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Bubble Column Bioreactors

Tower Bioreactors Without Mechanical Agitation

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Summary

The present article investigates the behavior of bubble column bioreactors with yeast culture media in the absence of cells. To aid in the assessment of these reactors the following properties were estimated and partly theoretically treated: relative mean gas hold-up, bubble swarm velocity, bubble size, gas/liquid interfacial area, energy requirement for aeration, oxygen transfer coefficient across the gas/liquid interface and backmixing in the liquid phase. All of these properties are strongly influenced by the composition of the culture medium and the type of aerator. It is shown that in bubble column bioreactors, in the absence of antifoam agents and with low viscosity culture medium, high oxygen transfer rates can be achieved at low energy requirement. By application of multistage columns particular properties of the bubble column can be varied significantly. A comparison of bubble column reactors with mechanically agitated,

as well as with air-lift bioreactors, indicates that bubble columns are economical reactors, especially for aerobic cultivations.

Introduction

Bubble column reactors are popular in the chemical industry because of their versatile use and economical advantages i.e., low investment costs due to their simple construction and low variable costs of production due to low energy requirement of their operation, which is maintained by fluid dynamical mixing and dispersion of the phases. All these advantages are also valid for their application in biotechnology. However, with few exceptions, bubble column bioreactors have not been introduced into industry yet because of the lack of the necessary know-how in their design and operation.

A further reason for the delay of the application of bubble column bioreactors is an economic one. The replacement of sterile stirred tank bioreactors by new, more economical, reactor types is often unattractive due to high initial costs and long durability of the existing equipment.

In stirred tank bioreactors the construction of the equipment, especially that of the aerator, is not as decisive as in the case of bubble column bioreactors, since the performance of the stirred tank bioreactor can be improved up to a limit by an increase of the mechanical energy input. The lack of such a safety factor increases the risk of the applied bubble column bioreactor not giving the required performance. Therefore more careful and accurate design than for stirred tank bioreactors is necessary to lower the risk. The necessary data for this design exist only partly. The aim of this paper is to present more basic data for bubble column bioreactor design and operation, especially with regard to SCP production.

1. Application of Bubble Column Bioreactors in Industry

Large scale industrial application of bubble column bioreactors is rare [1, 2]. After a series of patents had been granted [8–13] on so-called 'tower fermentors' for the production of alcoholic liquids, in particular beer, the first application was realized [3, 4, 14–17], in pilot plant and then in production-scale.

The commercial production of beer in tower fermentors has been carried out in continuous operation over a period of many years. The beer produced is for all practical purposes indistinguishable from that produced in the conventional batch fermentation. For the successful continuous operation of a tower bioreactor it is essential to use a flocculent yeast, which is easy to separate from the beer at the tower head, since otherwise the yeast would be washed out and an insufficient yeast concentration maintained. The mean (wet) yeast concentration 25% w/w is generally attained with values as high as 30–35% w/w at the bottom and as low as 5–10% w/w at the top. These bioreactors are also applied in the U.K. in vinegar production [4]. Newer applications of such bioreactors without mechanical agitation have been worked out for SCP-production. Since

the planned commercial units are larger than the usual bioreactors, by the application of standard stirred tank bioreactors, one would run into several difficulties due to the necessity for heat removal in external cooling loops with sufficiently high pumping rates, and to the intensive aeration as well as agitation required. Their high energy requirement would prevent the economical operation of a large commercial plant. To avoid these difficulties, especially the external cooling of the fermentation medium which is necessary to remove the great amount of heat produced by mechanical stirring, new pneumatic bioreactors were developed. Air-lift bioreactors became popular. One of the first patents for the use of this bioreactor was granted to Lefrancois in 1955 [18], and several units which are in use are described in the literature [19–25]. ICI has developed a bubble column bioreactor with external recycling [the pressure cycle fermentor (PCF)] which has operated very satisfactorily in pilotscale production of ca. 1000 tons per year protein [26]. Pilot plant air-lift bioreactors have been applied by BP Proteins Ltd. [37]. The Kanegafuchi Chemical Industry Co., Ltd., Japan, has also developed a bubble column bioreactor with external recycling for n-paraffin solutes [28]. The air-lift bioreactor of Gulf Research and Development Co., Pittsburgh, is supplied by a draft tube and applied in the semicommercial petroprotein unit at Vasco, California [29]. A bench-scale bubble column bioreactor has been used for yeast production in Prague [5].

Different modifications of bubble column bioreactors, e.g. multistage tower reactors with a mechanical stirrer, have also been developed [6, 7].

To further extend the application of these pneumatic tower bioreactors (bubble column reactors with and without recycling) more data are needed which are evaluated under fermentation conditions.

2. Properties of Bubble Columns and Their Characterization

The main task of bubble columns for aerobic cultivation is the dispersion of air in the liquid to maintain the high oxygen transfer rates, OTR's, necessary to high productivity. The OTR depends on the overall volumetric mass transfer coefficient and the oxygen driving force. Since in common cultivation systems the gas side mass transfer resistance can usually be neglected, one considers only the resistance in the liquid phase. This assumption is made in the present paper.

The following definitions are used:

The oxygen driving force is the difference between the oxygen concentration in the liquid at the interface C_L^* and in the bulk C_L. It is assumed that C_L^* can be calculated by the partial pressure of oxygen in the gas phase and the Henry coefficient H_e of oxygen, i.e. at the interface distribution equilibrium of oxygen prevails.

Instead of the over all mass transfer coefficient the individual mass transfer coefficient of the liquid phase k_L is used, which is defined by Eq. (1):

$$Q_{O_2} = k_L a' (C_L^* - C_L) \tag{1}$$

where $Q_{O_2} = \left(\frac{\text{mass } O_2 \text{ transferred}}{\text{time}}\right)$

C_L, C_L^* = concentration of O_2 in the liquid bulk phase and/or at the interface $(\frac{\text{mass } O_2 \text{ dissolved}}{\text{liquid volume}})$

a' = gas/liquid interfacial area

$$k_L = \frac{Q_{O_2}}{a'(C_L^* - C_L)} = \left(\frac{\text{volume of liquid}}{\text{interfacial area} \times \text{time}}\right) \text{ or}$$

$$k_L a = \frac{k_L a'}{V_L} = \frac{Q_{O_2}}{V_L} \frac{1}{C_L^* - C_L} = \left(\frac{1}{\text{time}}\right)$$

with $a = \frac{a'}{V_L}$ specific interfacial area $(\frac{\text{gas/liquid interfacial area}}{\text{volume of liquid}})$.

The correlations for the mass transfer coefficient are usually expressed in dimensionless form:

$$Sh = C_1 (SC)^n (Gr)^m \tag{2}$$

where $Sh = \frac{k_L \cdot d_B}{D_L}$ Sherwood number

$Sc = \frac{\nu_L}{D_L}$ Schmidt number

$Gr = \frac{d_B^3 \rho L \Delta \rho g}{\eta_L^2}$ Grashoff number

d_B = mean bubble diameter

D_L = diffusivity of O_2 in the liquid phase

$\nu_L = \frac{\eta_L}{\rho_L}$ kinematic viscosity of the liquid phase

η_L = dynamic viscosity of the liquid phase

ρ_L = density of the liquid phase

$\Delta\rho = \rho_L - \rho_g$

ρ_g = density of the gas phase

g = acceleration due to gravity

n, m and C = constants.

Because bubbles of different size behave dissimilarly the experimental correlations are valid only for a given range of d_B: e.g. for small bubbles ($d_B < 2.5$ mm) Calderbank *et al.* [30] gave Eq. (2) with

$$C_1 = 0.31, \qquad n = 0.33, \qquad m = 0.33$$

and for large bubbles ($d_B > 2.5$ mm) with

$$C_1 = 0.42, \qquad n = 0.5, \qquad m = 0.33.$$

According to these equations k_L is independent of bubble size within these two ranges and depends only on the physical properties of the system [31].

The specific interfacial area *"a"* can be calculated for a swarm of nearly spherical bubbles by Eq. (3):

$$A = \frac{a'}{V} = \frac{6\,E_G}{d_s} = a \cdot (1 - E_G). \tag{3}$$

In Eq. (3) E_G is the mean relative gas hold up defined by Eq. (4):

$$E_G = \frac{V - V_L}{V} = \frac{H - H_L}{H} \tag{4}$$

where V = volume of the bubbling layer
V_L = volume of the bubble free liquid layer
H = height of the bubbling layer
H_L = height of the bubble free liquid layer
a = a'/V_L specific interfacial area

d_s is the "Sauter" mean or surface volume mean diameter:

$$d_s = \frac{\sum_1^N n_i d_i^3}{\sum_1^N n_i d_i^2} \tag{5}$$

where n_i = the frequency of the bubbles with the diameter d_i.

According to Oels [32] a simple relation between E_G and d_s holds:

$$E_G = C_2 Fr^p \tag{6}$$

where Fr = $\frac{w_{SG}}{\sqrt{g d_s}}$ Froude number
w_{SG} = superficial gas velocity
C_2 and p are constants.

Therefore the specific interfacial area A depends only on w_{SG} and d_s:

$$A = \frac{C_3 {w_{SG}}^p}{g^{0.5p} {d_s}^{1+0.5p}} \tag{7}$$

where C_3 is a constant.

According to Eq. (7) A can be enlarged either by increasing w_{SG} or by diminishing d_s. Economical production demands as low energy input as possible to keep low the amount of heat produced by energy dissipation and the cooling capacity needed to remove this heat.

The increase of w_{SG} means higher compression energy (and sometimes heavier foam problems), the decrease of d_s can be achieved in different ways. Since the bubble diameter plays a decisive role in aerobic fermentors, especially in bubble columns with regard to the OTR, its dependence on the most important design and process parameters has to be considered.

In stirred tank reactors the air is injected into the liquid at the base of the mixing vessel by a simple gas intake system. The dispersion of the injected gas phase is achieved by

mechanical agitator which produces dynamic pressure by means of turbulence.
In the turbulent field the large bubbles are unstable, they disintegrate. Their size is controlled by the dynamical equilibrium bubble size. In bubble column reactors often flat gas distributors (perforated or porous plates) are applied which produce small bubbles. The initial size of these bubbles depends on the forces acting on them during their formation. Several investigations have been carried out on single bubble formation at orifices and nozzles [44]. Since perforated plate distributors are multi-orifice and porous plate distributors are multinozzle systems, the initial bubble size can be calculated by the relations developed for single bubbles, as long as the interaction of the bubbles is low and the bubble formation frequency remains below a limit. At high bubble formation frequency coalescence can occur during the formation (pairing of bubbles [45–48]). However, if the oxygen requirement is low, relative low gas flow rates are used, therefore it is possible to apply the well known relations developed for single bubbles [44] to calculate the initial bubble size.
In general, bubble formation occurs in two stages, i.e. the expansion and ascending stages. During the expansion stage the bubble is kept on the nozzle- or orifice-opening. It grows by the inflowing gas. According to the static theory [44], the first stage is finished when the buoyancy force becomes greater than the forces which act downwards on the bubble. At this point the bubble begins to ascend. During the ascending stage the bubble remains connected with the nozzle and/or orifice opening by a tail, which has the diameter of the opening. Across this tail the bubble is fed further by gas. The bubble formation is stopped by the disconnection of the tail. According to the dynamical theory [49] the lift-off of the bubbles from the orifice (or nozzle) is caused by the inward radial motion of the liquid which narrows the tail of the bubble up to detachment.
For constant gas flow rate Q, which is applied in the present investigation, the final volume of a single bubble V_B is given by Eq. (8):

$$V_B = V_E + Q\,t_c. \tag{8}$$

Here t_c is the duration of the ascending stage and V_E the volume of the bubble at the point of lift-off [44]:

$$V_E^{5/3} = 0.047\,\frac{Q^2}{g} + 2.41\,\frac{\nu_L}{g}\,Q\,V_E^{1/3} + 3.14\,\frac{D_\delta\sigma}{g\rho_L}\,V_E^{2/3}. \tag{8a}$$

The final volume of the bubble can be estimated by Eq. (8b):

$$r_E = \frac{B}{2\,Q(A+1)}\,(V_B^2 - V_E^2) - \frac{C}{AQ}\,(V_B - V_E) - \frac{3\,G}{2\,Q\,(A-\frac{1}{3})}\,(V_B^{2/3} - V_E^{2/3}) \tag{8b}$$

where $r_E = (\frac{3}{4\,\pi})^{1/3}\,V_E^{1/3}$

$$A = 30.6\,r_E\,\nu_L/Q$$

$$B = 1.45\,\frac{g}{Q}$$

$$C = \frac{4.55\,D_\delta\sigma}{\rho_L Q}$$

$$G = 3.51\,\nu_L.$$

Equation (8) can only be applied in the range in which separate bubbles are formed. With increasing gas flow rate a transition at the aerator from bubbling gas into gas jet occurs. The critical flow rate of this transition is given by Eq. (9a) and/or (9b):

$$Q'_{cr} = 20.4 \frac{\sigma}{\rho_L} \sqrt{\frac{D_{\ddot{o}}}{g}} \quad (cm^3/s) \tag{9a}$$

according to Brauer [108] and

$$Q_{cr} = \sqrt{\frac{2\pi^2 D_{\ddot{o}}^3 \sigma}{16 \rho_G}} \quad (cm^3/s) \tag{9b}$$

according to Ruff [109]. Here ρ_G = the density of the gas phase.
These two equations yield rather different results. However, one can consider Q'_{cr} as the upper and Q_{cr} as the lower limit of the critical flow rate. If a gas jet forms in the laminar liquid at the orifice or nozzle it disintegrates in a given distance from the opening due to the instability of the gas-liquid interface. For the systems investigated in the present paper the viscosity terms can be neglected, hence the inequality (10a) prevails [110]:

$$\frac{\alpha \rho_L}{\eta_L} \gg k^2, \tag{10a}$$

where α = growth rate of disturbance cm^{-1}
k = wave number of disturbance cm^{-1}.

The general stability equation then simplifies to [110]:

$$\alpha^2 = \frac{\sigma(1 - k^2 a^{*2}) k a^*}{\rho_L a^{*3} K_0(ka^*)/K_1(ka^*)}, \tag{10b}$$

where a^* = jet radius,
K_0 = modified Bessel function of the second kind or zeroth order,
K_1 = modified Bessel function of the second kind of first order.
This equation was first derived by Rayleigh [111]. The controlling wave length corresponds to the dimensionless wave number $(ka^*)_{max} = 0.485$.
Equation (10b) can be applied, if

$$\frac{\sigma \rho_L D_{\ddot{o}}}{\eta_L} > 36. \tag{10c}$$

With the media, perforated an porous plate used in this investigation inequality (10c) is always fulfilled.
Since the size of the bubbles formed from laminar cylindrical gas jets is controlled by the amplification of disturbances which result from surface instability, one can calculate the bubble volume, if one assumes that it is equal to the volume of the cylinder having the radius of the jet and the length λ, the acutal wave length of dominant wave [112]:

$$V_B = \pi a^{*2} \lambda \tag{10d}$$

where $\lambda = \frac{2\pi a^*}{ka^*}$,

hence

$$V_B = \frac{2\pi^2 a^{*3}}{(ka^*)_{max}} . \tag{10e}$$

By substituting the nozzle or orifice radius for the jet radius one obtains bubble volumes which agree fairly well with the experiments. Relation (10c) can be applied up to the gas flow rates where at the aerator no turbulence prevails.

In the presence of local turbulence at the aerator the ratio of the dynamic pressure force of the local turbulence to the interfacial force controls the bubble size. Therefore the initial bubble size at the gas distributor is controlled by the buoyancy and interfacial forces [Eq. (8)] at low gas flow rates (bubbling gas range), by the instability of the gas/liquid interface of the gas jet [given by Eq. (10b)] at intermediate gas flow rates, and by the ratio of the dynamical pressure force of the local turbulence to the interfacial force at high gas flow rates.

However, this initial bubble size is not necessarily preserved in the entire column. The ascending bubbles coalesce, if the initial bubble size is smaller than the local dynamical equilibrium bubble size in the column and the coalescence it not supressed, alternatively the bubbles disintegrate if the initial bubble size is larger than the local dynamical equilibrium bubble size. In systems with hindered coalescence the bubbles formed at the gas distributor can be preserved, therefore the size of the bubbles can be smaller than the dynamical equilibrium size, if the initial bubble diameter is below the dynamical equilibrium diameter in the column.

In pure liquids the coalescence/redispersion rate is high, therefore the bubbles quickly attain the equilibrium size. In this case and in systems with gas distributors which produce initial bubble sizes larger than the equilibrium size, the bubble diameter is not influenced by the gas distributor plate. The bubble size is controlled only by the dispersion equilibrium in the column. The dispersion equilibrium is reached when the ratio of dynamic to surface tension forces has a particular value which is characteristic for the system. This force ratio is given by the Weber-number *We*:

$$We = \frac{\tau d_B}{\sigma} \tag{11a}$$

where τ = dynamic pressure,
σ = surface tension.

For dynamic equilibrium Eq. (11b) holds:

$$We_{eq} = \frac{\tau d_{B\,max}}{\sigma} \tag{11b}$$

where $d_{B\,max}$ the maximum possible diameter of the bubble which can survive at dynamic equilibrium in a flow or turbulent field of dynamic pressure τ. In a one stage bubble column, in which the gas bubbles ascend due to the buoyancy forces with the relative velocity w_R with respect to the liquid the *We*-number is given by [38]:

$$We^2 = \frac{\rho_L w_R^2 d_B}{2\sigma} \tag{12}$$

for nearly spherical bubbles with a diameter of d_B, if one can neglect the viscous and inertia forces. Equation (12) holds for low viscosity liquids, as investigated in this paper, and for systems in which the bubble movement is not influenced by external forces (except gravity).

The Bond number, *Bd*, accounts for the gravitational and surface tension forces:

$$Bd^2 = \frac{\rho_L g d_B^2}{4\,\sigma}. \tag{13}$$

Berghmans [38] evaluated the boundary between the stable and unstable regions for bubble swarms as function of the *We*- and *Bd*-numbers by neglecting the viscous and intertia forces.

Calculating *We*- and *Bd*-numbers by means of the measured ρ_L, w_R, σ, and d_B the position of the bubbles on the stability diagram can be estimated [50]. If they are in the stable region the dynamical coalescence-redispersion equilibrium is not important. The bubble diameter is not influenced by $d_{B\max}$, but by the initial bubble diameter at the gas-distributor. If the bubbles are at the stability boundary, dynamical equilibrium prevails and $d_B \cong d_{B\max}$.

It is difficult to estimate the dynamic pressure τ of Eq. (11) for a complex turbulent flow. Such turbulence prevails, e.g. in a bubble column with nozzle aeration, near to the nozzle. Turbulent flow produces primary eddies which have a scale of similar magnitude to the dimensions of the main stream.

These large primary eddies are unstable and disintegrate into smaller eddies until all their energy is dissipated by viscous flow. During the transfer of the energy from primary eddies to small eddies the directional nature of primary eddies is gradually lost [40]. According to Kolmogoroff [39] the smallest eddies which are responsible for the energy dissipation are statistically independent of the primary eddies and have locally isotropic character. The scale of these smallest eddies l is given by Eq. (14):

$$l = \frac{\eta_L^{3/4}}{\rho_L^{1/2}} \left(\frac{E}{V_L}\right)^{-1/4} \tag{14}$$

where $\frac{E}{V_L}$ is the rate of energy dissipation per unit volume of the liquid.

If one assumes that in the presence of a bubble the local structure of the turbulence does not alter, the maximum stable diameter of the bubble is given by the ratio of the attacking shear stresses and the surface tension resisting the deformation of the bubble, i.e. by the *We*-number:

$$We = \frac{\overline{u^2(d_{B\max})}\,\rho_L\, d_{B\max}}{\sigma} \tag{15}$$

where $\overline{u^2(d_{B\max})} = \overline{(u_1 - u_2)^2}$

and u_1 and u_2 are the local velocities of the liquid at the maximum distance of $d_{B\max}$.

If $L \gg d_B \gg l$, where L the scale of primary eddies and l the scale of the smallest eddies $\overline{u^2(d_{B\max})}$ can be calculated by Eq. (16) [41]:

$$u^2(d_{B\max}) = C_4 \left(\frac{E}{V_L}\right)^{2/3} \left(\frac{d_{B\max}}{\rho_L}\right)^{2/3}. \tag{16}$$

Putting Eq. (16) into Eq. (15) and comparing it with Eq. (11) one obtains the theoretical relation (17) for τ

$$\tau = C_4 \rho_L \left(\frac{E\, d_{B\max}}{V_L \rho_L}\right)^{2/3} \tag{17}$$

and for d_{max}

$$d_{max} = C_5 \frac{\sigma^{0.6}}{\left(\frac{E}{V_L}\right)^{0.4} \rho_L^{0.2}} \tag{18}$$

where C_4 and C_5 are constants.

In a given system (C_5, ρ_L and σ are constant) $d_{B\max}$ depends only on the rate of energy dissipation $\frac{E}{V_L}$, i.e. on the power input per unit volume of the liquid. Therefore one can produce small bubbles ($d_{B\max}$ is small) by a high rate of energy dissipation. However, high $\frac{E}{V_L}$ means also high power input per unit volume, i.e. high energy requirement and high variable costs. Economical operation demands low power input.

If the coalescence rate in the fermentation medium is low, it is more economical to apply the energy in a small volume at the site of bubble formation, i.e. to apply a high rate of energy dissipation locally and to retain overall a relatively low energy requirement [42]. Thus one can form small bubbles due to small $d_{B\max}$ in this volume. By delayed coalescence this small bubble size can be preserved and a high specific interfacial area can be achieved with relatively low energy input. Coalescence can be delayed or completely supressed by additives (e.g. C_1–C_2 alcohols etc.) which are often used as substrates. The influence of the substrate on "a" should be considered, both when the substrate is selected and on the specification of "a".

Longitudinal mixing also influences the operation of continuous bubble column fermentors.

In continuous stirred tank fermentors it is assumed that the mixing is "perfect", therefore the ideal continuous stirred tank reactors (CSTR) model can be applied. According to this model the agitation is sufficient to assume homogeneous conditions so that the composition of the effluent from the vessel is always the same as the composition of the contents. The material balance over the vessel with respect to the cell mass X in the vessel is given by Eq. (19)

$$\frac{dX}{dt} = D\,(X_0 - X) + \mu X \tag{19}$$

where X_0 = cell concentration in the feed,

D = $\frac{E}{V_L} = \bar{t}^{-1}$ dilution rate or reciprocal residence time

F = feed

V_L = volume of the liquid in the vessel.

Under steady state conditions:

$$\frac{dX}{dt} = 0 \quad \text{and with}$$

sterile feed, $X_0 = 0$, the specific growth rate μ equals the dilution rate:

$$D = \mu. \tag{20}$$

If the intensity of the mixing is less than "perfect", the actual wash out rate of organism is less than μ unless the liquid culture is (frequently or continously) reinoculated. This question was treated by Erickson *et al.* [33, 34]. On the other hand the utilization of the substrate is much better, if the intensity of the longitudinal mixing is low. Thus the optimal operation of a reactor and its productivity depends on the longitudinal mixing of the phases in the reactor.

The intensity of axial mixing is usually described by longitudinal dispersion models [36, 37] or back flow cell models [35, 36]. If the oxygen partial pressure in the gas phase changes only slightly, one can neglect the longitudinal dispersion in the gas phase and consider it only in the liquid phase. For this case the estimation of the longitudinal fluid dispersion and the application of a one-phase model is sufficient to characterise the axial mixing in the fermentor. In the present paper only the axial mixing in the liquid phase is considered and only the longitudinal dispersion model is applied.

The dispersion model is described by the following dimensionless equation, derived from an unsteady state material balance on the tracer component.

$$\frac{\partial C^*}{\partial \theta} + \frac{\partial C^*}{\partial x^*} = \frac{1}{Pe} \frac{\partial^2 C^*}{\partial x^{2*}} \tag{21}$$

where C^* = dimensionless concentration
θ = dimensionless time
x^* = dimensionless axial distance.

Equation (21) is used to estimate the model parameter [37, 43].

This model is based on the assumption that the two transport mechanisms bulk flow and longitudinal dispersion are independent of the position in the reactor. The dimensionless model parameter, the Peclet number Pe:

$$Pe = \frac{w_L L}{D_{L\,\mathrm{eff}}}$$

indicates the degree of mixing within the reactor. Here w_L is the effective flow rate of the liquid, $D_{L\,\mathrm{eff}}$ the effective longitudinal diffusivity and L is the test section.

In view of the foregoing considerations the following parameters are going to be used to characterise the bubble column fermentor:

E_G	average relative gas hold up
w_R	relative velocity of the bubble swarm
d_s	"Sauter" mean diameter of bubbles
We	Weber number of the bubble column
Bd	Bond number of the bubble column
a, A	specific interfacial area gas/liquid
$k_L a$	volumetric mass transfer coefficient of oxygen across the gas/liquid interface.
k_L	mass transfer coefficient of oxygen across the gas/liquid interface
Sh	Sherwood number

$\frac{E}{V_L}$ or $\frac{E}{V}$ rate of energy dissipation necessary to produce the specific interfacial area a.

D_L coefficient of longitudinal dispersion and/or back mixing in the liquid phase.

Several investigations have been carried out for the estimation of E_G, A, k_La and D_L in bubble columns of pure liquids (mostly water). Most recent evaluations for E_G [51], A [52] and Sh [53] are given by Gestrich and for D_L by Eissa [54] and Todt [36]. However, fermentation media have a complex composition and no general correlations are available for liquid mixtures.

3. Systems and Procedures

a) Biological System

Since the general aim of the current investigations is the optimization of yeast (*Candida boidinii*) production from alcohol in bubble column fermentors the culture medium given below was used with various substrates.

1 g	KH_2PO_4/l
2 g	$KHPO_4$/l
2 g	$(NH_4)_2SO_4$/l
2 g	$(NH_4)_2NO_3$/l
1 g	$Na_2HPO_4 \cdot 2H_2O$/l
0.2 g	KCl/l
0.2 g	$MgSO_4 \cdot 7H_2O$/l
0.5 mg	H_3BO_3/l
0.04 mg	$CuSO_4 \cdot 5H_2O$/l
0.1 mg	KI/l
0.2 mg	$FeCl_3 \cdot 6H_2O$/l
0.4 mg	$MnSO_4 \cdot H_2O$/l
0.4 mg	$ZnSO_4 \cdot 7H_2O$/l
0.2 mg	Ammoniumheptamolybdat/l.

The yeast (*Candida boidinii*) and the composition of the above culture medium originate from "Gesellschaft für Biotechnologische Forschung e. V." Stöckheim [55], our partner in cooperative research.

The following substrates were used in conjunction with the medium:

methanol
ethanol and/or
glucose
and for comparison
n-propanol
n-butanol and/or
10% Na_2SO_4.

The latter corresponds to the commonly used sulphite oxidation system for the estimation of the specific gas/liquid interfacial area [56].

To investigate the influence of the phosphates and the different substrates separately the following media were used: