

AIRLIFT BIOREACTORS WITH PACKED BEDS OF IMMOBILIZED BIOCATALYSTS: Theoretical Evaluation of the Liquid Circulation Performance

Y. CHISTI and M. MOO-YOUNG

Department of Chemical Engineering, University of Waterloo, Waterloo, Ontario, Canada

The energy balance approach is used to develop a method for prediction of the induced liquid circulation velocity in airlift bioreactors containing packed beds of catalyst in the downcomer. The method accounts for the effects of airlift and packed bed geometry, the fluid properties and the gas flow rate on the circulation of liquid. The technique is potentially a powerful tool for reactor design and scale-up.

The liquid circulation rate is modelled for an air-water system in an airlift ($h_L = 8$ m; $A_r/A_d = 1.0$) containing various depths of either spherical bead or Rashig ring packing. The type and the size ($2-10 \times 10^{-3}$ m diameter) of packing correspond to those commonly used in various bioreactors, e.g., immobilized enzyme reactors. The effects of the riser gas flow ($0 < U_{Gr} \leq 0.12$ ms $^{-1}$), the depth of packing ($0 \leq L \leq 4$ m), and the size and shape of particles on the rate of liquid circulation are examined with a view to evaluation of the airlift-packed bed hybrid bioreactor for potential large-scale applications.

In the ranges examined, the airlift-packed bed bioreactor was predicted to generate enough liquid flow for successful operation with some cell culture and immobilized enzyme systems.

INTRODUCTION

Airlift and packed bed bioreactors have been widely accepted in commercial fermentation, cell culture and immobilized enzyme applications. A combination of those distinct reactor concepts into an airlift-packed bed hybrid bioreactor is potentially useful. An airlift reactor containing a packed bed of biocatalyst in the downcomer (Figure 1) is one way of implementing the hybrid design. The success of the design depends entirely on the ability of the airlift to drive the liquid through the packing at the required rate, which depends on the oxygen requirements of the packed bed and on the need to attain particular levels of solid-liquid mass transfer in the packing. Although fluidized bed bioreactors may be employed for reactions involving solid biocatalysts, packed systems can attain higher solid-liquid mass transfer rates (at lower energy inputs) because of the higher relative velocities between the liquid and solid phases in these systems¹. Additionally, the kinetics of particular reactions may have a plug flow requirement which is easily met in packed beds. Hence, an evaluation of the liquid circulation phenomenon in the airlift-packed bed combination is necessary. Here we develop a method for predicting the velocity of the circulatory flow and examine the factors which affect circulation. The magnitude of circulation determines the residence time of the liquid in the packed bed, the solid-liquid mass transfer in the packing, and the turbulence and shear levels in the riser and the bed. The rate of circulation is critically dependent on pressure drop through the packed section.

The air (or other gas) injected into the riser of the airlift (Figure 1) leads to a higher gas holdup in the riser than in the downcomer containing the packed bed. The consequent difference in the bulk densities of the fluid in the riser and the downcomer induces the liquid circulation in the airlift loop and through the packed bed of immobilized biocatalyst. To ensure that the gas bubbles do not build up in the packing to the detriment of liquid

circulation, the reactor can be designed such that all gas bubbles escape the liquid prior to it recirculating into the downcomer. This gas-liquid separation has been discussed² and comprehensive design guidelines for ensuring complete disengagement of gas from liquid have been published³.

Although no engineering analysis of the hybrid device has been attempted so far, the concept of airlift-packed bed combination is not new. Anchorage dependent animal cells have been grown on the surface of microbeads in beds irrigated by airlift driven culture fluid^{4,5}. Such devices have been applied at 0.1–100 l scales for the production of foot-and-mouth disease vaccine⁵ using cells supported on 3×10^{-3} m diameter glass beads. A superficial liquid velocity of $\sim 3 \times 10^{-3}$ ms $^{-1}$ through the packing has been reported⁵. Similar reactors have been used to grow hybridoma cells for the production of monoclonal antibodies⁶. These examples demonstrate that the airlift-packed bed combination is a practical idea, not just a curiosity. The riser of the hybrid reactor offers a better mixed zone than the packed section; the pH, temperature and the dissolved oxygen levels of the recirculating fluid can be easily controlled in the riser. Hence the hybrid design overcomes some of the shortcomings of packed bed bioreactors. Despite these enhancements, the use of packed bed airlifts is unlikely to be feasible for microbial cultivation (except perhaps for non-growing immobilized cells) because of possible difficulties with clogging of the bed by biomass. Immobilized animal cells and immobilized enzymes are expected to be the main users of airlift-packed bed bioreactor technology.

THEORY

Liquid circulation in airlift reactors without packed sections, that is in liquid phase free-suspension cultures, has received much attention^{2,7-9} and a unified theory for the prediction of circulation velocity has emerged^{2,10}. The

0960-3085/93/\$05.00 + 0.00

© Institution of Chemical Engineers

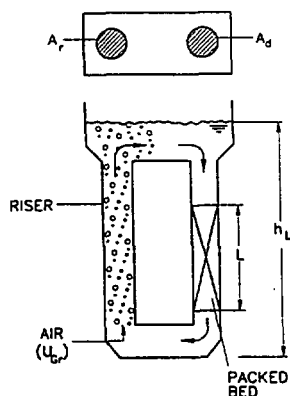


Figure 1. Airlift-packed bed hybrid reactor.

prediction is based on equations obtained by energy balance over the airlift loop: rate of energy input into the reactor = rate of energy dissipation, or

$$E_i = E_R + E_D + E_B + E_T + E_F \quad (1)$$

where E_i = energy input due to isothermal gas expansion in the riser; E_R = energy dissipation due to wakes behind bubbles in the riser; E_D = energy loss due to stagnant gas in the downcomer; $E_{B(T)}$ = energy loss due to fluid turn around at the bottom (top) of the reactor; E_F = energy loss due to friction in the riser and the downcomer.

Equation (1) does not contain an energy loss term for the biocatalyst particles because only free cells are present in the reactor. Also, the kinetic energy input associated with sparging of the gas has been disregarded because it is usually negligible for well designed gas spargers as demonstrated elsewhere².

The energy balance approach which is successful in the simple airlift loop, can be extended to airlift systems with packed beds of catalysts. Because viscous fluids and non-Newtonian media containing solids are not suitable for use in packed bed airlifts, only Newtonian low-viscosity (water-like) flows will be considered in the following development. Under these conditions, the wall friction associated energy losses can be neglected⁷ in comparison with other terms in equation (1); thus E_F will be ignored. However, energy dissipation due to the bed must be accounted for by addition of a term (E_P) to equation (1). On the other hand, the energy loss due to stagnant gas in the downcomer (E_D) would not occur in the packed bed airlift because, to ensure stable operation, the reactor will have to be designed for complete disengagement of the gas in the headspace³. Hence, E_D will be disregarded. Equation (1), therefore, is modified to:

$$E_i = E_R + E_B + E_T + E_P \quad (2)$$

The energy dissipation due to the wakes behind the bubbles in the riser (E_R) can be obtained⁷ by an energy balance on the riser as the control volume. E_R is given by

$$E_R = E_i - \rho_L g h_D U_{Lr} A_r \epsilon_r \quad (3)$$

The energy loss in the top and the bottom sections of the airlift is given² as:

$$E_B + E_T =$$

$$\frac{1}{2} \rho_L A_r U_{Lr}^3 \left[\frac{K_T}{(1 - \epsilon_r)^2} + K_B \left(\frac{A_r}{A_d} \right)^2 \frac{1}{(1 - \epsilon_d)^2} \right] \quad (4)$$

where K_T and K_B are the friction loss coefficients for the top and the bottom connection sections between the riser and the downcomer. Because the downcomer is assumed to be free of gas, $\epsilon_d = 0$, and equation (4) simplifies to

$$E_B + E_T = \frac{1}{2} \rho_L A_r U_{Lr}^3 \left[\frac{K_T}{(1 - \epsilon_r)^2} + K_B \left(\frac{A_r}{A_d} \right)^2 \right] \quad (5)$$

By analogy with pipe flow, the energy dissipation rate in the packed bed (E_P) can be written as

$$E_P = U_{Ld} A_d \Delta P \quad (6)$$

where ΔP is the pressure drop through the bed, and U_{Ld} is the superficial liquid velocity in the downcomer. Because the continuity relationship for incompressible flow governs the flow between the riser and the downcomer, we have

$$U_{Lr} A_r = U_{Ld} A_d \quad (7)$$

which can be substituted into equation (6) to obtain E_P in terms of U_{Lr} :

$$E_P = U_{Lr} A_r \Delta P \quad (8)$$

Substitution of equations (3), (5) and (6) into equation (2) leads to

$$E_i = E_i - \rho_L g h_D U_{Lr} A_r \epsilon_r + \frac{1}{2} \rho_L A_r U_{Lr}^3 \left[\frac{K_T}{(1 - \epsilon_r)^2} + K_B \left(\frac{A_r}{A_d} \right)^2 \right] + U_{Lr} A_r \Delta P \quad (9)$$

or

$$0 = -g h_D \epsilon_r + \frac{U_{Lr}^2}{2} \left[\frac{K_T}{(1 - \epsilon_r)^2} + K_B \left(\frac{A_r}{A_d} \right)^2 \right] + \frac{\Delta P}{\rho_L} \quad (10)$$

Equation (10) is the basis of the method for prediction of the liquid circulation rate. The parameters K_B and K_T (equation (10)) may be calculated as outlined in Appendix 1 and other publications^{2,7}. Equation (10) requires a knowledge of the riser gas holdup (ϵ_r) which depends on the superficial gas velocity (U_{Gr}) and the liquid flow (U_{Lr}), according to the well known Ellis's equation cited by Hills⁹ and given below in a rearranged form:

$$\epsilon_r = \frac{U_{Gr}}{0.24 + 1.7 (U_{Lr} + U_{Gr})^{0.7}} \quad (11)$$

Equation (11) applies to air-water system when ($U_{Lr} + U_{Gr}$) < 1.3 ms⁻¹. The calculation of pressure drop through the packing (ΔP) for use in equation (10) is explained below.

Pressure Drop Through the Packed Bed (ΔP)

Two common cases are of importance in immobilized biocatalysis: (a) beds composed of spherical catalyst particles such as those used in anchorage dependent cell culture^{4,5} or enzyme columns¹², and (b) beds of more open structure as produced by ring packing such as Rashig rings.

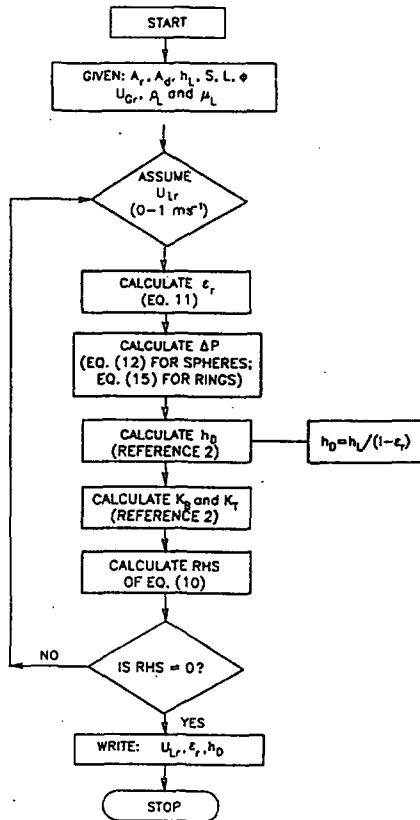


Figure 2. Algorithm for the prediction of liquid circulation velocity (U_{Lr}) in airlift-packed bed system.

Spherical particles

Pressure drop through beds of uniform particles can be satisfactorily correlated by the Carman-Kozeny equation applicable to laminar as well as turbulent flow¹³. In terms of U_{Lr} , the equation is

$$\Delta P = \frac{\rho_L U_{Lr}^2 S(1-\phi)L}{\phi^3} (5 Re^{-1} + 0.4 Re^{-0.1}) \left(\frac{A_r}{A_d}\right)^2 \quad (12)$$

where ϕ is the void fraction of the bed, L is the depth of packing and $S (=6/d)$ is the surface area per unit volume of the particles. The definition of the Reynolds number (Re) employed by Coulson and Richardson¹³ in equation (12) can be adapted for the airlift:

$$Re = \frac{U_{Lr} \rho_L}{S(1-\phi)\mu_L} \left(\frac{A_r}{A_d}\right) \quad (13)$$

Substitution of equation (12) into equation (10) gives an expression which can be solved for U_{Lr} .

Rashig rings

Equation (12) gives consistently low results¹³ for hollow packing. Flow through such packing is better described¹³ by the semi-empirical Ergun equation written below in terms of U_{Lr}

$$\Delta P = \left(150 \frac{(1-\phi)^2 \mu_L U_{Lr}}{\phi^3 d^2} + 1.75 \frac{(1-\phi) \rho_L U_{Lr}^2}{\phi^3 d} \left(\frac{A_r}{A_d}\right) \right) \left(\frac{A_r}{A_d}\right) L \quad (14)$$

Following the approach of Coulson and Richardson¹³, the particle diameter (d) in equation (14) can be replaced with $6/S$, and upon rearrangement we obtain

$$\Delta P =$$

$$\left[4.17 \mu_L S(1-\phi) U_{Lr} + 0.29 \rho_L U_{Lr}^2 \left(\frac{A_r}{A_d}\right) \right] \left(\frac{A_r}{A_d}\right) \frac{(1-\phi)}{\phi^3} S L \quad (15)$$

Substitution of equation (15) into equation (10) leads once again to an expression which may be solved for U_{Lr} .

Calculation of the superficial Liquid Velocity in the Riser (U_{Lr})

For calculation of liquid circulation velocity in a reactor of specified geometry (i.e., A_r , A_d , h_L , S , L and ϕ), fluid (i.e., ρ_L and μ_L), and riser gas flow (U_{Gr}), the following procedure is used:

1. A value for U_{Lr} ($0-1 \text{ ms}^{-1}$) is assumed.
2. The riser gas holdup (ϵ_r) is calculated using the assumed U_{Lr} (step 1), and known U_{Gr} , in equation (11).
3. The pressure drop through the packed section (ΔP) is calculated using either equation (12) or equation (15), depending on the type of packing (spheres or Rashig rings).
4. The height of gas-liquid dispersion (h_D) is now estimated²: $h_D = h_L / (1 - \epsilon_r)$.
5. The geometry dependent parameters K_T and K_B are calculated as explained in Appendix 1.
6. The right hand side of equation (10) is solved using the parameters determined in steps 1-5. If the $RHS = 0$, the initially assumed U_{Lr} (step 1) constitutes a solution. For $RHS \neq 0$, steps 1-6 must be repeated with a new assumption for U_{Lr} . The ϵ_r and h_D corresponding to a solution are the predicted riser gas holdup and the gas-liquid dispersion height, respectively.

The foregoing procedure is illustrated in Figure 2.

RESULTS AND DISCUSSION

The theoretical developments described in the previous section were used for several test case calculations of liquid circulation velocity in airlift-packed bed combinations of hypothetical geometry. The aim was simply to gain insight into the behaviour of circulation with respect to such design parameters as the type of packing, the size of the catalyst support particles, the depth of the packed zone, and the gas flow rate in the riser.

The superficial liquid velocity calculations were for air-water system ($\mu_L = 10^{-3} \text{ Pas}$; $\rho_L = 10^3 \text{ kgm}^{-3}$) in an external-loop airlift ($A_r/A_d = 1.0$; $K_B = K_T = 11.4$; $h_L = 8 \text{ m}$) shown in Figure 1. The riser superficial air velocity (U_{Gr}) range for the computations was $0-0.12 \text{ ms}^{-1}$. The height (L) of packing in the downcomer ranged from $L = 0$ (i.e., no packing) to $L = 4 \text{ m}$. Two types of packings were investigated, spheres ($d = 2-10 \times 10^{-3} \text{ m}$) and porcelain Rashig rings (0.006 and 0.01 m nominal size). The surface-to-volume ratio (S) of the various particles is shown in Table 1. The beds of spheres were assumed to

Table 1. Properties of packing.

Packing	Size ($\times 10^3$ m)	S (m^{-1})	ϕ (—)
Spheres	2	3000	0.4
	4	1500	0.4
	6	1000	0.4
	10	600	0.4
Rashig rings	6 (nominal)	710	0.62
	10 (nominal)	481	0.67

have a void fraction of 0.4, which is usual for uniform spheres¹³; the ring packings¹⁴ had a much higher voidage (>0.6 , Table 1). The size and the geometry of the packings represented typical biocatalyst support material used for enzymes^{12,15} and animal cells^{4,5}.

The predicted liquid circulation rate as a function of the riser superficial air velocity is shown in Figure 3 for the reactor without any packing. The circulation follows a previously observed^{2,8} behaviour: a rapid initial increase followed by a more gradual rise. The predicted magnitude (Figure 3) of the U_{Lr} is in keeping with results expected for a reactor with a $K_B = 11.4$. The introduction of even a one metre deep bed ($\phi = 0.4$; $L/h_L = 0.125$) of spheres ($d = 0.01$ m) caused a dramatic reduction in U_{Lr} to $\sim 13\%$ of the value in a packing-free airlift. For smaller packing, e.g. 0.002 m diameter beads, the liquid circulation was only $\sim 4\%$ of that obtained in the absence of the packing (Figure 4). Note also (Figure 4) that beyond a U_{Gr} of ~ 0.02 ms^{-1} , the normalized liquid velocity (U_{Lr}/U_{Lr0}) for any given particle size was nearly constant, i.e., the reduction in U_{Lr} relative to the packing-free mode of operation, was independent of U_{Gr} . This independence happened because the flow in the beds was turbulent ($Re > 10$ for $U_{Gr} > 0.02$ ms^{-1}), and in turbulent flow the friction factor through the packing is known to be relatively insensitive to further increase in liquid flow¹³ which accompanies the rise in gas flow, U_{Gr} . Although the normalized liquid flow (Figure 4) is a good indicator of the reduction in liquid circulation due to the packing, absolute values of U_{Lr} (Figure 5) are more meaningful for judging performance. As shown in Figures 4 and 5, for a bed of fixed height ($L = 1$ m), the circulation velocity declined with decreasing diameter of the particles, even though the bed voidage was held constant ($\phi = 0.4$). Notice though (Figure 5), that despite the small beads, the flow velocity exceeded 3×10^{-4} ms^{-1} , a value employed for culture of anchorage dependent cells on 0.003 m glass

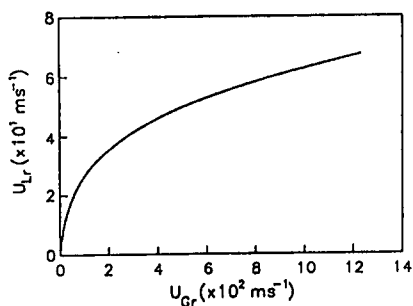


Figure 3. Superficial riser liquid velocity (U_{Lr}) vs superficial air velocity in riser (U_{Gr}) for the airlift without packed bed.

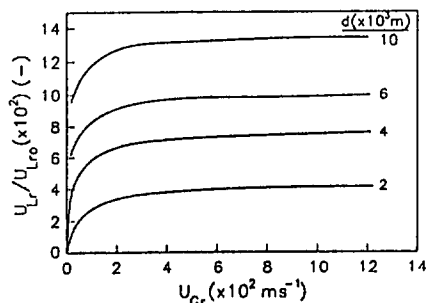


Figure 4. Normalized liquid velocity (U_{Lr}/U_{Lr0}) vs gas flow in riser for a 1 m deep bed of spheres.

spheres in airlift-packed bed bioreactors⁵. For industrial immobilized enzyme packed bed reactors we estimate (Appendix 2) a flow velocity requirement of only 1×10^{-3} ms^{-1} based on a typical residence time of ~ 30 minutes¹². The rate of circulation was higher than necessary for the cases cited; however, the rate can be easily controlled by manipulation of the gas input to the riser provided the change does not affect oxygen requirements. Other possible constraints on the upper limit for flow of gas are

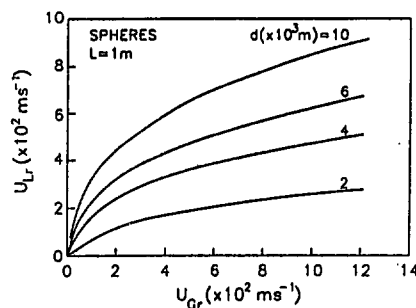


Figure 5. Riser liquid flow vs gas flow for 1 m deep bed of spherical particles: effects of gas flow and particle size.

related to such factors as foaming, slugging in the riser and liquid blow out. Sufficiently large liquid flows can be attained in still deeper beds as illustrated in Figure 6 for beads 0.01 m in diameter. The flow declined as the fractional depth (L/h_L) of the packed section was increased (Figure 6).

A comparison of the Rashig ring and the bead packing is shown in Figure 7. The results are for 0.006 m particles. For both packings, the liquid circulation decreased with increasing depth (L/h_L) of packing; however, a 2 m deep

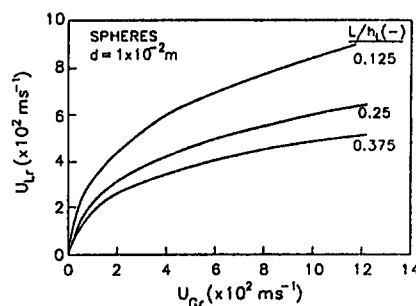


Figure 6. Riser liquid flow vs gas flow for packed beds of 0.01 m spherical particles: effects of depth of packing.

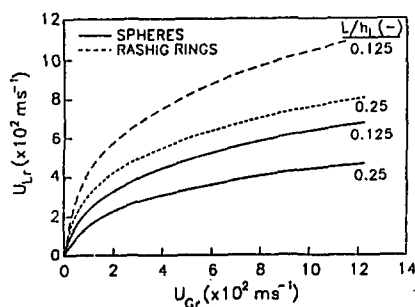


Figure 7. Riser liquid flow vs gas flow for Rashig rings and spheres of 0.006 m size: effects of type and depth of packing.

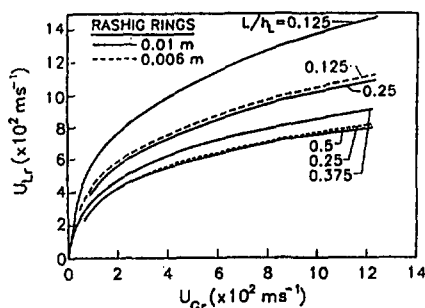


Figure 8. Riser liquid flow vs gas flow for 0.006 m and 0.01 m Rashig rings at various depths of packing: a 4 m deep bed of 0.01 m particles allows as much flow as a 2 m deep bed of smaller (0.006 m) particles.

bed ($L/h_L = 0.25$) of Rashig rings allowed a significantly higher flow (Figure 7) than a bed of spheres which was half as deep ($L/h_L = 0.125$). The differences were due to the higher voidage ($\phi = 0.62$) of the ring packing relative to the bed of spherical particles ($\phi = 0.4$). The airlift could drive useful amounts of liquid through beds constituting 50% or more of the height of the reactor. For example, Figure 8 shows the expected flow through a 4 m deep ($L/h_L = 0.5$) bed of 0.01 m Rashig rings. Flow through a 2 m deep ($L/h_L = 0.25$) bed of 0.006 m rings was determined to be virtually the same as attainable in 4 m deep beds of slightly larger packing ($d = 0.01$ m) (Figure 8).

In general, in a packed bed airlift device, an increase in the overall height will enhance liquid circulation for a fixed depth of packing. Increase in the depth of packing or decrease in the diameter of particles will slow down the circulation for a given gas flow. For otherwise equal conditions, increased bed voidage will improve the circulation of liquid.

While the results are simulations, all the component parts of the theory have been rigorously proven separately: the energy balance approach has been experimentally demonstrated⁷ for 13 different airlift reactors (without packed beds) over a broad range of operating scale (0.06–1.06 m³ liquid volume); Ellis's equation has been independently confirmed, and Carman-Kozeny and Ergun equations have been extremely well established over the years for pressure loss calculations in packed columns commonly employed in the chemical industry.

CONCLUSIONS

Based on theoretical developments, a sufficiently wide range of induced circulatory flow of liquid can be attained

in airlift-packed bed combinations to make those bioreactor systems worthwhile for anchorage-dependent animal cell culture and immobilized enzyme catalysis. For any such application, a careful evaluation of the minimum and the maximum required levels of circulation is necessary. The selection of type, size and depth of the packing is based on the required range of liquid flow, the acceptable riser gas velocity and the desired surface area for supporting the catalyst. The suitable range of liquid flow rates is determined by the axial depletion of oxygen in the packed zone and solid-liquid mass transport considerations.

Any selection of the parameters can be evaluated by simulation using the procedures developed here; hence, the experimental effort can be concentrated upon fewer variables or a more narrow range of variables. Furthermore, the approaches used are adaptable to prediction of circulation in airlifts with static mixers¹⁶ or other devices, e.g., heat exchangers. The ability to predict the rate of circulation is a prerequisite to predicting the solid-liquid mass transfer and heat transfer coefficients within the bed. These transport properties have been thoroughly studied in packed beds as evidenced by major reviews^{17,18}. Once the airlift driven liquid circulation velocity through the packing has been quantified, the transport rates in the bed can be calculated with existing correlations^{1,17,18}.

APPENDIX I: CALCULATION OF COEFFICIENTS K_B AND K_T

For the simulations reported in this work the geometry-dependent frictional loss coefficients were assumed to be equal, $K_T = K_B = 11.4$, as would be the case when the top and the bottom zones connecting the riser and the downcomer have similar geometries^{2,3}. A high value of 11.4 was used for these coefficients to simulate a restricted flow situation to account for such factors as pressure drop through the plate supporting the packed bed. Normally, $K_B \approx 5$ for airlift reactors having the geometric ranges $A_b/A_d = 1-2$, $A_b/A_r = 0.25-1$ and $L_{cp}/d_{cp} = 2-7$ ^{2,19}, where A_b is the cross-sectional area of the connecting pipe, L_{cp} is its length and d_{cp} is its diameter. In external-loop airlift reactors without packed beds, Choi and Lee²⁰ experimentally measured liquid circulation velocities and gas hold-ups and correlated their data with the well known equation developed by Chisti *et al.*⁷:

$$U_{Lr} = \left[\frac{2g h_D (\varepsilon_r - \varepsilon_d)}{K_B \left(\frac{1}{(1 - \varepsilon_r)^2} + \left(\frac{A_r}{A_d} \right)^2 \frac{1}{(1 - \varepsilon_d)^2} \right)} \right]^{0.5} \quad (A1)$$

Note that equation (A1) contains only K_B because K_B and K_T are assumed to be equal⁷. The values of K_B required to achieve best fit of the data with equation (A1) were calculated²⁰ and the calculated K_B was correlated with the geometric variables using the equation:

$$K_B = 12.705 \left(1 + \frac{A_d}{A_r} \right)^{2.05} \left(1 + \frac{L_{cp}}{L_h} \right)^{-1.119} \quad (A2)$$

which applied for K_B s in the range 10–25. The L_h in equation (A2) is the vertical distance between the lower and upper pipes which connect the riser and the downcomer. For practical purposes L_h may be taken to equal

h_L , the static liquid height. As a cautionary note, equation (A2) has not been proven to be generally applicable nor does it have a basis in fundamentals of fluid mechanics.

APPENDIX 2: THE REQUIRED U_{Lr} FOR AN IMMOBILIZED ENZYME COLUMN

The residence time (t_R) of the liquid in a once-through packed bed system is

$$t_R = \frac{\text{liquid volume of bed}}{\text{flow rate}} = \frac{A_d L \phi}{A_r U_{Lr}} \quad (\text{A3})$$

when $A_d = A_r$,

$$t_R = \frac{L \phi}{U_{Lr}} \quad (\text{A4})$$

A typical residence time for immobilized enzyme columns is ~ 30 minutes¹². Thus, the required U_{Lr} for a 6 m deep bed ($\phi = 0.4$) is

$$U_{Lr} = \frac{L \phi}{t_R} = \frac{6 \times 0.4}{30 \times 60} = 0.001 \text{ ms}^{-1}$$

NOTATION

A_b	Cross-sectional area of the connecting pipe (m^2)
A_d	Cross-sectional area of downcomer (m^2)
A_r	Cross-sectional area of riser (m^2)
d	Diameter of particle (m)
d_{cp}	Diameter of the connecting pipe (m)
E_B	Energy dissipation due to fluid turnaround at bottom (W)
E_D	Energy dissipation rate due to gas in downcomer (W)
E_F	Energy dissipation due to wall-friction (W)
E_i	Energy input rate (W)
E_P	Energy dissipation rate in the packed bed (W)
E_R	Energy dissipation due to bubbles in riser (W)
E_T	Energy dissipation due to fluid turnaround at top (W)
g	Gravitational acceleration (ms^{-2})
h_D	Height of gas-liquid dispersion (m)
h_L	Height of gas-free liquid (m)
K_B	Frictional loss coefficient for the bottom (—)
K_T	Frictional loss coefficient for the top (—)
L	Depth of the packed bed (m)
L_{cp}	Length of the connecting pipe (m)
L_h	Vertical distance between the top and the bottom connecting pipes (m)
ΔP	Pressure drop through the packing (Pa)
Re	Reynolds number defined by equation (13) (—)
S	Surface area per unit volume of particle (m^{-1})
t_R	Residence time of liquid in the packed bed (s)
U_{Gr}	Superficial gas velocity in the riser (ms^{-1})
U_{Ld}	Superficial liquid velocity in the downcomer (ms^{-1})
U_{Lr}	Superficial liquid velocity in the riser (ms^{-1})
U_{Lro}	U_{Lr} in the airlift without any packing (ms^{-1})

Greek Letters

ε_d	Gas holdup in the downcomer (—)
ε_r	Gas holdup in the riser (—)
μ_L	Viscosity of the liquid (Pas)
ρ_L	Density of the liquid (kgm^{-3})
ϕ	Void fraction of the packed bed (—)

REFERENCES

- Mao, H. H., Chisti, Y. and Moo-Young, M., 1992, Multiphase hydrodynamics and solid-liquid mass transport in an external-loop airlift reactor—A comparative study, *Chem Eng Commun*, 113: 1–13.
- Chisti, M. Y., 1989, *Airlift Bioreactors*, 203–229 (Elsevier Applied Science, London).
- Chisti, Y. and Moo-Young, M., 1993, Improve the performance of airlift reactors, *Chem Eng Progress*, 89 (6) 1: 38–45.
- Spier, R. E. and Whiteside, J. P. 1976, The production of foot-and-mouth disease virus from BHK 21 C 13 cells grown on the surface of glass spheres, *Biotechnol Bioeng*, 18: 649–657.
- Whiteside, J. P. and Spier, R. E., 1981, The scale-up from 0.1 to 100 liter of a unit process system based on 3-mm-diameter glass spheres for the production of four strains of FMDV from BHK monolayer cells, *Biotechnol Bioeng*, 23: 551–556.
- Murdin, A. D., Thorpe, J. S., Kirkby, N., Groves, D. J. and Spier, R. E., 1987, Immobilization and growth of hybridomas in packed beds, in *Bioreactors and Biotransformations*, Moody, G. W. and Baker, P. B. (editors), 99–110 (Elsevier Applied Science, London).
- Chisti, M. Y., Halard, B. and Moo-Young, M., 1988, Liquid circulation in airlift reactors, *Chem Eng Sci*, 43: 451–457.
- Jones, A. J., 1985, Liquid circulation in a draft-tube bubble column, *Chem Eng Sci*, 40: 449–462.
- Livingston, A. G. and Zhang, S. F., 1993, Hydrodynamic behaviour of three-phase (gas-liquid-solid) airlift reactors, *Chem Eng Sci*, 48: 1641–1654.
- Chisti, Y. and Moo-Young, M., 1988, Prediction of liquid circulation velocity in airlift reactors with biological media, *J Chem Technol Biotechnol*, 42: 211–219.
- Hills, J. H., 1976, The operation of a bubble column at high throughputs I: gas holdup measurements, *Chem Eng J*, 12: 89–99.
- Chaplin, M. F. and Bucke, C., 1990, *Enzyme Technology*, 167–196 (Cambridge University Press, Cambridge).
- Coulson, J. M. and Richardson, J. F., 1978, *Chemical Engineering*, volume 2 (3rd edition), 126–132 (Pergamon Press, Oxford).
- Backhurst, J. R. and Harker, J. H., 1973, *Process Plant Design*, 108 (Heinemann, London).
- Messing, R. A. (editor), 1975, *Immobilized Enzymes for Industrial Reactors* (Academic Press, New York).
- Chisti, Y., Kasper, M. and Moo-Young, M., 1990, Mass transfer in external-loop airlift bioreactors using static mixers. *Can J Chem Eng*, 68: 45–50.
- Zenz, F. A. and Othmer, D. F. 1960, *Fluidization and Fluid-Particle Systems*, 427–433, 467–470 (Reinhold, New York).
- Lemcoff, N. O., Pereira Duarte, S. I. and Martinez, O. M., 1990, Heat transfer in packed beds, *Reviews in Chemical Engineering*, 6: 229–292.
- Chisti, Y. and Moo-Young, M., 1991, Fermentation technology, bioprocessing, scale-up and manufacture, in *Biotechnology: The Science and the Business* (Moses, V. and Cape, R. E., editors), 167–209, (Harwood Academic Publishers, New York).
- Choi, K. H. & Lee, W. K., 1993, Circulation liquid velocity, gas holdup and volumetric oxygen transfer coefficient in external-loop airlift reactors, *J Chem Technol Biotechnol*, 56, 51–58.

ADDRESS

Correspondence concerning this paper should be addressed to Professor Y. Chisti, Department of Chemical Engineering, University of Waterloo, Ontario, Canada N2L 3G1.

This manuscript was received 25 January 1993 and accepted for publication after revision 25 May 1993.