

# Optimisation of agitation and aeration in fermenters

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**Abstract** The problem of optimising agitation and aeration in a given fermenter is addressed. The objective function is total electric power consumed for agitation, compression and refrigeration. The major constraint considered is to ensure that the dissolved oxygen concentration is above the critical value. It is shown that it is possible to analytically calculate the optimal pair (air flowrate, stirrer speed) and that, at least for the industrial antibiotics fermentation used as case-study, the optimum lies within a window for satisfactory operation, limited by other possible constraints to the problem. Savings achievable by optimal operation as compared with current industrial procedure were found to be around 10% at pilot plant scale (0.26 m<sup>3</sup>) and 20% at full scale (85 m<sup>3</sup>).

## List of symbols

A	fermenter cross sectional area (m <sup>2</sup> )	$n^*$	number of impellers
C	dissolved oxygen concentration (mole m <sup>-3</sup> )	N	rotation speed (s <sup>-1</sup> )
C*	DO concentration in equilibrium with the gas (mole m <sup>-3</sup> )	$N_F$	rotation speed at flooding (s <sup>-1</sup> )
$C_{crit}$	critical DO concentration (mole m <sup>-3</sup> )	$N_p$	unaerated power number
$C_p$	specific heat of air at constant pressure (J kg <sup>-1</sup> K <sup>-1</sup> )	$N_{pg}$	aerated power number
$C_{sp}$	dissolved oxygen set point (mole m <sup>-3</sup> )	OUR	Oxygen Uptake Rate (mole m <sup>-3</sup> s <sup>-1</sup> )
$C_v$	specific heat of air at constant volume (J kg <sup>-1</sup> K <sup>-1</sup> )	$p_0$	atmospheric pressure (N m <sup>-2</sup> )
D	agitator diameter (m)	$p_1$	compressor exit pressure (N m <sup>-2</sup> )
f	pressure correction of air flow-rate	$p_2$	pressure at the bottom of the fermenter (N m <sup>-2</sup> )
$(Fl_g)_F$	aeration number at flooding	$p_3$	pressure at the top of the fermenter (N m <sup>-2</sup> )
$(Fr_g)_F$	froude number at flooding	$P_c$	compression power (W)
k	coefficient in expression for mass transfer coefficient	$P_d$	power added by expansion (W)
$K_L a$	volumetric oxygen transfer coefficient (s <sup>-1</sup> )	$P_{ev}$	power removed by evaporation (W)
m	power exponent in expression for mass transfer coefficient	$P_g$	agitation power (W)
n	gas flow rate exponent in expression for mass transfer coefficient	$P_m$	power added by metabolism (W)
		$P_r$	power removed by refrigeration (W)
		$P_t$	total power (W)
		Q	air flow-rate at atmospheric conditions (m <sup>3</sup> s <sup>-1</sup> )
		$Q_f$	air flow-rate at average fermenter conditions (m <sup>3</sup> s <sup>-1</sup> )
		$s_0$	absolute humidity at atmospheric conditions
		$s_3$	absolute humidity at fermenter exit
		T	tank diameter (m)
		V	liquid volume (m <sup>3</sup> )
		$v_s$	gas superficial velocity (m s <sup>-1</sup> )
		$\alpha_i$	parameter defined in the text
		$\beta$	safety margin for dissolved oxygen (mole m <sup>-3</sup> )
		$\gamma$	ratio of specific heats of air
		$\eta_g$	agitation efficiency
		$\eta_c$	compression efficiency
		$\eta_r$	refrigeration efficiency
		$\rho$	liquid density (kg m <sup>-3</sup> )
		$\rho_g$	air density (kg m <sup>-3</sup> )
		$\lambda$	latent heat of vaporisation of water (J kg <sup>-1</sup> )

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## 1

### Introduction

Energy is a major cost in aerobic fermentations. Energy is consumed in agitation, air compression and refrigeration. A first stage in fermenter energy optimisation is through geometry, in particular through appropriate agitator choice. This subject has received considerable attention in the literature, both scientific and commercial.

Once fermenter geometry has been fixed, however, a second stage in energy minimisation is still possible, namely through optimal operation of agitation and aeration. The idea is to find the pair (air flow rate, agitation speed) that will correspond to



a minimum total energy cost, while satisfying any constraints related either to fermenter capacity or to the proper running of the fermentation. Usually, the constraint which affects the optimisation problem is the requirement to maintain dissolved oxygen concentration above a critical value, below which microorganism productivity decreases.

This optimisation problem has been almost completely neglected in the literature. Recently, however, Singh<sup>1</sup> and Singh et al.<sup>2</sup> devised a control algorithm, in which air flow rate and stirrer speed are varied according to a simplex method for  $OTR/P_i$  minimisation, where  $OTR$  is the oxygen transfer rate and  $P_i$  is the sum of dissipated agitation and gas expansion power. An alternative optimal control algorithm was developed by Shields and Kao.<sup>3</sup> This algorithm is quicker, since it uses knowledge of the system to manipulate agitation speed in order to approach the dissolved oxygen constraint. Minimum total power is found by Fibonacci search on a second variable, the aeration number, from which the air flow rate can be calculated.

Neither of these research groups, however, deals with the optimisation problem for a given set of conditions. Although fermentations are dynamic, optimisation may be useful in establishing targets and improving fermenter operating procedures without advanced bi-variable computer control.

## 2 Theory

### 2.1 Power (objective function)

The total electrical power consumed in a fermenter is the sum of three components:

$$P_t = \frac{P_g}{\eta_g} + \frac{P_c}{\eta_c} + \frac{P_r}{\eta_r} \quad (1)$$

$P_g$ ,  $P_c$ , and  $P_r$  are respectively the useful power dissipated in agitation, air compression and refrigeration.  $\eta_g$ ,  $\eta_c$  and  $\eta_r$  are the corresponding global efficiencies.

The power required for agitation under aeration,  $P_g$ , is assumed to be given by:

$$P_g = \sum_i^{n^*} N_{pgi} \cdot \rho \cdot N^3 D^5, \quad (2)$$

where  $D$  is the stirrer diameter,  $N$  is the stirring speed, and  $\rho$  is the liquid density. The aerated power number of the  $i$ th turbine,  $N_{pgi}$ , depends mainly on the stirrer unaerated power number,  $N_p$ , and on the actual air flowrate,  $Q_i$ :<sup>4</sup>

$$N_{pgi} = N_p \cdot F_i(Q_f) = N_p \cdot F_i(Q \cdot f), \quad (3)$$

where  $Q$  is the air volumetric flow rate at standard conditions,  $f$  is the respective correction factor for temperature and pressure and  $F_i$  is some function which depends on geometry.

If compression power,  $P_c$ , is assumed to be adiabatic, we shall have:

$$P_c = \alpha_1 \cdot Q, \quad (4)$$

with

$$\alpha_1 = \frac{\gamma}{\gamma - 1} P_0 \left[ \left( \frac{p_1}{P_0} \right)^{(\gamma-1)/\gamma} - 1 \right], \quad (5)$$

where  $P_0$  is the atmospheric pressure,  $p_1$  is the compressor outlet pressure, and  $\gamma = C_p/C_v = 1.4$  for air compression.

Refrigeration power is the sum of four terms:

$$P_r = P_m + P_g + P_d - P_{ev}, \quad (6)$$

On the one hand, refrigeration has to remove the power input due to metabolism,  $P_m$ , due to agitation,  $P_g$ , and due to the isothermic expansion of air bubbles as they rise in the fermenter,  $P_d$ , given by:

$$P_d = \alpha_2 \cdot Q, \quad (7)$$

with

$$\alpha_2 = f \cdot p_2 \cdot \ln \left( \frac{p_2}{p_3} \right), \quad (8)$$

where  $p_2$  and  $p_3$  are pressures at the bottom and the top of the fermenter, respectively.

Refrigeration is helped, on the other hand, by evaporative cooling, as the air stream becomes saturated with water vapour at fermentation temperature, hence the negative sign in Eq. (6), affecting  $P_{ev}$ , given by:

$$P_{ev} = \alpha_3 \cdot Q, \quad (9)$$

with

$$\alpha_3 = \rho_g \lambda \cdot (s_3 - s_0), \quad (10)$$

where  $\rho_g$  is the gas density at standard conditions,  $\lambda$  is the latent heat of vaporisation of water, and  $s_3$  and  $s_0$  are the absolute humidities of air at the top of the fermenter and at atmospheric conditions, respectively.

### 2.2 Oxygen concentration (major constraint)

The dissolved oxygen concentration,  $C$ , has to be kept above the critical concentration,  $C_{crit}$ . The constraint to the problem is, therefore:

$$C \geq C_{crit}. \quad (11)$$

Since power increases with  $C$  both at constant  $N$  and at constant  $Q$ , this is equivalent to:

$$C = C_{sp} = C_{crit} + \beta, \quad (12)$$

where  $C_{sp}$  is the dissolved oxygen set point and  $\beta$  is a safety term.  $C$  can be calculated from a steady state oxygen balance:

$$OUR = K_L a (C^* - C), \quad (13)$$

where  $OUR$  is the oxygen uptake rate,  $K_L a$  is the volumetric global mass transfer coefficient and  $C^*$  is the DO concentration in equilibrium with the gas. For the sake of mathematic simplicity,  $C^*$  is assumed to be independent of  $Q$ , which is a reasonable assumption, except when very low values of air flowrate coincide with high values of  $OUR$ . Only then does oxygen depletion in the air become significant.



The volumetric global mass transfer coefficient is assumed to be given by the usual type of correlation:

$$K_L a = k \left( \frac{P_g}{V} \right)^m (v_s)^n = k \left( \frac{P_g}{V} \right)^m \left( \frac{Q \cdot f}{A} \right)^n, \quad (14)$$

where  $V$  is the fermenter volume,  $A$  is the fermenter cross-sectional area,  $v_s$  is the superficial velocity.  $k$ ,  $m$  and  $n$  are parameters which depend mainly on broth properties<sup>5,6</sup>.

### 2.3 Optimisation

The desired optimisation corresponds to a minimisation of total power,  $P_t$ , given by Eqs. (1)–(10), subjected to the constraint, Eq. (12). Minimum total power corresponds to:

$$\frac{dP_t}{dQ} = \frac{d(P_g/\eta_g + P_c/\eta_c + P_r/\eta_r)}{dQ} = 0. \quad (15)$$

$P_c$  and  $P_r$  may be replaced as functions of  $Q$  using Eqs. (4)–(10), taking into account also that  $P_m$ , the power due to metabolism, does not vary with  $N$  or  $Q$ .  $P_g$ , on the other hand, may be eliminated as a function of  $Q$ , using the constraint, through Eqs. (12), (13) and (14), as follows:

$$P_g = \alpha_4 Q^{-n/m}, \quad (16)$$

with

$$\alpha_4 = V \left[ \frac{K_L a}{k} (A/f)^n \right]^{1/m}, \quad (17)$$

and

$$\frac{K_L a}{k} = \frac{OUR/k}{(C^* - C_{sp})}. \quad (18)$$

Thus Eq. (15) becomes an equation which can be solved for  $Q$  as the single unknown, yielding an optimal value of air flowrate of:

$$Q_{opt} = \left( \frac{\alpha_1 + \alpha_2 - \alpha_3}{n \cdot \alpha_4} \times \frac{\eta_c + \eta_r}{1/\eta_g + 1/\eta_r} \right)^{-m/(n+m)}. \quad (19)$$

The corresponding optimal value of agitation power,  $P_{gopt}$ , may then be obtained from Eq. (16) and then  $N_{opt}$  can be determined combining Eqs. (2) and (3), and solving for  $N$ .

### 2.4 Representation of operating states and constraints

A map of the possible states of a given fermenter with a particular broth can be drawn in a  $N$  vs.  $Q$  space, since  $N$  and  $Q$  are the only independent variables of interest. In this space, one can plot, eg, iso-power curves, iso-oxygen curves, the optimum operating point, and constraints to the problem.

Iso-power curves are curves of constant  $P_t$ , given by Eq. (1). The terms on the right hand side may all be expressed as a function of  $N$  and  $Q$ , yielding an equation which may be solved for  $N$  as a function of  $Q$ . Iso-oxygen curves may similarly be determined by fixing  $C$  in Eq. (13) and then combining and manipulating Eqs. (13), (14), (2) and (3). Typical iso-power and iso-oxygen curves are shown in Figs. 1 and 2.

Besides minimum acceptable DO, there are other constraints which set allowable limits to  $N$  and  $Q$ . Although Eq. (12) is usually the constraint which affects the optimisation problem, it is conceivable that, in certain cases, one of the other constraints may be the one determining the optimisation result. These may include, for example: (i) installed compressor capacity, (ii) maximum installed stirrer speed; (iii) maximum tip speed before damage to fragile cells occurs; (iv) maximum allowable dissolved  $\text{CO}_2$  concentration; (v) minimum stirrer speed for acceptable mixing; (vi) avoidance of flooding of the (lowest) turbine; (vii) minimum heat transfer coefficient allowable. In some cases, these may have to be plotted on the  $N$  vs.  $Q$  graph to see whether they may interfere with the optimisation exercise.

## 3 Results and discussion: A case study

Fermentation of a strain of *Streptomyces Aureofaciens* for the production of demethylchlortetracycline is used as a case study. Two scales of operation are considered, 0.26 m<sup>3</sup> and 85 m<sup>3</sup>, corresponding to actual pilot plant and full scale fermentations. Equations were solved using a spread-sheet.

### 3.1 Pilot-plant scale

The pilot plant fermenter is fully baffled and has 0.26 m<sup>3</sup> useful capacity. It has an aspect ratio of 1, and a single Rushton turbine with half the tank diameter and a clearance from bottom of  $T/3$ .

Parameters used in the equations are shown in Table 1.  $OUR$  and  $K_L a$  data were determined using techniques described elsewhere.<sup>7</sup> Measured  $OUR$  in the production stage of the fermentation varied in the range 6 to 18 g m<sup>-3</sup> min<sup>-1</sup>. The reference value used in this case study is a high value, typical of the beginning of the production stage. The critical dissolved oxygen value is a tentative one, even if it was based on data from about 20 pilot-plant fermentations at various oxygen concentrations. No safety margin,  $\beta$ , was added. The value of  $C^*$  used corresponds to 90% saturation of the liquid by air at average fermenter pressure. The function in Eq. (3) for this particular geometry was experimentally determined, as:

$$F = N_{pg}/N_p = 0.44 + 0.56 \cdot \exp(-569 \cdot Q \cdot p_0/p_2). \quad (20)$$

Figure 1 shows iso-oxygen and iso-power curves obtained for this system using the reference parameters from Table 1. The optimum, as calculated using Eq. (19), is shown. It corresponds to a tangent of the critical iso-oxygen curve with some iso-power curve, and can therefore be visually estimated as well.

The determined optimum pair  $(Q, N)_{opt}$  is a reasonable operating point, well within aeration and agitation capacities of this system ( $Q_{max} = 0.009 \text{ m}^3 \text{ s}^{-1}$  and  $N_{max} = 6 \text{ s}^{-1}$ ). It corresponds to slightly over 1 vvm and a stirring speed a little lower than the usual operating speed, hence no damage to cells is expected (*Streptomyces* cells are not very fragile, anyway). Mixing time, which varies with the reciprocal of the stirrer speed, will still be acceptable, and heat transfer limitations are not expected. The constraint posed by flooding of the turbine is



Table 1. Parameters used in the case-study (SI units)

Parameters	Pilot scale (0.26 m <sup>3</sup> )	Industrial scale (85 m <sup>3</sup> )	Observations
<b>Biological:</b>			
OUR	8.2 × 10 <sup>-3</sup>	*	experimental
C <sub>crit</sub>	0.119	* 76	experimental
<b>Geometrical</b>			
D	0.35	1.24	
n*	1	3	
N <sub>p</sub>	4.4	5	experimental
T	0.7	3.4	
V	0.26	85	
<b>Mass transfer</b>			
k	1.7 × 10 <sup>-3</sup>	*	experimental
m	0.58	*	experimental
n	0.39	*	experimental
<b>Operational</b>			
C*	0.375	0.484	calculated (see text)
p <sub>0</sub>	1.0 × 10 <sup>5</sup>	1.0 × 10 <sup>5</sup>	
p <sub>1</sub>	3.0 × 10 <sup>5</sup>	3.0 × 10 <sup>5</sup>	
p <sub>2</sub>	1.6 × 10 <sup>5</sup>	2.5 × 10 <sup>5</sup>	
p <sub>3</sub>	1.5 × 10 <sup>5</sup>	1.5 × 10 <sup>5</sup>	
s <sub>0</sub>	0.0215	0.0215	assumed
s <sub>3</sub>	0.0072	0.0072	saturation, 25 °C
β	0	0	assumed
η <sub>g</sub>	0.7	0.7	assumed
η <sub>c</sub>	0.7	0.7	assumed
η <sub>r</sub>	4	4	assumed
<b>Physical properties</b>			
ρ	1000	1000	
ρ <sub>g</sub>	1.2	1.2	
λ	2.4 × 10 <sup>6</sup>	2.4 × 10 <sup>6</sup>	
γ	1.4	1.4	

\*assumed the same as pilot

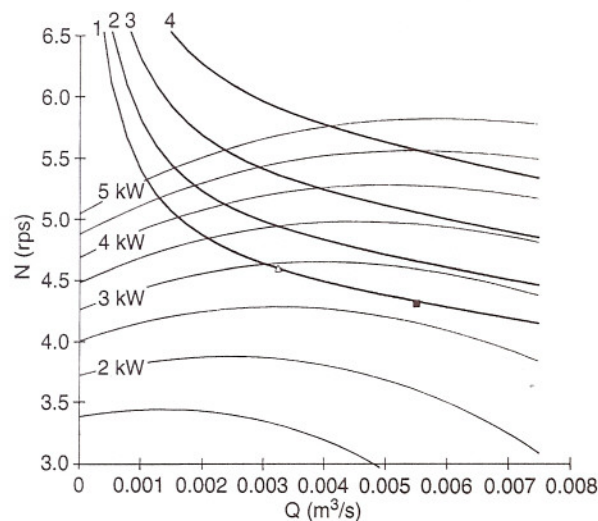


Fig. 1. Map of dissolved oxygen and total power as a function of air flowrate and stirrer speed for the 0.26 m<sup>3</sup> fermenter. (■ -optimal operation; ▲ -typical operation; iso-oxygen curves in bold: 1 - 0.12 mol m<sup>-3</sup>; 2 - 0.15 mol m<sup>-3</sup>; 3 - 0.18 mol m<sup>-3</sup>; 4 - 0.21 mol m<sup>-3</sup>)

not easy to establish, since there are no general correlations for shear thinning broths. A correlation for water is:<sup>8</sup>

$$(FL_g)_F = 30 \cdot (D/T)^{3.5} (Fr)_F, \tag{21}$$

where (FL<sub>g</sub>)<sub>F</sub> and (Fr)<sub>F</sub> are, respectively, the aeration and the Froude numbers at flooding. This corresponds to a relationship between N and Q. According to this correlation, flooding is not a problem (minimum N to avoid flooding is always below 2 s<sup>-1</sup> within the range of air flow rates of interest).

Figure 1 also shows that the single variable oxygen control used in current industrial practice may keep the system far from the energy optimum, since any point along the critical iso-oxygen curve satisfies the DO set point, with varying total power requirement. The factory procedure for control of this fermentation, for example, was to set a constant stirrer speed at 275 rpm (related to some tip speed recommendation) and leave air flowrate as the manipulated variable. If the DO set point is the critical value, then the operating point using factory procedure with single variable control is the other point shown in the figure. Optimization would therefore lead to savings of about 10% in power.

### 3.2 Full industrial scale

The full scale fermenter is fully baffled (banks of tubes) and has 85 m<sup>3</sup> useful capacity. It has an aspect ratio of 3, and three Rushton turbines, with spacing equal to D, and a clearance from bottom of T/3. Turbine and tank diameters are shown in Table 1, as well as other parameters used in Eqs. (1)–(19). OUR and critical oxygen, being related to the microorganism, are assumed to be fermenter independent, and hence the values determined in the pilot plant are used. The correlation used for K<sub>L</sub>a is also the same as the one determined in the pilot plant, as its parameters depend mainly on broth properties.<sup>5,6</sup> The value of C\* used corresponds to 90% saturation of the liquid by air at average fermenter pressure. The aerated power numbers, for this particular geometry were determined using the following assumptions: (i) The form of the function in Eq. (3) for the bottom turbine is as in Eq. (20); (ii) the two constants in the expression for the bottom turbine were determined by fitting to values of P<sub>g</sub>/P obtained using Warmoeskerken's correlations<sup>9</sup> for a typical operating value of N = 1.67 s<sup>-1</sup>; (iii) the equation thus obtained for the bottom turbine is independent of N; (iv) the two upper turbines suffer a power reduction half of that of the lowest turbine. The following relationship was obtained for P<sub>g</sub>:

$$P_g = [0.90 + 2.1 \cdot \exp(-7.32 \cdot Q \cdot p_0/p_2 \cdot)] \cdot N_p \cdot \rho \cdot N^3 D^5. \tag{22}$$

Results are shown in Fig. 2. Optimum operating conditions are compared with operating conditions at typical fixed operating speed. Power savings achievable are of the order of 20%.

As in the case of the pilot plant, the optimal (Q, N)<sub>opt</sub> is still a reasonable operating point. It corresponds to 0.3 vvm and a stirring speed a little lower than the usual operating speed, well within the system capacities for aeration and agitation. The constraint posed by flooding of the turbine is not important, as shown in Fig. 2. Heat transfer limitations are not expected. Mixing, however, presents a problem, in its



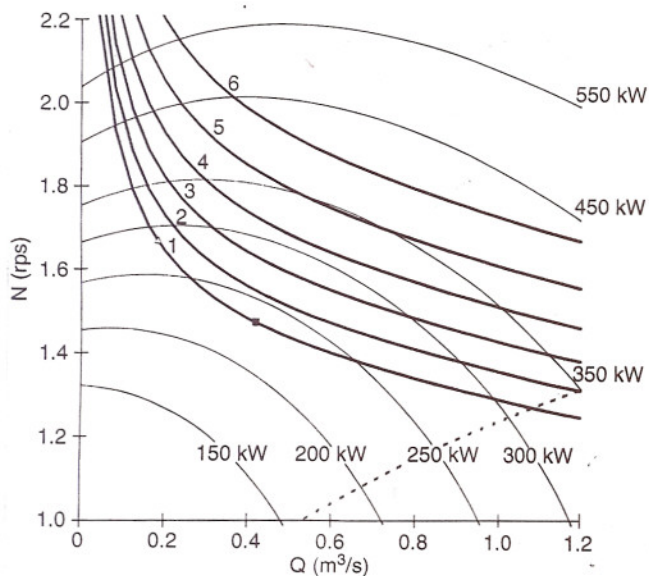


Fig. 2. Map of dissolved oxygen and total power as a function of air flowrate and stirrer speed for the 85 m<sup>3</sup> fermenter. (■ - optimal operation; ▲ - typical operation; - - - flooding of the lowest impeller; iso-oxygen curves in bold: 1 - 0.12 mol m<sup>-3</sup>; 2 - 0.15 mol m<sup>-3</sup>; 3 - 0.18 mol m<sup>-3</sup>; 4 - 0.21 mol m<sup>-3</sup>; 5 - 0.24 mol m<sup>-3</sup>; 6 - 0.27 mol m<sup>-3</sup>)

interaction with mass transfer. The constraint used was to keep an average DO equal to the critical value. Now, with a large fermenter with three radial stirrers, mixing between agitation stages is less than perfect, and, since mass transfer on the top stage is poorer, DO will be less than average at the top of the fermenter. One way to deal with this problem is to make use of the safety margin to the critical oxygen,  $\beta$ , reflecting expected axial gradients of DO along the fermenter. For the sake of simplicity, this was not done.

#### 4

#### Conclusions

This work shows that there is scope for optimisation of fermenter agitation and aeration with constraints, for a given set of conditions and provided that correlations and parameters describing oxygen transfer and agitation power are known. Other conclusions are:

- (i) Plotting of fermenter states as a function of the two independent variables,  $Q$  and  $N$ , is helpful. Iso-power curves, iso-DO curves and other constraints may be studied in this graph.
- (ii) The optimal operating point can be analytically calculated or visually determined.
- (iii) For a typical antibiotics fermentation, the optimum lies within the window for satisfactory operation, both at pilot- and full-scale operation.
- (iv) Optimisation corresponds to significant savings in power as compared to usual factory control procedure ( $\sim 10\%$  at pilot plant scale,  $\sim 20\%$  at industrial scale).

#### References

1. Singh, V.: Scale-up and optimization of fermentor mass transfer. PhD thesis. The State University of New Jersey, U.S.A., 1988
2. Singh, V.; Fuchs, R.; Hensler, W.; Constantinides, A.: Scale-up and optimisation of oxygen transfer in fermenters. *Annals of the New York Academy of Sciences*, 589 (1990) 616-641
3. Shields, R.W.; Kao, E.L.: An energy cost minimizing strategy for fermentation dissolved oxygen control. *Bioprocess Eng.*, 10 (1994) 91-97
4. Luong, H.T.; Voleski, B.: Mechanical power requirements of gas-liquid agitated systems. *AIChE J.*, 25(5) (1979) 893-895
5. Van't Riet, K.: Review of measuring methods and results in non-viscous gas-liquid mass transfer in stirred vessels. *Ind. Eng. Chem. Proc. Des. Dev.*, 18(3) (1979) 357-364
6. Bailey, J.E.; Ollis, D.F.: *Biochemical Engineering Fundamentals*. 2nd ed., McGraw-Hill, 1986
7. Vasconcelos, J.M.T.; Alves, S.S.: Direct dynamic  $k_L a$  measurements in viscous fermentation broths - the residual gas hold-up problem. *Chem Eng. J.*, 47 (1991) B35-B44
8. Nienow, A.W.; Konno, M.; Warmoeskerken, M.M.C.G.; Smith, J.M.: On the flooding/loading transition and the complete dispersal condition in aerated vessels agitated by a Rushton turbine. In: *Proc. 5th European Conf. on Mixing*, pp. 143-154. BHRA, Cranfield, 1985
9. Warmoeskerken, M.M.C.G.: Gas-liquid dispersing characteristics of turbine agitators. PhD thesis. University of Delft, The Netherlands, 1986