospective energy-saving measure for bioprocess improvement.

The extended uniform distribution in the case of slotted blades, e.g. SB2, PfB, STB, can be explained by fluid dynamics effects, e.g. accelerated flow through the slots that imposes pressure recovery at the blade rear. This way the impellers produce a mighty convective flow due to enhanced circulation in both directions. Referring to the role of turbulent diffusion, the moderate effect on $k_L$ is due to improved volumetric distribution of $\varepsilon$ in the case of the slotted designs compared to the conventional impeller versions which is seen in Fig. 3 and Fig. 4.

### Conclusions

Targeting bioprocess production rate enhancement by improving the mixing flow field, two component properties of
a model bioreactor flow field, namely, circulation flow rate and kinetic energy dissipation rate were studied. Three versions of two major impeller designs – a flat-blade one and inclined blade, were compared and their differences and achievements were revealed. Comparing the distribution of $\varepsilon$, the slotted designs showed good performance in the reactor bulk. This may be explained by possible flow acceleration and pressure recovery at the blades’ rear. The simulation data for the slotted inclined-blade impeller revealed up to 18% increase of $\varepsilon$ in the reactor bulk accompanied by a possible 12% increase of $k_L$ per unit input power, which improves the energy efficiency of the studied equipment. The fluid dynamics analysis opens the slotted impeller designs for further examination at real bioprocess conditions.

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