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ORIGINAL PAPER

Comparative analysis of oxygen transfer rate distribution in stirred bioreactor for simulated and real fermentation broths

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Abstract Study of the distribution of the oxygen mass transfer coefficient, k_la, for a stirred bioreactor and simulated (pseudoplastic solutions of carboxymethylcellulose sodium salt) bacterial (*P. shermanii*), yeast (*S. cerevisiae*), and fungal (*P. chrysogenum* free mycelia) broths indicated significant variation of transfer rate with bioreactor height. The magnitude of the influence of the considered factors differed from one region to another. As a consequence of cell adsorption to bubble surface, the results indicated the impossibility of achieving a uniform oxygen transfer rate throughout the whole bulk of the microbial broth, even when respecting the conditions for uniform mixing. Owing to the different affinity of biomass for bubble surface, the positive influence of power input on k_la is more important for fungal broths, while increasing aeration is favorable only for simulated, bacterial and yeast broths. The influence of the considered factors on k_la were included in mathematical correlations established based on experimental data. For all considered positions, the proposed equations for real broths have the general expression $k_la = \alpha C_X^{\beta}\left(\frac{P_a}{V}\right)^{\gamma} v_S^{\delta}$, exhibiting good agreement with experimental results (with maximum deviations of ±10.7% for simulated broths, ±8.4% for *P. shermanii*, ±9.3% for *S. cerevisiae*, and ±6.6% for *P. chrysogenum*).

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List of symbols

C_X	Biomass concentration, g/l d.w.
E_{O_2}	Oxygen mass transfer efficiency, m^3/J
k_la	Oxygen mass transfer coefficient, /s
P_a	Power consumption for mixing of aerated broths, W
P_a/V	Specific power input, W/m^3
v_S	Superficial air velocity, m/s
V	Volume of medium, m^3
η_a	Apparent viscosity, Pa s
α, β, γ, δ	Parameters of empirical correlations (2) and (3)

Introduction

One of the particularities of biosynthesis processes is the polyphasic composition of the broths, being generally triphasic (gas–liquid–solid) or tetraphasic (gas–liquid–liquid–solid). Consequently, mass transfer (of carbon and energy sources, organic nitrogen, and oxygen) is more complex than that required for chemical processes and controls bioreactor performance.

The oxygen supply into broths constitutes one of the decisive factors for cultivated microorganism growth and plays an important role in the scale-up and economy of aerobic biosynthesis systems. The aeration efficiency depends on the oxygen solubilization and diffusion rate into the broth, as well as on the capacity of the

bioreactor to satisfy the oxygen demands of the microbial population.

Oxygen mass transfer can be analyzed and described by means of the mass transfer coefficient, k_la, being the most important parameter for the design and operation of mixing/sparging equipment for aerobic bioreactors. k_la values are affected by many factors, such as the geometrical and operational characteristics of the vessel, medium composition, microorganism concentration and morphology, and biocatalyst properties (particle size, porosity, etc.) [1, 7, 9, 16, 17, 20].

Stirred bioreactors are widely used in biotechnology, because they provide large values of heat and mass transfer rate, due to the intense mixing. These bioreactors are recommended for broths containing suspended particles with a pronounced tendency for deposition or for fermentations where oxygen supply is the limiting factor. However, an important challenge for the design and operation of such bioreactors is the nonuniform distribution of the energy promoted by mixing, with direct consequences on the distribution of mixing efficiency and mass/heat transfer rate [6].

Although the literature offers correlations for k_la, there are still many uncertainties concerning the accuracy of such k_la predictions, owing to the strong influence of the bioreactor geometry and the range of operating variables for which the proposed models are adequate, and due to the experimental methods used for k_la determination [15, 21]. Moreover, these correlations can be applied for certain microorganism cultures only, and describe the system behavior for a given region without indicating the oxygen transfer rate distribution throughout the whole bulk volume of the broth.

Recent reports from the literature have underlined the possibility of characterizing the performance of stirred bioreactors by means of the computational fluid dynamics (CFD) method, which has previously been applied to analyze the distribution of flow streams and velocity, gas holdup, air bubble size, interfacial area, and bubble coalescence or formation [2, 3, 8, 10, 11, 13, 14], as well as oxygen transfer in stirred vessels containing tap water [12]. Although oxygen transfer is directly related to the processes that have been studied and modeled using CFD, there is no information concerning the oxygen transfer rate distribution in stirred bioreactors with multiple impellers, probably due to the larger number and complexity of the factors involved.

For this reason, the aim of the experiments described herein is to analyze the oxygen transfer rate distribution as a function of liquid height, through the oxygen mass transfer coefficient, k_la, for a stirred bioreactor and different fermentation broths without biomass (simulated broths) and with microorganisms (bacteria *Propionibacterium shermanii*, yeast *Saccharomyces cerevisiae*, and fungus *Penicillium chrysogenum* free mycelia), for a large domain of operating variables. To quantify the effects of the considered factors (apparent viscosity, concentration and morphology of the different microorganisms, specific power input, and superficial air velocity) on k_la and its distribution, mathematical correlations are established for a number of positions in the bioreactor. The proposed equations could be useful for mass transfer optimization or scale-up.

Materials and methods

The experiments were carried out in a 5 l (4 l working volume, ellipsoidal bottom) laboratory bioreactor (Biostat A; B. Braun Biotech International), with parameter values controlled and recorded by computer. The bioreactor and impeller characteristics have been presented previously [4].

The bioreactor mixing system consisted of two Rushton turbine impellers (diameter 64 mm) and three baffles. The lower stirrer was placed 64 mm from the bottom of the bioreactor. The upper stirrer was placed on the shaft at the optimum distance from the lower one according to the type of broth studied, namely at 128 mm for simulated broths and at 64 mm for the real broths, as demonstrated in previous work [5]. The rotation speed was maintained below 600 rpm. The experiments were carried out at Reynolds number up to 15,200, a domain which corresponds to a laminar, transitory, low-turbulent flow regime and that avoids cavity formation at the broth surface.

The sparging system consisted of a single ring sparger with 64 mm diameter, placed 15 mm from the vessel bottom, with 14 holes of 1 mm diameter. The volumetric air flow rate was varied from 75 to 450 l/h, corresponding to superficial air velocity of 0.84×10^{-3} to 5×10^{-3} m/s.

In the experiments, simulated and real broths were used. The simulated broths were carboxymethylcellulose sodium salt solutions with pseudoplastic behavior and apparent viscosity in the range 15–96 cP. The following real broths were studied:

- Bacteria (*Propionibacterium shermanii*), with C_X of 30.5–120.5 g/l d.w.
- Yeast (*Saccharomyces cerevisiae*), with C_X of 40–150 g/l d.w.
- Fungus (*Penicillium chrysogenum* free mycelia), with C_X of 4–36 g/l d.w.

Owing to the difficulty of in situ viscosity measurements during the experiments, the viscosity was measured before and after each experiment using a rotary viscometer (Hake Viscometer 6 Plus). Both the experiments and viscosity measurements were carried out at temperature of 25°C. Any viscosity or morphology changes were recorded during the experiments.

For determination of k_la, the static method was used [7, 17, 19]. This method has the advantages that it can be applied for different media (to establish the effect of media components on oxygen mass transfer) and does not involve chemical reactions that could affect measurement accuracy. According to this method, values of k_la were calculated from the slopes of straight-line plots of $\ln \frac{C_l^*}{C_l^* - C_l}$ versus time.

The concentrations of oxygen dissolved in the broth were measured using an oxygen electrode (InPro 6000 series, Mettler Toledo). As underlined in the literature, because the k_la values were in all cases less than 0.1/s, it was assumed that the response of the oxygen electrode to the change in the oxygen concentration was sufficiently fast and did not affect the determination accuracy [15, 19].

Because the static method is adequate for nonrespiring systems only, the respiratory activity of microorganisms was inhibited by suspending the biomass in a solution of 0.2% pyrogallic acid and 0.4% potassium hydroxide for about 30 min, then the biomass was filtered, washed with distilled water, and used for preparation of the above-mentioned suspensions [7].

To analyze the oxygen transfer rate distribution in the broth, the oxygen electrode was introduced at four different positions, located vertically from the bottom of the bioreactor as follows:

- Position 1: at 20 mm
- Position 2: at 70 mm
- Position 3: at 120 mm
- Position 4: at 170 mm

The variations of dissolved oxygen concentration were recorded by the bioreactor computer recording system and were analyzed to calculate k_la values.

Mathematical correlations describing the influences of the considered factors on k_la for the four positions in the broth were developed using MATLAB software. For the experimental data, multiregression analysis was performed, with the difference between experimental and modeled values being subjected to least-squares minimization. Using MATLAB, the regression coefficients and standard deviations were calculated.

Each experiment was carried out three times, under identical conditions, and the average value of k_la was used. The maximum experimental errors varied between ±4.36% and ±5.88%.

Results and discussion

Increase of broth viscosity as a result of compositional change during fermentation significantly reduced the oxygen mass transfer rate. This phenomenon is a consequence of the reduction of turbulence in the system. Furthermore, the biomass exhibited a significant effect on the oxygen mass transfer. In principle, the influence of cells is the result of [7]:

- Modification of the rheological characteristics of the broth during the fermentation process, especially the increase of apparent viscosity due to biomass accumulation, an effect that is less pronounced for bacterial cultures. The increase of viscosity induces two major direct effects on oxygen mass transfer: reduction of turbulence and perturbation of bubble dispersion–coalescence equilibrium.
- Obstruction of mass transfer, owing both to the reduction of oxygen solubility and to the blocking effect created by cell adsorption to air bubble surface. However, adsorbed solid particles can promote surface renewal, with a favorable effect on oxygen mass transfer.

Bubble dispersion–coalescence equilibrium is also affected by the presence of a solid phase, which can amplify or diminish the coalescence process, depending on the concentration and morphological conformation of the microorganism [21]. Therefore, the appearance of small bubbles is promoted, leading to increase of the interfacial area for oxygen mass transfer. However, owing to the high retention time in the broth, the oxygen concentration gradient between the two phases and the oxygen mass flow are both reduced [7]. These phenomena induce a heterogeneous distribution of air bubbles, of gas–liquid interfacial area, and thereby of oxygen transfer rate in the broth.

For these reasons, use of a single mathematical model and a single/average value for k_la for a given fermentation broth does not provide the accuracy required to operate the bioreactor under optimum conditions. Consequently, by means of the experimental data, a map of the oxygen transfer rate distribution in the microbial broth must be plotted.

Simulated broths

Figure 1 indicates the different variations of k_la for the simulated broths as a function of the specific power input for the four considered positions. Thus, although the shapes of the recorded curves are similar, the magnitude of the influence of the mixing intensity differs considerably from one position to another.

For the more viscous broths, k_la increases with greater mixing for all oxygen electrode positions, reaches a maximum value, then decreases. This variation could be the result of modification of the mixing mechanism in the presence of air bubbles, and thereby of the extent of turbulence, with increasing specific power input. Thus, at low

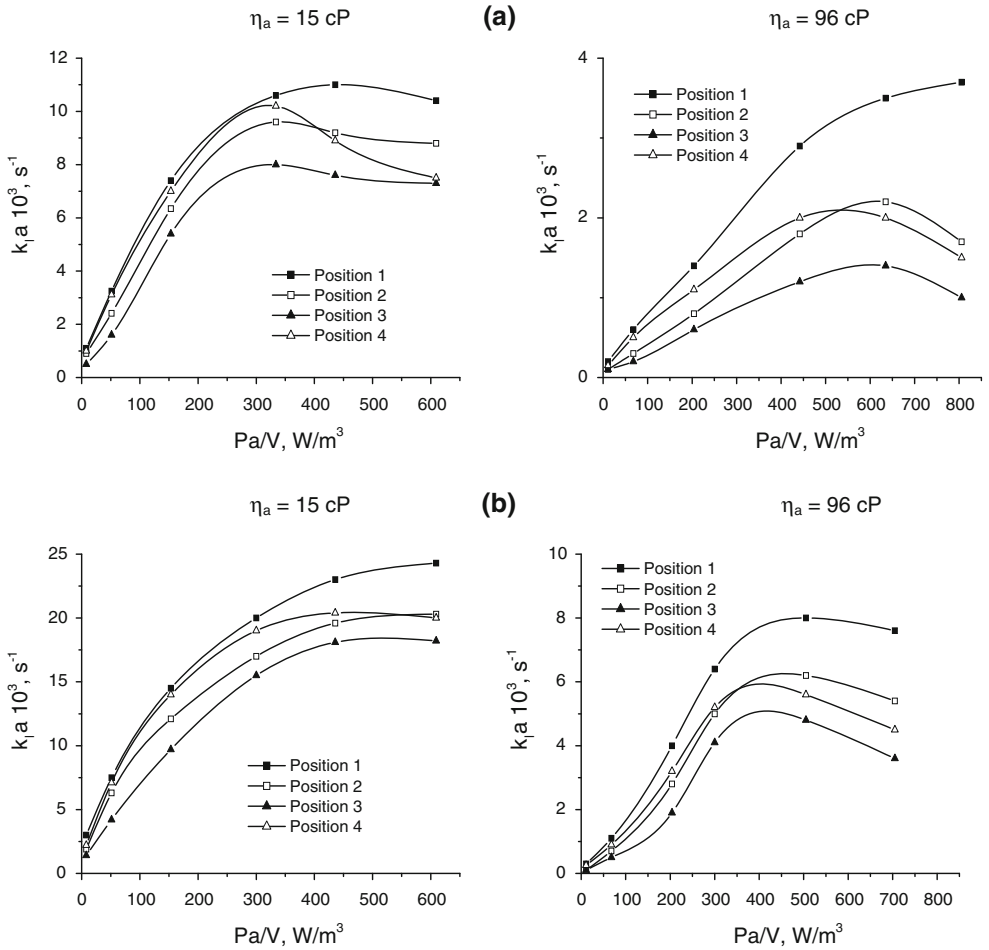

Fig. 1 Influence of specific power input on the oxygen mass transfer coefficient for the simulated broths for: **a** $v_S = 8.4 \times 10^{-4}$ m/s, and **b** $v_S = 5 \times 10^{-3}$ m/s

rotation speed, the contribution of pneumatic mixing to dispersion circulation is important, and increasing the rotation speed further intensifies broth agitation in the bioreactor. At higher rotation speeds, the bubble retention time increases, the gas–liquid dispersion flow becomes more complex, and its circulation velocity becomes lower than that of the flow streams promoted by mechanical mixing in unaerated media. Moreover, air retention diminishes the oxygen concentration gradient between the gaseous and liquid phases, thus also affecting the mass transfer.

The decisive influence of media circulation on the oxygen transfer rate is underlined by results previously obtained for the mixing time distribution in fermentation broths [5]. The cited study indicated that maximum mixing efficiency is achieved for specific power input values close to those corresponding to maximum k_la, and that the mixing intensity distribution is similar to that of the oxygen transfer rate. The highest values of k_la were recorded for position 1, due to the presence of the impeller and the close vicinity of the sparger. The oxygen transfer rate gradually reduced towards the top of the bioreactor, due to the decreased turbulence at positions 2 and 3 [5] and the increased separation from the sparger.

At lower specific power input, the variation of the oxygen transfer rate obtained for position 4 was similar to that recorded for position 1, owing to the presence of the impeller. At higher mixing intensity (specific power consumption above 400–450 W/m^3), the values of k_la for the upper region become lower than those for position 2.

The shapes of the above-discussed variations (Fig. 1a) remain similar with increasing apparent viscosity, but the oxygen transfer rate decreased and the differences between its values for the four regions became more pronounced. Moreover, the maximum k_la was achieved at higher specific power input. These phenomena are a result of the influence of the apparent viscosity on the extent of turbulence and the interfacial area. Thus, for low-viscosity broths, Newtonian broths or for media containing electrolytes, tensides, or polymeric compounds, bubble coalescence is avoided and the average bubble size is small. For broths with apparent viscosity above 10 cP or exhibiting

non-Newtonian behavior, the equilibrium between dispersion and coalescence of bubbles is perturbed and large bubbles are formed, a phenomenon which induces a decrease of the gas–liquid interfacial area and a heterogeneous air distribution in the broth [7, 21]. In this case, bubble coalescence occurs around the impellers, especially around those placed near the sparger, with the larger bubbles rising with high velocity along a preferential central route.

Owing to air accumulation, especially around the lower impeller, and to the nonuniform rising of larger bubbles, the bubble distribution in region 4 is heterogeneous, and the volumetric air fraction is low. Consequently, although the second impeller is placed in this region, the k_la values recorded for position 4 become lower than those at position 2.

Increasing aeration rate promotes intensification of turbulence and a homogeneous air distribution in the broth and increases the oxygen concentration gradient between the gaseous phase and the media, thus having a favorable effect on oxygen mass transfer, as shown in Fig. 1b. For this reason, the above-discussed variations of k_la recorded at superficial air velocity of 0.84×10^{-3} m/s are similar to those corresponding to 5×10^{-3} m/s. However, at higher aeration rates, the magnitude of these variations is diminished, while the maximum values of k_la and the differences between the four positions become less evident.

Analysis of the oxygen transfer rate distribution as a function of broth height confirms the above conclusions. Therefore, Fig. 1 indicates also the nonuniform distribution of k_la, with its minimum value being reached for position 3. Although the values of k_la obtained for lower dissipated mechanical energy (100–200 W/m^3) and superficial air velocity of 0.84×10^{-3} m/s, and for higher values of dissipated mechanical energy (600–800 W/m^3) and superficial air velocity of 5×10^{-3} m/s, could be assumed to be similar, they do not clearly indicate a uniform oxygen transfer rate distribution. These results are in agreement with the mixing intensity distribution in the broth [5].

Mixing intensification leads to an increase of the oxygen transfer rate, but this effect does not counteract the corresponding increase of power consumption required. Therefore, for better characterization of bioreactor performance from the viewpoint of oxygen transfer, the oxygen transfer efficiency parameter, E_{O_2}, is introduced, defined as [6]:

$$E_{O_2} = \frac{k_1 a}{\frac{P_a}{V}}. \quad (1)$$

As can be observed from Fig. 2, the variation of the oxygen transfer efficiency with specific power input is contrary to that of k_la with the same parameter, an evolution that suggests that high oxygen mass transfer rate values can be reached in stirred bioreactors, but with considerable energy consumption for mechanical mixing. The intensification of aeration from 0.84×10^{-3} to 5×10^{-3} m/s induces 1.9–2.3 times increased oxygen transfer efficiency, as a result of increased turbulence and air–broth interfacial area.

The aeration rate controls the oxygen mass transfer through the air hold-up, interfacial area, and medium circulation in the bioreactor, the magnitude of its effect being directly related to the apparent viscosity. Therefore, Fig. 3 indicates the variation of the oxygen transfer rate with the superficial air velocity for different electrode positions and broth apparent viscosities. For water and simulated broths with lower viscosity (below 25 cP), increasing the superficial air velocity exerts a favorable effect on k_la in all considered regions in the bioreactor. Increase of the apparent viscosity modifies this influence, with the appearance of important differences between the impeller regions (positions 1 and 4) and the intermediary regions (positions 2 and 3).

Aeration intensification up to superficial air velocity of 1.7×10^{-3} m/s initially results in an increase of the oxygen transfer rate. Above this level of aeration rate, the dependence of k_la on the superficial air velocity is controlled by the apparent viscosity. In the case of fermentation broths with apparent viscosity of 25–60 cP, further increase of aeration rate does not exert a strong influence on k_la, which increases slightly or remains constant. For more viscous broths (apparent viscosity above 60 cP), aeration intensification above 1.7×10^{-3} m/s induces a reduction of k_la, an effect that is larger for the upper region (position 4). For the lower region (position 1), at apparent viscosity of 96 cP, a particular sinusoidal variation of the oxygen transfer rate with increasing aeration was recorded.

Comparative analysis of the correlations between mixing efficiency and oxygen transfer rate or aeration rate showed similar results. The variation of k_la with the superficial air velocity was directly related to the variation of the mixing intensity with the same parameter [5]. Thus, for positions 1 and 4, at lower volumetric air flow, the bubble coalescence rate was high and remained unaffected by the low degree of turbulence, resulting from the reducing of the interfacial area and the heterogeneous air distribution in the bioreactor. These phenomena are amplified at higher apparent viscosity. Aeration intensification exerted an important positive effect on the oxygen mass transfer, because it promotes turbulence, and thereby reduction of bubble coalescence and increase of the air–media interfacial area.

However, for constant specific power consumption, further increase of the aeration rate leads to decrease or disappearance of the above-presented positive effect at positions 1 and 4. According to the results of previous studies on the influence of aeration on mixing efficiency [5], this variation is due to the formation of smaller

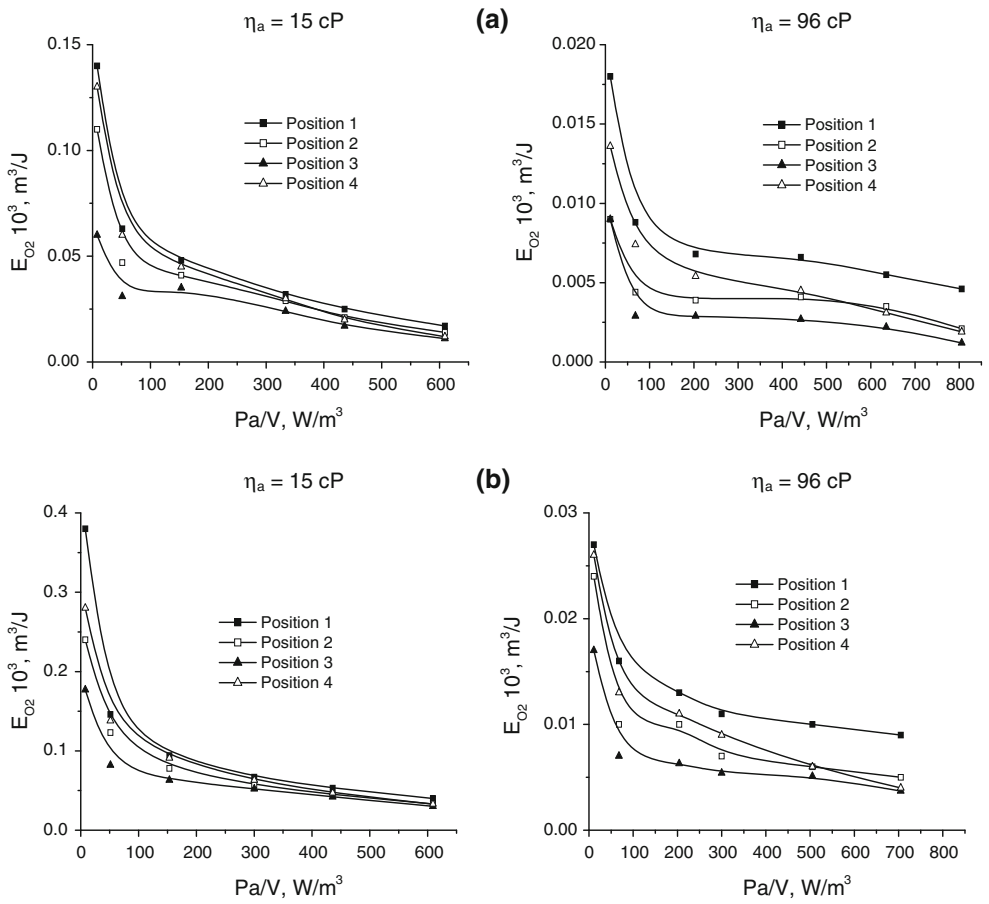

Fig. 2 Influence of specific power input on the oxygen transfer efficiency for simulated broths for: **a** $v_S = 8.4 \times 10^{-4}$ m/s, and **b** $v_S = 5 \times 10^{-3}$ m/s

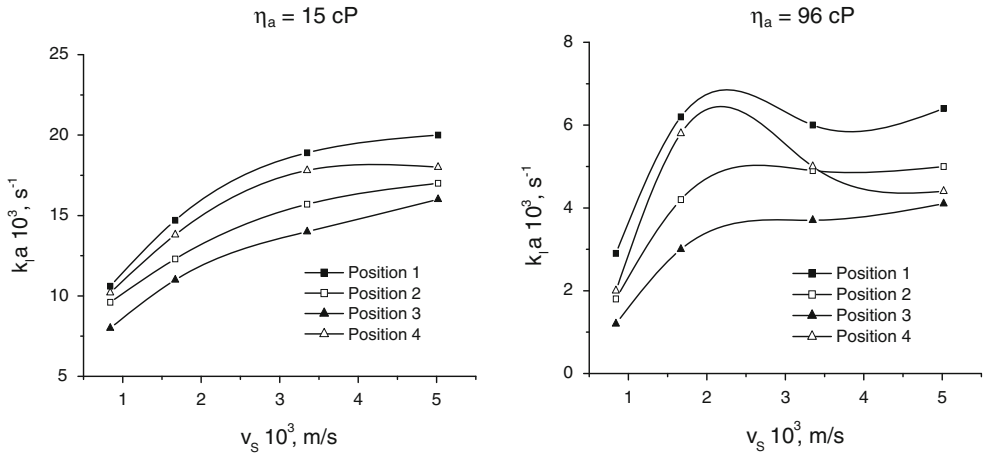

Fig. 3 Influence of superficial air velocity on the oxygen mass transfer coefficient for simulated broths ($P_a/V = 300$ W/m^3)

bubbles with slower rising velocity, inducing increased gas hold-up with a direct influence on the decrease of the dispersion circulation velocity and oxygen concentration gradient between the two phases. Because this effect becomes more pronounced with increasing apparent viscosity, it underlines the major role played by viscosity in reduction of turbulence and formation of small bubbles at low circulation velocity. Furthermore, the decrease of oxygen transfer rate suggests that the relative magnitude of these negative influences exceeds that of the positive effect of the increase of interfacial area due to the dispersion of small bubbles.

The sinusoidal variation of k_la recorded for position 1 for superficial air velocity above 3.4×10^{-3} m/s could be explained by the appearance of flooding, as the energy dissipated by the air exceeds that of the impeller, especially close to the sparger [19, 21]. At this point, the rising velocity of the air increases simultaneously with the intensification of the media circulation and oxygen transfer. This flooding phenomenon is specific to high-viscosity media, due to inefficient mechanical mixing which promotes air accumulation around the impellers [5, 21].

Because the mixing intensity at the intermediary positions 2 and 3 was significantly lower than that at positions 1 and 4 [5], aeration intensification exerts a continuous positive influence on oxygen transfer, due to the amplification of turbulence. Evidently, for the above-discussed reasons, the increase of the apparent viscosity diminishes the magnitude of this positive influence of aeration.

Propionibacterium shermanii broths

From Fig. 4 it can be observed that, for all positions, the oxygen transfer rate increased with increasing specific power input, reached a maximum value, then decreased, similar to the variation recorded for simulated broths. However, because the apparent viscosity of the bacterial broth is rather low, this variation cannot be attributed mainly to modification of the mixing mechanism with increasing specific power input in the presence of air bubbles, as in the case of simulated broths. For systems containing *P. shermanii* cells, mixing intensification initially compensates for the negative effect of bubble surface blockage by redistributing adsorbed cells and renewal of the gas–liquid interface. For higher specific power input, bubble coalescence is reduced and small bubbles are formed, thus increasing the relative importance of the blocking effect.

The maximum of the oxygen mass transfer coefficient is more evident at lower aeration rate and biomass concentration, being reached at specific power consumption of 250 W/m^3 (Fig. 4a).

As discussed above, increasing the superficial air velocity contributes to additional bubble dispersion through pneumatic mixing, owing to the intensification of turbulence, and to increase of air hold-up in the broth. Consequently, cell adsorption to bubble surface is partly avoided, a phenomenon that is more pronounced for lower amount of *P. shermanii*. In these circumstances, for biomass concentration up to 43 g/l d.w. and superficial air velocity of 5×10^{-3} m/s, the variation of k_la is attenuated (Fig. 4b). The favorable contribution of aeration intensification is also suggested by the extension of the domain in

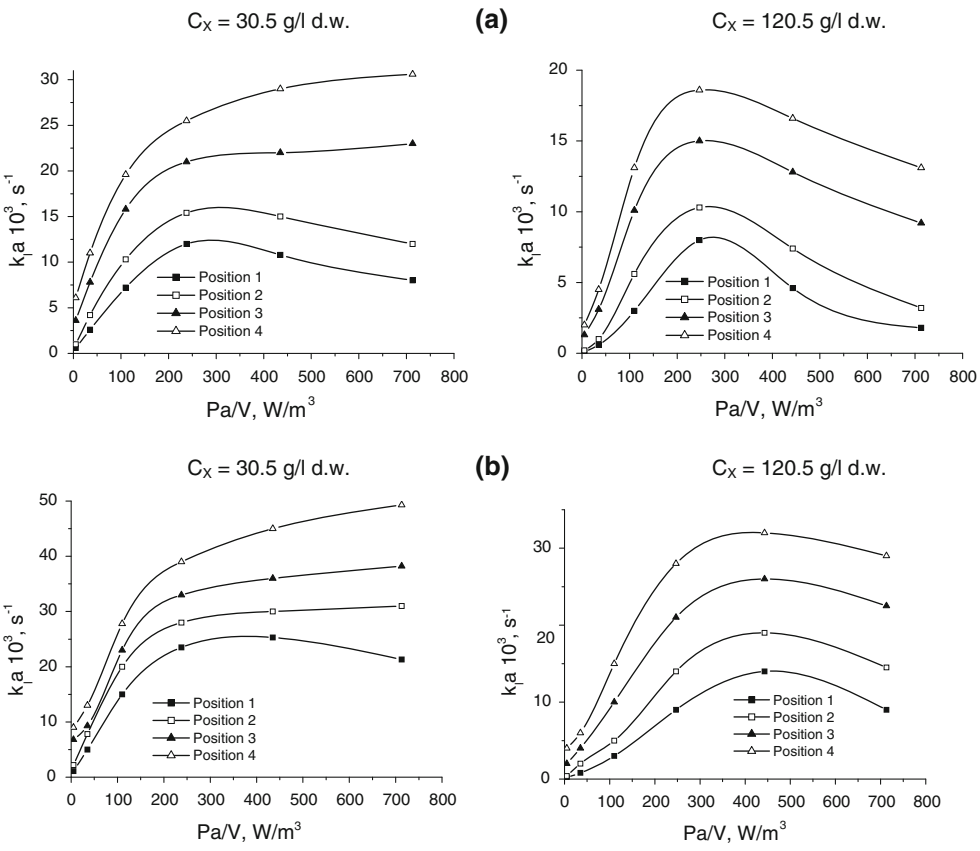

Fig. 4 Influence of specific power input on the oxygen mass transfer coefficient for *P. shermanii* broths for: **a** $v_S = 8.4 \times 10^{-4}$ m/s, and **b** $v_S = 5 \times 10^{-3}$ m/s

which the mixing exhibits a favorable influence on oxygen transfer, with the specific power consumption value required for the maximum k_la increasing to 430 W/m^3.

According to previous study on the mixing distribution in aerated *P. shermanii* broths [5], the specific power input which leads to the maximum oxygen transfer rate corresponds to minimum levels of mixing time.

Contrary to the results obtained for the simulated broths, for bacterial suspensions the lowest values of oxygen mass transfer coefficient are found for position 1, due to the highest concentration of biomass at the bottom of the bioreactor. Accumulation of bacterial cells due to deposition affects the favorable effect of the sparger and the lower impeller in this region. The conclusion that the oxygen transfer is controlled by the solid phase and not by the apparent viscosity is underlined by the gradual increase of k_la from position 1 to 4, in direct relation to the reduction of biomass amount with bioreactor height. Thus, the shapes of the curves describing the correlations between k_la and the specific power consumption (Fig. 4) are identical for positions 1 and 2, being modified for the upper positions. Moreover, the maximum of the oxygen transfer rate is less evident for positions 3 and 4.

Biomass accumulation leads to decrease of the oxygen transfer rate, irrespective of bioreactor operational parameters or position in the broth. Thus, for 300 W/m^3 and cell accumulation from 30.5 to 120.5 g/l d.w., k_la was reduced about 1.3–2.4 times, with the largest reduction being recorded for positions 1 and 2.

The experiments carried out for simulated broths, without biomass, and bacterial broths with the same apparent viscosities and using identical operating conditions showed that the oxygen mass transfer rate in biomass suspensions is lower than that recorded in simulated broths. The blocking effect due to cell adsorption to bubble surface can be described by the ratio of the oxygen mass transfer coefficient for biomass suspensions, $(k_la)_C$, to that for simulated broths without biomass, $(k_la)_0$, obtained using similar experimental conditions [7].

Besides the blocking effect, adsorption of cells to the gas–liquid interface, combined with the apparent broth viscosity, promotes bubble coalescence, leading to formation of large bubbles and decrease of the interfacial area. Consequently, the air is nonuniformly distributed in the broth [7, 17, 19].

From Fig. 5 it can be observed that the presence of cells results in a significant reduction of the oxygen mass transfer coefficient compared with the k_la value recorded for simulated broths (at 300 W/m^3, k_la decreased about 1.22–4.54 times, with the effect being more pronounced for lower aeration rates and higher biomass concentrations).

In all cases, increasing the specific power input intensified the effect of cell adsorption, because the air is finely dispersed and the free surface of small bubbles is easily occupied by cell adsorption. These results confirm those

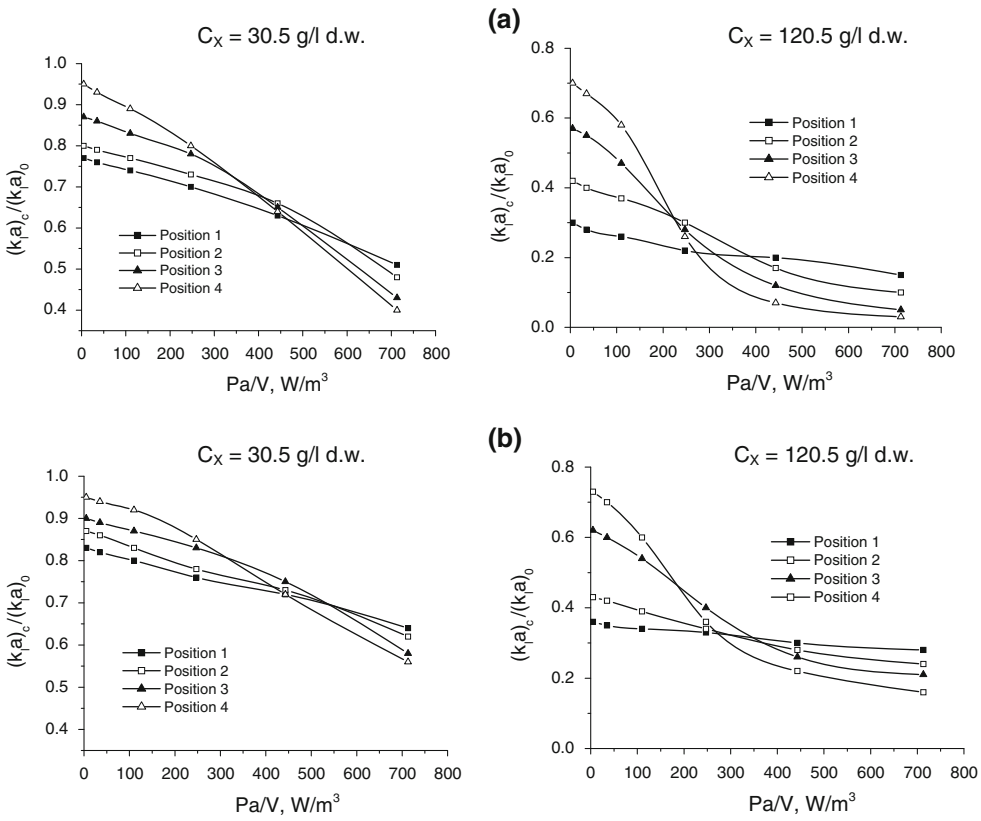

Fig. 5 Effect of cell adsorption to bubble surface on oxygen mass transfer coefficient for *P. shermanii* broths for: **a** $v_S = 8.4 \times 10^{-4}$ m/s, and **b** $v_S = 5 \times 10^{-3}$ m/s

previously reported by other authors [10, 22]. However, this effect is more important for upper regions, with the ratio $(k_la)_C/(k_la)_0$ decreasing faster at positions 3 and 4 compared with at positions 1 and 2. Due to the deposition of solid phase at the bottom of the bioreactor, the extent of bubble surface blockage by cell adsorption is maximum in this region, thus the value of the ratio $(k_la)_C/(k_la)_0$ is lower and less affected by modification of the mixing intensity or aeration rate. In contrast, for the upper region, intensification of the broth circulation generates biomass dispersion also in these regions and, consequently, exhibits a strong blocking effect of bubble surface. For this reason, for specific power consumption above a certain level, the ratio $(k_la)_C/(k_la)_0$ for positions 3 and 4 becomes lower than for positions 1 and 2. The value of the specific power input corresponding to the change of the relative magnitude of the blocking phenomenon with bioreactor height is defined as the critical specific power input and varies from 450 to 250 W/m^3 with *P. shermanii* cell accumulation.

The above-discussed effects are attenuated with increasing aeration rate, owing to the increase of the volumetric air fraction in the broth, although the shape of the dependence of the ratio $(k_la)_C/(k_la)_0$ on the mixing intensity remains similar.

Analysis of the oxygen transfer rate distribution as a function of bioreactor height indicates that the minimum value of k_la was recorded for position 1, and its maximum for position 4. These results confirm the decisive control of the bacterial biomass on oxygen transfer from the gaseous to the liquid phase. The closest values of oxygen mass transfer coefficient were obtained for lower specific power input (35 W/m^3) with intense aeration, without evident uniformity of the oxygen transfer rate. These data are in agreement with the variation of mixing efficiency in the fermentation broth [5]. These previous studies concluded that uniform mixing could be achieved using the same experimental conditions, because cell adsorption to bubble surface affected only oxygen transfer but not broth circulation.

Aeration intensification exerts a favorable effect also for bacterial broths (Fig. 5); for example, at 300 W/m^3, increase of the superficial air velocity from 0.84×10^{-3} to 5×10^{-3} m/s leads to increase of k_la by 1.2–1.9 times, with this effect being more important at lower *P. shermanii* biomass concentration. For the above-presented reason, although the influence of the specific power input is similar over the entire experimental range of superficial air velocity, the magnitude of its effect is diminished at higher aeration rate (the maximum of k_la is less pronounced or is not reached for lower biomass amount and upper positions, and the differences between the plotted variations are attenuated).

Compared with the simulated broths, the influence of aeration on k_la for bacterial cultures is different. Therefore, Fig. 6 shows that aeration intensification exerts a continuous, favorable effect on the oxygen transfer rate for all considered positions in the broth. The biomass accumulation does not change this influence (in the case of simulated broths, increase of the apparent viscosity leads to differentiation of the shapes of the dependence of k_la on superficial air velocity for the four positions). Moreover, the effect induced by aeration intensification is less significant for suspensions containing bacterial cells, because the increased turbulence promotes more efficient cell dispersion throughout the whole bulk volume of the broth and thereby extension of bubble surface blockage due to cell adsorption.

Contrary to the simulated broths without biomass, the strong acceleration of broth circulation, as reported in previous study [5], does not induce significant intensification of oxygen transfer in the bacterial cultures, due to the supplementary dispersion of cells in the broth.

From Fig. 7a, b, plotted for the two considered values of aeration rate, it can be observed that increase of the superficial air velocity exerts a favorable effect on the oxygen transfer efficiency, enhancing it about 1.3–1.9 times (with the effect being more pronounced at lower cell concentrations), as a result both of turbulence intensification due to the additional contribution of pneumatic mixing to broth circulation (similar to in the simulated broths), and of increase of the area of nonblocked interface needed for interphasic transfer of oxygen.

Saccharomyces cerevisiae broths

Owing to the similar viscosities of the bacterial and yeast broths at the same biomass concentration, the variations of k_la and the phenomena inducing these variations for *S. cerevisiae* cultures were similar to those recorded for *P. shermanii* cultures.

Aeration also exerts a favorable effect on oxygen transfer for all positions studied in the bioreactor. Thus, for biomass concentration up to 75 g/l d.w. and superficial air velocity of 5×10^{-3} m/s, k_la either increases continuously with the specific power input or reduces slowly after its maximum value (Fig. 8). Moreover, for the upper region, the biomass concentration range corresponding to a positive influence of mixing is extended from 75 g/l d.w., for 8.4×10^{-4} m/s, to 100 g/l d.w., for 5×10^{-3} m/s.

The maximum of the oxygen mass transfer coefficient is more evident at lower aeration rate and higher biomass concentration. A favorable contribution of aeration is also suggested by the increase of the specific power consumption needed to achieve the maximum level of oxygen transfer, from 250 W/m^3, at 8.4×10^{-4} m/s (Fig. 8a), to 430 W/m^3, at 5×10^{-3} m/s (Fig. 8b).

However, the greater tendency of yeast cells to deposit on the bottom of the bioreactor leads to biomass accumulation at position 1, a phenomenon that is stronger than for

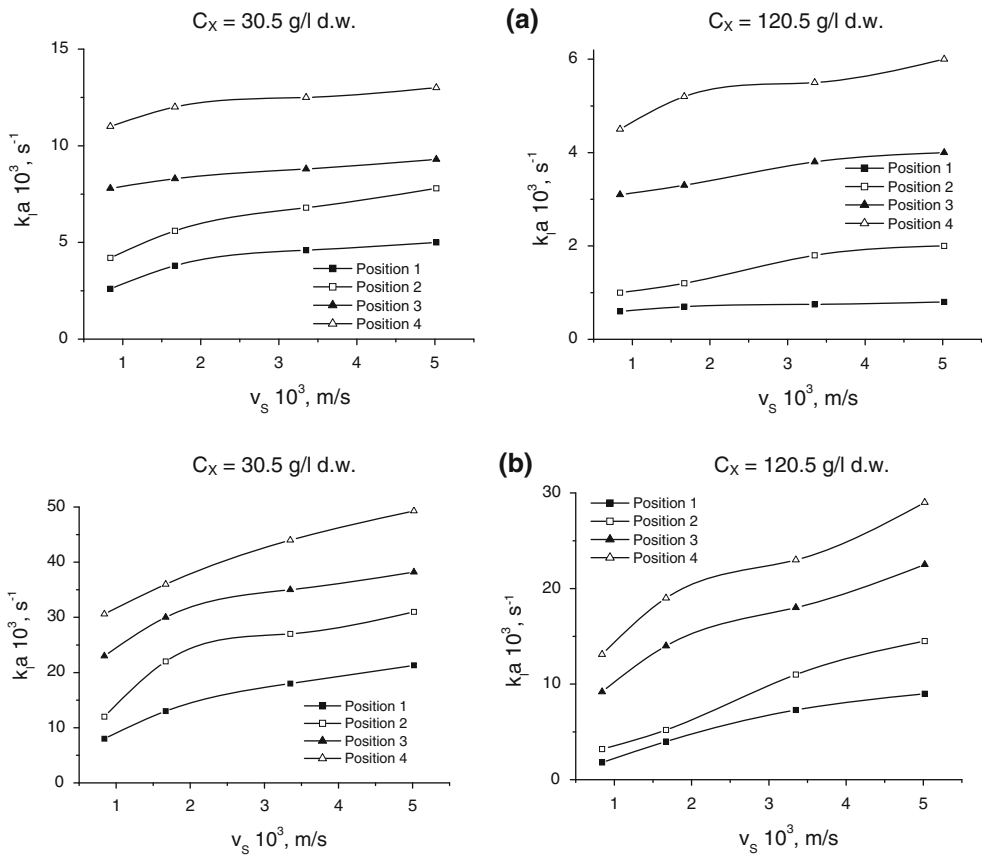

Fig. 6 Influence of superficial air velocity on the oxygen mass transfer coefficient for *P. shermanii* broths for: **a** $P_a/V = 35$ W/m^3, and **b** $P_a/V = 715$ W/m^3

the *P. shermanii* suspensions, due to the larger size of the yeast cells, Thus, the maximum of k_la becomes less evident and the differentiation between positions 1, 2 and 3, 4 becomes more pronounced. For this reason, the lowest values of the oxygen mass transfer coefficient are achieved for position 1, with its value increasing from the lower to upper region of the bioreactor (Fig. 8).

Also in the case of the yeast broths, the values of the specific power input corresponding to the maximum oxygen transfer rates are those that induce the most efficient mixing [5].

For specific power input of 300 W/m^3, cell accumulation from 40 to 150 g/l d.w. reduced k_la by about 1.8–3 times, this effect being more significant for the lower positions 1 and 2; this effect was stronger than that observed for bacterial broths. The presence of cells significantly decreases the oxygen transfer rate compared with its value recorded for simulated broths and leads to a nonuniform distribution of k_la.

For yeast cultures, the value of the critical specific power input varies from 550 to 350 W/m^3 with biomass accumulation, being greater than that recorded for *P. shermanii*.

Owing to the lower affinity for bubble surface and the greater deposition rate of yeast cells compared with bacterial cells, the blocking effect is less important in the case of *S. cerevisiae*. The diminution of this effect in yeast broths is suggested by the higher values of the ratio $(k_la)_C/(k_la)_0$ obtained for yeast, as well as by the flattening of the curves describing the variation of this ratio with the power input (Fig. 9).

The magnitude of the influence of aeration on oxygen transfer for the yeast cultures is rather similar to that observed for *P. shermanii* broths, with k_la being increased by 1.1–2 times on modifying the aeration rate over the studied range.

However, due to the more pronounced influence of yeast biomass, the superficial air velocity exerts a stronger, positive influence on the oxygen transfer efficiency, with its increase amplifying E_{O_2} by about 1.2–3 times.

Penicillium chrysogenum broths

Accumulation of fungus biomass induces a significant increase of broth viscosity and controls the rheology of the suspension, exerting a direct influence on the broth

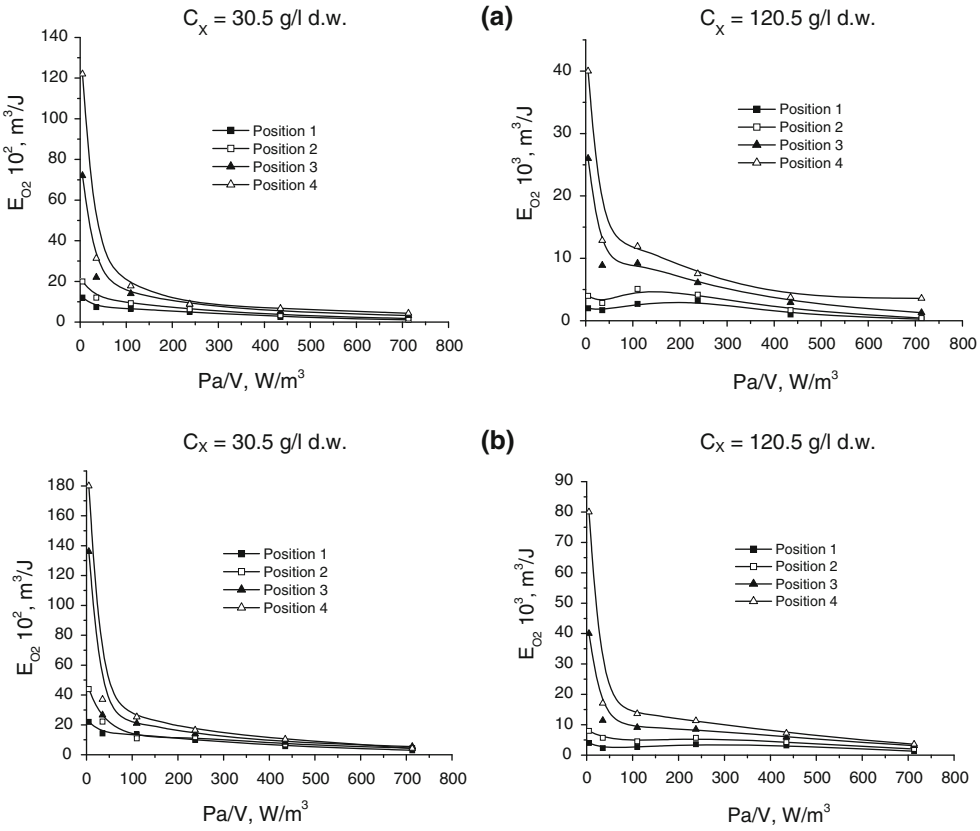

Fig. 7 Influence of specific power input on the oxygen transfer efficiency for *P. shermanii* broths for: **a** $v_S = 8.4 \times 10^{-4}$ m/s, and **b** $v_S = 5 \times 10^{-3}$ m/s

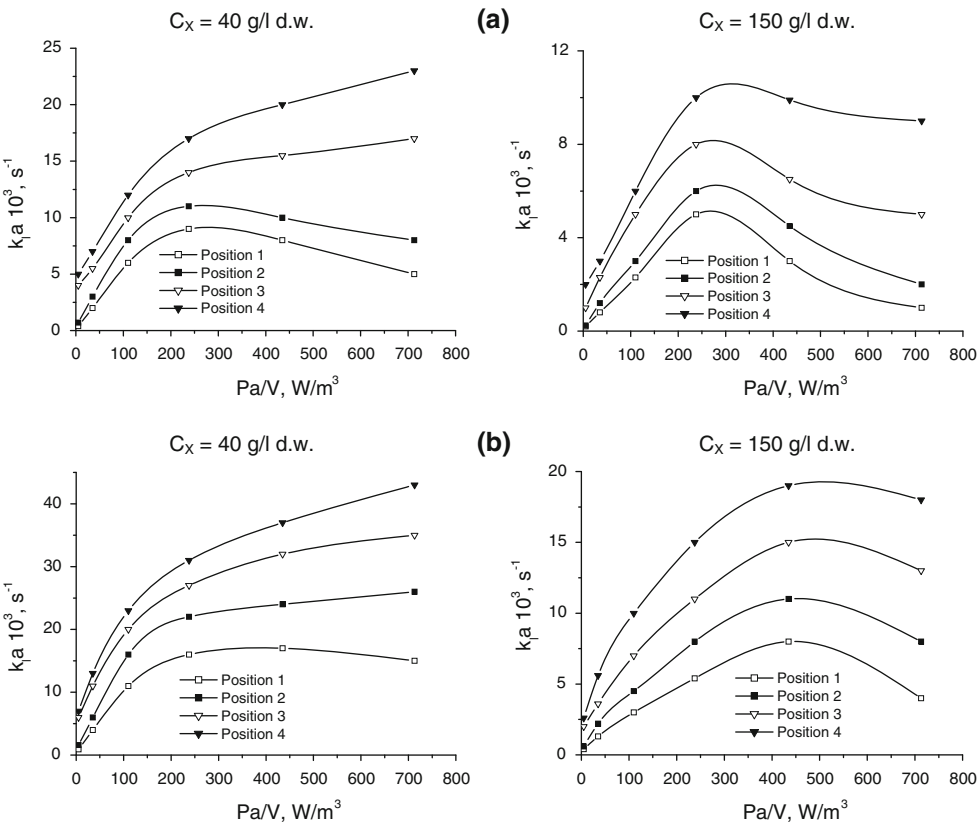

Fig. 8 Influence of specific power input on the oxygen mass transfer coefficient for *S. cerevisiae* broths for: **a** $v_S = 8.4 \times 10^{-4}$ m/s, and **b** $v_S = 5 \times 10^{-3}$ m/s

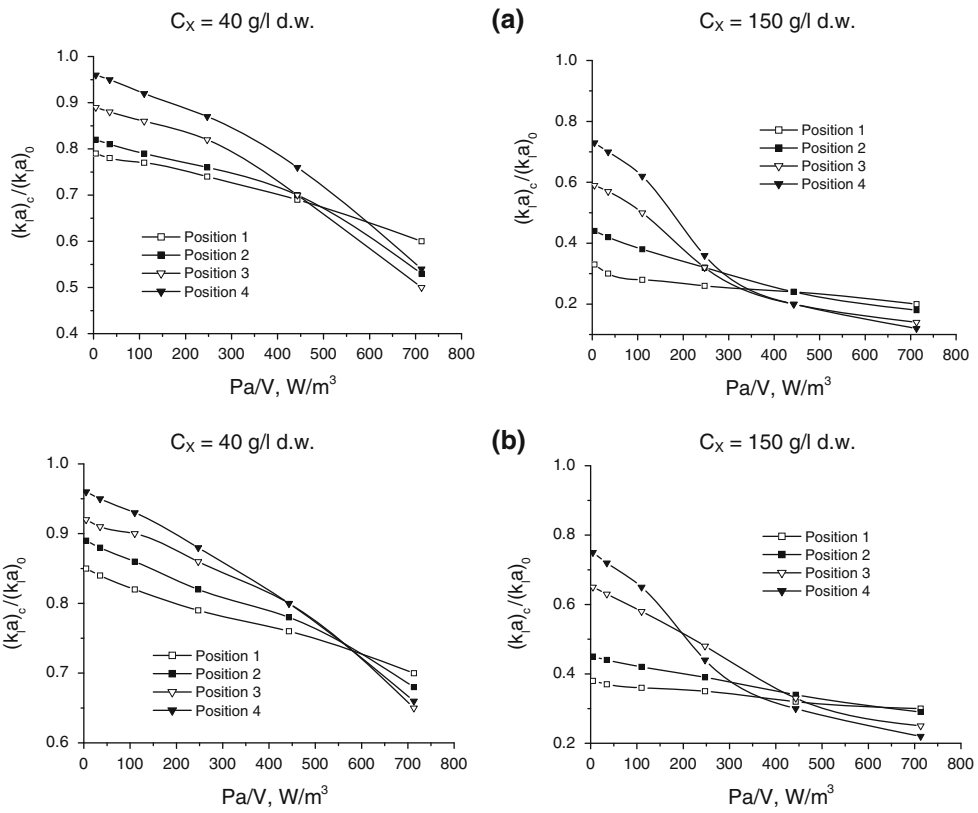

Fig. 9 Effect of cell adsorption at bubble surface on the oxygen mass transfer coefficient for *S. cerevisiae* broths for: **a** $v_S = 8.4 \times 10^{-4}$ m/s, and **b** $v_S = 5 \times 10^{-3}$ m/s

hydrodynamics and mass/heat transfer efficiency. Irrespective of the morphology (free mycelia or pellets), the apparent viscosity of fungus broths is considerable greater than that of bacterial or yeast cultures [7]. Among the two morphological conformations of *P. chrysogenum*, the apparent viscosity of free mycelia suspensions is greater compared with that of pellet suspensions (for biomass concentration of 33.5 g/l d.w. the apparent viscosity of free mycelia suspensions was 172.5 cP, versus 88.4 cP for pellet suspensions) [18].

Compared with the bacterial and yeast broths, the oxygen transfer rate in *P. chrysogenum* broths exhibited a particular variation as a function of the specific power input (Fig. 10).

Thus, for positions 1 and 3 and biomass concentration up to 24 g/l d.w., mixing intensification leads to a continuous acceleration of the oxygen transfer rate (Fig. 10a). For greater amounts of *P. chrysogenum*, k_la increases with increasing specific power input, reaches a maximum value, then decreases, with this variation being more pronounced for position 3. This microorganism possesses lower capacity to block bubble surface compared with the bacteria or yeast. In these systems, the apparent viscosity, which is significantly higher than that of the bacterial or yeast cultures, is the main factor controlling oxygen transfer from the gaseous phase to the microorganisms via the liquid phase. Mixing intensification only partially counteracts the negative effect of the apparent viscosity, inducing an increase of k_la for the regions associated with the two impeller positions (i.e., positions 1 and 3).

For higher fungus concentration and specific power input above 400 W/m^3, bubble coalescence is diminished and the surface of the small bubbles formed is blocked by biomass adsorption, which leads to a slow decrease of the oxygen transfer rate. The maximum of k_la is more evident for position 3, because the above-discussed phenomenon is combined with biomass dispersion from the lower region under intense mixing.

The dependence of k_la on power consumption recorded for positions 2 and 4 indicates the existence of a maximum level of oxygen transfer rate for the fungal free mycelia cultures, followed by a strong reduction. Although the variations of k_la for these two positions are similar, the phenomena generating them are different. For position 2, which is located between the two impellers, the diminution of k_la above a certain mixing intensity can be correlated with the reduction of broth circulation velocity, due to the interference of adjacent streams induced by the impellers. According to previous study on the hydrodynamics of *P. chrysogenum* free mycelia broths [5], this effect becomes more important at higher apparent viscosity and at high biomass concentration. Because position 4 is located outside the upper impeller region, the increase of the energy dissipated by mixing initially promotes a positive

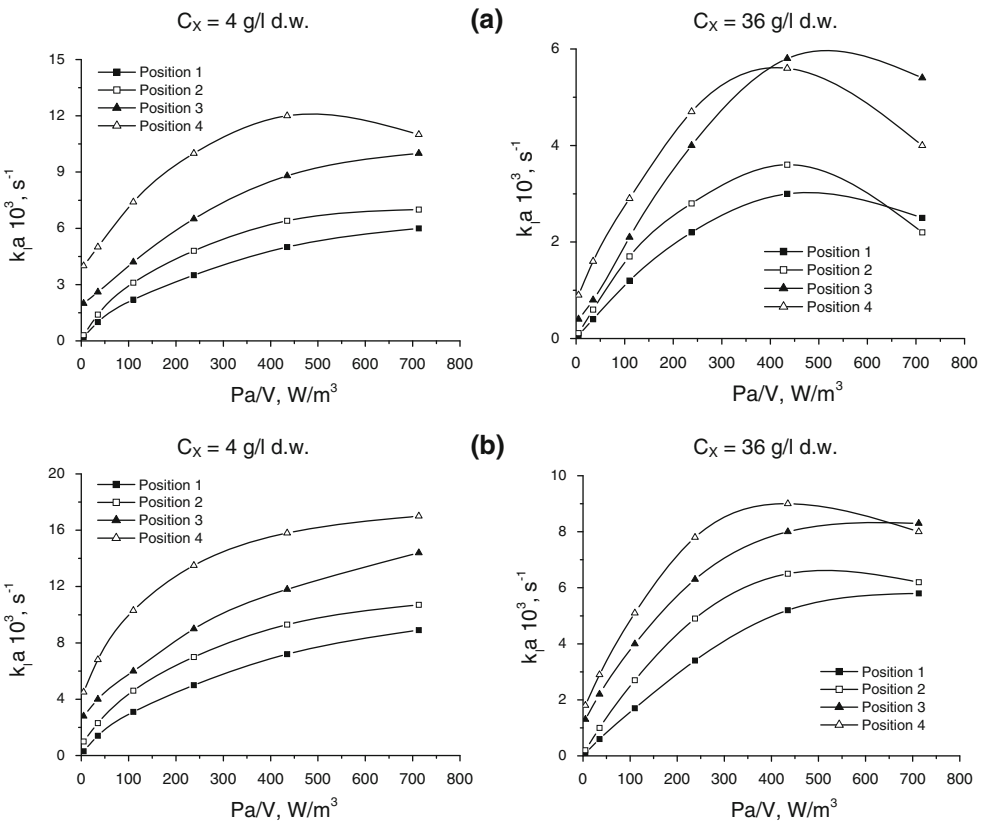

Fig. 10 Influence of specific power input on the oxygen mass transfer coefficient for *P. chrysogenum* broths for: **a** $v_S = 8.4 \times 10^{-4}$ m/s, and **b** $v_S = 5 \times 10^{-3}$ m/s

effect on oxygen transfer. However, at higher power input, the biomass is more uniformly dispersed, the amount of fungus at the top of the bioreactor increases, and thereby the oxygen mass transfer coefficient is reduced.

Evidently, the accumulation of biomass amplifies these phenomena. Therefore, for *P. chrysogenum* concentration above 24 g/l d.w. and higher mixing intensity, the values of k_la recorded for positions 2 and 4 become lower than those for positions 1 and 3, respectively. For all four positions, the maximum k_la is reached at critical specific power input of 430–450 W/m^3.

At higher aeration rate, the combination of mechanical with pneumatic mixing promotes extension of the turbulence in the broth. Consequently, the negative influence of the apparent viscosity is diminished and the maximum level of k_la is either eliminated, for positions 1 and 3, or attenuated, for positions 2 and 4 (Fig. 10b). The maximum of the oxygen transfer rate, recorded for positions 2 and 4 at higher biomass concentration, is also achieved at critical specific power input of 450 W/m^3.

As was concluded in previous study on the hydrodynamics of aerated broths of *P. chrysogenum* free mycelia, the value of the critical power input coincides with that needed to achieve the minimum mixing time or the maximum mixing efficiency [5].

Similar to the cultures of *P. shermanii* and *S. cerevisiae*, the lowest values of the oxygen transfer rate were obtained for position 1, due to the highest amount of biomass at the bottom of the bioreactor. Owing to the biomass deposition, the positive effects of the presence of the impeller and sparger at the bottom of the bioreactor on k_la are attenuated.

Furthermore, the oxygen transfer rate in the fungus broths is considerably lower than that for the bacterial or yeast broths, for the same biomass concentration, as a result of the higher apparent viscosity of the fungus suspensions (at 450 W/m^3 and biomass concentration of 36 g/l d.w., the value of k_la for *P. chrysogenum* broths was 5 times lower than that for *P. shermanii* broths and 4 times than that for *S. cerevisiae* broths).

Comparatively analyzing the graphical dependences of k_la on the specific power input for bacteria, yeast, and fungus, it can be observed that the values of k_la recorded for the four considered positions in the fungus broth are more similar. This result suggests that the influence of fungus biomass is less important compared with bacterial or yeast biomass, with the apparent viscosity being the main parameter which controls oxygen transfer.

As can be seen from Fig. 10, accumulation of *P. chrysogenum* from 4 to 36 g/l d.w. leads to reduction of the oxygen transfer rate by 1.3–2.1 times (at 450 W/m^3), with the effect being more pronounced at lower aeration rate. For the above-discussed reasons, the influence of the fungus biomass was weaker than in the case of bacteria and yeast.

Comparative analysis of the effect of blocking induced by *P. shermanii*, *S. cerevisiae*, and *P. chrysogenum* emphasizes the specific behavior of the fungus. As discussed above, in the case of *P. shermanii* and *S. cerevisiae* broths, mixing intensification invariably leads to decrease of the ratio $(k_la)_C/(k_la)_0$, due to the fine dispersion of the air and thereby faster blockage of free surface of small bubbles due to cell adsorption. In contrast, Fig. 11 indicates that the ratio $(k_la)_C/(k_la)_0$ for *P. chrysogenum* initially increases with increasing power consumption, reaches a maximum value, then decreases. As mentioned above, this evolution is the result of the lower affinity of fungus biomass for air bubbles compared with the other two microorganisms, with the values of the ratio $(k_la)_C/(k_la)_0$ for fungus being higher [at 36 g/l d.w. and 450 W/m^3, the ratio $(k_la)_C/(k_la)_0$ for *P. chrysogenum* was about 1.25 times greater than that for *P. shermanii* and about 1.15 times greater than that for *S. cerevisiae*].

The appearance of the maximum of the ratio $(k_la)_C/(k_la)_0$ is the result of two contrary phenomena occurring with mixing intensification: removal of biomass from bubble surface, at lower specific power input, and formation of smaller bubbles which are more easily occupied by fungus, at higher power consumption.

In all cases, the maximum value of this ratio was reached at 250 W/m^3, for all considered positions in the broth. However, by increasing the fungus concentration, the reduction of the ratio $(k_la)_C/(k_la)_0$ becomes more pronounced, owing to the amplification of the blockage phenomenon (Fig. 11a). Although the shape of the dependence of the ratio $(k_la)_C/(k_la)_0$ on the power consumption remains the same, the negative effect of bubble surface blockage is diminished by aeration (Fig. 11b).

The variation of the oxygen transfer rate with broth height shows the increase of k_la from position 1 to 4, with exceptions recorded for higher specific power input (above 450 W/m^3 for superficial air velocity of 8.4×10^{-4} m/s, or above 700 W/m^3 for superficial air velocity of 5×10^{-3} m/s) and biomass concentration over 12 g/l d.w. The maximum value of the oxygen transfer rate was recorded for position 3, for the reasons discussed above. According to previous study, the maximum of k_la is directly related to the most intense circulation of fungal broths [5].

Due to the higher apparent viscosity of the fungus cultures, the magnitude of the positive effect of aeration on k_la is diminished compared with that observed for bacterial or yeast broths. Thus, for the critical specific power input (450 W/m^3), increase of the superficial air velocity from 0.84×10^{-3} to 5×10^{-3} m/s induces intensification of the oxygen transfer by 1.3–1.7 times, with the highest values being reached for higher amounts of *P. chrysogenum* biomass.

Moreover, in contrast to the systems containing *P. shermanii* or *S. cerevisiae*, aeration intensification does

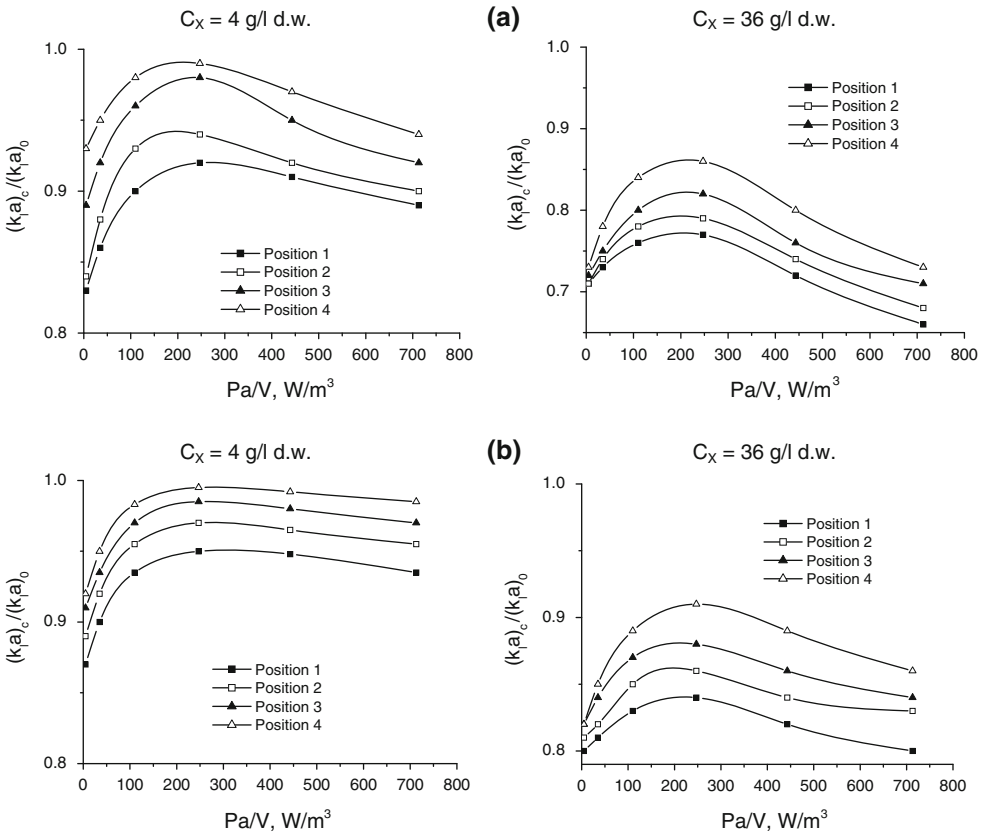

Fig. 11 Effect of biomass adsorption at bubble surface on the oxygen mass transfer coefficient for *P. chrysogenum* broths for: **a** $v_S = 8.4 \times 10^{-4}$ m/s, and **b** $v_S = 5 \times 10^{-3}$ m/s

not lead to continuous acceleration of the oxygen transfer rate in the fungus broths. From Fig. 12 it can be seen that increase of the superficial air velocity initially induces a reduction of k_la to a minimum value, followed by an increase of this parameter. This phenomenon, which is apparently unexpected, can be correlated with the variation of broth circulation intensity as a function of volumetric air flow. Previous experiments on the hydrodynamics of *P. chrysogenum* free mycelia suspensions indicated that, by intensifying the aeration, the mixing time increased to a maximum value then decreased above a certain aeration rate [5].

This variation is the result of the formation of small bubbles, due to air dispersion and mechanical agitation, as well as to the presence of biomass, which avoids bubble coalescence. These small bubbles exhibit a negative effect on broth circulation, reducing its velocity and thereby the mixing intensity. At higher air flow rate values, the energy dissipated by the air exceeds that of the stirrer, resulting in the appearance of flooding [5, 7, 21]. At the flooding point, the rising velocity of the air strongly increases, generating a simultaneous increase of the velocity of media circulation and thereby an increase of the oxygen transfer rate. The value of the aeration rate corresponding to the flooding point is called the critical superficial air velocity [7] and depends on the amount of mycelia and the power consumption, being the same for all the positions analyzed in the bioreactor.

The value of the critical volumetric air flow needed for the minimum level of k_la becomes lower with biomass accumulation. Thus, for *P. chrysogenum* concentration of 36 g/l d.w., the effect of aeration is positive for the entire experimental range of superficial air velocity. However, intensification of the mechanical mixing is associated with higher values of critical volumetric air flow, owing to the greater contribution of mechanical agitation to the turbulence in the broths (for fungus concentration below 24 g/l d.w., increase of the power consumption from 35 to 710 W/m^3 induced an increase of the critical superficial air velocity from 1.7×10^{-3} to 3.4×10^{-3} m/s) (Fig. 12).

Similar to the bacterial and yeast broths, the variation of the oxygen transfer efficiency with specific power input is contrary to that of k_la with specific power input. The intensification of aeration in the experimental range induces greater enhancement of oxygen transfer efficiency than for the other two studied cultures (by about 1.2–2.2 times).

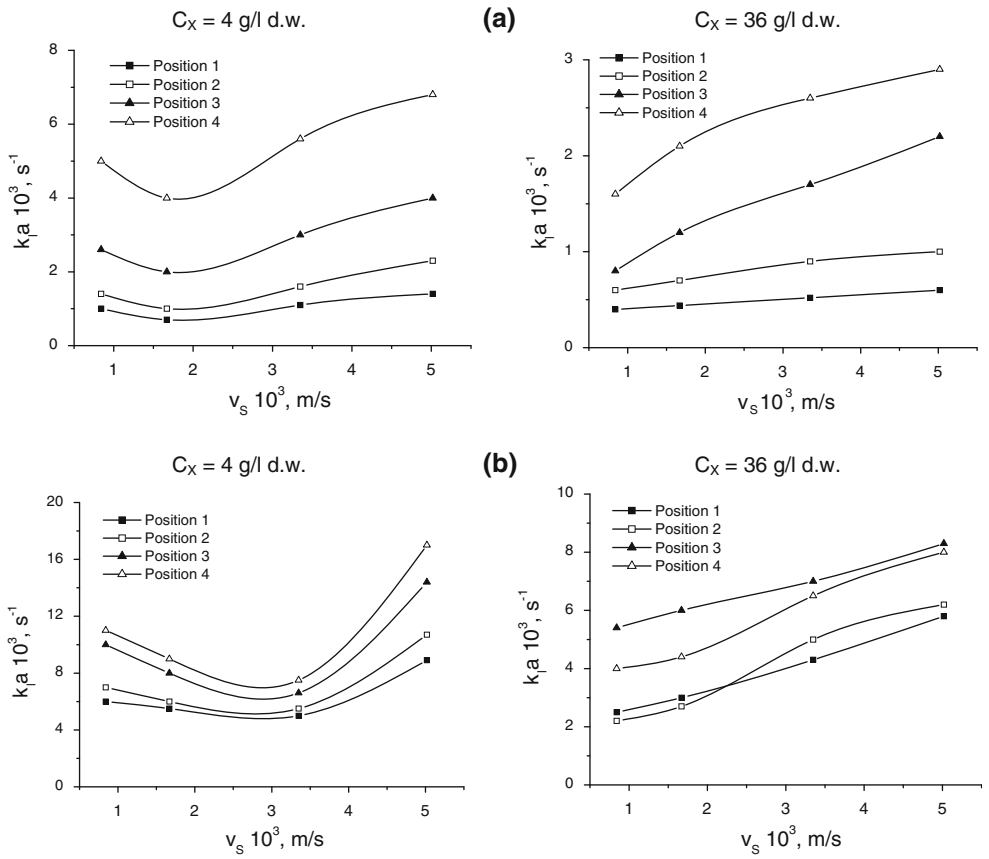

Fig. 12 Influence of superficial air velocity on the oxygen mass transfer coefficient for *P. chrysogenum* broths for: **a** $P_a/V = 35$ W/m^3, and **b** $P_a/V = 715$ W/m^3

Mathematical correlations for k_la

The above-discussed experimental data were included in mathematical correlations to describe the influences of apparent viscosity or biomass concentration, specific power input, and superficial air velocity on the oxygen mass transfer coefficient at different positions in the bioreactor. The general expression of the proposed equations is

$$k_la = \alpha\eta_\alpha^\beta\left(\frac{P_a}{V}\right)^\gamma v_S^\delta \quad (2)$$

for simulated broths, or

$$k_la = \alpha C_X^\beta\left(\frac{P_a}{V}\right)v_S^\delta \quad (3)$$

for bacterial, yeast, and fungal broths.

The influence and the relative importance of the considered variables are suggested by the values of the coefficients α, β, γ, and δ. The values of these coefficients are specific for each broth type and were calculated by the multiregression method using MATLAB software. Thus, the following correlations have been established:

(a) Simulated broths:

- Position 1

$$k_la = 0.26\frac{v_S^{0.45}\left(\frac{P_a}{V}\right)^{0.42}}{\eta_a^{0.56}}, s^{-1} \quad (4)$$

- Position 2

$$k_la = 0.62\frac{v_S^{0.58}\left(\frac{P_a}{V}\right)^{0.47}}{\eta_a^{0.45}}, s^{-1} \quad (5)$$

- Position 3

$$k_la = 0.29\frac{v_S^{0.54}\left(\frac{P_a}{V}\right)^{0.37}}{\eta_a^{0.55}}, s^{-1} \quad (6)$$

- Position 4

$$k_la = 0.55\frac{v_S^{0.54}\left(\frac{P_a}{V}\right)^{0.28}}{\eta_a^{0.46}}, s^{-1} \quad (7)$$

(b) Bacteria (*P. shermanii*):

- Position 1

$$k_la = 65.82\frac{v_S^{0.43}}{C_X^{0.28}\left(\frac{P_a}{V}\right)^{0.029}}, s^{-1} \quad (8)$$

- Position 2

$$k_la = 55.29\frac{v_S^{0.35}}{C_X^{0.68}\left(\frac{P_a}{V}\right)^{0.45}}, s^{-1} \quad (9)$$

- Position 3

$$k_la = 22.57\frac{v_S^{0.19}}{C_X^{0.49}\left(\frac{P_a}{V}\right)^{0.45}}, s^{-1} \quad (10)$$

- Position 4

$$k_la = 44.15\frac{v_S^{0.41}}{C_X^{0.40}\left(\frac{P_a}{V}\right)^{0.46}}, s^{-1} \quad (11)$$

(c) Yeast (*S. cerevisiae*):

- Position 1

$$k_la = 5.24\frac{v_S^{0.51}}{C_X^{0.70}\left(\frac{P_a}{V}\right)^{0.076}}, s^{-1} \quad (12)$$

- Position 2

$$k_la = 5.03\frac{v_S^{0.23}}{C_X^{0.34}\left(\frac{P_a}{V}\right)^{0.17}}, s^{-1} \quad (13)$$

- Position 3

$$k_la = 3.89\frac{v_S^{0.21}}{C_X^{0.29}\left(\frac{P_a}{V}\right)^{0.20}}, s^{-1} \quad (14)$$

- Position 4

$$k_la = 59.82\frac{v_S^{0.14}}{C_X^{0.38}\left(\frac{P_a}{V}\right)^{0.43}}, s^{-1} \quad (15)$$

(d) Fungus (*P. chrysogenum*) free mycelia:

- Position 1

$$k_la = 3.36\frac{v_S^{0.94}\left(\frac{P_a}{V}\right)^{0.046}}{C_X^{1.01}}, s^{-1} \quad (16)$$

- Position 2

$$k_la = 1.10\frac{v_S^{0.26}\left(\frac{P_a}{V}\right)^{0.68}}{C_X^{0.32}}, s^{-1} \quad (17)$$

- Position 3

$$k_la = 5.31\frac{v_S^{0.22}\left(\frac{P_a}{V}\right)^{0.40}}{C_X^{0.29}}, s^{-1} \quad (18)$$

- Position 4

$$k_la = 11.22\frac{v_S^{0.17}\left(\frac{P_a}{V}\right)^{0.029}}{C_X^{0.36}}, s^{-1} \quad (19)$$

The proposed models exhibit good agreement with the experimental data, the maximum deviation being ±10.7% for simulated broths, ±8.4% for *P. shermanii*, ±9.3% for *S. cerevisiae*, and ±6.6% for *P. chrysogenum*.

Analyzing the corresponding determination coefficients, which represent the squared correlation coefficients for the proposed equations, it can be concluded that the considered factors influence the mixing efficiency and distribution to an extent of 94.8% for simulated broths, 96.2% for *P. shermanii*, 97.7% for *S. cerevisiae*, and 95.7% for *P. chrysogenum*, respectively. The remaining 5.2%, 3.8%, 2.3%, and 4.3%, respectively, can be attributed to the effect of other factors, namely number, position and geometry of baffles, sparger diameter, temperature, etc.

Conclusions

This study on the oxygen transfer rate distribution in a stirred bioreactor underlines the different behavior of the simulated and real broths (bacterial, yeast, and fungal cultures) from the viewpoint of the correlations between k_la and the considered parameters (apparent viscosity or biomass concentration, rotation speed, and aeration rate). Moreover, the amplitude of the influences of the considered factors differs according to the region of the broth.

The increase of the mixing energy consumed indicates the existence of a critical specific power input corresponding to the maximum k_la. The value of the critical rotation speed depends on the position considered in the broth, the apparent viscosity or biomass concentration, the aeration rate, and the type of microorganism.

Except for the simulated broths, the experiments suggest the impossibility of achieving a uniform oxygen mass transfer rate throughout the whole bulk of the broth, even when the operating conditions for uniform mixing are obtained. This is the consequence of cell adsorption to bubble surface, a phenomenon that especially affects the oxygen transfer and less so the broth circulation.

Owing to the different affinity of biomass for bubble surface, the influence of power input on k_la differs between bacterial and yeast cultures versus fungal ones.

The effect of aeration intensification is positive for simulated, bacterial and yeast broths, for all considered positions in the bioreactor. However, for *P. chrysogenum* cultures, increase of the superficial air velocity initially induces a reduction of k_la to a minimum value, followed by an increase. This variation, which correlates directly with the variation of broth circulation intensity, is a result of the formation of small bubbles, at lower superficial air velocity, and of flooding, at intense aeration. The value of volumetric air flow corresponding to the flooding point depends on the amount of mycelia and the power consumption, irrespective of the position studied.

These results underline that aerobic bioreactor scale-up has to consider the oxygen transfer rate distribution in the broth, because otherwise, even when respecting geometrical similarity, it is possible that a similar variation of k_la will not be achieved at larger scale. Scale-up of aerobic stirred bioreactors using the oxygen transfer criterion constitutes the ongoing subject of our experimental work.

The influences of the considered factors on k_la were included in mathematical correlations established based on the experimental data. The proposed equations allow the oxygen mass transfer coefficient to be predicted in different regions of the bioreactor for simulated, bacterial, yeast, and fungal broths, and exhibit good agreement with the experimental results (the maximum deviation varied between $\pm 6.6\%$ for *P. chrysogenum* and $\pm 10.7\%$ for simulated broths).

References

1. Aiba S, Humphrey AE, Millis NF (1973) Biochemical engineering. Academic, New York
2. Bakker A, Van Den Akker HEA (1994) Gas-liquid contacting with axial flow impellers. Chemical engineering research and design. Trans I Chem E Part A 72:573–582
3. Bujalski JM (2003) Ph.D. thesis, University of Birmingham
4. Caşcaval D, Galaction AI, Folescu E, Turnea M (2006) Comparative study on the effects of n-dodecane addition on oxygen transfer in stirred bioreactors for simulated, bacterial and yeasts broths. Biochem Eng J 31:56–66
5. Caşcaval D, Galaction AI, Turnea M (2007) Comparative analysis of mixing distribution in aerobic stirred bioreactor for simulated, yeasts and fungus broths. J Ind Microbiol Biotechnol 34:35–47
6. Chisti Y, Jauregui-Haza UJ (2002) Oxygen transfer and mixing in mechanically agitated airlift bioreactors. Biochem Eng J 10: 143–153
7. Galaction AI, Caşcaval D, Oniscu C, Turnea M (2004) Prediction of oxygen transfer coefficients in stirred bioreactors for bacteria, yeasts and fungus broths. Biochem Eng J 20:85–94
8. Hjertager BH (1998) Computational fluid dynamics (CFD) analysis of multiphase chemical reactor. Trends Chem Eng 4:45–92
9. Ho CS, Olshue JY (1987) Biotechnology processes scale-up and mixing. American Institute of Chemical Engineering, New York
10. Ju LK, Sundararajan A (1994) The effects of cells on oxygen transfer in bioreactors: physical presence of cells as solid particles. Chem Eng J 56:B15–B22
11. Kerdouss F, Bannari A, Proulx P (2006) CFD modeling of gas dispersion and bubble size in a double turbine stirred tank. Chem Eng Sci 61:3313–3322
12. Kerdouss F, Bannari A, Proulx P, Bannari R, Skrga M, Labrecque Y (2007) Two-phase mass transfer coefficients prediction in a bioreactor with a CFD model. Comput Chem Eng. doi:10.1016/j.compchemeng.2007.10.010
13. Lane GL, Schwarz MP, Evans GM (2002) Predicting gas-liquid flow in a mechanically stirred tank. Appl Math Model 26: 223–235
14. Lane GL, Schwarz MP, Evans GM (2005) Numerical modeling of gas-liquid flow in stirred tanks. Chem Eng Sci 60:2203–2214
15. Montes FY, Catalan J, Galan MA (1999) Prediction of k_La in yeasts broths. Proc Biochem 34:549–555

16. Moo-Young M, Cooney CL, Humphrey AE (1985) Comprehensive biotechnology, vol 2. Pergamon, Oxford
17. Miyachi M, Iguchi A, Uchida S, Koide K (1981) Effect of solid particles in liquid-phase on liquid-side mass transfer coefficient. Can J Chem Eng 59:640–645
18. Oniscu C, Galaction AI, Caşcaval D, Ungureanu F (2002) Modeling of mixing in stirred bioreactors. 2. Mixing time for non-aerated fermentation broths. Biochem Eng J 12:61–69
19. Ozbek B, Gayik S (2001) The studies on the oxygen mass transfer coefficient in a bioreactor. Proc Biochem 36:729–741
20. Puthli MS, Rathod VK, Pandit AB (2006) Optimization of lipase production in a triple impeller bioreactor. Biochem Eng J 27: 287–294
21. van't Riet K, Tramper J (1991) Basic bioreactor design. M. Dekker, New York
22. Weber ME, Paddock D (1983) Interceptional and gravitational collision efficiencies for single collectors at intermediate Reynolds numbers. J Colloid Interface Sci 94:328–335