Mass transfer, gas hold-up and cell cultivation studies in a bottom agitated draft tube reactor and multiple impeller Rushton turbine configuration

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Abstract

Gas-liquid mass transfer is an important phenomenon in aerobic microbial cultivations, and the mass transfer performance of an industrial reactor strongly affects the overall process economics. Traditionally, industrial and laboratory bioreactors have been agitated with flat disc turbines (Rushton turbines) although there are many variants to this design. In addition, pneumatically agitated reactors such as bubble columns and airlift reactors have been studied and used by the industry.

In this study we utilize an agitated draft tube reactor in cell cultivation and mass transfer studies. A standard reactor geometry agitated with three Rushton turbines was compared to Outotec OKTOP®9000 reactor which is a draft tube reactor agitated with a single impeller located just below the draft tube. The experiments included cell cultivation with *Pichia pastoris* yeast, determination of overall mass transfer coefficient by dynamic gassing in method and measurement of local gas hold-up by electrical impedance tomography (EIT). In addition, agitation power was estimated from the power consumption of the DC-motor.

OKTOP®9000 reactor was found to have higher k_{La} values than the STR with similar agitation power and gas flowrate. The overall gas hold-up was similar in both geometries at same power inputs and gas flow rates. However, some significant differences were detected in the distribution of gas phase between the two geometries especially in the axial direction. Also changes in the gas dispersion regime can be detected from the spatial distribution of the gas hold-up measured by EIT. The cell cultivation experiments showed the applicability of this type of agitated draft tube reactor to bioprocesses although a direct comparison with Rushton geometry is not straightforward.

Keywords

Stirred tank, draft tube, k_{La} , hold-up, yeast cultivation, bioreactor

29 Nomenclature

30	A	reactor cross sectional area (m^2)
31	B_w	baffle width (mm)
32	C	impeller off bottom clearance (mm)
33	C_l	dissolved oxygen concentration (mg/l or %)
34	$C_{l,p}$	dissolved oxygen probe reading (mg/l or %)
35	C_g	dispersed gas oxygen concentration (%)
36	C^*	saturation concentration of oxygen in liquid phase (mg/l or %)
37	D_i	impeller diameter (mm)
38	D_{dt}	draft tube diameter (mm)
39	g	gravitational acceleration (m/s^2)
40	H	liquid level height (mm)
41	H_{dt}	draft tube height
42	$k_L a$	overall mass transfer coefficient (s^{-1} or h^{-1})
43	M	torque (Nm)
44	m	dimensionless partition coefficient for gas/liquid equilibrium (dimensionless)
45	N	impeller revolution rate (s^{-1} or min^{-1})
46	N_p	impeller power number (dimensionless)
47	P	impeller power input (W)
48	P_{gas}	power input by gas buoyancy (W)
49	P_{tot}	total power input by impeller and gas buoyancy
50	Q_g	volumetric gas flow rate (l/min or m^3/s)
51	S	impeller spacing (mm)
52	T	tank diameter (mm)
53	v_s	superficial gas velocity (m/s)
54	V	volume (l)
55	X	cell mass concentration (g/l)

57 Abbreviations

58	AL	airlift reactor
59	BSM	basal salt medium
60	CDW	cell dry weight (g/l)
61	DO	dissolved oxygen (%)
62	STR	stirred tank reactor
63	OD	optical density
64	OUR	oxygen uptake rate of cells
65	OTR	oxygen transfer rate of a reactor
66	YPD	yeast extract, peptone, dextrose medium

68 Greek letters

69	α, β, γ	parameters in $k_L a$ correlation
70	ϵ	gas hold-up (dimensionless)
71	ϵ_{avg}	average hold-up over the reactor or measurement volume
72	ϵ_{vis}	visually measured overall hold-up
73	θ_m	mixing time (s)
74	σ_l	liquid phase electrical conductivity (mS/cm)
75	σ_m	measured dispersion conductivity (mS/cm)
76	ρ	density (kg/m^3)
77	τ_r	DO-probe response time (s)

78 1 Introduction

79 Micro-organisms are used to produce different chemicals, enzymes and medicines. A majority of these
80 production processes are aerobic. In aerobic processes, the cells utilize oxygen, dissolved in the liquid
81 medium, in their metabolism as the final electron acceptor. In addition, there are so-called gas-fermentation
82 processes in which carbon and/or energy is provided through the gas phase (Munasinghe and Khanal, 2010).
83 Therefore, the most common reactors are gas-liquid contactors. The microbial cells can be considered as a
84 solid phase. However, their density is near to that of water, reducing the terminal settling velocity, and they
85 are often neglected when considering only the hydrodynamics of bioreactors. Especially in bulk enzyme and
86 chemical production, the reactor volumes may be several hundred cubic meters, and the efficiency of gas-
87 liquid mass transfer and bulk mixing becomes an important design parameter. Stirred tank reactors (STR)
88 with height to diameter ratio (H/T) above 2 are common in large scale industrial processes and, therefore,
89 they are often equipped with multiple impellers. Alternatives for STR include pneumatically agitated bubble
90 column and airlift reactors. In the latter, a draft tube or other internal structure is constructed to enhance
91 recirculation.

92 For STR, various impeller configurations have been proposed and tested. The traditional approach is to use
93 several Rushton turbines for gas dispersion and mixing. Other options include concave disc turbines for better
94 gas handling capacity and axial impellers to enhance liquid circulation. The axial impellers have been used
95 both in up and down pumping modes (Moucha et al., 2003).

96 Gas flow regimes in a conventional STR are often characterized based on gas flow number ($Fl_g = Q_g N^1 D^3$) and
97 Froude number ($Fr = N^2 D g^{-1}$) to flooding, loading and complete dispersion. Impeller flooding should be
98 avoided in all cases. In addition, superficial gas velocity ($v_s = Q_g A^{-1}$) is often used to describe a scale
99 independent value for gas flow. At homogeneous regime ($v_s < 0.02$ to 0.03 m/s), impeller controls the flow
100 pattern and bubble size whereas at heterogeneous regime ($v_s > 0.02$ to 0.03 m/s) flow is controlled by the
101 gas velocity. (Paul et al., 2004). At homogeneous regime and non-flooded conditions, a following correlation
102 is often written for overall gas-liquid mass transfer coefficient:

$$103 \quad k_L a = \alpha \left(\frac{P}{V} \right)^\beta v_s^\gamma$$

104 Where P is agitation power, V is the liquid volume, v_s is superficial gas velocity and α , β and γ are adjustable
105 parameters. Sometimes, overall power input due to agitation and gas buoyancy is used instead of agitation
106 power. Pneumatic power input per liquid volume can be calculated as $P_{gas} V^{-1} = \rho g v_s$. Similar correlations
107 exist for airlift reactors although it is sufficient to use either superficial gas velocity or pneumatic power input
108 as the variable, and some authors utilize superficial gas velocity based on the riser cross sectional area. In

109 addition, the ratio of downcomer and riser cross sectional area is often included in the correlations. (Chisti,
110 1989)

111 One option to enhance the performance of stirred tank and airlift reactors is a sort of a hybrid between the
112 two reactors. These are often called stirred airlift reactors or stirred draft tube reactors. We prefer the latter
113 name since, strictly speaking, an airlift reactor refers to a system where flow is induced only by the gas phase
114 buoyancy and related density gradients. Various designs have been studied in the previous literature with
115 varying impeller number, type(s) and location, flow direction in the draft tube, and other geometrical
116 parameters. A short summary of these studies is presented in Table 1.

117 Moo-Young et al. (1993) found hydrofoil-agitated AL-STR hybrid bioreactor superior to either basic airlift or
118 stirred tank in the production of mycoprotein foods from *Neurospora sitophila* where the culture medium
119 becomes highly viscous and pseudoplastic. Pollard et al. (1997) studied baker's yeast fermentation and the
120 mixing performance of a pilot scale concentric airlift bioreactor agitated with a marine propeller located near
121 the bottom of the downcomer. They found that agitation reduced dissolved oxygen heterogeneity within the
122 reactor and increased the oxygen uptake rate (OUR) of the cells. Furthermore, it was stated that the
123 maximum OUR depended more on the lowest dissolved oxygen (DO) value than the circulation time which is
124 related to the frequency at which cells experience changes in DO.

125 Chisti and Jauregui-Haza (2002) also found mechanically agitated airlift reactor to increase mixing
126 performance and oxygen transfer although the oxygen transfer efficiency in terms of power consumption
127 decreased compared to a regular airlift reactor. Rostami et al. (2005) compared agitated draft tube reactor
128 with airlift reactor and measured lower hold-up and k_La values for the agitated draft tube geometry. They
129 also proposed different designs be tested in agitated draft tubes for air distribution as well as for agitation,
130 such as utilizing radial flow impellers instead of axial flow impellers that were used in their study. Lueske et
131 al. (2015) compared a stirred draft tube reactor with regular down pumping STR and measured higher k_La
132 but lower gas hold-up for the draft tube reactor at the same power input.

133 Ahamed and Vermette (2010) used an airlift reactor with and without agitation in the production of cellulases
134 with *Trichoderma reesei*. Their experiments yielded higher enzyme productivity and activity without
135 agitation, a result which they mainly accounted for morphological differences observed during the cultivation
136 with the two reactors. The axial impeller was located inside the draft tube which was the riser part of the
137 reactor and is therefore different from the examples described above in which the flow direction in the draft
138 tube is downwards. However, Bang et al. (1998) and Jesus et al. (2015) both reported improved mass transfer
139 performance when agitation was added to an airlift reactor with draft tube as the riser part. Jesus et al. (2015)
140 used highly viscous and non-Newtonian liquids and either radial or axial impeller and concluded that the
141 radial impeller performed better. Bang et al. (1998) also noted that the gas flow rate in airlift reactors

required for sufficient mass transfer and solids suspension is often much higher than stoichiometric requirements. Therefore, mechanical stirring could be an option if there is a need to reduce exhaust gas recirculation back to the reactor.

Table 1. Summary of agitated draft tube reactors in the literature

Flow direction in DT	Total number, type and positioning of the impeller(s)	Measured responses	Variables	correlation for $k_L a$	Reference
Up	1; axial (propeller) inside DT	Microbial growth and product formation	Agitation (on/off)	-	Ahamed and Vermette, 2010
Down	2; axial (hydrofoil) impellers inside DT	Gas hold-up, $k_L a$, liquid circulation	Agitation, gas flow, liquid viscosity	$\left[0.04387 - 1.598 \times 10^{-9} \left(\frac{P}{V}\right)^{2.67}\right] \times v_{s,riser}^{0.406[N-4.3609]^{0.3777}}$	Chisti and Jauregui-Haza, 2002
Down	2; axial (hydrofoil) impellers inside DT	Microbial growth	Draft tube (with/without)	-	Moo-Young et al., 1993
Down	1; axial (propeller) at the lower part of DT	Microbial growth, OUR, DO-heterogeneity, gas hold-up, $k_L a$, liquid circulation	Agitation, gas flow, H/T	-	Pollard et al., 1997
Down	2; axial (hydrofoil) impellers inside DT	Gas hold-up, $k_L a$	Agitation, gas flow, liquid viscosity	$5.6 \times 10^{-5} \left(\frac{P_{tot}}{V}\right)^{0.97}$	Rostami et al., 2005
Up	1; axial (propeller) or radial below DT	Gas hold-up, $k_L a$	Agitation, gas flow, liquid viscosity, impeller type	$0.02 \left(\frac{P}{V}\right)^{0.1} v_s^{1.42} g^{-0.21}$ (CMC) $0.02 \left(\frac{P}{V}\right)^{0.11} v_s^{0.99} g^{-0.08}$ (xanthan)	Jesus et al., 2015
Down	3; 2 axial (hydrofoil) impellers inside DT and a Rushton turbine below DT	Gas hold-up, $k_L a$, gassed power	Agitation, gas flow	$0.395 \times \left(\frac{P}{V\rho}\right)^{0.391} v_{s,riser}^{0.338}$	Lueske et al., 2015
Up	1; axial (propeller) at the lower part of DT	Gas hold-up, $k_L a$, liquid circulation	Agitation, gas flow, liquid viscosity, solid content	$3.1 \times 10^{-3} \left[\left(\frac{P}{V}\right)^{0.47} + \left(\frac{P_{gas}}{V}\right)^{0.81}\right]$	Bang et al., 1998
Down	2; 1 axial above DT and 1 radial below DT	$k_L a$	Agitation, gas flow, drag-reducing agent concentration	$1.222 \times \left(\frac{P + P_{gas}}{V}\right)^{0.5} v_s^{1.0}$	Kura et al., 1993

Agitated draft tube reactor in this study is Outotec OKTOP®9000 which is different compared to the previous ones used in microbial cultivations. The reactor type is originally developed for direct leaching of zinc concentrate and is now in use at production plants worldwide with reactor volumes ranging around 1000 m³. Gas to liquid mass transfer is an important issue also in hydrometallurgy since, due to low oxygen solubility and high oxygen demand, several hydrometallurgical operations are controlled by the rate of oxygen transfer from the gas to the aqueous phase. OKTOP®9000 reactor is designed to have high gas to liquid mass transfer capacity and good oxygen utilization efficiency with a relatively low agitation power. Therefore, this type of a reactor could also be suitable for fermentation processes that require high gas-liquid mass transfer capacity. Gas-liquid mass transfer studies in this type of a reactor have been published by Kaskiala (2005).

156 The OKTOP®9000 reactor (Figure 1) is agitated with a single impeller located just below the draft tube. The
 157 impeller disperses the gas that is introduced below it and induces recirculation through the draft tube so that
 158 the direction of flow is downwards inside the tube and upwards outside of it. This gas dispersion duty is very
 159 different compared to the other previously proposed agitated draft tube geometries in which the impeller is
 160 merely used for liquid pumping. The described geometry is compared to a standard stirred tank geometry
 161 utilizing three Rushton turbines in cell cultivation, mass transfer and gas hold-up experiments.

162 2 Materials and methods

163 2.1 Reactor geometries

164 The two reactor types were constructed in the same vessel by changing the inner structures. The reactor
 165 diameter ($T = 190$ mm) and liquid height ($H = 470$ mm) were the same for both geometries. The reference
 166 geometry was a STR equipped with three Rushton turbines whereas OKTOP®9000 is an agitated draft tube
 167 reactor in which the agitator is placed just below the draft tube. The geometries of both reactor types is
 168 presented in Table 2 and in Figure 1. Rushton geometry was equipped with four baffles and the draft tube
 169 geometry was designed so that the structures to attach the draft tube at the bottom part worked also as
 170 baffles up to the height of 125 mm. The impeller was placed at 75 mm clearance from the bottom so that the
 171 structure covered the impeller region and prevented vortex formation. There were three vertical structures
 172 with 120° angle between them. The impeller was placed as near to the draft tube as possible without a
 173 physical contact between the tube and the impeller. A distance of 1.8 cm from the end of the tube to the
 174 plate of the impeller was considered safe even with high agitation and aeration. The draft tube was attached
 175 to the reactor lid with two rods that extended 6 cm below the liquid surface.

176 Cell cultivation and mass transfer experiments were conducted in a Biostat C-DCU stainless steel bioreactor
 177 (Sartorius, Germany). The material used in the draft tube and related structures was also stainless steel. The
 178 gas hold-up measurements by electrical impedance tomography (EIT) were conducted in a separate,
 179 geometrically similar vessel made out of plastic (PMMA). To prevent the interference of structures with high
 180 electrical conductivity in the electrical measurements, plastic (PMMA and PVC) was used also for the draft
 181 tube and the related structures of this vessel. The impeller for the OKTOP®9000 geometry was 3d-printed
 182 from alumina reinforced plastic.

183 Table 2. Geometry of the two reactor types

	Rushton	OKTOP® 9000
T (mm)	190	190
H (mm)	470	470
D_i (mm)	75	73
C (mm)	75	75
S (mm)	150	-

184

D_{dt} (mm)	-	56
H_{dt} (mm)	-	360
B_w (mm)	15	20

Figure 1. Reactor geometries and dimensions, Rushton (left) and OKTOP®9000 (right)

2.2 Cell cultivation

Pichia pastoris X33 yeast was used in the cell cultivation experiments. It is a Crabtree negative yeast and therefore suitable for batch cultivation since high initial glucose concentration does not lead to fermentative metabolism of the cells. The batch process was chosen in order to maintain the liquid volume and height at a constant level during the cultivation. The yeast was maintained on YPD (Yeast extract, Peptone, Dextrose) agar plates and seed culture for inoculum was cultivated in a liquid YPD-medium.

The bioreactor cultivations were carried out in basal salt medium (BSM) supplied with PTM₁ trace salt solution (4.3 ml PTM₁ per 1 liter BSM). A detailed composition of the medium is listed in Table 3. The liquid

height for the cultivations was 470 mm, yielding a total volume of 12.45 liters. The BSM medium was sterilized in-situ in the reactor before adding the sterile-filtered PTM₁-solution. The sterilization sequence increases the temperature of the medium to 121 °C. Normally during sterilization the liquid is circulated at an agitation rate of 100 rpm to ensure adequate heat transfer between the liquid and the heat transfer jacket. However, since the OKTOP® impeller was 3d-printed from alumina enforced plastic, agitation was switched off at temperatures above 80 °C to prevent any deformation of the impeller blades due to softening of the material.

Ammonium hydroxide was used to control the pH during the cultivation. An antifoam agent (Antifoam 204, Sigma-Aldrich) was used for foam control. The level of dissolved oxygen (DO) was controlled by increasing the inlet air flow rate after DO reached the set point of 30 % of air saturation. In addition to regular DO-measurement from the side-port at the lower part (10 cm from the bottom) of the bioreactor, dissolved oxygen was measured also at 40 cm liquid level. Dissolved oxygen control was done based on the lower probe (Oxyferm FDA 120, Hamilton, Switzerland) and the higher probe (Visiform, Hamilton Switzerland) was for monitoring only. The Oxyferm probe was calibrated to 0 % during sterilization and to 100 % before inoculation when the cultivation medium was fully saturated with oxygen. Concentration of oxygen and carbon dioxide in the off-gas were measured with an Innova 1313 gas analyzer (LumaSense, Denmark).

Manual samples were taken during the fermentation to measure optical density (OD), cell dry weight (CDW) and glucose concentration. The optical density was measured at 600 nm wavelength and samples were diluted in MilliQ water to reach a measured absorbance value less than 0.8. For CDW and glucose measurements, 2 ml samples were centrifuged and the supernatant was removed for sugar analysis. The remaining cell pellet was suspended to 0.9 % NaCl solution, centrifuged again and the remaining liquid was discarded. Samples were then dried at 60 °C for 24 hours for the CDW measurement. All manual samples were made in triplicates.

Table 3. BSM and PTM₁ composition.

Basal Salt Medium			PTM ₁ Trace Salts		
Phosphoric acid (85 %)	24.0	ml/l	Copper sulfate (pentahydrate)	6	g/l
Calcium sulfate	0.93	g/l	Sodium iodide	0.08	g/l
Potassium sulfate	18.2	g/l	Manganese sulfate (monohydrate)	3	g/l
Magnesium sulfate (heptahydrate)	14.9	g/l	Sodium molybdate (dihydrate)	0.2	g/l
Potassium hydroxide	4.13	g/l	Boric acid	0.02	g/l
Glucose	40	g/l	Cobalt chloride	0.5	g/l
			Zinc chloride	20	g/l
			Ferrous sulfate (heptahydrate)	65	g/l
			Biotin	0.2	g/l
			Sulfuric acid	5	ml/l

2.3 Mass transfer experiments

Overall gas-liquid mass transfer coefficient ($k_L a$) was measured by gassing in / gassing out –experiments in the same reactor that was used in cell cultivation experiments. Prior to each experiment, the liquid was sparged with nitrogen to displace all dissolved oxygen. When DO had reached 0 %, agitation and nitrogen flow were stopped for a brief moment to let entrained gas bubbles escape before switching on agitation and air flow. Dissolved oxygen concentration was measured from two liquid levels, and $k_L a$ was calculated from the saturation phase. Same equipment was used as in cell cultivation experiments but the zero calibration for DO-probes was done by nitrogen displacement of oxygen.

Mass transfer experiments were done in 0.03 mol/l MgSO_4 solution to simulate similar coalescence behaviour as in the cultivation medium. MgSO_4 was also used in the cultivation medium with concentration higher than 0.03 mol/l but, according to (Kaskiala, 2005) the effect of MgSO_4 on bubble diameter is negligible with concentrations above 0.03 mol/l. This was confirmed by visual inspection of the gas hold-up, which increased up to this concentration but further addition did not increase hold-up with constant N and Q_g .

In mass transfer modelling, a perfectly mixed model was used for the liquid phase whereas a plug flow model was adopted for the gas phase (Pinelli et al., 2010). Values for $k_L a$ were estimated from the following equations:

$$\frac{\partial C_g}{\partial t} = \frac{v_s}{\varepsilon} \frac{\partial C_g}{\partial z} - \frac{k_L a}{\varepsilon} \left(\frac{C_g}{m} - C_l \right)$$

$$\frac{dC_{l,p}}{dt} = \frac{C_l - C_{l,p}}{\tau_r}$$

$$\frac{dC_l}{dt} = \frac{k_L a}{1 - \varepsilon} (\bar{C}^* - C_l)$$

$$\bar{C}^* = \frac{\bar{C}_g}{m}$$

Where C_g is the gas phase oxygen concentration, $C_{l,p}$ is the concentration of oxygen in the liquid phase measured by the DO-probe, C_l is the actual dissolved oxygen concentration, $\bar{C}^*$ is the saturation concentration of oxygen, ε is the gas hold-up, m is partition coefficient, and τ_r is the probe response time. Response time has been determined in an experiment where a step change in oxygen concentration was established by transferring the probe from nitrogen saturated liquid to oxygen saturated liquid with vigorous agitation. The value for response time of the lower probe is 15 s. Gas hold-up was estimated from the hold-up experiments described in the next section. A central difference scheme was used to transfer the partial differential equation for C_g to a series of ODEs. The differential equations were solved in Matlab (ode15s – solver), and the value for $k_L a$ was estimated using a nonlinear least squares method (lsqnonlin –routine in

247 Matlab) where the object function was the sum of squared residuals between measured values during the
248 saturation phase and the corresponding model values for probe reading. The experimental data used in the
249 parameter estimation was restricted to dissolved oxygen concentration < 98% of the saturation
250 concentration.

251 2.4 Measurement of local gas hold-up

252 Local values for gas hold-up were measured by electrical impedance tomography (EIT). The measurement
253 method is based on electrical conductivity of the dispersion and has previously been used for gas hold-up
254 measurements in a flotation cell as well as for the measurement of solids distribution in a stirred tank
255 (Kourunen et al., 2011; Tervasmäki et al., 2014). A total of 32 electrodes were distributed in 4 measurement
256 layers with 8 electrodes in each layer. Electrode layers were at heights of 4.5, 12.9, 25.5 and 33.9 cm from
257 the vessel bottom. From the 32 electrodes, 22 were current carrying electrodes and current injection was
258 made by a slightly modified opposite injection pattern with 14 current injections. The resulting potential
259 between all the adjacent electrodes were then measured. Amplitude in the current injection was 0.7 A at 10
260 kHz frequency.

261 Since the highest electrode layer was 13 cm lower than the unaerated liquid height, reconstruction mesh did
262 not reach this level but was restricted to 38.4 cm. The outer diameter of the draft tube was more than 30%
263 of the tank diameter and, therefore, the volume occupied by the draft tube was removed from the
264 reconstruction mesh. Other innards such as sparger, baffles and impellers were smaller and reference
265 measurement without gas inflow was considered adequate to account for their effect on the measurement
266 of conductivity distribution. The reconstruction meshes for both geometries are presented in Figure 2.

Figure 2. Reconstruction mesh in the EIT measurements. Black planes mark the vertical position of the impellers.

Tap water was used as the liquid medium and reference data with no gassing was measured with N below 200 rpm to prevent surface aeration. Reconstructed conductivity values were converted to gas volume fraction by following equation which is derived from Maxwell model with an assumption that dispersed phase conductivity is zero.

$$\varepsilon = \frac{\sigma_l - \sigma_m}{\sigma_l + 0.5(\sigma_m)}$$

Where σ_l is the conductivity of the liquid phase and σ_m is the measured conductivity (mS/cm). In addition to EIT-measurement, overall gas hold-up was measured visually as the difference between the dispersion height and ungassed liquid height. A slide caliper was used to measure the dispersion level at the wall of the transparent vessel during the EIT-measurements.

2.5 Power consumption of agitation

Power consumption of the agitator motor was estimated from the current and voltage data of the servomotor amplifier. Torque was estimated from the current data by using a manufacturer supplied parameter and agitation power was calculated by the following equation.

$$P = 2\pi MN$$

Where P is power (W), M is the torque determined from the current data (Nm) and N is the impeller revolution rate (s^{-1}). Losses caused by the bearings and mechanical seal were estimated as a function of revolution rate in empty reactor and subtracted from the measured value.

286 3 Results and Discussion

287 3.1 Cell cultivation

288 Online measurements and results from manual samples of the cell cultivation experiments are presented in
289 Figure 4 and Figure 3, respectively. Overall trend in the online measurements is very similar between the two
290 reactor geometries. For dissolved oxygen, a following differential equation can be written which accounts for
291 oxygen transfer rate (OTR) of the reactor and oxygen uptake rate of the cells (OUR).

$$292 \frac{dC_l}{dt} = OTR - OUR = k_L a (C^* - C_l) - OUR$$

293 Where C_l is the dissolved oxygen concentration C^* is the oxygen saturation concentration in the broth. OUR
294 of the cell culture depends on the cell mass, growth rate and the yield of cell mass per oxygen. In this type of
295 batch cultivation, OUR increases during the process mainly due to increase in the cell mass.

296 In the beginning, Q_g and N are maintained constant and also $k_L a$ can be considered constant and, therefore,
297 the only factor that affects OTR is the driving force ($C^* - C_l$). Since the number of cells increases and also the
298 growth rate of cells increase after a short adaptation phase, the oxygen uptake rate of the cell population
299 increases. This results in a decrease of dissolved oxygen concentration and set point for DO (30 %) is reached
300 within 9 hours after inoculation for both geometries. At this point, airflow is started to increase in order to
301 maintain the oxygen concentration at the set point level. During the increase of airflow, the two geometries
302 behave in a slightly different way. For the Rushton geometry, the DO-level at the upper probe increases while
303 DO at lower probe is constant. For the OKTOP® geometry, increasing flow rate has only a minor effect on DO-
304 levels at the upper probe. Some of these observations can be explained by the results from the mass transfer
305 and gas hold-up measurements and will be discussed later on.

306 Another noticeable difference in the online measurement data is the large variation of measurement values
307 in the OKTOP® geometry after the increase of airflow at about 10 hours. This can be noticed from both DO-
308 probes and off gas CO_2 measurements and, therefore, cannot be accounted only for measurement noise.
309 This also results in a sudden increase of Q_g to maximum level at 10 hours when DO suddenly drops below set
310 point. After reaching maximum value for Q_g , DO suddenly rises causing Q_g to decrease for a while before
311 rising back to maximum level.

312 For the lower DO-probe, it can be seen that DO-values are under 0% at the end of the fermentation. This is
313 probably a result from the calibration procedure in which the zero point was calibrated during sterilization
314 with temperature above 100 °C when oxygen solubility is zero. However, a significant amount (250 ml) of
315 28% ammonium hydroxide was added after the sterilization sequence to adjust pH to target level which was
316 5.0. This, with the fact that temperature compensation is done on a broad scale (100 °C during zero
317 calibration to 30 °C during fermentation), may have some effect on the measured values.

318 Depletion of glucose, which is used as a primary carbon and energy source by the cells can be detected in the
 319 rise of DO between 16 and 17 hours of cultivation. Fermentation with OKTOP® geometry was continued for
 320 a short moment after depletion of glucose and aeration was switched off and N was set to 200 rpm to prevent
 321 surface aeration. Even after depletion of glucose, the cells still consume some oxygen and, with OTR = 0,
 322 oxygen concentration dropped to -8.7% which is lower than the lowest value measured during the cultivation
 323 (-5.2%). It is also close to the lowest value that was recorded during the cultivation with Rushton geometry
 324 in which DO clearly reached a minimum value that was maintained for few hours. Therefore, it can be
 325 concluded that DO at the lower measurement point reached zero during the cultivations with Rushton
 326 geometry but some dissolved oxygen was remaining in the OKTOP® fermentations. At the higher
 327 measurement point DO did not reach zero in either case.

328 This result may imply similar phenomena as reported by Pollard et al. (1997) where they found more uniform
 329 DO distribution in agitated draft tube reactor although the reference case was a regular airlift reactor in their
 330 study. As will be shown in the mass transfer results, the overall mass transfer coefficient in the cultivation
 331 conditions at highest air flow rate is about 225 and 277 h⁻¹ for OKTOP (650 rpm) and Rushton (450 rpm)
 332 geometry, respectively. Thus, the characteristic times for mass transfer are 16 and 13 s. Mixing time for the
 333 Rushton geometry can be estimated by a correlation presented below (Rodgers et al., 2011) for a system of
 334 three Rushton turbines to be about 20 s. However, this should be considered only as an approximate value
 335 and it is very close to the characteristic time for mass transfer. Therefore, it can be stated that both the mass
 336 transfer and liquid circulation may have an effect on the DO distribution within the reactor.

$$337 \quad \theta_m = N^{-1} 5.2 N_p^{-1/3} \left(\frac{D}{T} \right)^{-2} \left(\frac{H}{T} \right)^{2.5}$$

338 Sugar consumption and cell growth can be seen from the manual samples taken during the fermentation in
 339 Figure 3. The samples follow similar trend with online measurements with little variation between the two
 340 geometries. Final cell dry weight is somewhat higher with the Rushton geometry. However, during the
 341 fermentation with OKTOP® geometry, occasional creaky noise was heard from the mechanical seal and
 342 inspection after the experiment revealed fouling of the seal. It may be that during sterilization sequence with
 343 no agitation, some components in the cultivation medium have burnt on the heating jacket, thus affecting
 344 the medium components.

Figure 3. Glucose concentration, optical density (OD) and cell dry weight (CDW) during the cultivations. Error bars are for 2 x standard deviation of triplicate samples.

Figure 4. Dissolved oxygen at 10 cm and 40 cm from reactor bottom, inlet gas flow rate and off gas CO₂ concentration during cell cultivations.

3.2 Power consumption

Measurements for power consumption were carried out during the hold-up experiment. Impeller power numbers and the effect of gas on the power consumption were estimated from this data for both reactor geometries. The following equation was used to correlate the power consumption with N and v_s .

$$P = (N_p - kv_s)\rho N^3 D_i^5$$

Where ρ is the liquid density (kg/m³), D_i is the impeller diameter (m), N is the impeller revolution rate (s⁻¹), v_s is the superficial gas velocity (m/s) and N_p and k are adjustable parameters. This is similar to the equation for power number but with an additional term $k^* v_s$ which decreases the power number with aeration. Coefficient values with 95% confidence intervals are listed in Table 4.

N_p represents the ungassed power number and the overall power number decreases with gassing depending on the value of k . The ungassed power number for three Rushton turbines is in accordance with literature values. The value of k describes how the power number drops with increasing gas flow rate and much higher values are found for the Rushton geometry even if scaled with N_p . Therefore, the gas-handling capacity of the OKTOP® impeller can be considered to be better of the two. However, the relation of gassed and ungassed power consumption is rather complex and cannot be fully described by the one parameter model presented here. It can still be considered applicable at the scale and operational ranges used in this study, and the power consumption values presented in the later sections are calculated by using this approach.

Table 4. Coefficients for power consumption estimation with 95 % confidence bounds.

Parameter (95% cb)	OKTOP®	3xRushton
N_p	2.09 (1.97, 2.22)	10.6 (10.0, 11.1)
k	33.8 (19.7, 47.8)	508 (421, 595)
R^2	0.99	0.98

3.3 Mass transfer

There was a slight overpressure in the reactor depending on the gas flow rate and the highest pressure was 300 mbar at the highest gas flow rate. Therefore, the saturation concentration for dissolved oxygen exceeded 100 % and was determined separately for each experiment from the measurement data.

Figure 5 shows dimensionless dissolved oxygen and off-gas concentrations during the saturation phase. For a constant agitation rate, it is clearly seen that the off-gas oxygen concentration increases more rapidly with increasing inlet gas flow rate. This can be expected since the gas phase residence time decreases with increasing flow rate and similar gas dispersion and recirculation capacity. However, there is a significant time delay and axial dispersion when gas exits the dispersion and flows through the head space and piping to the off-gas analyzer. Therefore, it should not be interpreted directly as the dispersed gas oxygen concentration.

Figure 5. Dimensionless dissolved oxygen and off-gas oxygen concentrations measured with OKTOP® geometry at constant N .

The measured dimensionless DO and off-gas O_2 concentration during saturation are plotted in Figure 6 with model values for DO, estimated DO-probe reading and the mean value of dispersed gas phase oxygen concentration. The fit of the model to the experimental DO-measurements is good, and the average R^2 -value of all measurements is 0.99. The effect of gas phase oxygen concentration on the $k_L a$ -estimation is best seen in subplots b and c with high gas flow and low/moderate agitation (b) and high agitation and low gas flow. In the former case, in which the estimated gas phase residence time is 3.6 s, the model predicted dispersed gas O_2 -concentration increases almost instantaneously to the inlet gas concentration whereas there is some delay in the latter case with longer gas residence time (8.5 s). Although the time delay is still quite small, the assumption of constant O_2 concentration for the dispersed gas equal to inflowing gas O_2 (no depletion model) results in 11% lower $k_L a$ -value. In the case of shorter gas residence time, no depletion model and plug flow model for gas phase both give the same value for $k_L a$.

The values for $k_L a$ are also sensitive to the response time, and values fitted to a model with no response time are plotted in Figure 7. The lowest $k_L a$ -values are similar for both cases, and the relationship is almost linear up to 0.04 s^{-1} . At higher $k_L a$ -values when the inverse of $k_L a$ approaches the value of response time, the deviation becomes large and nonlinear. The estimation of $k_L a$ was done with a constant value for response time. In these experimental conditions, mixing is assumed to be adequate to minimize any additional diffusion resistance between the DO-probe membrane and bulk fluid. Varying response time may become an issue if measurements are made at low agitation rates or in very viscous fluids.

400 Figure 6. Saturation phase DO and off-gas O_2 measurements and model values (dimensionless) with Rushton geometry.

Figure 7. Effect of probe response time on the value of $k_L a$.

Mass transfer coefficients for both geometries and four gas flow rates as a function of N are plotted in Figure 8. $k_L a$ increases with agitation and aeration although the effect of gas flow rate is rather small at the lowest agitation rates for both geometries. Gassed power consumption was estimated by the equation presented earlier and the mass transfer coefficient for both geometries and three gas flow rates are plotted in Figure 9. When the agitation power is low (< 500 W/m³), the measurements at a constant gas flow rate are at the same range regardless of the geometry. With increasing agitation power, however, the $k_L a$ values measured by OKTOP®9000 geometry are higher at similar power consumption. It also seems that the difference arises at lower power consumption when the air flow rate is low (6.5 l/min). However, when the agitation rate is increased excessively (> 4000 W/m³) with $v_s = 0.006$ m/s, the increase in $k_L a$ is small for both geometries. Unfortunately, higher gas flow rates could not be used at the highest agitation rates due to excessive increase in the gas hold-up.

The measured $k_L a$ -values were also fitted to correlation functions presented in Table 1. The best fit was for the type of equation used by Lueske et al. (2015) which is very similar to the equations used with traditional stirred tanks but with superficial gas velocity calculated based on the riser cross sectional instead of the reactor cross sectional area. To compare also the traditional STR, a following equation was used to fit the $k_L a$ -data with P/V and v_s as variables:

$$k_L a = \alpha \left(\frac{P}{V} \right)^\beta v_s^\gamma$$

The parameters α , β and γ are presented in Table 5 for different scenarios. First, the parameters were fitted separately for both geometries. The largest variation was on the parameter α which should be strongly dependent on the liquid phase properties rather than the geometry of the system (Doran, 2012). Therefore, the parameters were also fitted for both geometries simultaneously and this value was used to estimate β and γ for both geometries separately with α fixed at 0.452. The experimental data can be fitted satisfactorily with the traditional correlation but the identification of the parameters remain poor. This is especially true for α for which the lower 95% confidence interval is negative when the parameters are estimated from the measurements with OKTOP®-geometry. Furthermore, in order to reliably capture the effect of scale-independent values for operating conditions (v_s and P/V and their exponents), measurements should be done in more than one scale.

Table 5. $k_L a$ -correlation parameters fitted separately for each geometry, together for both geometries and separately for both geometries with fixed value for parameter A

Data used in fitting	α (95% CI)	β (95% CI)	γ (95% CI)	R^2
Rushton	0.416 (0.0618 0.770)	0.297 (0.209 0.385)	0.733 (0.549 0.917)	0.856
OKTOP®	0.343 (-0.124 0.811)	0.373 (0.252 0.494)	0.778 (0.530 1.03)	0.846
Rushton&OKTOP®	0.457 (0.111 0.804)	0.314 (0.242 0.386)	0.766 (0.612 0.920)	0.824
Rushton	0.457 (fixed)	0.295 (0.213 0.378)	0.749 (0.626 0.872)	0.856
OKTOP®	0.457 (fixed)	0.364 (0.259 0.470)	0.823 (0.672 0.975)	0.845

Figure 8. $k_L a$ as a function of agitation and different gas flow rates. OKTOP®9000 (left) and Rushton geometry (right).

Figure 9. $k_L a$ as a function of measured power consumption for three gas flow rates. Dashed (OKTOP®9000) and dotted (Rushton) lines are fitted using the parameter values in Table 5 with fixed value for α ($\alpha = 0.457$) and separately estimated values for β and γ .

3.4 Gas hold-up

Average measurement values during 20 s of data collection in a steady state was used to calculate the hold-up values. The estimation of local gas hold-up was calculated from the three-dimensional conductivity distribution measured by EIT as described in previous sections. Thus, the gas hold-up was obtained in the three-dimensional tetrahedral mesh (Figure 2). An example of average gas hold-up during measurements with both geometries at constant gas flow rate and increasing agitation is presented in Figure 10 with isosurfaces covering hold-up values 3, 5, 7.5, 10 and 12.5%. For OKTOP®9000 at low agitation, the highest hold-up values are found around the impeller near the draft tube and below the impeller. Visually this corresponds to a situation in which the impeller speed is just adequate to disperse the gas so that it does not flood the impeller and flow into the draft tube but is dispersed to the annulus region. Only by increasing the agitation the inflowing gas is properly circulated towards the reactor walls and lower parts of the reactor. For the multiple Rushton agitated reactor, the highest hold-up values are first found from the upper part of the reactor whereas increasing the agitation makes the gas recirculate also at the lower part.

451 Figure 10. Isosurfaces of 3, 5, 7.5, 10 and 12.5 % hold—up for both geometries at $Q_g=18$ l/min ($v_s=0.011$ m/s). Isosurfaces with highest
452 hold-up value are filled with values larger than 12.5 %.

453 Overall hold-up was calculated from the EIT-measurements by volume averaging the hold-up values over the
454 tetrahedral mesh. Overall hold-up is plotted as a function of visually measured hold-up in Figure 11. It should

455 be noted that the EIT-measurement covered liquid heights up to 384 mm whereas the original liquid height
 456 was 470 mm. In the case of OKTOP®9000 geometry, the EIT-measurement covered only the annulus of the
 457 draft tube section whereas visually measured overall hold-up accounts for both inside and outside of the
 458 draft tube. However, the total volume of the draft tube is small (<10 %) compared to the volume of annulus
 459 and bottom part of the reactor.

460 The overall hold-up measured by EIT is plotted as a function of agitation for different gas flow rates and both
 461 geometries in Figure 12, and hold-up vs. power consumption is plotted in Figure 13. It can be clearly seen
 462 that the overall hold-up as a function of power consumption is very similar to both reactor geometries. Only
 463 at high gas flow rates, higher overall hold-up is detected for the Rushton geometry. This quite different from
 464 the overall mass transfer coefficient as higher k_La -values were measured with OKTOP®9000 with similar
 465 power input and gassing rates. In addition, more uniform dissolved oxygen concentration profile was
 466 measured during the fermentation with the draft tube geometry. The reason for this and the better mass
 467 transfer performance of the draft tube geometry may partly be explained by high energy dissipation rate at
 468 the mixer region and efficient liquid circulation through the draft tube.

469
 470 Figure 11. Overall hold-up determined from EIT-measurement and visually measured hold-up.
 471

Figure 12. Hold-up vs. N for OKTOP® (left) and Rushton geometry (right) for different superficial gas velocities.

Figure 13. Hold-up vs. calculated power consumption for both geometries and different gas flow rates.

Figure 14 and Figure 15 present contour maps in which the hold-up values in z - r plane were calculated as an average of 20 evenly distributed angular coordinates. For the OKTOP® geometry, it can be seen that increasing the impeller revolution rate at a constant gas flow rate the gas hold-up shifts more towards the lower part of the vessel. Furthermore, especially at lowest N and highest Q_g (450 rpm and 25 l/min), the impeller does not disperse the gas as desired and most of the gas flows upwards in the inner part of the

annulus just outside the draft tube. With higher impeller revolution rates, the gas is also recirculated to lower parts of the vessel below the impeller. A similar trend can be seen for the Rushton turbine – the poorest gas dispersion is at highest Q_g and lowest N (25 l/min and 310 rpm, Figure 14) when the lowest impeller was flooded. This can be seen as low hold-up values at heights below the lowest impeller near the reactor wall.

The two geometries differ quite significantly in the axial distribution of the dispersed gas. For the OKTOP® geometry, the highest hold-up values are in the lower parts of the vessel near the impeller. The highest hold-up values for three Rushton turbines are detected at top part of the vessel except for the lowest gas flow rate at 830 rpm and 10 l/min. Only at this situation can a completely dispersed regime be assumed.

Overall mass transfer coefficient and gas hold-up are largely affected by the same parameters, N and Q_g . Both measured parameters are plotted in Figure 16 in which a clear correlation can be seen for both geometries. It should be noted that the EIT-measurements for hold-up and mass transfer measurements were made in different liquid phase, tap water and 0.03 mol/l $MgSO_4$ solution, respectively. Therefore, direct estimation of k_La from the measured hold-up is not straightforward since hold-up during mass transfer experiments has been higher because of non-coalescing liquid and smaller bubble size.

From the hold-up contours (Figure 14 and Figure 15), it can be concluded that the hold-up distribution is more uniform with the traditional STR geometry agitated with three Rushton turbines. Also the local mass transfer coefficient is expected to be more uniformly distributed with this geometry compared to the draft tube agitated with a single impeller. However, the dissolved oxygen profile during the fermentation was more uniform with the OKTOP®9000 reactor and also higher overall k_La -values were measured with similar agitation power and gas flow rates.

We suggest that this could be explained by enhanced liquid circulation with the draft tube and the fact that the mass transfer rate is very high at the bottom of the reactor near the impeller. This is also the location at which air introduced into the reactor and, during fermentation, the gas bubbles are continuously depleted from oxygen as they move upward in the reactor. Therefore, the driving force for mass transfer at upper impellers in the Rushton geometry is smaller although local k_La -values are high near the impellers. In the OKTOP® geometry, high local k_La -values are in the same region where air is introduced and also the driving force is high. In fact, if the proposed mechanisms are significant factors in the observed phenomena, it is expected that the differences would increase in larger scale due to hydrostatic pressure which increases the oxygen solubility at the bottom and further the driving force for mass transfer. Further studies in larger scale and with the usage of CFD and other more detailed modelling approaches are being planned to test these hypotheses.

513 Figure 14. Local gas hold-up contour plots with $Q_g = 25$ l/min OKTOP®9000 (upper figures) and Rushton (lower figures). Agitation
514 power is estimated from equation presented earlier.

Figure 15. Local gas hold-up contour plots with $Q_g = 10$ l/min OKTOP®9000 (upper figures) and Rushton (lower figures). Agitation power is estimated from equation presented earlier.

Figure 16. k_La vs. overall gas hold-up.

4 Conclusions

Higher k_La values were achieved with similar agitation power input in OKTOP®9000 reactor compared to STR. This suggests that the OKTOP®9000 reactor attains higher mass transfer efficiency. At least partial explanation may be high energy dissipation at the impeller region with high gas hold-up and better recirculation and bulk mixing in the draft tube reactor. For further studies, more detailed modelling of the gas and liquid flow in k_La -estimation could be beneficial, especially if results from different scales are to be compared.

Gas hold-up distribution was measured by EIT and an overall value was measured visually. Overall values calculated from the EIT-measurements correlated well with the visually measured values, and the overall hold-up was rather similar for both geometries when compared in terms of power consumption. However, 2D and 3D figures from the EIT-measurements reveal significant differences in the hold-up distribution. These can be used to compare local conditions between different geometries as well as to distinguish different flow regimes depending on the agitation and gas flow rate.

Both geometries were suitable for cell cultivations but the problems with cultivation medium, possibly related to sterilization without agitation, made it difficult to directly compare the results in cell yield. Additional studies of liquid mixing time could reveal differences in bulk liquid mixing and the effect of gas on it. Flow pattern in the OKTOP®9000 geometry is well defined compared to multiple Rushton geometry and

536 recirculation should be efficient. At least the uniformity of dissolved oxygen was better in the agitated draft
537 tube geometry.

538 A fermentation process with high oxygen demand and sensitivity to environmental gradients (dissolved
539 oxygen, nutrients) could also reveal more differences between reactor geometries. In previous literature,
540 agitated draft tubes have been found to be very efficient in mycelial cultivations with high viscosity and
541 pseudoplastic rheology and in baker's yeast production where more uniform DO was achieved to enhance
542 oxygen uptake of the cells. These reactor geometries and agitators have been different from the draft tube
543 geometry used in this study.

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