NON-IDEAL FLOW PHENOMENA IN TUBULAR FERMENTATION SYSTEMS—FUNDAMENTALS, AND INFLUENCE ON EQUIPMENT DESIGN

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ABSTRACT

Tubular fermenters are treated from the point of view of their most important property with respect to their successful application— the deviation from plug flow behaviour. Firstly, the models of non-ideal flow suitable for various types are discussed. The axially dispersed plug-flow model is so far the most frequently used. Secondly, an improved method for the evaluation of the dispersion characteristics in this model, taking account of the low Peclet numbers encountered in most practical equipment, is proposed. The method of moments, again a very frequently used tool can give confusing results in this region. Finally, the perspectives of a more adequate treatment of non-ideal flow in tower systems not mechanically agitated is discussed, based on the mixing models of Prandtl and Kármán and on velocity profiles.

INTRODUCTION

In any microbiological process problem, the fermenter is undoubtedly the key equipment of the system. Of the two major equipment types—the perfectly mixed and the tubular—the tubular are in some cases a perspective equipment. These cases involve the formation of a secondary metabolite at the end of the growth phase, growth or product-formation best represented by an autocatalytic first order reaction, optimal volume resulting when these are in combination with a perfectly mixed system, and rational liquid substrate utilization, (a case of operating economy), to state their main features.

However, all the major cases mentioned require the condition of perfect plug flow in the equipment to be met exactly. This is never the case and that equipment will work best where the approximation to this condition is best. It is therefore necessary to know when selecting an equipment, how much imperfect flow behaviour can be expected within it. The tools for this investigation have been long since provided by control engineering and chemical engineering and those known already have been criticized elsewhere[1]. We shall in this contribution review their suitability for aerated and non-aerated fermentation systems, starting from the simplest equipment—a

bubble column—and treating the most sophisticated forms—the mechanic-ally-mixed vertical sectioned columns. The statistical frequency-response techniques will be mentioned for their suitability for obtaining dispersion characteristics in dispersed plug-flow based models, and the actual status of non-ideal flow in some simpler apparatus forms will be suggested.

SELECTION OF APPROPRIATE NON-IDEAL FLOW MODEL

Generally, tubular systems may be either horizontal, or vertical, the decisive parameter being the length to width ratio. Chemical process indus-tries (apart from a few rather eccentric cases encountered a few years ago) have decided in an overwhelming majority for the vertical systems. The reasons for this decision—better distribution of liquid and gas in systems where a gas takes part in the reaction, simpler equipment hydraulics, and decreased land cost—are also valid in the fermentation industries.

From the point of view of apparatus design, two basic column types can be distinguished, those operating with a basically single-phase flow (non-aerated systems), and those treating a two-phase system (aerated systems), using the very frequent simplification which regards the system liquid substrate-microorganism as an essentially homogeneous phase. This division then affects the selection of apparatus proper. Two basic types can be distinguished here (a) that without any mechanical aids for contacting of the phases, and (b) that provided with such means, or mechanically agitated tower fermenters. The first group can be subdivided into two categories a(i) systems without phase redistribution (empty or bubble columns), and a(ii) systems sectioned into smaller compartments (where phase separation may take place). Mechanically agitated systems are not generally further subdivided, as mixed columns must anyway have some partitions to prevent the column from being totally mixed.

Let us now take as an illustration how widely different ideas can be obtained in backmixing studies of the simplest apparatus form, viz. the bubble column. Backmixing column studies concerning possible applications in chemical process industries are surprisingly numerous over the past few years. The backmixing conditions can be used for fermentation cases as well. Tower fermenters of the empty column type can be operated both in aerobic and anaerobic systems. The first case is rather simple when the quasi-single phase simplification can safely be adopted. The backmixing description will be done most appropriately using the model of Taylor diffusion[2] in laminar flow of the fluid, or by the axially-dispersed plug-flow model[3] when the suspension flows under turbulent conditions. A comparatively large amount of plug-flow behaviour can be expected in this case.

The situation becomes far more involved when the gas phase also comes into consideration as is the case with bubble columns. The actual hydraulic conditions in this case will be treated in more detail at the end of this paper. From the existing literature it can be seen that most of the work done on backmixing in these simple systems from the point of view of apparatus form is based on the axially-dispersed plug-flow model and, surprisingly, not only in the liquid, but also in the gas phase[4]. Again, though there has been little reported on correlating dispersion coefficients in fermenters, there is a

plentitude of data on bubble columns both co-current, and counter-current obtained mostly on simple model systems[5-19]. Some results seem to confirm this very much simplified assumption as suitable for industrial equipment design, e.g. published reports on the successful transfer of design data from a 16 mm diameter laboratory column to a 300 mm column[13,18], and in the successful use of mass transfer coefficients $k_L a$ obtained under the assumptions of an axially-dispersed plug-flow model in laboratory apparatus to plant-size equipment[17]. The data correlation is however rather scattered and this gives some doubt on the use of these two cases as confirmation of the realistic possibilities of application of this model. More doubt emerges when considering the low Péclet numbers generally observed in these columns where the model is itself in doubt from purely theoretical considerations[1,3]. This uncertainty can be felt also from the work of Ohki and Inoue[15] who suggest three separate regions for the operation of the bubble columns, covering the laminar to turbulent flow conditions $(40 \lesssim D_l < 700 \text{ cm}^2 \text{ s}^{-1})$, viz. the bubble-(the isolated bubble), confused-(the regime mostly encountered in fermentations) and the coalesced-bubble-(slug-) flow regimes. The confused-flow regime is claimed to be impossible to correlate, whereas the remaining two are correlated by the dispersion model (in the following examples of correlation, reference to original work follows after the relation in parentheses)

$$D_l = 0.3 d_0^2 u_G^{1.2} + 170 \, d_0 \text{ (15, bubble flow)} \tag{1}$$

$$D_l = 14 \, d_c/(1 - \varepsilon)^2 \text{ (15, slug flow)} \tag{2}$$

$$D_l = 4.2 d_c + 1.67 d_c u_\infty (u_G/u_0)^{\frac{3}{4}} (13) \pm 30\% (1 - \varepsilon) u_l < 4.2 \text{ cm s}^{-1} \tag{3}$$

$$D_l = 4.2 d_c + 12.1 d_c (u_l/(1 - \varepsilon))(u_G/u_0)^{3} (13)(1 - \varepsilon) u_l > 4.2 \text{ cm s}^{-1},$$
$$u_0 = 4\sigma^2 g/k\rho\eta \tag{4}$$

$$D_l = 0.055 \exp(19.3 \, \dot{V}_G) (12) \tag{5}$$

$$Pe_l = 4.5 (14) \tag{6}$$

apart from many graphical correlations, mostly non-linear and some showing extremums. The gas dispersion number has been correlated by

$$D_G = 3.54 \, u_G^{0.91} (\pm 30\%) (4) \tag{7}$$

The scatter of correlations, where given, and the rather inconsistent way of correlation of one simple phenomenon in a very simple apparatus using a fairly restricted set of systems (mostly water–air, N_2, CO_2) can most appropriately be attributed to the restricted applicability of the model to this system. This is, as already mentioned, also substantiated by the low Peclet numbers mostly reported[5,6,11,12,14] when the method of evaluation used in these contributions, the method of moments, can itself be in doubt[20].

Nevertheless, we can make two conclusions on the use of bubble columns for aerated systems: (1) some more adequate description of the hydraulic conditions within the system is to be found, and (ii) as substantial backmixing is present in this simplest apparatus type, some more suitable apparatus should be sought. Let us consider the second case first, when gas-suspension systems must be treated.

The simplest way of reducing the macro-flows along the column axis is the introduction of some partitions, permitting in a restricted way the flow of both phases involved. Some form of sieve plates is usually used. Cases of fermentation experiments on such equipment have already been reported[21,22]. The operation problem which arises in this case is however in the reduced gas redistribution from gas pools accumulating frequently below the plates resulting in the formation of slugs of air. This naturally reduces the use of the gaseous substrate. The only remedy to this phenomenon leads directly to the use of mechanical mixing to aid gas–liquid redistribution within the compartments. As reported in Ref. 7, column sectioning without agitation does not substantially influence the amount of backmixing, but rather the gas hold-up. Extensive data is available on the subject of mechanically-aided gas–liquid contractors, which will not be treated here. The fact which is important for our treatment here, viz. the very frequent use of the dispersion model in its simplest form, will only be noted at this place.

RECOMMENDED MODELS FOR TOWER FERMENTORS

As follows from the previous model, the axially-dispersed plug-flow model is a frequently-used tool, and in some cases this is justified. Let us now mention the cases when this is so. There are actually three related ways of describing the backmixing phenomenon in its uni-dimensional or two-dimensional simplification—Taylor diffusion, the axially (and/or radially) dispersed plug-flow model[30] and the model of a series of perfectly mixed cells.

Taylor diffusion model

Provided the spreading of a substance takes place in laminar flow as is frequently the case in fermentations where long reaction times are encountered, the resulting residence time (or the concentration profile) will also be affected by the laminar velocity profile[2]. In this case, the effective longitudinal diffusivity $(D_l)_{eff}$ must also be taken account of in the process of mass transfer which follows from

$$(D_l)_{eff} = a^2 u^2 / 192 \mathscr{D}_r \qquad (8)$$

as shown also by Aris[24]. However, the molecular diffusion processes may still be comparable to those taking place by this form of eddy diffusion, to which $(D_l)_{eff}$ is proportional, and the appropriate term in the general expression of the mass transfer rate

$$-K \partial^2 C/\partial x^2 + \partial C/\partial \theta = R \qquad (9)$$

is then

$$K = \mathscr{D} + (D_l)_{eff,av} \qquad (10)$$

R is the right hand side corresponding to a given mass transfer case, and $K = \mathscr{D}$ when processes take place by molecular diffusion only, and $K = (D_l)_{eff}$ when $(D_l)_{eff} \gg \mathscr{D}$.

Dispersion model

This model is justified only when turbulent flow takes place in the equipment and the velocity profile becomes essentially flat. Provided fully-developed turbulence at a section of the column can be assured the other simplification used practically throughout the existing work, viz. that of the axially-dispersed plug-flow model, can also be used (assuming $D_r = \infty$). Apart from Ref. 34, this has been confirmed in all other experimental work on tubular reactors[10]. The dispersion model in its uni-dimensional form is described by

$$-D_l \partial^2 C/\partial x^2 + u \partial C/\partial x + \partial C/\partial \theta = R \qquad (10a)$$

for the case of an unsteady state operation or tracer injection. This simplifies for steady state conditions when $\partial C/\partial \theta = 0$. Relation (10a) is also the main relation used for the determination of D_l using tracer input and output information[1,3].

The methods most frequently used (in the order of preference given to them by the authors of various contributions) are the statistically-based method of moments[3] which has been critically reviewed in Ref. 20, and the 'transfer function' method which in the present form inevitably brings about operation in the complex domain. A simplification of the second method was suggested by the authors of this contribution[1] avoiding the necessity of calculating in the complex domain. As this method is fairly general for cases where the conditions more or less strictly correspond to the definition of the axially-dispersed plug-flow model, it will be briefly reviewed here as the recommended method for evaluation of D_l. The method is based on the transfer function and the simplification lies in the fact that the Laplace transform of a convolution of two functions is equal to the product of Laplace transforms of the respective functions. This assumption then brings the entire calculation to the time domain only. Numerical curve fitting is then used for obtaining Pe or D_l rather than the statistical evaluation of the output curves using generally the first and second moments. As criteria of the final fit, the areas under the theoretical and experimental curves, standard errors, position of the peak (a clear indication of the suitability of the dispersed plug-flow model), etc., can be used. In the case of more skewed tracer output curves, when the methods regarding the variance as the highest moment used are not adequate[1], the mean residence time becomes the second iterated variable and this can account for slight deviations from the strict conditions of the dispersed plug-flow model.

Perfectly-mixed cell model

This model can be safely used for non-ideal mixing explanation in a single mixed vessel, or for non-ideal flow in a tubular system provided the number of (assumed) perfectly-mixed cells within it, j, is large. In this case, as reviewed in, for example, Ref. 25, the model has been used successfully by many investigators, as the evaluation procedure is simpler. The condition of applicability (j is large) was not always perfectly met[21]. The simplicity of evaluation lies in the fact that the concentration or velocity profiles are sought using first order finite difference equations

$$rC_{i-1} - rC_i = V_i dC_i/d\theta \text{ for } i = 1, 2, \ldots, j \qquad (11)$$

As the method is strictly applicable only to small deviations from plug flow (j is large) it actually becomes a finite difference approximation of the continuous problem solved otherwise more accurately by the continuous dispersion model[25]. The number of the perfectly-mixed cells j is obtained by analogous procedures as the dispersion number D using the method of moments, or of the transfer function. Serious complications are encountered mainly in the second case, when j is not a whole number[26]. This involves rather problematic operations with the transfer function or some model distortions[27].

Concluding this part it may be worth quoting the statement made by Horn and Parish[25]: 'Since both the series of mixers model and the Taylor diffusion model of tubular reactors can be approximated by the dispersion model, it is appropriate to use that model as a basis of calculation.' It may therefore be recommended to use the dispersion model to characterize backmixing in tubular fermenters in all conditions where the physical state of the system allows it. More clearly-distinguished advantages of its use follow when the dispersion characteristics are used not only with respect to mass transfer but also in combination with a chemical or biological reaction. The series of perfectly-mixed cells model has however undisputable advantages when dead zones or defined macroscopic back-flows occur in the equipment[28, 29, 32].

Non-ideal flow with chemical reaction

The situation becomes ever more complicated when a chemical, biological or both kinds of reaction are also involved. A reasonably difficult problem arises only when a zeroth or first order reaction takes place. The latter assumption is actually a very frequently used simplification in biological systems, even if it is not always justified. Combining reaction rate equations with some adequate description of the non-ideal flow in the system leads to fairly complicated relations even in the very simplest approximation using the axially-dispersed plug-flow model. This case has been recently treated for any reaction type with a known rate in a multicomponent system[25] using the perturbation technique. This includes using a correction term for the concentration which would result in plug flow thus giving the assumed actual concentration and in including a second correction term for concentration changes near the system boundary. A similar approach was suggested using collocation methods[33] permitting the minimization of the number of steps necessary in a numerical approximation of input and final concentration in reactions up to the third order with reasonable accuracy. There is one problematic point in the verification part of this contribution, and that is the comparatively low Peclet numbers ($Pe = 1$-5) where the applicability of the dispersion model to such a degree of backmixing in the system is doubtful. Laminar flow systems, which are of particular interest to slow biological reactions, were treated in Ref. 35. It is shown that the axial dispersion approximation holds well only for slow and medium rate reactions; large deviations were observed for fast reacting systems where considerable influence of increasing turbulence on increased accuracy is

observed. This may be in contradiction to the previously stated facts, yet we must bear in mind that the non-ideal flow description using the axially-dispersed plug-flow model is in this case only an approximation which proved useful even in the laminar flow.

When analysed on a really sophisticated basis biological systems will bring about far greater complications as all kinds of consecutive, inhibiting etc. reactions will have to be considered. This will naturally only be possible when data on such kinetic models become reliably available. By then, the analysis offered for the relative influence of any number of dependent and independent variables in an engineering problem[31], enabling a pre-selection for the experimenter of those variables at a determined level of influence, may become of importance.

PERSPECTIVES IN THE INVESTIGATION OF TUBULAR SYSTEMS FOR NON-IDEAL FLOW

Bubble columns undoubtedly represent the simplest form of equipment available generally. For anaerobic conditions with small amounts of gases evolved during fermentations, this equipment is adequate and the conditions for flow within it can be ascertained using either the Taylor diffusion, or the dispersed plug-flow models, depending on the predominant type of flow. There is little justification in this case for the use of the model of perfectly-mixed cells, as the definition of a perfectly-mixed physical unit within the system is rather artificial.

The picture changes abruptly when larger amounts of gases (limiting hold-up being at about $\varepsilon \leqslant 2.5$ per cent) are present. The situation is less difficult when the gases get into the system by reaction in an anaerobic case, it is more complicated when gas is being actually blown into the system. *Figure 1* shows the conditions at the limiting hold-up, with laminar flow of liquid. At first sight, the interface between the injected dye and the remaining liquid is rather different from that which one expected in dispersed plug flow. In the case of the anaerobic system with gases evolved rising predominantly by buoyancy to the liquid level, the recirculation models of Hochman[36] and Mah[37] can be used. The models assume a core of flow around the centre of the column flowing in the main flow direction, and a recirculating flow of the gasified suspension or liquid near the wall, with exchange of material between both annular flows. When operating amounts of air (5 per cent $< \varepsilon < 10$ per cent) are being introduced by distributors into the column system, the description by any of the models described previously becomes absurd. Even in the case of perfectly designed, machined and operated distributors of gas (which will never be the case in industrial practice), liquid maldistribution over any column cross-section will be completely stochastic in nature, with streams of different densities flowing up and down, causing some mixing on the large scale. The stochastic nature of this process leads directly to the idea of which model should be preferred in such a case—the model of turbulent jet or turbulent wake mixing being the appropriate ones[38]. The mixing characteristic of this model is the eddy diffusivity itself, or the related Prandtl mixing length, which are both related by known relations to the amount of mass transferred:

$$D_e = L_P^2 |d\bar{u}/dy| \qquad (12)$$

and

$$N \, dy = -D_e \, d\bar{n}(y) \qquad (13)$$

where D_e and L_P are the eddy diffusivity and the Prandtl mixing length, respectively, $|d\bar{u}/dy|$ is the absolute value of the shear rate based on the average liquid flow rate, $d\bar{n}(y)$ is the average concentration of the transferred
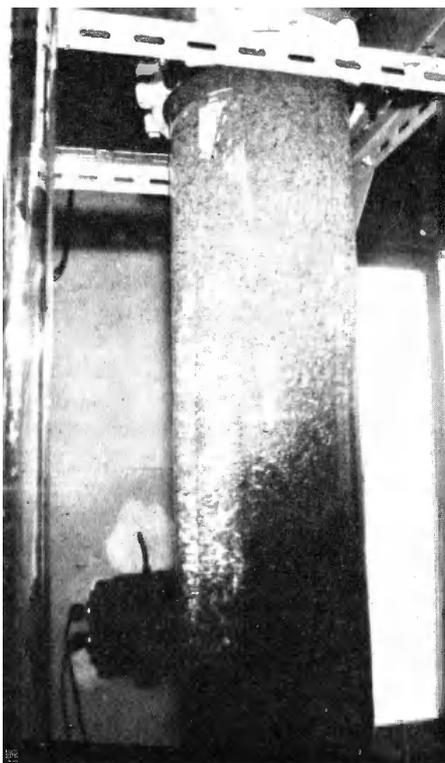
Figure 1. Dye liquid interface after dye injection upstream, liquid rate $u_1 = 6 \, \mathrm{cm \, s^{-1}}$, air hold-up $\varepsilon = 2.5$ per cent, bubble column $d_c = 0.25 \, \mathrm{m}$.

material, and N is the number of particles (or mass) transported per unit area in unit time. From the relations stated it follows that the other obvious limitation was taken account of, i.e. that of the turbulence to be homogeneous and isotropic. The Prandtl mixing length may have some advantage over the eddy diffusivity in actual measurements in respect to the fact suggested by Prandtl[39] that L_P is, in free turbulent layers (jets and wakes), constant in the isolated jet or wake and proportional to their widths.

The importance of the turbulent wake formation for mass transfer in chain bubbling was recognized and discussed by Yeheskel and Kehat[40]. In the case of chain bubbling their results confirm the recirculation models

mentioned earlier[36, 37]. On the other hand, the authors have found that the amount of liquid entrained in the wake of a single bubble is decreased in the case of chain bubbling. Future research on hydraulic conditions in bubble columns might pursue these suggested paths, rather than expanding the already known facts on backmixing obtained by the simple models. This is also the way which is taken at present at the Microbiological Institute.

Sectioning of aerated tubular reactors alone was reported earlier to have beneficial influence on gas hold-up rather than on decrease in backmixing. This fact, supported by experimental work on such fermenters,[21] suggests that in this case, too, the turbulence approach is closer to reality.

IMPACT OF NON-IDEAL FLOW CONDITIONS ON APPARATUS FORM

Despite the ways of measuring more accurately the deviation from ideal plug flow as described in the previous paragraph, it is an indisputable fact that considerable backmixing is and will continue to be present in simple and sectional bubble columns. Bearing in mind the strict conditions which the biological system within such a column brings about, there remain for consideration some systems which will improve the amount of plug flow present in the equipment. This cannot be done at present otherwise than by the introduction of mechanical aids into the systems, taking into consideration, naturally, the increased expenditure due to them. Sectioned tubular systems, vertically aligned and provided with some kind of mixing are then the obvious solution to this problem. The backflows between single compartments must be minimized in this case, as they are the main reason for increasing the over-all amount of liquid backmixed.

The efforts in inventing such equipment should therefore concentrate on designing a type distinguished by: (i) low pressure drop of gas at appreciable height of the equipment, (ii) high gas hold-up and gas utilization (large inner recirculation of gas) (iii) minimal liquid backflows between stages, (iv) low power consumption for mixing. These demands are not always easy to meet in the microbial-suspension–air mixture, mainly in cases of sterile operation. Some possible hints to the solution of the problem are illustrated in *Figure 2*.

Any tower equipment can be divided into two distinct categories— continuous or stagewise contact. Both categories can be operated in the co-current or in countercurrent flow of gas and suspension. The first category has definite advantages in non-aerated systems (cf. condition (iii) above), whereas the second group is recommended for thoroughly aerated systems. The systems depicted in *Figure 2* are briefly described as follows: RDF (rotating disk fermenter) gives good approximation of axially-dispersed plug flow at reasonable energy consumption and reasonable gas holding times at 300–600 r.p.m. Preliminary gas distribution must be efficient. There are several variations to this theme, serrated disks, perforated disks, and (aimed at reducing the equipment operation to stages), the pulse disk RDPF (the second system depicted). By varying the times of rotation and of the transporting single pulse motion a broad range of residence times in the compartment can be achieved. Both types are at present investigated in

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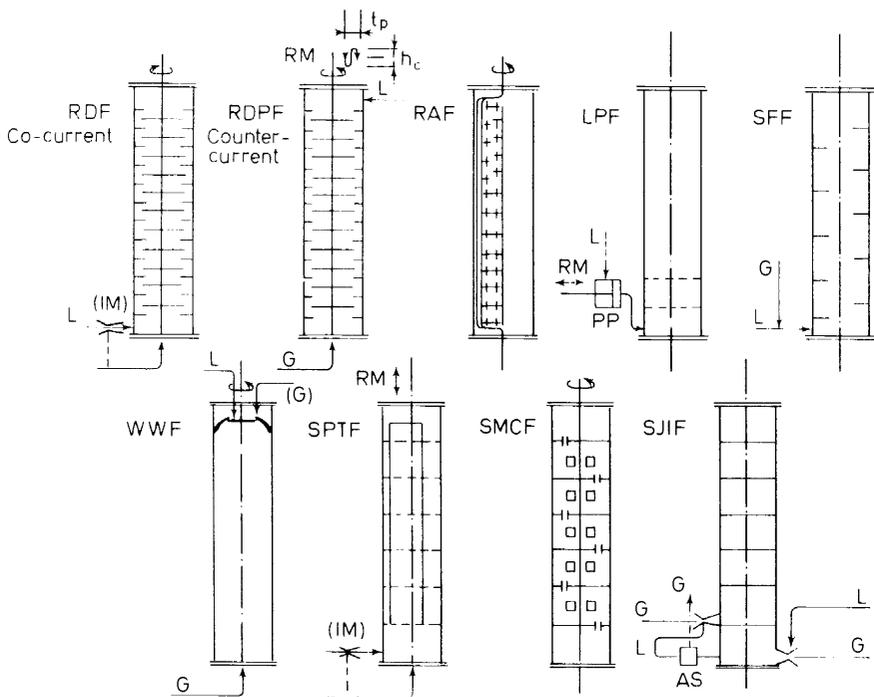
Figure 2. Possible arrangements of tubular fermentation systems IM injection mixer of suspension and air (L and G), AS—air separator, LP liquid pulsator, RM reciprocating motion. For explanation see text.

detail. The RAF (the rotating arm fermenter) is suitable for organisms tending to settle on the walls as e.g. the photosynthesizing ones. The basic simple type can be provided with vertical and horizontal baffling and this may considerably improve the operation of a simple bubble column at low cost. The LPF (liquid pulsed fermenter) improves operation by external pump pulses without the introduction and sealing of any rotating part. In the SFF (spiral flow fermenter) the path of the liquid becomes more organized by tangential liquid inlet (or liquid and gas mixture) than in an empty column. Baffles (stationary) may aid to organize the liquid motion. The WWF (wetted wall fermenter) is a laboratory rather than industrial type apparatus for measurements of transfer phenomena at a defined transfer surface. The SPTF (staged pulse tray fermenter), coming to the stagewise operated types, is a version which should be preferred to simple sectioned columns as the tray motion aids the gas redistribution and breaking up of slugs. The SMCF (sectioned mixed compartment fermenter) is suitable provided backflow between compartments can be avoided : this type has also been used several times with minor modifications but it is a rather costly arrangement justified only when breaking up of air into very small bubbles is requested. The SJIF sectioned jet (2- or 3-phase) injection fermenter should provide an energetically cheap arrangement limiting backflow to a minimum

and still providing a very fine gas–liquid emulsion. All the above-mentioned equipment types can be operated in co-current or counter-current arrangement; the depicted systems of flow were chosen quite arbitrarily.

It is needless to say that extensive research work is still needed to provide methods and means for *a priori* elucidation of the optimal fermenter type for a given operation, which is undoubtedly the aim of fermenter design engineers. Not only design relations must be known, but also properties of the systems, kinetic data and correlations. Only then can the fermentation process become a system and be treated as such.

NOTATION

a	column radius;
C	concentration, dimensionless;
$\mathscr{D}$	molecular diffusivity;
D	dispersion coefficient;
D_e	eddy diffusivity;
d	diameter;
g	acceleration due to gravity;
h_c	compartment height;
j	number of perfectly-mixed cells;
k	constant;
L	length;
L_P	Prandtl mixing length;
N	number of molecules transferred;
$\bar{n}(y)$	average concentration of transferred substance;
Pe	Peclet number $= uL/D$;
t	time;
u	velocity;
$\dot{V}$	volumetric rate:
v	volume;
$y(x)$	axial distance;
θ	dimensionless time;
σ	surface tension;
ρ	density;
η	viscosity;
ε	gas hold-up:

Indices

a	axial;
av	average;
G	gas;
i	initial;
i	i-th;
l	liquid, longitudinal;
o	opening;
p	pulse;
r	radial;
∞	terminal velocity of a single bubble.

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