Biochemical Engineering Journal 118 (2017) 70–81

Contents lists available at ScienceDirect

Biochemical Engineering Journal

journal homepage: www.elsevier.com/locate/bej

Regular article

Hydrodynamics and mass transfer in bubble column, conventional airlift, stirred airlift and stirred tank bioreactors, using viscous fluid: A comparative study

Sérgio S. de Jesus*, João Moreira Neto, Rubens Maciel Filho

Laboratory of Optimization, Design and Advanced Control, Bioenergy Research Program, School of Chemical Engineering, University of Campinas, P.O. 6066, Zip: 13083-852 Campinas/SP, Brazil

ARTICLE INFO

Article history:
Received 8 June 2016
Received in revised form
17 November 2016
Accepted 21 November 2016
Available online 22 November 2016

Keywords:
Bioreactors
Hydrodynamics
Mass transfer
Newtonian fluids
Non-Newtonian fluids

ABSTRACT

The performance of four bioreactors (bubble column, concentric tube airlift, concentric tube stirred airlift, and mechanically stirred tank) were evaluated in this study in terms of the hydrodynamics and mass transfer, using viscous a Newtonian fluid (glycerol 65%) and a non-Newtonian fluid (xanthan 0.25%). The experimental results showed that the gas holdup and mass transfer coefficient were higher in the stirred airlift and stirred tank, on the other hand these reactors had high shear rates. In relation to power consumption, lower values were obtained in the bubble column and airlift bioreactors. In a viscous medium in which microorganisms or shear-sensitive cells are used, the use of airlift bioreactors may be the best choice for presenting a low shear environment and a reasonable oxygen transfer rate, in addition to the low power consumption. On the other hand, if the process involves microorganisms that require high oxygen rates, a stirred airlift bioreactor may be the best choice.

1. Introduction

The oxygen or other gas from a gaseous to liquid form is one of the main challenges for reactor engineering. Thousands of biological processes occur in the presence of aerobic microorganisms, and in the highly viscous medium, which implies a great challenge for the aeration system, stirring and mixing, with the purpose of supplying oxygen gas in liquid form for cell growth and maintenance in order to achieve a given product. Studies with different mediums and microorganisms reported that several factors must be taken into account for choosing the correct bioreactor. These factors include their geometry, their stirring and aeration system and the ease of operation and control, their ability to separate the product from the medium or from the by-products, energy consumption, and finally, their relative ease of post-process cleaning [1–3]. Understanding the hydrodynamic behavior of the reactor is a very important parameter, which is necessary to understand the transport phenomena involved in their operation; some parameters such as liquid circulation velocity, mixing time, gas holdup, bubble diameter, mass transfer (k_La) and shear rate should be taken into consideration [4]. For proper oxygen transfer from the gas phase to the liquid phase, the generation of regions of high shear should be avoided, since these affect the cells and produce irreversible morphological changes to the microorganism. For this reason, the stirring effect on the morphology of submerged cultures must be carefully evaluated. On the other hand, the stirrer velocity and the mixing intensity have an important role in the rupture of bubbles. To create greater turbulence in the medium and break the bubbles, many bioreactors use a set of baffles, which can also lead to an increased shear rate [5].

In submerged cultures involving aerobic organisms, the stirred tank bioreactor is the most used. This equipment has impellers for mechanical stirring of the broth [6,7]. This stirring is intended to enhance mixing, to break bubbles and to increase the turbulence of the liquid medium. The main advantage of these bioreactors is the good uniformity of the medium around the tank, avoiding the formation of aggregates, being widely used for cultures with formation of broths with complex rheological characteristics, generally mediums with non-Newtonian behavior, which require high speeds of heat and mass transfer, and in these cultures, achieving a perfect mixture is difficult, causing aeration problems [6]. Furthermore, these reactors have some disadvantages, particularly in

* Corresponding author.
E-mail address: ssjesus@gmail.com (S.S. de Jesus).

http://dx.doi.org/10.1016/j.bej.2016.11.019
1369-703X/

Nomenclature

a, b, c, d	Parameters of eq. (14) and (15) [-]
e, f, h, i,j	Parameters of eq. (20) and (21) [-]
w, x, y, z	Parameters of eq. (22) and (23) [-]
A_D	Cross-sectional area of downcomer [m^2]
A_R	Cross-sectional area of riser [m^2]
C	Instantaneous concentration of dissolved [kmol m^{-3}]
C_0	Initial concentration of dissolved oxygen [kmol m^{-3}]
C^*	Saturation concentration of dissolved oxygen [kmol m^{-3}]
D_T	Tank diameter [m]
d_i	Diameter of the impeller [m]
E	Fractional approach to equilibrium defined by eq. (4) [-]
g	Gravitational acceleration [m s^{-2}]
h_D	Height of gas-liquid dispersion [m]
h_L	Height of gas free liquid [m]
k	Consistency index [Pa.s^n]
k_La	Overall volumetric gas–liquid mass transfer coefficient [s^{-1}]
M	Torque [N m]
M_0	Torque due to gearbox, bearings and seals [N m]
n	Flow behavior index
N	Rotational speed of the impeller [s^{-1}]
N_p	Impeller power number [-]
P	Power consumption [W m^{-3}]
P_G	Power input due to gassing [W]
P_0	Power drawn under ungassed conditions [W]
Q	Specific air flow rate [vvm]
Re	Reynolds number [-]
t	Time [s]
t_0	Initial or start time [s]
U_G	Superficial gas velocity based on the total [m.s^{-1}]
V_L	Volume of liquid [m^3]
ε_G	Overall fractional gas holdup [-]
$\dot{\gamma}$	Shear rate [s^{-1}]
γ_{AV}	Average shear rate [s^{-1}]
μ	Dynamic viscosity [Pa s]
μ_{ap}	Apparent viscosity [Pa s]
ρ_L	Density of the liquid [kg m^{-3}]
τ	Shear stress [Pa]

cultures with shear-sensitive cells, such as plant and animal cells that may be damaged due to their reduced viability with an increase in the stirring velocity [5]; the use of highly viscous mediums which exhibit non-Newtonian behavior can also be a disadvantage of this type of reactor, since the impeller presents flooding, and cannot be aerated at high gas velocities, resulting in poorer mixing patterns in comparison with the airlift-type reactor [7].

There are also other types of bioreactors which are very important and industrially used, called pneumatic bioreactors, in which medium stirring is performed by air bubbling. Bubble columns and airlift bioreactors can be included in this group [8]. These reactors are generally cylindrical in shape, where homogenization of the medium and aeration are carried out by air injection or the injection of other gases through a sparger located in the base to maintain a proper level of stirring and oxygen transfer, it is operated with high air flow [8,9]. The main advantages are low operating costs and maintenance due to the absence of moving parts, and ease of operation. However, the use of non-Newtonian viscous fluids is considered a limiting factor in choosing this equipment, since high viscosity decreases gas holdup and prevents the formation and stability of a bed of homogeneous bubbles, this also has a negative impact in gas-liquid mass transfer [10–14].

In order to overcome some airlift bioreactor and some stirred tank bioreactor limitation, mechanically agitated airlift bioreactors were proposed [7,15,16]. Although this type of bioreactor has not yet been used industrially, it has demonstrated a high standard of mixing of fluid-gas in the laboratory, which results in an oxygen transfer increase to the reaction system, the performance increase of the bioreactor is mainly due to mechanical stirring, which can achieve high fluid circulation due to the highly directional flow pattern [7]. These bioreactors still require more detailed studies, at both experimental and computational levels.

Comparative studies, listing the main advantages and disadvantages of these reactors, even at laboratory level, have not yet been described. Studies in the literature are limited in their comparisons between pneumatic and conventional bioreactors, with a lack of comparative studies also with hybrid bioreactors. The objective of this study was to compare, in order to list, the advantages and disadvantages of conventional, pneumatic and hybrid bioreactors. In this work the performances of four bioreactors (bubble column, airlift, stirred airlift and stirred tank) were analyzed with regards to hydrodynamics and mass transfer. In order to analyze the performance of these reactors, viscous fluids with Newtonian behavior (glycerol 65%) and non-Newtonian behavior (xanthan 0.25%) were used. For comparison purposes, the experiments were performed with the same volume of fluid and gas sparger. In experiments with mechanical stirring, a Rushton turbine impeller was used due to its wide use in laboratories and industry [17], with the same geometric similarity given by the relation $(D_T/d_i) = 3$. The results of the advantages and disadvantages of each bioreactor were enumerated.

2. Materials and methods

2.1. Bioreactors

2.1.1. Stirred tank bioreactor

A 5.0 L benchtop bioreactor was used (Bioflo III fermentor, New Brunswick Scientific, USA) with a maximum working volume of up 4.0 L. The gas sparger was adapted and built for this study and consisted of a circular perforated plate with 0.05 m diameter, with 90 holes of 0.001 m in diameter. A dissolved oxygen electrode (O2-sensor InPro6800/12/220 Mettler Toledo, Switzerland) and pH probe (405-DPAS-SC-K8S/225 Mettler Toledo, Switzerland) were used. The stirring was promoted by a Rushton turbine impeller with six blades, 0.06 m in diameter. The impeller clearance was 0.01 m. The relationship between the diameter of the impeller and the diameter of the tank $(D_T/d_i) = 3$. The dimensions of the equipment are described in Fig. 1.

2.1.2. Stirred airlift bioreactor

A concentric draft tube stirred airlift bioreactor with a working volume up to 4.0 L, described in de Jesus et al. [16] was used for the experiments. The stirring in the bioreactor was promoted by a Rushton turbine impeller with six blades, 0.06 m in diameter. The impeller clearance was 0.01 m, and $(D_T/d_i) = 3$. The air was sparged into the internal zone through a circular perforated plate with 0.05 m diameter, with 90 equidistant holes with 0.001 m diameter, located on the bottom of the bioreactor, concentric in relation to the area comprised by the riser. A dissolved oxygen electrode (O2-sensor InPro6800/12/220 Mettler Toledo, Switzerland) and two identical pH probes (405-DPAS-SC-K8S/225 Mettler Toledo, Switzerland) were used. To avoid vortex formation, four baffles

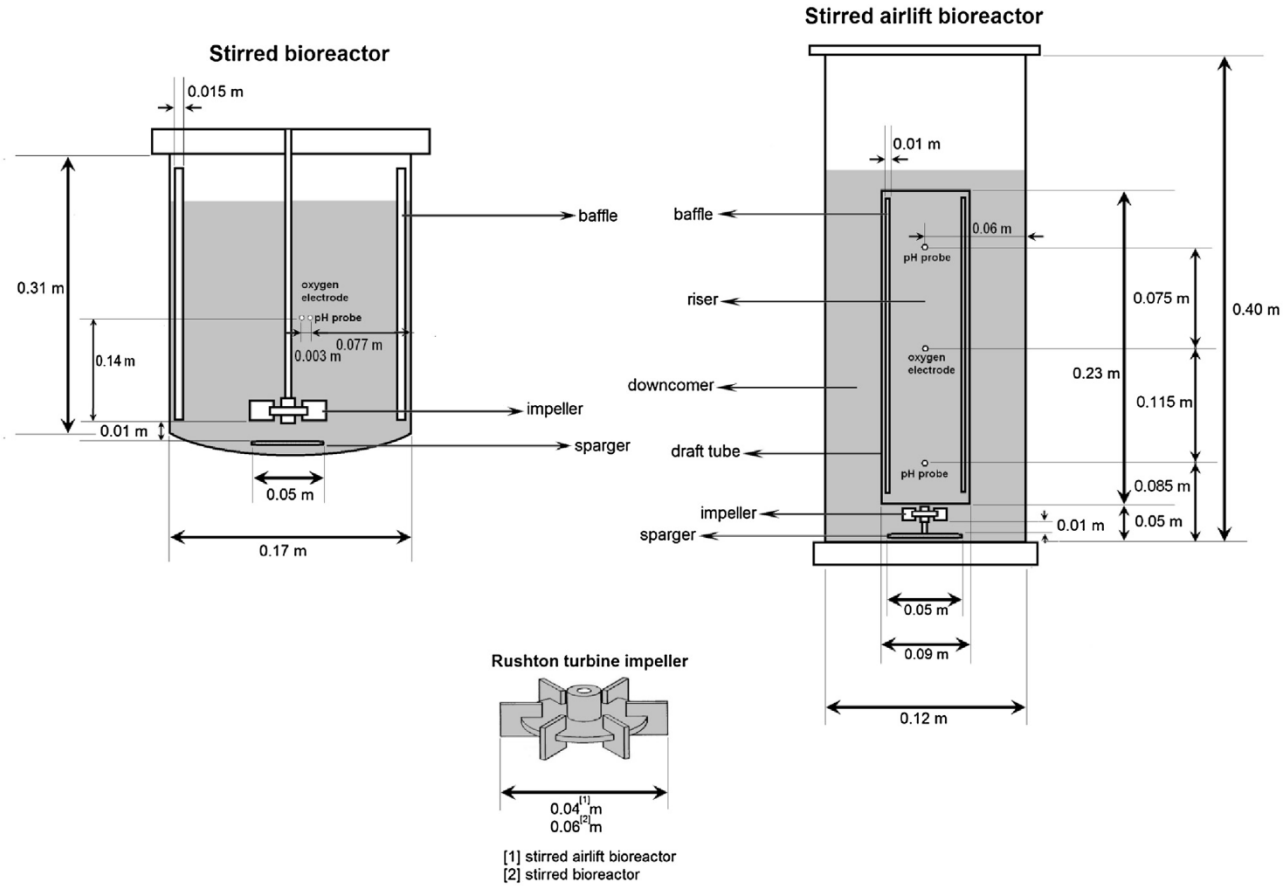

Fig. 1. The schematic diagram of the experimental bioreactors system.

were added inside the draft tube, in the region comprised of the riser.

This bioreactor was also operated without stirring, as in a conventional airlift bioreactor, and withdrawal of draft tube allowed it to function as a bubble column bioreactor. The dimensions of the equipment are described in Fig. 1.

2.2. Fluids

Glycerol 65% (99.5%, LabSynth Ltda., Brazil) and xanthan gum 0.25% (Sigma-Aldrich, Germany) were used as Newtonian and non-Newtonian fluids, respectively. The solutions were prepared with deionized water.

The specific air flow rate varied from 0.50 to 1.50 vvm. The volume of fluid in the reactors was 3.5 L.

The stirring speed ranged from 400 to 800 rpm. All experimental runs were carried out at atmospheric pressure and at 25 ± 2 °C.

2.3. The measurements

2.3.1. Rheology

The rheological behavior of the xanthan solution was correlated with the Power Law model (Ostwald-de Wale), given by:

$$\mu_{ap} = k\dot{\gamma}^{n-1} \tag{1}$$

Parameters k and n of Eq. (1) were experimentally obtained by coaxial cylinders ZA-30 (coquette) HAAKE Rheo-Stress 6000 rheometer (ThermoScientific, Victoria, Australia), with 60 mm in diameter.

2.3.2. Gas holdup

The gas holdup (ε_G) was estimated by visual observation of the increase in volume level caused by aeration or aeration/agitation, in this method, gas holdup is given by equation [4]:

$$\varepsilon_G = \frac{h_D - h_L}{h_D} \tag{2}$$

where h_D is the height of gas-liquid dispersion and h_L is the height of gas-free-liquid.

All experiments were performed in triplicate.

2.3.3. Volumetric oxygen transfer coefficient

The volumetric oxygen transfer coefficient (k_La) was measured with the dynamic gassing-in method [5].

The oxygen content in the fluid was eliminated by bubbling of gaseous nitrogen until the dissolved oxygen concentration was less than 5% air saturation, and then the reactor was aerated in accordance with the conditions of each experiment.

The dissolved oxygen concentration was collected every second through a computer program installed in the bioreactor. The increase in the dissolved oxygen concentration was followed over time until the fluid became saturated with oxygen (>90%). For each air velocities were collected approximately 40 points until oxygen saturation. All experiments were done in triplicate for each studied air velocity. k_La was calculated as the slope of the linear equation:

$$-ln(1 - E) = k_La(t - t_0) \tag{3}$$

where E is the fractional approach to equilibrium and can be estimated by:

$$E = \frac{C - C_0}{C^* - C} \tag{4}$$

Table 1
Properties of liquids used.

Fluid	ρ_L	$\mu \times 10^3$	n	k
Glycerol 65%[a]	1165	14.45	–	–
Xanthan 0.25%	996[b]	–	0.31[c]	0.47[c]

[a] Retired from Akita and Yoshida [20].
[b] Retired from Cerri and Badino [21].
[c] Experimental dates.

2.3.4. Power measurement

The power consumed for the reactors supplied for the stirring system was obtained experimentally. The number of power for each experimental condition was calculated using the equation given by [18]:

$$N_P = \frac{P_0}{\rho_L N^3 d_i^5} \tag{5}$$

The power (P_0) is related to the input torque (M) on the rotating shaft, by the relationship:

$$P_0 = 2\pi N(M - M_0) \tag{6}$$

The torque was determined by an optical-electronic measuring device (Dataflex 22/50, KTR, Germany).

The number of power was graphically correlated with Reynolds number (Re).

For Newtonian fluids, Re is given by:

$$Re = \frac{d_i^2 N \rho_L}{\mu} \tag{7}$$

In this work the Rieger and Novak method was adopted for Non-Newtonian fluid [19]. In this method the Reynolds number is modified in accordance with the rheology of the fluid, which consists of measuring the effective viscosity of the fluid at a shear rate equal to the rotation rate.

Using the power law viscosity model, this yields [19]:

$$Re = \frac{d_i^2 N^{2-n} \rho_L}{k} \tag{8}$$

The aeration power input for the bubble column was calculated using equation [7]:

$$\frac{P_G}{V_L} = \rho_L g U_G \tag{9}$$

For airlift reactors the aeration power input is given by [7]:

$$\frac{P_G}{V_L} = \frac{\rho_L g U_G}{1 + A_D/A_R} \tag{10}$$

For the stirred airlift bioreactor, total power input is given by the sum of the mechanical power input and the aeration power input [7,16].

3. Results and discussion

Table 1 presents the physical constants used for the calculations.

3.1. Gas holdup

Fig. 2 shows the specific air flow rate effect in the gas holdup of glycerol/air and xanthan/air systems for the four types of bioreactor.

The gas holdup showed a significant difference in the four reactors used in this study. Fig. 2 shows that regardless of the rheological behavior of the fluid used, bubble column and airlift reactors showed lower values. The fluid flow in these two reactors is caused only by the displacement of the injected air. The increase in the air flow rate implies an increase in gas holdup; however, the displacement of air is not strong enough to increase the gas holdup in the fluid as was the case in the other reactors studied, which have stirring systems. The use of viscous fluids has a negative effect on these hydrodynamic reactors. The increase of viscosity causes an increase in the size of the bubbles; this effect is primarily attributable to the existence of drag forces on the gas sparger zone, causing bubble coalescence. These bubbles have a short residence time, decreasing gas holdup [11]. The performance of bubble column reactors is strictly regulated by the flow regime prevailing in the column. By contrast, in airlift bioreactors, the presence of a draft tube produces a highly directional flow pattern, with recirculation of the fluid caused by air bubbles, causing the gas holdup to be greater than in the bubble column bioreactor. Moreover, bioreactors that have stirring systems had higher gas holdup; stirring helps in the bubble breaking regardless of the impeller used. The stirring velocity is essential to increase gas holdup, Fig. 2 shows increase of gas holdup due to stirring increase. The experiments revealed that at a rotation velocity of 400 rpm the gas holdup obtained in the stirred tank bioreactor was very close to those obtained in the airlift bioreactor, and similar observations were obtained when stirred airlift bioreactor was operated at 600 rpm; in this case, the gas holdup values were very close to the results obtained with the stirred tank bioreactor operated at 800 rpm. These observations are very important in choosing the bioreactor because stirring causes some side effects and increases power consumption (these observations are described later). Fig. 2 also shows that the hybrid bioreactor, that is, the mechanically stirred airlift bioreactor, had gas holdup values higher than the stirred tank bioreactor. This increase is mainly due to the greater height/diameter relationship of the reaction column and draft tube. Studies with this type of reactor showed that if the stirring system is located very near to the gas sparger it improves the breaking of gas bubbles, which favors better gas holdup in the reactor column [16].

While stirring was an important factor for gas holdup increases, in the studied reactors it was observed that stirring increases were not enough to break the coalescing bubbles into smaller bubbles. Foaming was observed in experiments using xanthan solution at a velocity of 800 rpm, which may result in biological processes and a loss of volatile metabolites, in addition to increase shear rate, which implies damage to cells which often cause the reduction of cell growth, and thus decreases the yield from the process [16]. Finally, in Fig. 2 we observed that the gas holdup of the xanthan solution had values greater than the glycerol solution. The hydrodynamics of bubbles in non-Newtonian fluids is quite different from that of Newtonian fluids; non-Newtonian fluid characteristics are responsible for a particular number of phenomena that are not observed in Newtonian fluids. In general, drag forces in a low viscosity liquid are not sufficient to increase the coalescence and, consequently, the coalescence rate of bubbles is lower in less viscous liquids; such bubbles are usually smaller, which result in a lower ascent speed, increasing the gas holdup. Moreover, with the increased viscosity, the turbulence and energy of eddies to break the bubbles is reduced and therefore bubble coalescence is promoted, leading to larger and faster bubbles and lower gas holdup [9]. The effect of increasing viscosity and elasticity has different effects on the gas holdup and on the coalescence of bubbles. In fluids with elastic behavior, such as xanthan gum, the increased specific air flow rate decreases the solution's viscosity, increasing the elastic effects, which can prevent the coalescence of bubbles, forming smaller bubbles. The glycerol solution is a highly viscous Newtonian fluid and inelastic. However, it is noteworthy that the gas holdup is the result of several factors such as stirring, impeller types and gas sparger as well as liquid properties and bubbles diameter, where the holdup is determined by the coalescence behavior of the liquid and initial bubble size at the gas sparger, to a non-coalescing system, the bubble diameter is com-

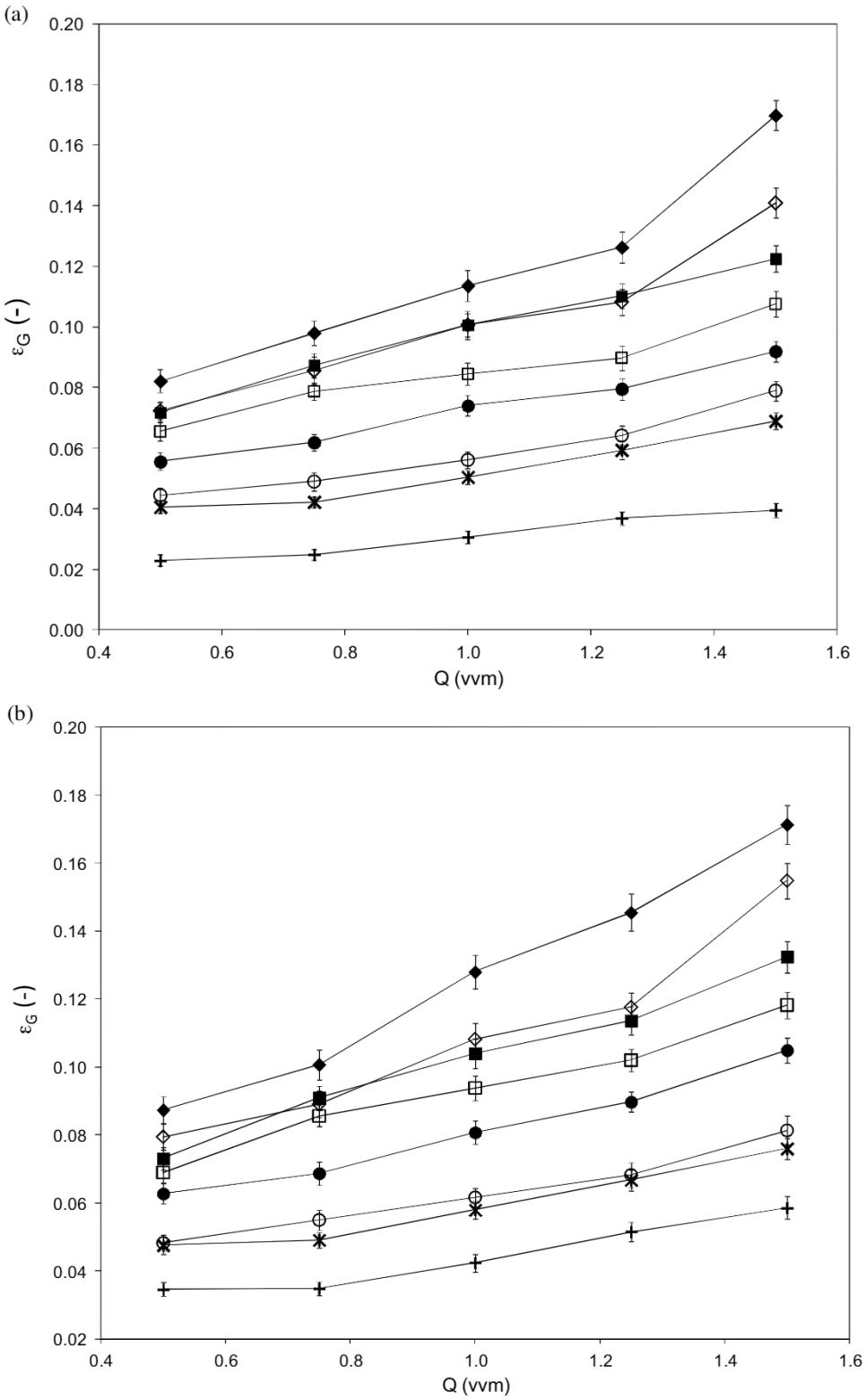

Fig. 2. Variation of gas holdup (ε_G) with specific air flow rate (Q) for glycerol 65% (a) and xanthan 0.25% (b).
where: (+) bubble column; (*) airlift reactor; (○) stirred tank reactor at 400 rpm; (□) stirred tank reactor at 600 rpm; (◊) stirred tank reactor at 800 rpm; (●) stirred airlift reactor at 400 rpm; (■) stirred airlift reactor at 600 rpm; (♦) stirred airlift reactor at 800 rpm.

pletely determined by the sparger, the impeller types and stirring input is merely complemented to improve the bubble breakage in smaller bubbles.

3.2. Volumetric oxygen transfer coefficient

The volumetric oxygen transfer coefficient (k_La) is an important parameter to be determined in the aerobic fermentative processes [5].

Studies were performed with airlift and stirred tank bioreactors [21–24], which are similar to those used in this paper. Those studies showed that the dissolved oxygen concentration is practically homogeneous along the reactor column due to the height being relatively small, which does not present significant concentration gradients and for this reason, there is no need the use of two or more probes.

Comparative experiments carried out with four different types of bioreactors showed that k_La increases with air flow in reactors which have moving parts, *i.e.* a stirring system, k_La also increased with increases in stirring (Fig. 3). The gas-liquid mass transfer is controlled by the liquid phase resistance and the contact area, and is directly related to hydrodynamics, with a k_La variation similar to the gas holdup.

Fig. 3 shows that the bubble column bioreactor had lower values of k_La. The low mass transfer of this bioreactor, compared to other studied devices using viscous fluids is the main reason for poor circulation of the liquid phase. According to Chaumat et al. [25] in bubble column bioreactors, two flow regimens are observed, which are controlled by the gas flow rate and by the properties of the liquid phase. The homogeneous bubble flow regime is observed at low gas velocities, being characterized by small-diameter bubbles and a uniform spatial dispersion of the gas holdup. In this regime there is no interaction between bubbles, their movement is more or less vertical. On the other hand, the heterogeneous system (churn turbulent flow) which is observed at speeds greater than 0.05 m s^{-1}, is characterized by a distribution of large-diameter bubbles along the column axis, causing macrocirculation and curved shape gas holdup profiles. In this regime the bubble size is established by the coalescence-break-up equilibrium. In this study, the gas velocities in the bioreactors were smaller than 0.05 m s^{-1}, which characterize the homogeneous regime; however, the formation of coalescent bubbles was observed. According to Deng et al. [11], the heterogeneous regime prevails in highly viscous liquids even at low superficial gas velocities, which can explain the low k_La values for the bubble column bioreactor, as the heterogeneous regime is characterized by a decrease of gas holdup and k_La. In general, in pneumatic bioreactors, k_La is directly related to the fluid properties, the height of the column and the type of gas sparger used, which determine the diameter of the bubbles formed and their gas holdup. Internal airlift loop bioreactors are basically a bubble column with a draft tube, which results in a highly directional flow pattern, increasing the fluid speed in the column and consequently increasing the k_La. Moreover, the gas-liquid mass transfer in airlift bioreactors is also related to the A_D/A_R ratio. Studies made by Pollard et al. [26], showed that with the increase of the A_D/A_R ratio an increase of oxygen transfer occurs, caused primarily by increased fluid speed in the riser, in their study a $A_D/A_R = 1.2$ ratio was used. Fig. 3 shows that k_La obtained in studies with the airlift bioreactor increased between 22 and 43% in relation to the bubble column bioreactor, in this work a draft tube $A_D/A_R = 1.8$ ratio was used. Fontana et al. [27] found that the gas-liquid mass transfer in an internal airlift loop bioreactor is roughly equivalent to results obtained with a stirred tank bioreactor at a rotation speed of 200 to 300 rpm. However, for speeds higher than 400 rpm, a significant increase in k_La occurred which, according to these authors, limits the use of airlift bioreactors in processes that require high liquid oxygen demands.

In processes in which viscous mediums are used, a great difficulty in the recycling of the liquid occurs, in this case, the stirring has a key role in increasing oxygen transfer. The stirring effect in the two bioreactors equipped with mechanical stirring can explain the performance of this equipment in relation to an increase of k_La with the increase of stirring. In stirred tank bioreactors, the hydrodynamics depends on their geometry and the impeller type. In general, the height/diameter is standardized and between 2 and 3, thus obtaining a high residence time of the bubbles is possible, improving the dissolution of oxygen in the liquid by increasing the pressure on the dispersion device. Studies made by Martín et al. [17] found that the position of the impeller has a great impact on mass transfer efficiency. According to these authors, the increase in impeller position relative to the gas sparger results in a loss of mass transfer efficiency at high rotational speeds where the main contribution to k_La is due to the rupture of bubbles. However, at low rotation speeds the main contribution to the k_La is based on the deformation of bubbles in the fluid flow so that the impeller position shows little effect on k_La. In this study, greater mass transfer occurred with the impeller at the lowest position, the clearance was 0.02 m. These observations are very important for choosing the impeller position in order to obtain the maximum mass transfer, the choice of the impeller position in the two bioreactors used in this study (Fig. 1) aimed to improve the breakage of bubbles into smaller bubbles, thereby forming small bubbles in the reaction vessel, which implies a considerable increase in mass transfer. Moreover, it was observed that in the stirred airlift bioreactor, the presence of stirring accelerates the rise of bubbles, and when these bubbles begin to rise, the shock between them increases considerably, increasing coalescence, which has a negative impact on k_La. However, the reduction of the coalescent bubbles is made by recirculating these bubbles between riser and downcomer so that these bubbles are broken when they come into contact with the impeller. It is important to point out that volumetric oxygen transfer coefficient will be the final result of the two systems sets: the first consists of the set of coarse bubbles, i.e. with average coalescent properties or coarse bubbles spargers and the second system consisting of fine bubbles, i.e. non-coalescent medium properties combined with fine bubble spargers. Recirculation of these bubbles between the riser and the downcomer implies an increase in turbulence and increase in k_La, which can be confirmed by the results shown in Fig. 3.

3.3. Shear rate

In biochemical processes the shear rate is a very important parameter, especially when employing microorganisms or shear-sensitive cells cultures, requiring bioreactors with considerably low shear levels. Therefore, determining the average shear rate ($_{\gamma AV}$) is essential for choosing the bioreactor, its design and operating conditions. Although excessive shear can result in a loss of viability and cell disruption, on the other hand, a certain degree of shear is required to achieve sufficient mass transfer and energy [28].

Despite shear rate being an important parameter, it is not easily characterized, restricting methods and theoretical models. Within these methodologies, proposals from Cerri et al. [22] and Bustamante et al. [23], may be used for various types of bioreactors, since they have the inclusion of a large numbers of parameters involved, such as operational conditions (N and Q) and the rheological properties of non-Newtonian fluid in turbulent regime as their main factors. In this methodology the shear rate ($\dot{\gamma}$) is calculated from the shear stress (τ) and dynamic viscosity (μ) for Newtonian fluid, which is given by:

$$\tau = \mu \dot{\gamma}^n \tag{11}$$

For pseudoplastic, non-Newtonian fluids, the relationship between shear stress and shear rate is nonlinear, and the flow curve is given by:

$$\tau = k\dot{\gamma}^{n-1} \quad n < 1 \tag{12}$$

According to Eq. (1), the apparent viscosity ($_{\mu ap}$) for pseudoplastic non-Newtonian fluids can be rewritten as:

$$\dot{\gamma} = \left(\frac{\mu_{ap}}{k}\right)^{1/n-1} \tag{13}$$

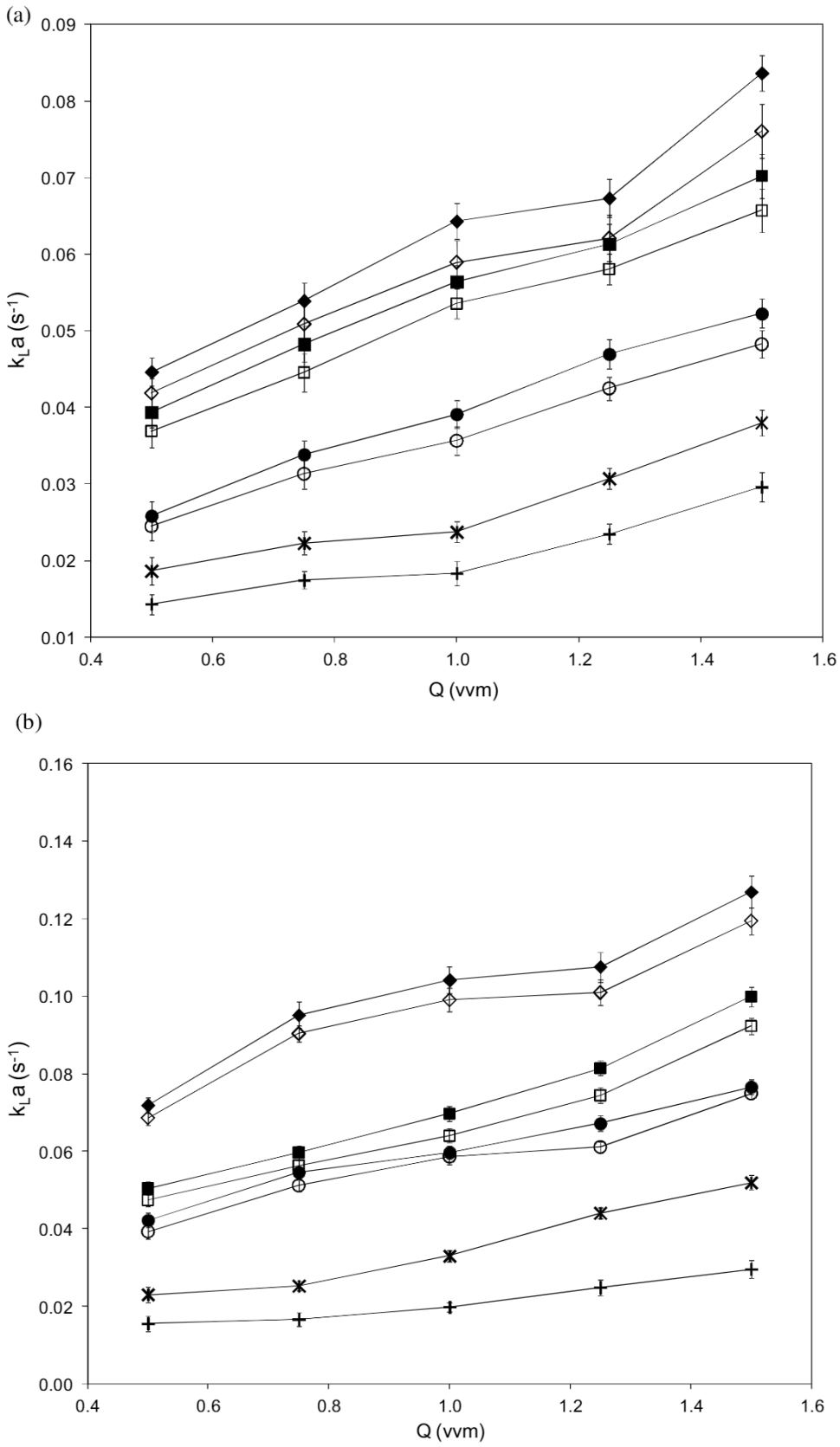

Fig. 3. Variation of volumetric oxygen transfer coefficient (k_La) with specific air flow rate (Q) for glycerol 65% (a) and (b) xhantan 0.25%.
where: (+) bubble column; (*) airlift reactor; (○) stirred tank reactor at 400 rpm; (□) stirred tank reactor at 600 rpm; (◊) stirred tank reactor at 800 rpm; (●) stirred airlift reactor at 400 rpm; (■) stirred airlift reactor at 600 rpm; (♦) stirred airlift reactor at 800 rpm.

To calculate the shear rate, first with k_La data for Newtonian fluids, we correlate with N, Q and μ, which results in the equations:

$$k_La = aQ^c\mu^d \text{ (bubble column and airlift bioreactor)} \quad (14)$$

$$k_La = aN^bQ^c\mu^d \text{ (stirred airlift and stirred bioreactor)} \quad (15)$$

Whereas Eqs. (14) and (15) are valid for Newtonian and non-Newtonian fluids, μ of Eqs. (14) and (15) may be replaced by μap of Eq. (13), obtaining the correlation of k_La for non-Newtonian fluids.

$$k_La = aQ^c\left(k\dot{\gamma}_{AV}^{n-1}\right)^d \text{ (bubble column and airlift bioreactor)} \quad (16)$$

$$k_La = aN^bQ^c\left(k\dot{\gamma}_{AV}^{n-1}\right)^d \text{ (stirred airlift and stirred bioreactor)} \quad (17)$$

Rearranging Eqs. (16) and (17), we have γ_{AV} as a function of operating conditions (N and Q), the volumetric oxygen transfer coefficient (k_La) and the rheological parameters of the fluid (k and n).

$$\gamma_{AV} = \left(\frac{k_La}{aQ^ck^d}\right)^{(1/d(n-1))} \text{ (bubble column and airlift bioreactor)} \quad (18)$$

$$\gamma_{AV} = \left(\frac{k_La}{aN^bQ^ck^d}\right)^{(1/d(n-1))} \text{ (stirred airlift and stirred bioreactor)} \quad (19)$$

The k_La data for non-Newtonian fluids can be correlated according to the following equations:

$$k_La = eQ^hk^in^j \text{ (bubble column and airlift bioreactor)} \quad (20)$$

$$k_La = eN^fQ^hk^in^j \text{ (stirred airlift, stirred bioreactor)} \quad (21)$$

Replacing Eq. (20) on Eq. (18) and Eq. (21) on Eq. (19), we obtain γ_{AV} as a function of N, Q, k and n.

$$\gamma_{AV} = \left(xQ^zk^wn^j\right)^{(1/d(n-1))} \text{ (bubble column and airift bioreactor)} \quad (22)$$

$$\gamma_{AV} = \left(xN^yQ^zk^wn^j\right)^{(1/d(n-1))} \text{ (stirred airlift and stirred bioreactor)} \quad (23)$$

where: $x = f/b$, $y = f\text{-}c$, $z = h\text{-}d$ and $w = i\text{-}e$.

The correlations given by Eqs. (22) and (23) were used to predict γ_{AV} from the xanthan 0.25% in function of N, Q, k and n, for all the studied reactors. The resulting equations below (Eqs. (24)–(35)) were obtained with the k_La data according to Fig. 3 and Eqs. (16)–(23).

Bubble column

$$\text{Glycerol}: k_La = 1.27\times10^{-2}Q^{0.51}\mu^{-0.12} \quad R^2 = 0.97 \quad (24)$$

$$\text{Xanthan}: k_La = 5.80\times10^{-3}Q^{0.66}k^{-0.50}n^{-0.80} \quad R^2 = 0.98 \quad (25)$$

$$\gamma_{AV} = (0.46Q^{0.15}k^{-0.38}n^{-0.80})^{[1/0.35(1-n)]} \quad (26)$$

Airlift bioreactor

$$\text{Glycerol}: k_La = 1.82\times10^{-2}Q^{0.60}\mu^{-0.10} \quad R^2 = 0.97 \quad (27)$$

$$\text{Xanthan}: k_La = 5.65\times10^{-3}Q^{0.77}k^{-0.13}n^{-1.50} \quad R^2 = 0.98 \quad (28)$$

$$\gamma_{AV} = (0.31Q^{0.17}k^{-0.04}n^{-1.50})^{[1/0.10(1-n)]} \quad (29)$$

Stirred airlift bioreactor

$$\text{Glycerol}: k_La = 2.63\times10^{-4}N^{0.50}Q^{0.66}\mu^{-0.50} \quad R^2 = 0.98 \quad (30)$$

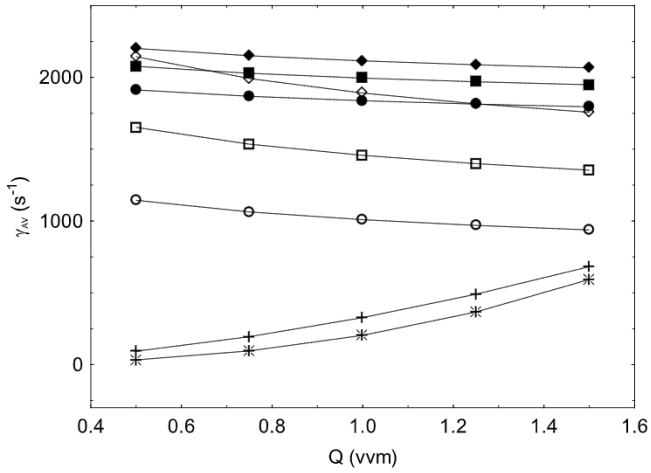

Fig. 4. Average shear rate (γ_{AV}) as a function of specific air flow rate (Q). where: (+) bubble column; (*) airlift reactor; (○) stirred tank reactor at 400 rpm; (□) stirred tank reactor at 600 rpm; (◊) stirred tank reactor at 800 rpm; (●) stirred airlift reactor at 400 rpm; (■) stirred airlift reactor at 600 rpm; (♦) stirred airlift reactor at 800 rpm.

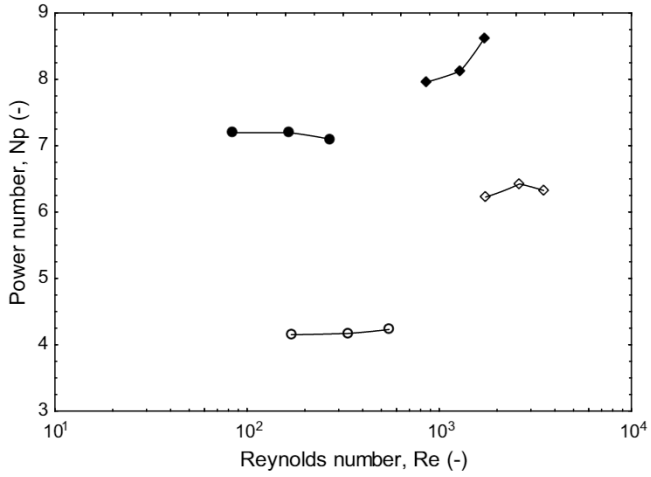

Fig. 5. Variation of the measured power number (Np) with Reynolds number (Re). where: (◊) stirred tank reactor – glycerol 65%; (○) stirred tank reactor – xanthan 0.25%; (♦) stirred airlift reactor – glycerol 65%; (●) stirred airlift reactor – xanthan 0.25%.

$$\text{Xanthan}: k_La = 9.00\times10^{-4}N^{0.63}Q^{0.64}k^{-0.10}n^{-0.32} \quad R^2 = 0.98 \quad (31)$$

$$\gamma_{AV} = (3.42N^{0.07}Q^{-0.02}k^{0.4}n^{-0.32})^{[1/0.50(1-n)]} \quad (32)$$

Mechanically stirred bioreactor

$$\text{Glycerol}: k_La = 1.84\times10^{-3}N^{0.25}Q^{0.70}\mu^{-0.40} \quad R^2 = 0.96 \quad (33)$$

$$\text{Xanthan}: k_La = 9.64\times10^{-4}N^{0.50}Q^{0.65}k^{-0.33}n^{-0.77} \quad R^2 = 0.97 \quad (34)$$

$$\gamma_{AV} = (0.53N^{0.25}Q^{-0.05}k^{0.07}n^{-0.77})^{[1/0.40(1-n)]} \quad (35)$$

Fig. 4 illustrates the shear rate (γ_{AV}) as a function of the specific air flow rate (Q). As can be observed in the pneumatic bioreactors, *i.e.*, bubble column and airlift, had lower shear rates; however, the

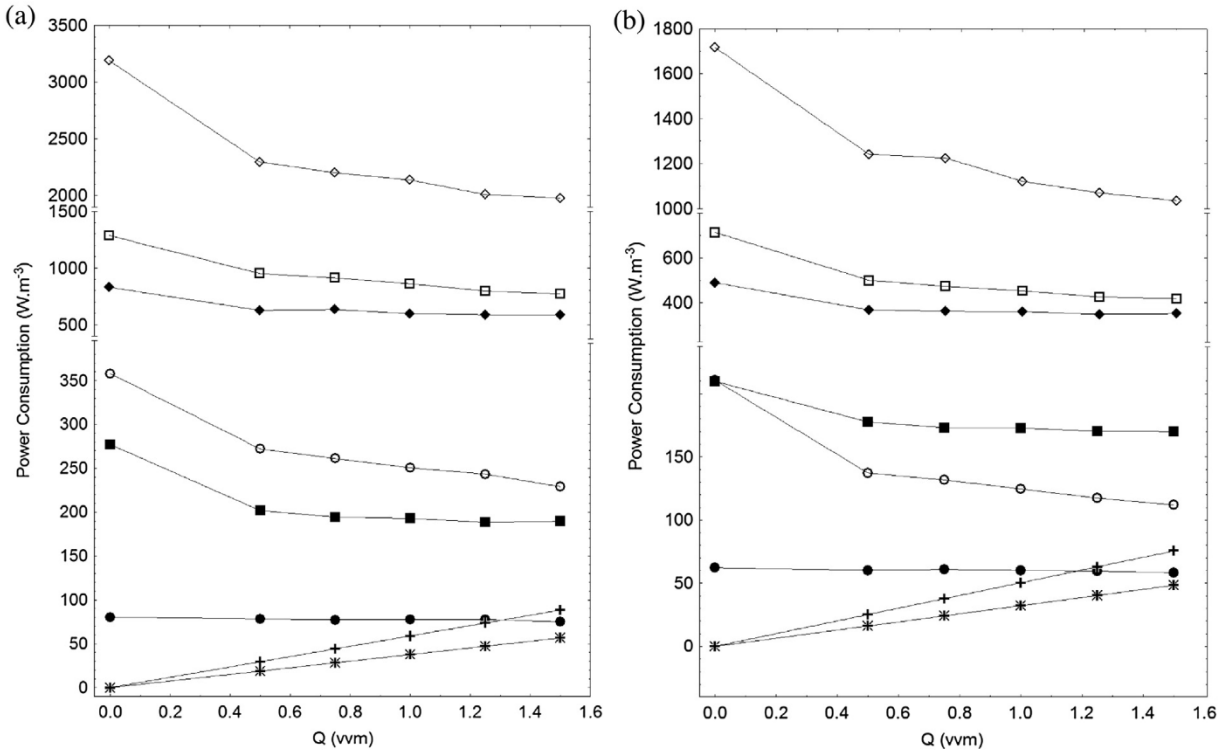

Fig. 6. Ungassed and gassed power requirements as a function of specific air flow rate (Q).
where: (+) bubble column; (*) airlift reactor; (◯) stirred tank reactor at 400 rpm; (□) stirred tank reactor at 600 rpm; (◊) stirred tank reactor at 800 rpm; (●) stirred airlift reactor at 400 rpm; (■) stirred airlift reactor at 600 rpm; (♦) stirred airlift reactor at 800 rpm.

Table 2
Performance of bioreactors studied using viscous fluids.

Bioreactor	Gas holdup (ε_G)	Mass transfer (k_La)	Shear rate (γ_{AV})	Power consumption (P)
Bubble column	low	low	low	low
Airlift	reasonable	reasonable	low	low
Stirred airlift	very high	very high	very high	high
Stirred tank	very high	very high	high	very high

shear rate increased linearly with the air velocity. According to Cerri et al. [22] in airlift internal circulation bioreactors at a superficial gas velocity $U_G < 0.05\ m\ s^{-1}$ there is an increase of shear rate, going through a maximum value; when $U_G > 0.05\ m\ s^{-1}$ the shear rate decreases due to bubble coalescence. On the other hand, various studies [29–31] have showed that the shear rate increases linearly with increasing air velocity, in contrast to the work of Cerri et al. [22], however these models take into account only the superficial gas velocity and the fluid properties [30]. In the model developed by Cerri and Badino [21] in addition to the rheological parameters, the volumetric oxygen transfer coefficient (k_La) is taken into consideration, which is a function of the operating conditions, the type of bioreactor, its geometry, and the rheology of the fluid used. Studies made by Thomasi et al. [24] with three different types of pneumatic bioreactors, had the same trend that was observed by Cerri and Badino [21], corroborating their methodology. It was also observed that the shear rate in the airlift bioreactor was lower than those found in bubble column reactors; these values are particularly related with the flow path defined in the liquid. The shear rate is primarily a function of the relative velocity between the bubbles and the liquid as well as between the liquid and the walls of the reactor. As seen in Figs. 3 and 4, for pneumatic bioreactors, increased k_La is directly related to increasing shear rate, with higher values obtained for the airlift bioreactor.

As seen in Fig. 4, reactors with moving parts showed a shear rate that was practically constant with the increase of the specific air flow rate at a given stirring speed. However, with increases in rotation speed, the shear rate increased. In these bioreactors the shear rate is dependent on the impeller's rotational frequency, of the rheological properties of the fluid, in particular by the consistency index and behavior index of fluid flow (k and n). The high shear produced by the stirred airlift bioreactor is due to the high turbulence that this equipment generates, generating eddies in the impeller, forming a wake of the impeller blades and generating a high shear environment. The wide liquid circulation in the column increases the liquid contact with the bioreactor wall contributing to increasing shear rate [16]. According to de Jesus et al. [16] and Chisti [32] the shear rate is dependent on the amount of hydrodynamics, the specific location of the impeller in the vessel or reaction column, the impeller type, the stirring speed and fluid properties. It should furthermore be noted that impellers with radial flow have higher shear rates than axial flow impellers.

3.4. Power measurement

The power consumption can be considered an important factor in the choice of bioreactor. Although the presence of stirring contributes to the increase of total power, choosing the appropriate

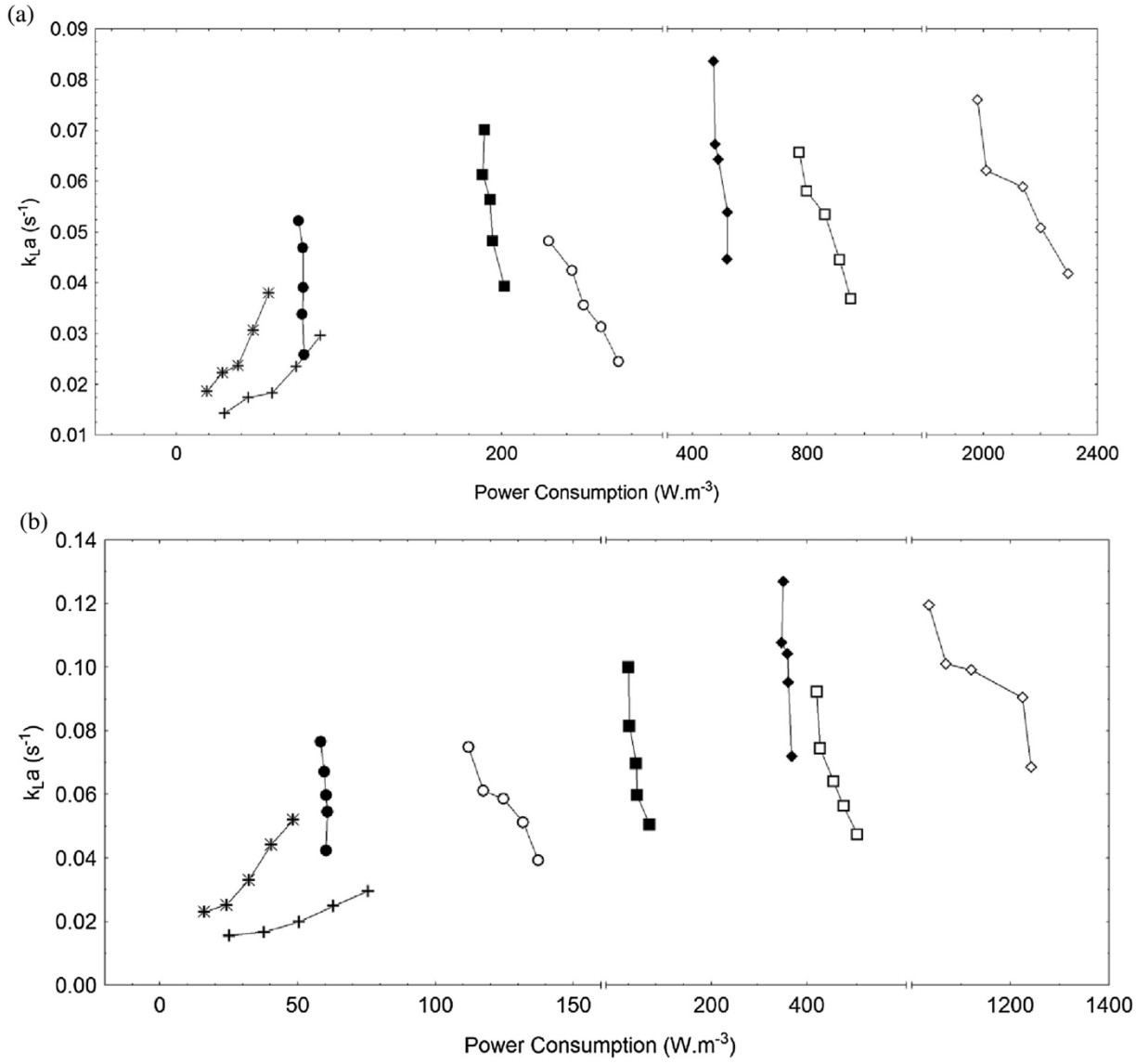

Fig. 7. Volumetric oxygen transfer coefficient (k_La) as a function of the power consumption.
where: (+) bubble column; (*) airlift reactor; (○) stirred tank reactor at 400 rpm; (□) stirred tank reactor at 600 rpm; (◊) stirred tank reactor at 800 rpm; (●) stirred airlift reactor at 400 rpm; (■) stirred airlift reactor at 600 rpm; (♦) stirred airlift reactor at 800 rpm.

impeller can optimize the power for smaller values and the mass transfer coefficient can be increased by more than 50%.

As mentioned above, Rushton turbine impellers are widely used in both industry and laboratories, and are recommended for processes that have mediums or fermentation broths with viscosities ranging from 10^{-3} to 8×10^2 Pa s [33].

Fig. 5 shows the dependence of the power number (*Np*) with the Reynolds number (*Re*) for Newtonian and non-Newtonian fluids of stirred tank and stirred airlift bioreactors in non-aerated system. The power number was defined by Eq. (5) and the Reynolds number by Eqs. (7) and (8). As noted, *Np* was determined in the transitional flow regime in which fluctuations in *Np* can be observed with the number of *Re*; in this regime the density, viscosity, as well as bioreactor geometry affect the required power, which may explain the difference between *Np* obtained for the two bioreactors and for the two fluids used. On the other hand, *Np* of the stirred tank bioreactor for glycerol solution was determined in the turbulent regime ($Re > 10^3$ or 10^4 for most impellers in vessels with baffles). In this regime the power required for turbulent flow is independent of the fluid viscosity but proportional to its density. We can also observe that the *Np* obtained for the stirred tank bioreactor was very close to the values reported in the literature for the Rushton impeller with six blades, which, in a transient regime, the *Np* can range between 3.5-4.5, and in the turbulent regime the *Np* is about 6 [34]. In general *Np* for Rushton turbine impellers is significantly higher than most other impellers. This indicates that this impeller transmits more energy to fluids than other impellers.

Fig. 6 shows the power consumption in the four reactors used for the two types of fluids studied under aerated and non-aerated conditions. As noted, in pneumatic bioreactors low power consumption occurred, and power input increases with increasing gas velocity; in these bioreactors all supplied power is derived from two sources: isothermal gas expansion, since it moves up the reactor and the kinetic energy of the gas injected into the reactor. In both studied pneumatic reactors the predominant source of power was the injected isothermal gas expansion, which was the lowest power consumption in the experiments with the airlift bioreactor, due to the standard defined of the injected gas flow.

Fig. 6 also shows that the impeller power consumption in the case of aerated systems is always lower than that found in unaerated systems since the transfer of power from the impeller to the fluid is greatly influenced by aeration. This power reduction is due to the formation of cavities behind the impeller blades and the different density of the fluid under gassed and ungassed conditions [35]. Fig. 6 also shows that power consumption increases with increasing rotational speed and causes a decrease in air velocity. In general it was observed that the power consumption stirred tank bioreactor was greater than in the stirred airlift bioreactor. In the stirred tank bioreactor, the energy transmitted to the fluid is made mainly through the impeller; in the stirred airlift bioreactor the total power input (P) is given by the sum of the power input due to aeration (P_G) and by the power input due to mechanical mixing (P_M). The kinetic energy contribution can be ignored as it only provided less than 1% of the total aeration power input. It was also noted that at the same rotational speed, power consumption in the stirred tank bioreactor can be up to 500% greater than in the stirred airlift bioreactor.

Power consumption has a major impact on the volumetric oxygen transfer coefficient, in general with increasing speed there is an increase in power consumption and in k_La. Fig. 7 shows the comparison of power consumption with the volumetric oxygen transfer coefficient (k_La) for all the studied reactors and operating modes. As can be seen, the pneumatic bioreactors power input has a proportional effect on k_La, that is, k_La increases with increasing power and is substantially linear. In reactors with mechanical stirring systems the increase in k_La is inversely proportional to the power consumption. Fig. 7 also shows that the increase or decrease in k_La has little impact on the power input in the stirred airlift bioreactor, with the rotational speed as the main factor for increasing the power consumption. It is also noted that when operating the stirred airlift bioreactor at $N = 400$ rpm, a high volumetric oxygen transfer coefficient can be obtained with lower power consumption than can be obtained in pneumatic bioreactors.

Table 2 summarizes the performance of each studied bioreactor with respect to hydrodynamics and mass transfer. However, we cannot forget that the performance of each bioreactor is also conditioned to the microorganism biochemicals used in the process.

4. Conclusions

In this work the performance of four bioreactors was studied using viscous fluids with Newtonian and non-Newtonian behavior. Through hydrodynamic experiments and mass transfer, the performance of these bioreactors was comparatively verified in order to highlight their use in biochemical processes when broths with complex rheological characteristics are used.

Through these observations, based on the results, we can conclude that in processes using viscous fluids the use of bubble columns reactors is not highly recommended, on the other hand, the use of airlift bioreactors can be an attractive alternative when cultures are sensitive to high shear rate, as these bioreactors have a low shear environment and a reasonable oxygen transfer rate in addition to low power consumption. But it is worth noting that the increase in viscosity negatively influences its performance and consequently its use.

Regarding the viscosity effect on the performance of mechanically stirred bioreactors, the hybrid bioreactor, *i.e.*, stirred airlift, is a viable alternative to stirred tank and pneumatic bioreactors, since it presented greater mass transfer and reasonable power consumption. However, this reactor has a high shear environment, thus its use is recommended with low rotational speeds to avoid high shear rates, which may damage cells resulting in the loss of its viability and even rupture, due to morphological damage during cell growth caused by hydrodynamic forces. It is very important to define in advance, aeration and stirring profile during the processes, with the correct choice of the impeller type being an important factor on the final yield.

Acknowledgments

The authors wish to acknowledge the financial support provided by the São Paulo Research Foundation (FAPESP, grants processes no 2008/57873-8, 2010/04903-7 and 2010/03764-3) and Coordination Improvement Higher Education Personnel (PNPD-CAPES).

References

[1] T. Moucha, V. Linek, E. Prokopová, Gas hold-up, mixing time and gas–liquid volumetric mass transfer coefficient of various multiple-impeller configurations: rushton turbine, pitched blade and techmix impeller and their combinations, Chem. Eng. Sci. 58 (2003) 1839–1846.
[2] F. Ju, Z.-M. Cheng, J.-H. Chen, X.-H. Chu, Z.-M. Zhou, P.-Q. Yuan, A novel design for a gas-inducing impeller at the lowest critical speed, Chem. Eng. Res. Des. 87 (2009) 1069–1074.
[3] J. Zhang, Z. Gao, X. Zhang, Z. Cai, Y. Bao, Gas-liquid mass transfer for coalescent system in a hot-sparged triple-impeller stirred reactor, J. Chem. Technol. Biotechnol. (2016), http://dx.doi.org/10.1002/jctb.4866.
[4] Y. Chisti, Airlift Bioreactors, Elsevier, New York, 1989.
[5] F. Garcia-Ochoa, E. Gomez, Bioreactor scale-up and oxygen transfer rate in microbial processes: an overview, Biotechnol. Adv. 27 (2009) 153–176.
[6] B. Kumar, K.A. Patel, A.R. Rao, Mass transfer and rate in baffled surface aerator, Korean J. Chem. Eng. 28 (2011) 502–506.
[7] Y. Chisti, U.J. Jauregui-Haza, Oxygen transfer and mixing in mechanically agitated airlift bioreactors, Biochem. Eng. J. 10 (2002) 143–153.
[8] A.A. Mouza, G.K. Dalakoglou, S.V. Paras, Effect of liquid properties on the performance of bubble column reactors with fine pore spargers, Chem. Eng. Sci. 60 (2005) 1465–1475.
[9] A. Esmaeili, C. Guy, J. Chaouki, The effects of liquid phase rheology on the hydrodynamics of a gas–liquid bubble column reactor, Chem. Eng. Sci. 129 (2015) 193–207.
[10] K. Mohanty, D. Das, M.N. Biswas, Hydrodynamics of a novel airlift multi-stage external loop airlift reactor, Chem. Eng. Sci. 14 (2006) 4617–4624.
[11] Z. Deng, T. Wang, N. Zhang, Z. Wang, Gas holdup: bubble behavior and mass transfer in a 5 m high internal-loop airlift reactor with non-Newtonian fluid, Chem. Eng. J. 160 (2010) 729–737.
[12] S. Drandev, K.I. Penev, D. Karamanev, Study of the hydrodynamics and mass transfer in a rectangular air-lift bioreactor, Chem. Eng. Sci. 146 (2016) 180–188.
[13] C. Wei, B. Wu, G. Li, K. Chen, M. Jiang, P. Ouyang, Comparison of the hydrodinamics and mass transfer characteristics in internal-loop airlift bioreactors utilizing either a novel membrane-tube sparger or perforated plate sparger, Bioprocess Biosyst. Eng. 11 (2014) 2289–2304.
[14] C.E. Mendes, A.C. Badino, Hydrodynamics of Newtonian and non-Newtonian in internal-loop airlift reactors, Biochem. Eng. J. 100 (2016) 137–152.
[15] W. Bang, I. Nikov, H. Delmas, A. Bascoul, Gas-liquid mass transfer in a new three-phase stirred airlift reactor, J. Chem. Technol. Biotechnol. 72 (1998) 137–142.
[16] S.S. de Jesus, J. Moreira Neto, A. Santana, R. Maciel Filho, Influence of impeller type on hydrodynamics and gas-liquid mass transfer in stirred airlift bioreactor, AIChE J. 61 (2015) 3159–3171.
[17] M. Martín, F.J. Montes, M.A. Galán, Bubbling process in stirred tank reactors II: agitator effect on mass transfer, Chem. Eng. Sci. 63 (2008) 3223–3234.
[18] M.O. Albaek, K.V. Gernaey, S.M. Stocks, Gassed and ungassed power draw in a pilot scale 550 litre fermentor retrofitted with up-pumping hydrofoil B2 impellers in media of different viscosity and with very high power draw, Chem. Eng. Sci. 63 (2008) 5813–5820.
[19] F. Rieger, V. Novak, Power consumption of agitators in highly viscous non-Newtonian liquids, Trans. IChemE. 51 (1973) 105–111.
[20] K. Akita, F. Yoshida, Bubble size interfacial area, and liquid-phase mass transfer coefficient in bubble columns, Ind. Eng. Chem. Process Des. Dev. 13 (1974) 84–91.
[21] M.O. Cerri, A.C. Badino, Oxygen transfer in three scales of concentric tube airlift bioreactors, Biochem. Eng. J. 51 (2010) 40–47.
[22] M.O. Cerri, L. Futiwaki, C.D.F. Jesus, A.J.G. Cruz, A.C. Badino, Average shear rate for non-Newtonian fluids in a concentric-tube airlift bioreactor, Biochem. Eng. J. 39 (2008) 51–57.
[23] M.C.C. Bustamante, M.O. Cerri, A.C. Badino, Comparison between average shear rates in conventional bioreactor with Rushton and Elephant ear impellers, Chem. Eng. Sci. 90 (2013) 92–100.
[24] S.S. Thomasi, M.O. Cerri, A.C. Badino, Average shear rate in three pneumatic bioreactors, Bioprocess Biosyst. Eng. 33 (2010) 979–988.
[25] H. Chaumat, A.M. Billet, H. Delmas, Hydrodynamics and mass transfer in bubble column: influence of liquid phase surface tension, Chem. Eng. Sci. 62 (2007) 7378–7390.

[26] D.J. Pollard, A.P. Ison, P.A. Shamlou, M.D. Lilly, Reactor heterogeneity with *Saccharopolyspora erythraea* airlift fermentations, Biotechnol. Bioeng. 58 (1998) 453–463.
[27] R.C. Fontana, T.A. Polidoro, M.M. Silveira, Comparison of stirred tank and airlift bioreactors in the production of polygalacturonases by *Aspergillus oryzae*, Bioresour. Technol. 100 (2009) 4493–4498.
[28] A. Contreras, F. Garcıía, E. Molina, J.C. Merchuk, Influence of sparger on energy dissipation shear rate, and mass transfer to sea water in a concentric-tube airlift bioreactor, Enz. Microb. Technol. 25 (1999) 820–830.
[29] M. Nishikawa, H. Kato, K. Hashimoto, Heat transfer in aerated tower filled with non-Newtonian liquid, Ind. Eng. Chem. Process Des. Dev. 16 (1977) 133–137.
[30] Y. Kawase, M. Moo-Young, Heat transfer in bubble column reactors with Newtonian and non-Newtonian fluids, Chem. Eng. Res. Des. 65 (1987) 121–126.
[31] L.K. Shi, J.P. Riba, H. Angelino, Estimation of effective shear rate for aerated Non-Newtonian liquids in airlift bioreactors, Chem. Eng. Commun. 89 (1990) 25–35.
[32] Y. Chisti, Hydrodynamic damage to animal cells, Crit. Rev. Biotechnol. 21 (2001) 67–110.
[33] R. Alcamo, G. Micale, F. Grisafi, A. Brucato, M. Ciofalo, Large-eddy simulation of turbulent flow in an unbaffled stirred tank driven by a Rushton turbine, Chem. Eng. Sci. 60 (2005) 2303–2316.
[34] A.W. Nienow, On impeller circulation and mixing effectiveness in the turbulent flow regime, Chem. Eng. Sci. 52 (1997) 2557–2565.
[35] N.K. Gill, M. Appleton, F. Baganz, G.J. Lye, Quantification of power consumption and oxygen transfer characteristics of a stirred miniature bioreactor for predictive fermentation scale-up, Biotechnol. Bioeng. 100 (2008) 1144–1155.