IMPROVEMENT OF AN UNBAFFLED STIRRED TANK MIXING CHARACTERISTICS USING VARIABLE SPEED IMPELLER

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Abstract

Unbaffled mixing tanks with magnetically driven impellers are increasingly used in biotechnological and pharmaceutical industries, combining the benefits of a closed, sterile environment with easy equipment cleanability. On the other hand, missing internals, such as baffles or cooling coils, have an adverse effect on the equipment mixing characteristics, namely the batch homogenization time. In our previous research, we uncovered that the eccentricity and inclination of the impeller – both employed routinely to enhance the mixing characteristics of unbaffled vessels – are not fully effective in the suppression of central vortex formation resulting in the increase in the homogenization time. In this work, we propose a simple solution to counteract the central vortex formation – a periodical variation of impeller rotational speed. This approach destabilizes the central vortex, significantly reducing homogenization time while maintaining the benefits of the original unbaffled setup. This innovation can seamlessly integrate into existing industrial setups, promising efficiency gains for biotech and pharmaceutical production.

Keywords: unbaffled mixing tanks, variable rotational speed, vortex destabilization, mixing time improvement

1 Introduction

Mixing is a fundamental unit operation in various industrial processes, used to achieve a uniform distribution of substances or temperatures inside a production vessel. The equipment most commonly used for mixing operations is a standard mixing vessel with four wall baffles and an impeller placed in the vessel axis. However, in the biotechnology or pharmaceutical industry, there are increased demands on the cleanability and sterility of the equipment, and therefore it is undesirable to install any internals or shaft seals in the vessel. To avoid this, stirred bioreactor manufacturers use unbaffled tanks with magnetically driven impellers. These do not require a shaft and its sealing, reducing significantly the potential threat of vessel content contamination. However, in order to drive the impeller magnetically, it must be installed directly on the vessel’s bottom, and impellers of smaller diameters \( D/T \sim 0.15 \) than those used in standard vessels \( D/T = 0.33 – 0.5 \) are preferred. In addition, to at least partially compensate for the missing baffles, the impeller is placed eccentrically and inclined on the bottom of the vessel [1]. While in the standard baffled vessels, sufficiently chaotic mixing and relatively fast homogenization of the batch are ensured, in these atypical stirred bioreactors, a poorly mixed segregated region at the site of the central vortex exists, which prolongs complete homogenization to an unbearable extent [2].

The formation of the segregated zone poses a risk to the microorganisms, especially in the situation when the aerobic process takes place. Therefore we aimed to enhance the mixing while maintaining all the advantages of the unbaffled arrangement with a magnetically driven impeller. During a literature survey, we found a promising method, which is currently used to improve especially the laminar mixing of viscous liquids in unbaffled tanks - a dynamic mixing protocol [3]. This method uses a change in the speed or even direction of rotation of the agitator to destabilize rotational flow patterns and thus improve the mixing of dead volumes. The use of forward-backward mixing protocol to promote the turbulent flow regime in unbaffled vessels has also been investigated experimentally [4] and by using computational fluid dynamics [5]. However, there are no mentions of the use of time-periodic changes in rotational speed to improve mixing performance in the developed turbulent flow regime. To fill this knowledge gap under the process
conditions suitable for shear-sensitive microorganisms, we present the data on the effect of mild impeller speed variations on the overall homogenization time in the pilot bioreactor with the magnetically driven impeller [2].

2 Materials and methods

The measurements were carried out in a pilot-plant mixed vessel of diameter $T = 390$ mm with a tap water system with a level height of $H = 600$ mm ($H/T \approx 1.5$) and volume of $V = 66$ dm$^3$. The experimental apparatus is partially modifiable – it allows operating in a standard fully-baffled or unbaffled configuration with an impeller mounted axially at the clearance $C = 50–200$ mm. In addition, it is possible to rearrange the apparatus to the unbaffled configuration with low-clearance ($C = 10$ mm) and eccentrically mounted impeller, which mimics the design of unbaffled bioreactors with magnetically-driven impellers (see Fig. 1A). In this investigation, two different Rushton turbines of the diameters $D$ equal to $60$ mm and $100$ mm were used, corresponding to the ratio $D/T \approx 0.15$ and $0.25$. The turbulent power number of both turbines, $P_0 = P/\rho N^3 D^5 = \text{const.}$, in the unbaffled configuration is equal to $3.1$ [2].

To enhance the mixing characteristics, a control system was implemented, which, in addition to mixing at constant speeds, enables precise periodic changes in the rotation speed. For both impellers, two primary rotational speeds, $N_p$, corresponding to specific power inputs of $10$ W/m$^3$ and $100$ W/m$^3$ were used. The data measured with the variable impeller speed are then presented in comparison with the data measured at the corresponding $N_p$. The typical course of the rotational speed $N$ for both constant and variable rotational speed measurements is depicted in Fig. 1B. One period of variable speed mixing may consist (in the case of $N_p > N_s$) of linear acceleration, $t_{\text{acc}} = 2$ s, to the primary test speed $N_p$, running for the time period of $\Delta t_p$, linear deceleration, $t_{\text{dec}} = 2$ s, to the secondary rotational speed $N_s$, and again running for the period $\Delta t_s$. A Burster 8645 torque meter ($\pm 2.5$ Nm, $<1\%$ F.S.) was used to measure the shaft torque $M$ from which the power input at a periodically varying rotational speed was calculated using $P = 2\pi MN$.

![Figure 1: (A) Sketch of the experimental vessel in the unbaffled configuration with eccentrically mounted RT impeller. (B) Typical time course of speed/power during one mixing period at constant (red line) and variable (blue line) impeller speeds.](image)

To visualize the mixing efficiency, the decolorization technique with the iodine-starch-sodium thiosulfate system was used. Before each measurement, the starch solution in the vessel (approx. $0.02$ g/L) was colored blue with an addition of iodine solution ($0.1$ M) and titrated with the $0.2$ M thiosulfate solution to the colorless equivalence point. Then, a volume of $(10 + 1)$ mL of the thiosulfate solution was added to the vessel and homogenized. The additional $1$ mL of thiosulfate solution ensures $10\%$ surplus of the reducing substance in the vessel corresponding roughly to the measurement of the time required for $90\%$ homogenization, $\theta_{90}$. The mixing time measurement
consisted of pouring 10 ml of a 0.1 M triiodide solution into the central poorly mixed zone and measuring the time required for complete decolorization of the vessel’s content from blue to colorless solution. The decolorization process is depicted in Fig. 2. Each measurement at given conditions was performed at least in triplicates, the results are presented as averaged values with their standard deviations as error bars.

Figure 2: Course of decolorization experiment under the conditions of $D/T \approx 0.25$, $H/T \approx 1.5$, $N = 5.9 \text{s}^{-1}$, and constant rotational speed of the impeller. The final mixing time for this specific measurement was equal to 280 s.

It should be noted here that the term mixing/homogenization time is not used in the strict sense in this work, as it does not correspond to the standard measurement of mixing times by conductometry or decolorization (e.g., [2]). In this work, it is taken as equivalent to the efficiency of breaking the segregated zone in the central vortex region. Corresponding to this purpose, it is measured by pouring the colored tracer directly into the vortex (segregated region), which results in better vortex visualization but also approx. 2-3 times longer homogenization times compared to the standard tracer injections outside this region.

Figure 3: (a) Dependence of mixing times on primary and secondary speed mixing duration. The mixing time average and standard deviation (SD) are listed above and below each point. (b) Dependence of mixing times on the frequency of speed change at variable speed rotation. An increasing ratio $\Delta t_p/\Delta t_s$ indicates a prolongation of the mixing period at primary speed with preservation of the period at the secondary speed $\Delta t_s = 5 \text{s}$. 
3 Results and discussion

3.1 Mixing time dependency on the frequency of speed changes

A parametric study was performed to map the effect of both delay durations \( (\Delta t_p, \Delta t_s) \) on the mixing time. The Rushton turbine of a diameter-to-tank ratio of \( D/T \approx 0.25 \) and the rotational speeds \( N_p = 5.9 \text{s}^{-1}, N_s = 3.7 \text{s}^{-1} \) \( (P_s/P_p = 0.25) \) were utilized. Fig. 3a) shows the obtained mixing times in the dependence on \( \Delta t_p \) and \( \Delta t_s \). It is evident that the best choice from the point of view of destabilization of the segregated region is the equal \( \Delta t_p = \Delta t_s = 5 \text{s} \).

In order to further investigate the course of the mixing time-\( \Delta t \) dependency, the data under constant \( \Delta t_s \) are plotted in Fig. 3b). As can be seen, increasing the ratio \( \Delta t_p/\Delta t_s \) leads to a gradual increase in the mixing time, and it can be assumed that with a further increase, the mixing time will eventually limit to the value measured for constant rotation of the impeller (orange line in Fig. 3b). Based on the data measured so far, it is not possible to reliably determine the mixing time dependency on speed change frequency, so further work will aim to measure the data and study the dependence over a broader range of frequencies. Knowledge of this data will be crucial for the design of industrial processes, as a balance will need to be found, for example, between more efficient destabilization of the segregated zone and the supplied power input, which affects the mass transfer characteristics of the process.

3.2 Mixing time dependency on amplitude

This type of experiment was focused on improving the mixing characteristics by varying the impeller speed with the same delay at primary and secondary speeds \( \Delta t_p = \Delta t_s = 5 \text{s} \). These experiments
were performed with both impellers at two default speeds corresponding to specific power inputs of 10 W/m$^3$ and 100 W/m$^3$. To allow a direct comparison of the effect of the periodic change in impeller rotational speed, the data are plotted against the theoretical ratio of power inputs that the impeller would have at steady mixing conditions at given speeds (see Fig. 4). A power ratio $P_s/P_p = 1$ corresponds to the steady mixing without the change of the rotational speed. On the other hand, a $P_s/P_p = 0$ corresponds to a complete stopping of the impeller for $\Delta t_s$, followed by an acceleration to $N_p$. It is obvious from Fig. 4a-d) that constant-speed mixing yields the highest mixing times in all cases, and even a slight variation in impeller rotational speed results in destabilization of flow patterns in the segregated region and thus lowers the mixing time.

The most intensive mixing between the segregated region and the main vessel’s volume was achieved by periodically stopping and starting the impeller. Under these conditions, the hydrodynamics of the mixed vessel was apparently different from the conditions with an unstopping impeller. With the unstopping impeller, the segregated zone was always present in the middle of the vessel, and the mixing limiting phenomena was apparently the radial transport of colored iodine-starch solution outside this zone. When stopping the impeller, the formation of the segregated zone in the vessel’s center was not observed. The colored tracer was dispersed in the whole upper part of the vessel within less than 30 seconds from the injection, and the mass-transfer limiting step was visibly the axial transport between the upper and lower parts.

**Relation to the mixing times measured via conductometry**

The improvements in the segregated zone mixing, achieved by the variable speed protocol cannot be directly interpreted as the improvement of the standard mixing time, $\theta_{95}$, measured in the previous work [2], where the tracer was injected close to the impeller and outside the segregated zone. However, some insight into possible improvements is offered by Table 1. It lists the homogenization times measured previously by standard conductometry ($\theta_{95}$) and decolorization ($\theta_{\text{decol}}$) and compares the values with the longest ($\theta^{\text{const}}$) and shortest ($\theta^{\text{var}}$) mixing times measured as part of this work non-standardly by injecting the tracer directly into the segregated vortex region.

### Table 1: Comparison of the homogenization and decolorization times measured using constant and variable impeller speed.

<table>
<thead>
<tr>
<th>Impeller</th>
<th>$P_p/V$ (W/m$^3$)</th>
<th>$N_p$ (s$^{-1}$)</th>
<th>$\theta_{95}$ (s)</th>
<th>$\theta_{\text{decol}}$ (s)</th>
<th>$\theta^{\text{const}}$ (s)</th>
<th>$\theta^{\text{var}}$ (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RT60</td>
<td>10</td>
<td>6.5</td>
<td>95</td>
<td>380</td>
<td>932</td>
<td>158</td>
</tr>
<tr>
<td>(D/T ≈ 0.15)</td>
<td>100</td>
<td>14.0</td>
<td>44</td>
<td>176</td>
<td>463</td>
<td>94</td>
</tr>
<tr>
<td>RT100</td>
<td>10</td>
<td>2.7</td>
<td>62</td>
<td>248</td>
<td>966</td>
<td>118</td>
</tr>
<tr>
<td>(D/T ≈ 0.25)</td>
<td>100</td>
<td>5.9</td>
<td>29</td>
<td>116</td>
<td>259</td>
<td>97</td>
</tr>
</tbody>
</table>

- **Relation to the mixing times measured via conductometry**

Apparently, due to the different measurement methodologies, the mixing times at constant stirrer speed obtained in this work are much longer than determined in [2]. Despite this methodology-related prolongation, the mixing times obtained with periodically stopping impeller, $\theta^{\text{var}}$, are lower than $\theta_{\text{decol}}$. These results indicate the great potential of the dynamic mixing protocol not only for the reduction of the segregated zone but also suggest a possible improvement in the homogenization time $\theta_{95}$, which will be investigated in the following work.

### 3.3 Power characteristics of variable speed impeller

Periodic acceleration and deceleration of the impeller, resulting in enhanced mixing characteristics, might be connected with the substantial increase in the impeller power input [4]. To investigate the effect of variable speed protocol on the power characteristics of a magnetically driven impeller, the torque $M$ and specific power input $P/V = 2\pi MN/V$ were measured for the 100mm impeller operated in three regimes: (i) at the constant speed of 5.9 s$^{-1}$, (ii) the speed alternating between 3.7 s$^{-1}$ and 5.9 s$^{-1}$ ($P_s/P_p = 0.25$), and (iii) with the periodically stopping impeller. The measured
data are shown in Fig. 5. It is evident, that at the constant speed, the specific power input of the impeller \( P/V \) is also constant at the value of 100 ± 8 W/m\(^3\), which agrees well with the previously measured impeller power number of 3.1 [2]. Surprisingly, neither with the alternating impeller speed nor with the stopping impeller, the peak torque notably exceeds the torque of the continuously running impeller. Apparently, using the alternating speed protocol for the magnetically driven impeller does not increase the impeller power number or peak shear stress during the acceleration and deceleration. From this point of view, the enhancement of mixing in the segregated region is achieved at no additional operational costs or risks. In fact, the variable speed protocol lowers mean energy demands for the mixing.

![Figure 5: Time course of (a) measured shaft torque \( M \), (b) calculated specific power input \( P/V \), and (c) rotational speed \( N \) for three experimental conditions: (●) constant impeller rotation at \( N = 5.9 \text{ s}^{-1} \) (equivalent of \( P/V = 100 \text{ W m}^{-3} \)), (●) periodically stopping the impeller to \( N_s = 0 \text{ s}^{-1} \) (equivalent of \( P_s/P_p = 0 \)), and (●) periodically slowing down impeller to \( N_s = 3.7 \text{ s}^{-1} \) (equivalent of \( P_s/P_p = 0.25 \)). Experimental conditions: \( D/T \approx 0.25 \), \( H/T \approx 1.5 \), \( N_p = 5.9 \text{ s}^{-1} \).](image)

4 Conclusions

This contribution brings a relatively simple method, which improves the mixing characteristics of stirred un baffled bioreactors with a magnetically driven impeller. The improvement was achieved by the employment of the dynamic mixing protocol– periodic variations of impeller rotation speed. The method was tested experimentally, using magnetically driven Rushton turbines of two diameters and two specific power dissipation rates. The obtained results revealed that the variation in the impeller speed destabilizes the central vortex region, which significantly reduces the tracer residence time there. Under the best operation conditions, the residence time reduction of up to 80% was achieved in contrast to constant speed mixing. It is also shown that periodically varying the impeller speed does not cause increased power dissipation or impeller maximum torque. Thus, the dynamic mixing protocol may be suitable for shear-sensitive processes in the pharmaceutical and biotechnology industries with no additional risks and high investment costs.

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Nomenclature

Symbols

- \( C \) \( \text{m} \) impeller clearance from the bottom
- \( D \) \( \text{m} \) impeller diameter
- \( E \) \( \text{m} \) impeller eccentricity
- \( H \) \( \text{m} \) liquid high
- \( M \) \( \text{Nm} \) torque measured on shaft
- \( N \) \( \text{s}^{-1} \) rotational frequency
- \( P \) \( \text{W} \) power input
- \( P_0 = \frac{P}{\rho N^3 D^5} \) power number
- \( T \) \( \text{m} \) vessel diameter
- \( t \) \( \text{s} \) time
- \( V \) \( \text{m}^3 \) vessel volume

\[ \alpha \] ° impeller inclination angle
\[ \Delta t \] s duration
\[ \rho \] kg m\(^{-3}\) liquid density
\[ \theta \] s mixing time

Subscripts, superscripts & abbreviations

- \( 90 \) 90\% homogeneity degree
- \( 95 \) 95\% homogeneity degree
- \( \text{acc} \) acceleration
- \( \text{const} \) constant
- \( \text{dec} \) deceleration
- \( \text{decol} \) decolorization
- \( p \) primary
- \( \text{RT} \) Ruston turbine impeller
- \( s \) secondary
- \( \text{SD} \) standard deviation
- \( \text{UBE} \) unbaffled with eccentrically mounted impeller
- \( \text{var} \) variable

References


