Monitoring gradient formation in a jet aerated bioreactor

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Jet aerated loop reactors (JLRs) provide high mass transfer coefficients ($k_L a$) and can be used for the intensification of mass transfer limited reactions. The jet loop reactor achieves higher $k_L a$ values than a stirred tank reactor (STR). The improvement relies on significantly higher local power inputs ($\sim 10^4$) than those obtainable with the STR. Operation at high local turnover rates requires efficient macromixing, otherwise reactor inhomogeneities might occur. If sufficient homogenization is not achieved, the selectivity of the reaction and the respective yields are decreased. Therefore, the balance between mixing and mass transfer in jet loop reactors is a critical design aspect. Monitoring the dissolved oxygen levels during the turnover of a steady sodium sulfite feed implied the abundance of gradients in the JLR. Prolonged mixing times at identical power input and aeration rates ($\sim 100\%$) were identified for the JLR in comparison to the STR. The insertion of a draft tube to the JLR led to a more homogenous dissolved oxygen distribution, but unfortunately a reduction of mixing time was not achieved. In case of increased medium viscosities as they may arise in high cell density cultivations, no gradient formation was detected. However, differences in medium viscosity significantly altered the mass transfer and mixing performance of the JLR.

KEYWORDS

dissolved oxygen gradient, jet loop reactor, macromixing, mass transfer, micromixing

1 | INTRODUCTION

The productivity of aerobic and mass transfer limited bioprocesses can be improved by increasing the oxygen transfer rate (OTR). The achievable space time yields of biochemical reactions are determined by both, local mass transfer effects and the overall mass transfer capacity of the reactor [1]. If high local reaction rates are achieved an efficient homogenization is required, otherwise oxygen and substrate gradients are formed and the aspired selectivity cannot be met [2,3]. Already a few seconds of oxygen limitation can induce genes for a metabolic shift towards the production of anaerobic byproducts [4–6].

In recent studies, an increase in mass transfer up to $\sim 200\%$ and therefore higher productivities were achieved in jet loop

reactors (JLRs) compared to stirred tank reactors (STRs) [7, 8]. Surprisingly in some cases the concentration of the anaerobic and overflow metabolite acetate was already increasing for cultivation at strictly aerobic conditions [9]. Therefore, the presence of oxygen- and substrate gradients within the JLR was considered as a possible reason for the observed acetate formation. To further evaluate that issue, a steady sodium sulfite feed was applied to the vessel and potential gradient formation was monitored. The results were compared to data obtained with an aerated stirred tank reactor (Figure 1).

1.1 | Balance of micro and macromixing

For JLRs, the efficient mass transfer performance relies on high local power inputs within the nozzle and subsequently the generation of a fine primary gas liquid dispersion [3]. In case of the STR, mixing and the secondary dispersion of the

Abbreviations: CMC, Carboxy methyl cellulose; JLR, Jet aerated loop reactor; OTR, Oxygen transfer rate; STR, Stirred tank reactor

FIGURE 1 Arrangement of 18 sensor positions in monitored sections 0.2–1.0 π at 6 reactor heights. (A) STR with 2 Rushton turbines, feed pipe, pipe sparger and 3 baffles (B) JLR with ejector, baffle plate, feed pipe and liquid outlet (C) JLR modified with draft tube. (D) Planar projection sensor positions, radian measure against reactor height. (E) Top view on reactor cover. Sensor ports at 0.2, 0.6 and 1.0 π

gas phase is taking place at multiple stirrer blades and at the installed baffles. Therefore, the distribution of power input is expected to be more homogenous. At identical overall power inputs, the local values found for the STR are lower than for the JLR [2]. Consequently, the gas liquid dispersion is worse and the mass transfer performance is reduced [10].

In general, mixing entails the distribution of miscible substances, an increase of the contact area between the substances, and molecular diffusion [10]. The term macromixing refers to the distribution of substances within the reactor, while the term micromixing describes mixing within the molecular scale [11–14]. For reactions limited by mass transfer, mixing time becomes important if the reaction rate and therefore the time constant for oxygen consumption is in the same order of magnitude [10]. For fast reactions, as they are aspired in process intensification, inhomogeneities are formed whenever micromixing is faster than macromixing [15]. The time scale for micromixing (θ_{micro}) is dominated by the local power input (ϵ_T), viscosity (ν) and diffusion (D_L) (Equation (1)) [16]. The time scale for macromixing

(θ_{macro}) can be correlated to the overall power input ($\bar{\epsilon}$) and geometric length scales of the reactor (e.g. the diameter d) (Equation (2)) [11].

$$\theta_{\text{micro}} \sim \left(\frac{\nu}{\epsilon_T} \right)^{1/2} \ln \left(\frac{\nu}{D_L} \right) \quad (1)$$

$$\theta_{\text{macro}} \sim \left(\frac{d^2}{\bar{\epsilon}} \right)^{1/3} \quad Re > 10^4 \quad (2)$$

The requirements for micro- and macromixing should be well known. If operated at identical overall power inputs ($\bar{\epsilon}$), the local power input (ϵ_T) and therefore the local reaction rates achieved in a jet aerated reactor are increased by multiple orders of magnitude in comparison to a STR. Consequently, a homogenous distribution of the reacting components must be ensured by intensified macromixing. Otherwise the generation of gradients and the formation of anaerobic byproducts or overflow metabolites becomes more likely.

1.2 | Role of hydraulic and pneumatic power input

For STRs, mixing and mass transfer can be regulated by the individual adaption of stirrer speed (hydraulic power input) and aeration rate (pneumatic power input). Mixing in JLRs is mainly facilitated by the entrained gas phase (pneumatic power input). However, for a JLR that is operated with an ejector nozzle the amount of entrained gas is directly correlated to the hydraulic power input. Pneumatic- and hydraulic power input cannot be adapted separately. For standard ejectors the major proportion of the provided power is unnecessarily dissipated in highly turbulent zones behind the nozzle outlet. This can be prevented by the installation of a draft tube. Thereby the momentum of the liquid jet is used more efficiently. A defined internal loop flow is implemented and a homogenous residence time distribution is achieved. For a JLR with an ejector installed in downflow configuration, a draft tube leads to higher local power inputs in the downcomer and lower local power inputs and less turbulence in the riser [17].

1.3 | Challenges arising from medium properties

The demands for mass transfer and mixing as well as the media properties can change significantly over fermentation time. JLRs work best for coalescence inhibited systems, where bubbles that are formed in the nozzle nearly remain their size during the circulation within the apparatus. However, the medium viscosity can increase with biomass growth and product formation. Increased viscosities can promote bubble coalescence and prolong the time constant for micromixing (Equation (1)). The rate constant of diffusion limited reactions (k_D) is decreased significantly with increasing viscosities. The changing rate constant can be correlated to the dynamic viscosity (η), the temperature (T) and the respective gas constant (R) (Equation (3) [18]). This implies, that a JLR with a high mass transfer performance in aqueous, coalescence inhibited salt medium, might lose its capabilities at an increased medium viscosity as can occur in high cell density cultures.

$$k_D \sim \frac{8 R T}{3 \eta} \quad (3)$$

2 | MATERIALS AND METHODS

2.1 | Reactor setups

The evaluated reactors were based on an Infors Labfors 5 fermentation unit with a total volume of 7.5 L and a $H_R:D_R$ ratio of 3. Controlled process variables were temperature,

airflow, agitator- (STR) and pump speed (JLR). The setpoint temperature of 37°C was measured by a PT100 sensor and maintained via the double jacket of the vessel. The integrated heating cartridge controlled the temperature of the thermostating liquid (1 % w/w diethylene glycol). Cooling was provided by a thermostat (FL601, Julabo, Germany). In both systems a mass flow controller (red-y smart controller GSC-C, Vögtlin, Switzerland) controlled (STR) or measured (JLR) the inflow of air. The dissolved oxygen level was measured by an optical oxygen sensor (PSt3, Presens, Germany). The achievable response time of the sensor t_{90} was < 3s. The sensor was inserted via the available 35 mm ports in the reactor cover (Figure 1E). Two clamp connectors attached to a guide rail provided mechanical stability and allowed an adjustment in variable axial positions.

The sensors were calibrated on 100% air saturation in 0.5 M sodium sulfate medium at 37°C at 1 atm. A peristaltic pump (Infors HT, Switzerland) added feed solution via the reactor head (STR) or via a feeding pipe close to the nozzle outlet (JLR). The STR was agitated via a mechanically sealed agitator shaft, powered by an electric motor (BG56 × 75SI, Dunkermotoren, Germany). Two six-bladed Rushton turbines with a diameter of 54 mm were installed at a distance of 180 mm and 55 mm from the reactor bottom. The reactor was equipped with three baffle plates with a width of 15 mm. Pressurized air was supplied via a J-formed open pipe sparger.

The JLR was equipped with an ejector nozzle (diameter orifice 1 mm, H804, Schlick, Germany). A gear pump (P72380, Gather, Germany) powered the liquid jet. The nozzle was mounted centrally in downflow configuration at a height of 150 mm from the reactor bottom. The pressure between the discharge side of the gear pump and the nozzle was measured via a manometer (Wika, Germany). A baffle plate installed above the liquid outlet prevented gas entrainment. The JLR was equipped with a removable draft tube with an inner diameter of 86 mm and a length of 100 mm. It was mounted to the ejector nozzle (80-180 mm from reactor bottom). The determination of k_L values and mixing times were performed at a liquid volume of 3.5 L (minimal filling level, maximal $\bar{\epsilon}$). For the visualization of potential gradient formation, the final filling level for 5.0 L liquid volume was chosen (maximal difference between ϵ_T and $\bar{\epsilon}$).

2.2 | Calculation of power input

The hydraulic power input (P_n) to the JLR was determined by the pressure drop over the liquid nozzle (Δp_n) and the liquid flow rate (Q_L) (Equation (4) [19]). An increase in pressure from 3.0 to 6.0 bar and liquid flow rates from 1.15 to 1.60 L min⁻¹ led to an absolute power input between 5.75 and 16.00 W.

$$P_n = \Delta p_n Q_L \quad (4)$$

The power input of the stirrer (P_s) was calculated by the density of the liquid phase (ρ_L), the stirrer diameter (d_s), the stirrer speed (n_s), the number of stirrers (m) and the power number (Po) (Equation (5)). The loss in power input by aeration was considered by a modified power number Po_b [20] (Equation (6)). For calculation of the modified power number, the reactor diameter (D_R) and the gravitational acceleration (g) were used. For superficial gas velocities (u_g) between $0.94 \times 10^{-3} \text{ m s}^{-1}$ and $4.71 \times 10^{-3} \text{ m s}^{-1}$ and turbulent conditions at 540 rpm ($Re: 2.7 \cdot 10^4$) and 1050 rpm ($Re: 5.3 \times 10^4$), hydraulic power inputs between 5.32 and 16.20 W were calculated.

$$P_s = m Po_b \rho_L d_s^5 n_s^3 \quad (5)$$

$$Po_b = \frac{Po_0}{\sqrt{1 + 490 \frac{u_g}{\sqrt{g} D_R}}} \quad (6)$$

In relation to the hydraulic power input, the maximum pneumatic power was accounted for < 2% of the total value. Therefore, the pneumatic power input was neglected within this study.

2.3 | Steady sulfite feeding method

In microbial systems oxygen consumption arises from substrate degradation and other metabolic processes. For the biocatalytic combustion of 1 mole glucose, 6 moles oxygen are required. Therefore, oxygen consumption in aerobic fed batch fermentations can be controlled by substrate limitation. For the presented characterization, the microbial system was replaced by a 0.5 M sodium sulfate solution (Equation (7), Equation (8)). Instead of a rate limiting carbon source (e.g. glucose), the oxygen consumption was controlled by a steady feed of sodium sulfite. It was expected that differences in the mass transfer- and mixing performance would lead to a locally different distribution of the reacting components (oxygen, sulfite) and therefore different reaction rates and consequently gradient formation.

The reactor were evaluated at operational parameters that are relevant for highly aerobic bioprocesses. In large scale stirred tank reactors the volumetric power input is limited to 5 kW m^{-3} [19]. Therefore, the reactors are compared for volumetric power inputs below 5 kW m^{-3} . For the volumetric power input (P/V) a value of 3.7 kW m^{-3} was chosen. The aeration rate (Q_g) was set to a value of $0.15 \text{ m}^3 \text{ h}^{-1}$. To prevent an accumulation of sodium sulfite, the oxygen consumption was adjusted to a constant value of $20 \text{ mmol L}^{-1} \text{ h}^{-1}$, a value below the overall mass transfer performance of the reactors ($STR \sim 100 \text{ mmol L}^{-1} \text{ h}^{-1}$, $JLR \sim 200 \text{ mmol L}^{-1} \text{ h}^{-1}$).

The dissolved oxygen levels were monitored via 3 ports at 0.2π , 0.6π , 1.0π radian measure (Figure 1E) and at reactor heights from 50 to 300 mm. Three different hardware setups were evaluated. A STR powered by Rushton turbines (Figure 1A), a JLR with a plunged ejector operated as free jet (Figure 1B) and a JLR equipped with a draft tube (Figure 1C) were evaluated. The measurements at each sensor position were performed for a time period of 2 min (sampling rate of 1 s^{-1} , standard deviation given). For visualization, the data were plotted in a planar projection (Figure 1D). The measured $p\text{O}_2$ values at the respective positions (0.2π - 1.0π) and reactor heights were depicted as a contour plot. A hypothetic gradient development between the monitored positions was calculated by linear interpolation of the measured dissolved oxygen levels.

2.4 | $k_L a$ determination with dynamic method

To obtain a measure for the dispersion of gas- and liquid phase, the volumetric mass transfer coefficient ($k_L a$) was determined. In the presented study the $k_L a$ is used as a measure of micromixing. As gradient formation was expected, ideally mixed conditions could not be stated. For gradient formation it was required that mass transfer and mixing were in the same order of magnitude. For the steady sulfite feeding method it was assumed, that high local $k_L a$ values (high micromixing) would improve local substrate conversion (O_2 consumption) and combined with inadequate mixing result in gradient formation.

In the region with the highest turnover the difference in the time scale for macromixing and micromixing should be maximal. Therefore, the sensor for the $k_L a$ determination was positioned in the highly aerated and turbulent regions at 0.6π at a height of 50 mm (Figure 1A,B,D).

The dissolved oxygen in the liquid phase was stripped with nitrogen gas. Subsequently, the aeration was started and the increasing oxygen concentration (c_{O_2}) was measured by an optical oxygen sensor. The $k_L a$ values were determined from the respective step response between 20 and 80% of the maximum dissolved oxygen concentration ($c_{\text{O}_2}^*$) (Equation [9]).

$$k_L a = \frac{\ln \left(\frac{c_{\text{O}_2}^* - c_{\text{O}_2,1}}{c_{\text{O}_2}^* - c_{\text{O}_2,2}} \right)}{t_2 - t_1} \quad (9)$$

2.5 | Mixing time determination with decolorization method

The mixing time was determined by a decolorization method. For colorization 5 mL of an 0.1 M iodine solution were added to 3.5 L of the respective medium. The addition of 10 mL saturated and filtrated starch solution intensified the colorization. For decolorization, 10 mL of 0.1 M sodium thiosulfate solution were added to the reactor. The mixing time was defined as the time that is required to obtain complete decolorization. The experiments were performed in triplicates. For evaluation the decolorization process was recorded with a camera.

2.6 | Determination of viscosity and shear rate

The effect of an altered medium viscosity on gradient formation, mixing time and $k_L a$ was tested in a pseudo plastic model medium that contained Carboxy methyl cellulose (CMC). However, for highly sheared pseudo plastic fluids, ideal viscous properties are found [21]. This allowed to assume ideal flow behavior for calculation of the shear rate ($\dot{\gamma}$) at the nozzle. The shear rates were calculated by the radius of the nozzle (r_n) and the liquid flow (Q_L) [22]. The apparent shear rate in the riser was calculated according to Equation (11) [23]. In bubble columns that are operated with non-Newtonian fluids, the shear rate was found to be a function of the superficial gas velocity (u_g) [24,25].

$$\dot{\gamma} = \frac{4 Q_L}{\pi r_n^3} \quad (10)$$

$$\dot{\gamma} = 5000 u_g \quad (11)$$

The range of relevant shear rates was estimated according to Equations (10) and (11). The viscosities of solutions containing 0.25–2.0 g L⁻¹ CMC were determined at apparent shear rates ($\dot{\gamma}$) ranging from 7 to 1000 h⁻¹ (rotational rheometer, RheoStress1, Haake Thermo Fischer Scientific Inc, USA).

3 | RESULTS AND DISCUSSION

3.1 | Gradient formation in JLR compared to STR

To generate a qualitative insight to gradient formation in JLR and STR, a steady sodium sulfite feed was applied to the reactors (Section 2.3). For the STR values between 22 and 85% dissolved oxygen concentration were determined in the evaluated section (Figure 2A). The lowest oxygen concentrations were found above the stirrers mounted at 50

and 180 mm reactor height. As described by Laufhütte und Mersmann [11], regions with a 70-fold increase in local power input and therefore high mass transfer rates can be found near the installed Rushton turbines. In comparison to the surroundings, zones of low dissolved oxygen concentration were identified at a position of 0.6π radian measure. As indicated by the dashed line, these zones are located behind the installed baffle at 0.55π radian measure. In the region below the upper stirrer (180 mm reactor height) and near the surface (300 mm reactor height), high dissolved oxygen levels ($pO_2 > 70\%$) were found. For the JLR without draft tube, dissolved oxygen concentrations between 29 and 71% were determined in the evaluated section (Figure 2B). Dissolved oxygen levels were increasing from 0.2π to 1.0π radian measure. Unfortunately, the main fraction of gas leaving the nozzle was swept to one side (0.2 – 0.4π) after flow deflection at the baffle plate. In the evaluated section of the reactor, axial and radial gradients were formed. The region with the lowest oxygen content was found in the upward directed flow after deflection at the baffle plate. An improvement of the local energy dissipation by the insertion of a draft tube significantly influenced the obtained results (Figure 2B). An asymmetric distribution of gas phase and feed solution was prevented. A defined gas liquid flow was implemented in the downcomer and in the riser section of the apparatus. For the evaluated segment of the reactor the installation of a draft tube successfully prevented the formation of gradients.

3.2 | Comparison of $k_L a$ and t_{mix} (P/V)

The results presented in Section 3.1 indicate that the mixing performance of the JLR without draft tube was worse compared to the STR. In case of the JLR, monitoring the dissolved oxygen levels implied unwanted gradient formation. Gradient formation occurs whenever micromixing is significantly faster than macromixing (1.1). Therefore, the micro- and macromixing abilities of the reactors were evaluated in more detail. The $k_L a$ value was determined as a measure of gas liquid micromixing. The mixing time was chosen as a measure that is mainly influenced by macromixing.

The achievable $k_L a$ values and the respective mixing times were determined for volumetric power inputs from 1.7 to 4.9 kW m⁻³. For the STR mixing times between 1.2 and 1.9 s were achieved. In comparison, the JLR achieved mixing times between 2.6 and 3.7 s (Figure 2D). The determined mixing times are in the same order of magnitude as the response time of the oxygen sensor. In general, this involves the risk to obtain high inaccuracies during $k_L a$ determination. Nevertheless, reproducible results with a low standard deviation were determined. The $k_L a$ values obtained by the JLR are 1.3 to 1.5 times higher than those achieved by the STR (Figure 2E). In case of the JLR, power input and gas dispersion is taking

FIGURE 2 Dissolved oxygen concentrations measured by steady sulfite feeding method and interpolated gradient. Internals pipe indicated by dashed lines (A) STR, standard deviation ± 2.26 (B). JLR with ejector, standard deviation $\pm 4.50\%$. (C) JLR with draft tube, standard deviation $\pm 0.92\%$. (D) Mixing times (t_{mix}) for STR and JLR without draft tube. (E) $k_L a$ for STR and JLR without draft tube. (F) Mixing times (t_{mix}) JLR without draft tube and JLR with draft tube

place in a very small volume within the nozzle. Compared to the values found for the STR, the local power inputs within the installed nozzle were increased by a factor of 10^4 . Consequently, smaller bubbles were formed and higher $k_L a$ values were achieved.

If however, the achieved mixing times and $k_L a$ values are considered, it turned out that for the STR the mixing time was decreasing with $t_{mix} \sim (P/V)^{-0.4}$ as the obtained $k_L a$ value was increasing with $k_L a \sim (P/V)^{0.4}$. For the JLR an increase in power input yielded $k_L a$ values increasing with $k_L a \sim (P/V)^{0.7}$ whereas the mixing time was decreasing only with $\theta_{macro} \sim (P/V)^{-0.3}$.

The found correlations for $k_L a \sim (P/V)^a$ and $t_{mix} \sim (P/V)^{-b}$, are in accordance with correlations found in the literature [10,15,19,26,27]. However, they might serve as indicators for the gradient formation caused by unbalanced macromixing and micromixing. In case of the JLR, the high $k_L a$ values and the relatively long mixing times might have promoted the formation of undefined inhomogeneities (Figure 2B). For the STR, macromixing and micromixing seemed to be well balanced. Local differences in dissolved oxygen concentration were clearly attributed to stirrers and baffles.

In case of the JLR, the formation of axial and radial gradients in the riser was prevented by the insertion of a draft tube (Figure 2C). The visual observation implied an improved and a more homogenous gas distribution compared to the operation without draft tube. The segmentation of

the apparatus led to an increased turnover of sulfite in the highly aerated downcomer at high local power inputs and consequently a lower oxygen consumption and increased dissolved oxygen levels in the riser. However, the mixing times were not significantly reduced compared the results obtained for the JLR without a draft tube (Figure 2F). Consequently, the diverging trend of $k_L a(P/V)$ and $t_{mix}(P/V)$ could not be converged by the insertion of a draft tube.

3.3 | Effect of pseudoplasticity on $k_L a$ and t_{mix}

Concerning bioprocesses, an increased biomass concentrations and product titers can change the intrinsic viscosity of the broth significantly. As outlined in Section 3.1, viscous forces have a strong influence on micromixing and diffusion. Especially polymer structures of biomass, feed compounds and product molecules can significantly alter the flow properties of the broth. Therefore, gradient formation, mixing times and $k_L a$ values in pseudo plastic, shear thinning media are of particular interest. In case of the JLR, high differences in local power input can be found between the highly turbulent flow in the nozzle and the relatively calm riser section. It is expected that the shear forces differed significantly across the reactor.

To evaluate the influence of an altered viscosity on gradient formation, the dissolved oxygen levels as well as the mass transfer- and mixing performance of a JLR were tested

FIGURE 3 (A) Oxygen gradient obtained for JLR 2 g L⁻¹ CMC and P/V: 3.7 kW m⁻³ standard deviation $\pm 1.33\%$, position of nozzle indicated by dashed line. (B) Calculated viscosities over shear rates for nozzle and riser (C) Obtained $k_L a$ values for JLR. (D) Obtained mixing times for JLR

for model media. The media contained CMC concentrations ranging from 0.5–2.0 g L⁻¹. The lowest viscosities were expected close to the nozzle (1.8–3.6 mPa s). The lowest shear rates and the highest viscosities should be found in the riser (38–6 mPa s) (Figure 3B). As reported by other authors [17] [28] [29] the determined $k_L a$ values were increasing with increasing CMC concentrations until a critical value was reached (1.0 g L⁻¹ CMC) (Figure 3C). For higher CMC concentrations, the effect of viscosity on the generation of gas liquid interface and diffusion became dominant and the measured $k_L a$ values were decreased with increasing CMC concentration. The obtained mixing times were prolonged with increasing CMC concentrations (Figure 3D). An elevated power input led to a reduction of mixing times which are comparable to the results obtained in aqueous solution (3.2). A CMC concentration of 2 g L⁻¹ was chosen to monitor gradient formation. For this medium composition, the mixing time was prolonged and the $k_L a$ value was decreased (Figure 3C/D). Interestingly, compared to the result obtained in Section 3.1, less inhomogeneities were found in the evaluated section (Figure 3A versus Figure 1B). A possible explanation could be originated in a decreased reaction rate constant k_D . According to Equation (3), k_D was decreased by the order of one magnitude in regions with low turbulence and maximal viscosity (Figure 3B). An increased medium viscosity hinders diffusion and therefore the reaction of dissolved oxygen with sulfite ions. Consequently, the local oxygen consumption

was slowed down and higher dissolved oxygen levels were found.

4 | CONCLUDING REMARKS

The steady sodium sulfite feeding method implied potential gradient formation in the evaluated JLR. The obtained results were supported by conventional mixing time- and $k_L a$ measurements. The local power inputs generated in a JLR are increased by the factor of 10^4 in comparison to the maximum values found in a STR. Therefore, higher $k_L a$ values were achieved with the JLR. Compared to the evaluated STR it was found, that the mixing time of the respective JLR was prolonged. Potential gradient formation was identified already at a low oxygen demand of 20 mmol L⁻¹ h⁻¹. For the STR, gradients could be attributed to highly turbulent zones above the stirrer and zones with low turbulence behind a baffle. In case of the JLR without draft tube, the pO₂ distribution could not be attributed to reactor internals. The main gas fraction was swept to one side after flow deflection at the baffle plate. Consequently, an undefined pO₂ distribution was obtained. This was addressed by the insertion of a draft tube. In the following, the uncontrolled formation of gradients in the monitored section was successfully prevented. The steady sodium sulfite feeding method confirmed the diverging relation between macromixing and mass transfer in the evaluated JLR. The disbalance of mixing and mass transfer

in JLRs reveals a critical design aspect, especially for the intensification of highly aerobic fermentation processes. To enhance understanding of gradient formation, additional calculations of computational fluid dynamics might be useful.

Nomenclature

c	[g L ⁻¹]	concentration
DR	[m]	reactor diameter
D	[m ² s ⁻¹]	mass diffusivity
d	[m]	diameter
g	[m s ⁻²]	gravitational acceleration
H _R	[m]	reactor height
k	[m ³ mol ⁻¹ s ⁻¹]	reaction rate constant
k _L a	[h ⁻¹]	mass transfer coefficient O ₂
m	[-]	number of stirrers
n _s	[s ⁻¹]	stirrer speed
p	[Pa]	pressure
P	[W]	power input
Po	[-]	power number
pO ₂	[%]	dissolved oxygen O ₂
Qg	[L min ⁻¹]	aeration rate
QL	[m ³ h ⁻¹]	liquid flow rate
R	[kg m ² s ⁻² mol ⁻¹ K ⁻¹]	gas constant
Re	[-]	Reynolds number
r	[m]	radius
T	[K]	temperature
t	[s]	time
ug	[m s ⁻¹]	superficial gas velocity
V	[m ³]	volume
*	[-]	saturated

Greek symbols

$\dot{\gamma}$	[s ⁻¹]	shear rate
Δ	[-]	delta
ϵT	[kW m ⁻³]	local power input
$\bar{\epsilon}$	[kW m ⁻³]	overall power input
η	[N s m ⁻²]	dynamic viscosity
θ	[s]	time scale
π	[-]	pi
ν	[m ² s ⁻¹]	kinematic viscosity
ρ	[kg m ⁻³]	density

Indices

0	unaerated
b	aerated / modified
L	liquid
mix	mixing
n	nozzle
s	stirrer
micro	microscopic
macro	macroscopic
D	diffusion

CONFLICT OF INTEREST

The authors have declared no conflict of interest.

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