DESIGNING OF AIRLIFT BIOREACTOR FOR DECREASING THE SHEAR STRESS ON THE CELL CULTURES

ABHINAV KAUSHAL (061552)

GYANENDU (061708)

MAY-2010

DEPARTMENT OF

BIOINFORMATICS & BIOTECHNOLOGY

JAYPEE UNIVERSITY OF INFORMATION TECHNOLOGY

WAKNAGHAT, SOLAN, HP, INDIA

CERTIFICATE

This is to certify that the work entitled, "DESIGNING OF AIRLIFT BIOREACTOR FOR INCREASING THE SHEAR SENSITIVITY FOR THE CELL CULTURING" submitted by **Mr Abhinav Kaushal (061552)** and **Mr. Gyanendu (061708)** in partial fulfillment for the award of degree of Bachelors of Technology in 2010 of Jaypee University of Information Technology has been carried out under my supervision. This work has not been submitted partially or wholly to any other University or Institute for the award of this or any other degree or diploma.

RUNNI MUKHERJEE

(Project Coordinator)

Lecturer,

Dept. of Bioinformatics and Biotechnology

Jaypee University of Information Technology

Waknaghat, Solan (H.P.).

ACKNOWLEDGEMENT

It has been a great pleasure working under the able guidance of faculty & staff in the Department of Bioinformatics and Biotechnology at Jaypee University of Information Technology, during our study as a B.Tech student. Thanks a lot to **Mrs. Runni Mukherjee**, our project advisor, for giving us the opportunity to undertake our B-tech final year project under her esteem guidance and guide us with the best of her knowledge and resources for the successful kick-off of this project and for her committed support in the forthcoming endeavors, otherwise, this research work would never have been possible.

Many people have contributed to this project in a variety of ways over the past few months. To the individuals who have helped me, I again express my appreciation. I also acknowledge the many helpful comments received from our teachers of the concerned department. I am indebted to all those who provided reviews & suggestions for improving the results and the topics covered in this project, and extend my apologies to anyone I may have failed to mention.

Thanks & Regards:

Abhinav Kaushal Abhinav

Gyanendu Gyanendu

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GREEK SYMBOLS

α-A parameter

β-A parameter

χ-A parameter

ρ_g- Density of gas (kgm^{-3})

ρ_L-Density of liquid (kgm^{-3})

μ_L- Viscosity of liquid (Pa s)

μ_g- Viscosity of gas (Pa s)

ε-Overall gas holdup

ε_d-Gas holdup in the downcomer

ε_r-Gas holdup in the riser

ABBREVIATIONS USED

G - glass,

SS - stainless steel,

AC - autoclavable,

SiS - sterilizable in situ,

SiP - sterilizable in the plant

ABSTRACT

Presently, there exist many designs for bioreactors and also airlift bioreactor in market but all these have certain limitations of which some significant ones have been improved upon in the proposed design. This innovative approach proposes a good air and liquid circulation, better mixing, better sparger location with its influence and also a fully new system of concurrent draft tubes for greatly improved influence in the mixing which are greatly required by the plant cells.The design has been supported with a mathematical model for calculation of various hydrodynamic parameters. The study of turbulence in the fluid present in different parts of the reactor has been mathematically calculated for the purpose of detecting levels of shear existing in various conditions. The major contribution of this novel design is that it can be directly used to provide better results for the industry application as it is based on mathematical hydrodynamic model, supported by equations and thus, just require scaling up to increasing capacity to meet a high working volume.

CHAPTER 1

INTRODUCTION

"Who knows that the work of Pasteur will lead to the innovation of bioreactor?"

This 21st century is turning into the age of biotechnology and almost every chemical, petrochemical, bioprocess, biotechnology industries are using these types of reactors. Commonly applications of these bioreactors are quiet diverse such as waste water treatment [12], production of e-polylysine, plant cell culturing, production of metabolites, fermentation [31] and many more. In chemical industries these bioreactor are the source of the low waste conversion of ethylene and chlorine to dichloroethane. These bioreactors are also recommended as promising photo bioreactors for the culturing of microalgae and cyanobacteria.

In biotechnology basically the metabolic activity of the microorganism is exploited to convert substrate into desired product. So, to optimize their productivity, the condition should be optimized properly. This necessitates a well balanced transport of nutrient to the cells and an efficient withdrawal of metabolites, especially if they are inhibiting or even toxic to the cell. These functions are well performed by this bioreactor.

A bioprocess model, thus, contains both, kinetics and transport description. In optimizing the performance of a biochemical production process, one must look for a well balanced interplay between kinetics and transport process. Both, the reactor as well as the organism must adapt to reach these goals. It is obvious that any transport becomes more difficult the longer the distances are which must be bridged. Hence, the relative importance of transport problems grow significantly with the scale of the reactor considered.

For the first time in 1940's the use of the stirred tank bioreactor came in picture during the world war1 in the chemical industry for the use in the first modern commercial fermentation that is of antibiotics production.

Later on the shortcomings of the stirred tank was substituted by the bubble columns and the modification of the bubble column resulted in a more refined version of invention i.e. airlift bioreactor which results in less damage to the shear sensitive cells. Airlift reactors have been

receiving much attention in research and industry because of their unique hydrodynamic characteristics.

According to the IUPAC definition it is defined as the bioreactor in which the reaction medium is kept fixed mixed and gassed by the introduction of gas or any other gas at the base of the column base equipped with either a draft tube or other device (external device) through which the reaction mixture is kept separated into the gassed and ungassed region. These airlift bioreactors are generally pneumatically agitated reactors that have no moving parts, low power consumption, good solid suspending , high mass and heat transfer characteristics and above all rapid mixing while retaining homogeneous shear stress [32]. In short, it can be considered as a gas induced circulation of liquid which would affect the overall operation and design. But problem is that how these circulations should be predicted and enhanced?

But, unfortunately the transport problem, microbial kinetics, and especially their interrelationship are not sufficiently understood, particularly in production scale reactor [36]. Much work must be invested in order to reach the final aim, the modeling of the entire systems in term of mathematical equation which can be solved with sufficient efficiency. A good airlift design requires knowledge of the effects of geometrical and operational parameters on hydrodynamics and mass transfer.

The fluid dynamics in bioreactor is reflected in many of the proceeding of the latest conferences on airlift bioreactor hydrodynamics [24]. Also, some reviews are also available on the industrial important bioreactor types such as Schugerl [37, 38].

The most important peculiarity of the current literatures on bioreactor fluid flow dynamics is that only very few experimental data are available which was obtained with simple laboratory conditions with simple model media.

The primary aim of this work is to enhance the understanding of airlift bioreactor. The emphasis is on the important aspects of the bioreactor design which has been characterized into three groups –mechanical factor (draft tube effect, sparger effect), thermodynamic factor (heat and mass transfer) and hydrodynamic factor (gas hold up effect, liquid circulation, mixing). Following these factors this review move to the measuring techniques that are considered which can be used in bioreactor during cultivation process or in model media which closely stimulate the production processes. Techniques which can only be employed in air-in water dispersion or similarly simple media is omitted. Similarly, problems related to the operation of airlift bioreactor are also worked out with great care. Better mixing, better gas hold up, collectively

leads to better mass and heat transfer which makes the airlift bioreactor – the reactor of choice. The absence of agitator adds to its benefits as it increases the shear sensitivity for the culturing of the cell. A work, done by Verschoor in 1985, reports that for industrial bubble column bioreactor the superficial velocity is of the order of 0.06m/s.in. Imperial Chemical Industry airlift reactor for single cell protein production, the superficial gas velocity has been increased to 0.22 m/s and this will increase oxygen transfer coefficient to 0.143 /s. This will certainly prove that liquid flow better than do the bubble column.

As there are many correlations given in many literatures choosing the best correlation between different parameters we would be able to scale up its production at low cost. The potential of this reactor to be further developed for many applications especially in plant biotechnology made this pneumatic device an important one.

Many literatures are present but none of the literatures combines all the factors affecting the working parameters altogether but this would be the first attempt which would take into account every factor related to the airlift bioreactor.

CHAPTER 2

LITERATURE REVIEW

What is Bioreactor..??

Bioreactor is a vessel in which is carried out a chemical process which involves organisms or biochemically active substances derived from such organisms.

Bioreactors are commonly cylindrical, ranging in size from some liter to cube meters,and are often made of stainless steel.

Bioreactor design is quite a complex engineering task. Under optimum conditions the microorganisms or cells will reproduce at an astounding rate. The vessel's environmental conditions like gas (i.e., air, oxygen, nitrogen, carbon dioxide) flowrates, temperature, pH and dissolved oxygen levels, and agitation speed need to be closely monitored and controlled. One bioreactor manufacturer, Broadley-James Corporation, uses vessels, sensors, controllers, and a control system, digitally networked together for their bioreactor system.

Continuous flow stirred tank reactors (chemostat): In the continuous flow, stirred tank reactor (CSTR or chemostat) fresh medium is fed into the bioreactor at a constant rate, and medium mixed with cells leaves the bioreactor at the same rate. A fixed bioreactor volume is maintained and ideally, the effluent stream should have the same composition as the bioreactor contents. The culture is fed with fresh medium containing one and sometimes two growth-limiting nutrients such as glucose. The concentration of the cells in the bioreactor is controlled by the concentration of the growth-limiting nutrient. A steady state cell concentration is reached where the cell density and substrate concentration are constant. The cell growth rate (μ) is controlled by the dilution rate (D) of growth limiting nutrient.

Cell culture bioreactors are categorized into two types: 1. those that are used for cultivation of anchorage dependent cells (e.g. primary cultures derived from normal tissues and diploid cell

lines. 2. Those that are used for the cultivation of suspended mammalian cells (e.g. cell lines derived from cancerous tissues and tumors, transformed diploid cell lines, hybridomas). In some cases the bioreactor may be modified to grow both anchorage dependent and suspended cells. Ideally any cell culture bioreactor must maintain a sterile culture of cells in medium conditions which maximize cell growth and productivity.

Fouling can harm the overall sterility and efficiency of the bioreactor, especially the heat exchangers. To avoid it the bioreactor must be easily cleanable and must be as smooth as possible (therefore the round shape).

Heat exchange is needed to maintain the bioprocess at a constant temperature. Biological fermentation is a major source of heat; therefore in most cases bioreactors need water refrigeration. They can be refrigerated with an external jacket or, for very large vessels, with internal coils.

Optimal oxygen transfer is perhaps the most difficult task to accomplish. Oxygen is poorly soluble in water -and even less in fermentation broths- and is relatively scarce in air (20.8%). Oxygen transfer is usually helped by agitation that is also needed to mix nutrients and to keep the fermentation homogeneous. There is however limits to the speed of agitation, due both to high power consumption (that's proportional to the cube of the speed) and the damage to organisms due to excessive tip speed.

Bioreactor treatment may be performed using microorganisms growing in suspension in the fluid or attached on a solid growth support medium. In suspended growth systems, such as fluidized beds or sequencing batch reactors, contaminated groundwater is circulated in an aeration basin where a microbial population aerobically degrades organic matter and produces carbon dioxide, water, and biomass. The biomass is settled out in a clarifier, then either recycled back to the aeration basin or disposed of as sludge. In attached growth systems, such as upflow fixed film bioreactors, rotating biological contactors (RBCs), and trickling filters, microorganisms are grown as a biofilm on a solid growth support matrix and water contaminants are degraded as they diffuse into the biofilm. Support media include solids that have a large surface area for bacterial attachment.

A bioreactor landfill operates to rapidly transform and degrade organic waste. The increase in waste degradation and stabilization is accomplished through the addition of liquid and air to enhance microbial processes. This bioreactor concept differs from the traditional "dry tomb" municipal landfill approach.

A bioreactor landfill is not just a single design and will correspond to the operational process invoked. There are three different general types of bioreactor landfill configurations:

Aerobic - In an aerobic bioreactor landfill, leachate is removed from the bottom layer, piped to liquids storage tanks, and re-circulated into the landfill in a controlled manner. Air is injected into the waste mass, using vertical or horizontal wells, to promote aerobic activity and accelerate waste stabilization. Anaerobic - In an anaerobic bioreactor landfill, moisture is added to the waste mass in the form of re-circulated leachate and other sources to obtain optimal moisture levels. Biodegradation occurs in the absence of oxygen (anaerobically) and produces landfill gas. Landfill gas, primarily methane, can be captured to minimize greenhouse gas emissions and for energy projects. Hybrid (Aerobic-Anaerobic) - The hybrid bioreactor landfill accelerates waste degradation by employing a sequential aerobic-anaerobic treatment to rapidly degrade organics in the upper sections of the landfill and collect gas from lower sections. Operation as a hybrid results in the earlier onset of methanogenesis compared to aerobic landfills The Solid Waste Association of North America (SWANA) has defined a bioreactor landfill as "any permitted Subtitle D landfill or landfill cell where liquid or air is injected in a controlled fashion into the waste mass in order to accelerate or enhance biostabilization of the waste." The United States Environmental Protection Agency (EPA) is currently collecting information on the advantages and disadvantages of bioreactor landfills through case studies of existing landfills and additional data so that EPA can identify specific bioreactor standards or recommend operating parameters.

Features Unique to Bioreactor Landfills: The bioreactor accelerates the decomposition and stabilization of waste. At a minimum, leachate is injected into the bioreactor to stimulate the natural biodegradation process. Bioreactors often need other liquids such as stormwater, wastewater, and wastewater treatment plant sludges to supplement leachate to enhance the microbiological process by purposeful control of the moisture content and differs from a landfill that simple recirculates leachate for liquids management. Landfills that simply recirculate leachate may not necessarily operate as optimized bioreactors.

Types of Bioreactor:

Several types of bioreactor enjoy use in both research and industry. Here are some of the most common:

CSTR – mechanical mixing and air-sparged liquid media

Airlift – uses air sparging to pneumatically mix the media

Combinations and variations of CSTR and Airlift reactors

Membrane – two permeable membranes to deliver nutrients and export wastes and products from bacteria in a center tube

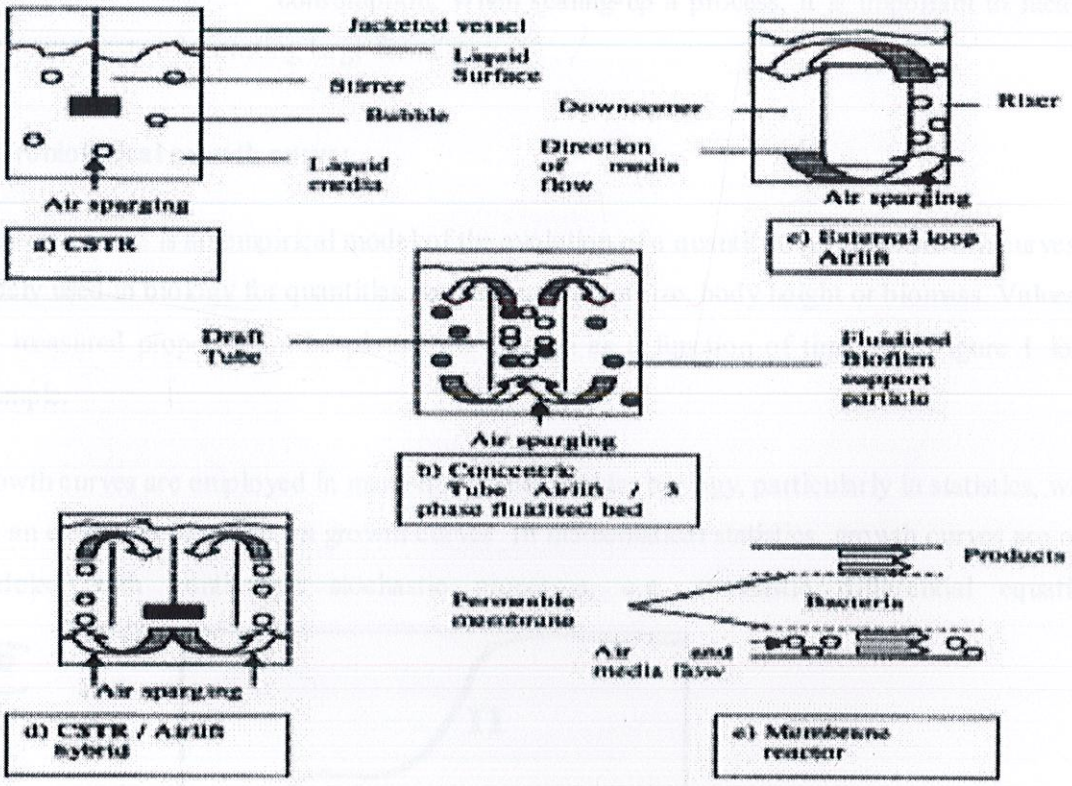
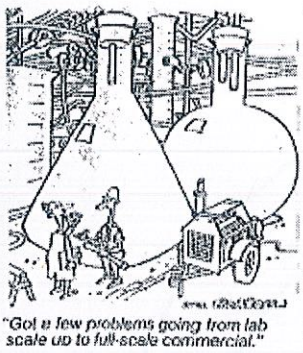


Figure 7: Types of Bioreactor

Scale up considerations:


"Got a few problems going from lab scale up to full-scale commercial."

This process is the important step for transferring bench-top fermentations to mass production. Scale-up would be very simple if all parameters affecting bacteria remained the same. Numerous empirical and semi-empirical relationships are often used to correlate variables such as shear rates and oxygen mass transfer with physical parameters such as impeller speed and reactor dimensions. One of the most important and often overlooked factors in scale-up is power consumption. When scaling-up a process, it is important to factor in the power costs of operating large fermenters.

Microbiological growth curve:

A growth curve is an empirical model of the evolution of a quantity over time.Growth curves are widely used in biology for quantities such as population size, body height or biomass. Values for the measured property can be plotted on a graph as a function of time; see Figure 1 for an example.

Growth curves are employed in many disciplines besides biology, particularly in statistics, which has an extensive literature on growth curves In mathematical statistics, growth curves are often modeled with continuous stochastic processes, e.g. stochastic differential equations.

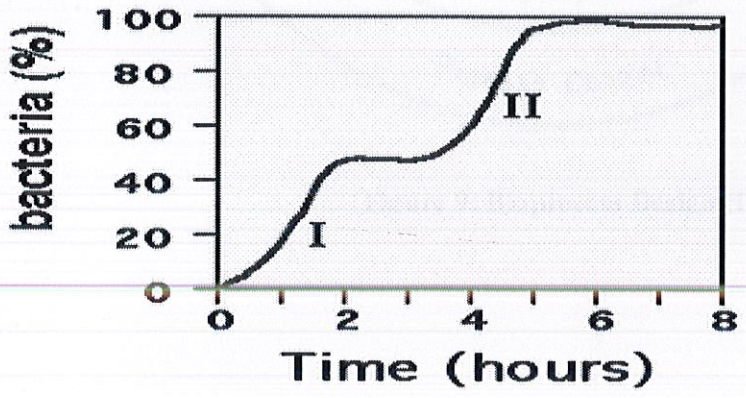


Figure 8: Microbiological growth curve

Bioprocess design hierarchy:

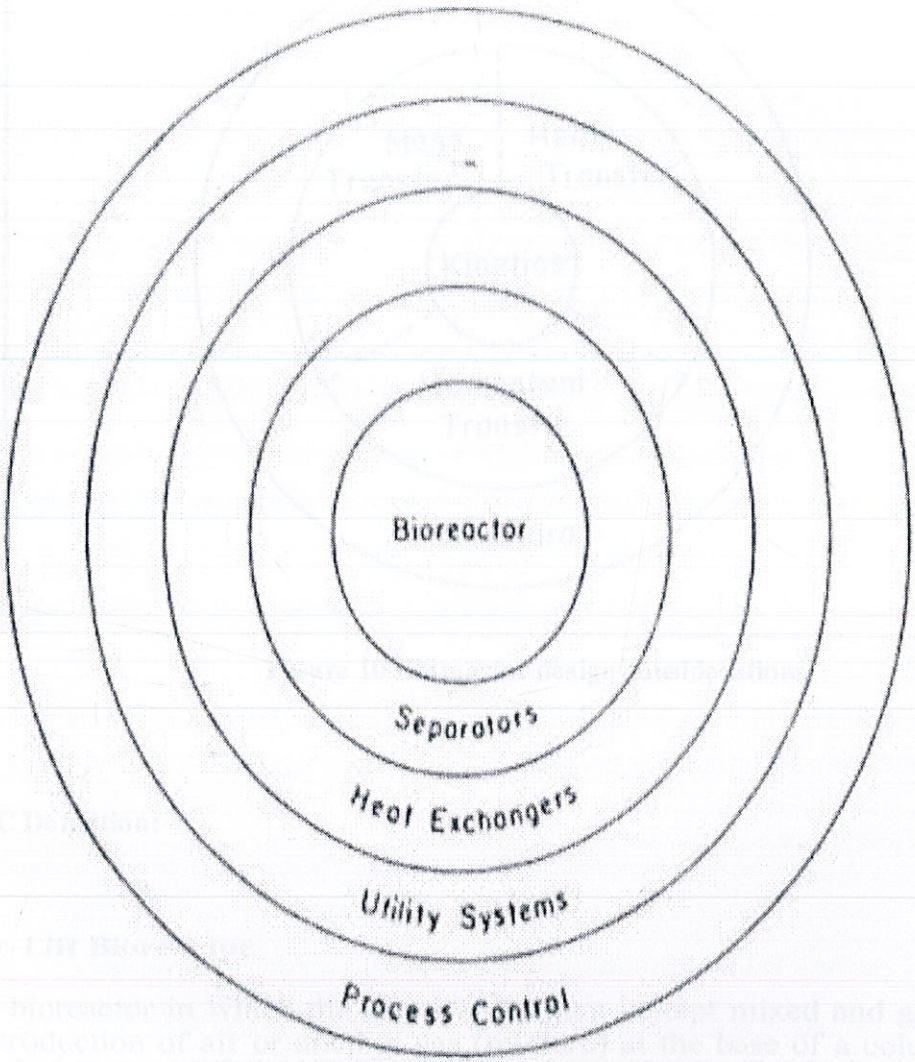


Figure 9: Bioprocess Design Hierarchy

Bioreactor design considerations:

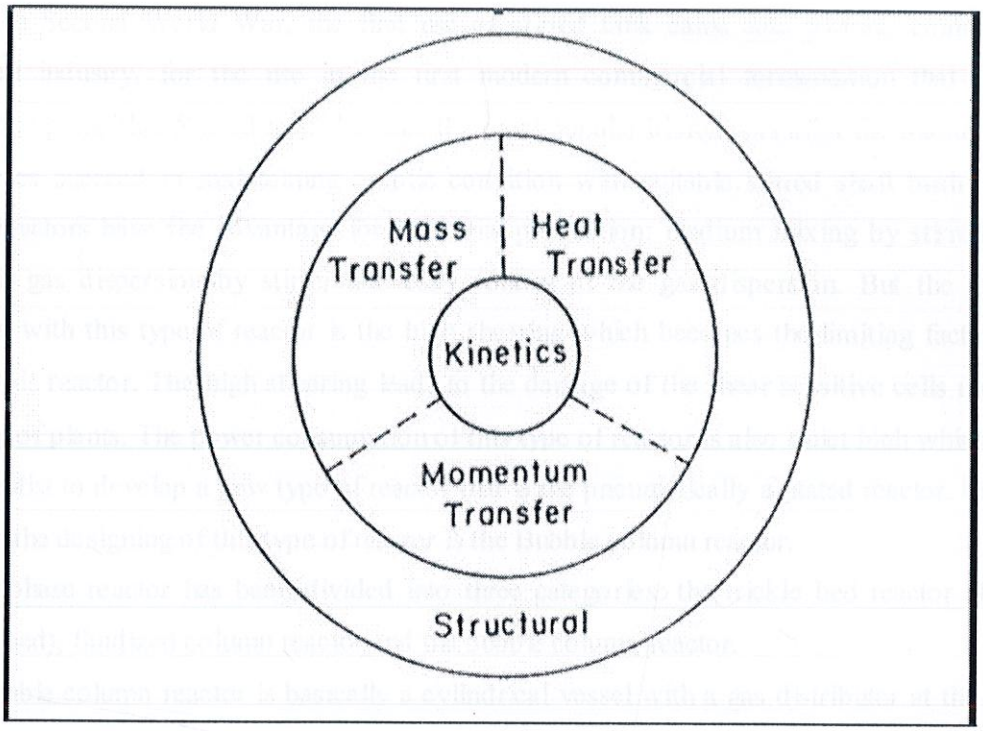


Figure 10 Bioreactor design considerations

IUPAC Definition:

Air-Lift Bioreactor

A bioreactor in which the reaction medium is kept mixed and gassed by introduction of air or another gas (mixture) at the base of a column-like reactor equipped either with a draught tube or another device (e.g. external tube) by which the reactor volume is separated into a gassed and an ungassed region thus generating a vertically circulating flow.
1992, *64*, 146

IUPAC Compendium of Chemical Terminology 2nd Edition (1997)

Pneumatically agitated reactor..?

After the Second World War, the first use of stirred tank came into picture, commonly in chemical industry, for the use in the first modern commercial fermentation that was the antibiotics penicillin. Stirred tanks became the most popular bioreactors after the manufacturing companies succeed in maintaining aseptic condition with suitable stirred shaft bush bearing. These reactors have the advantage for industrial production: medium mixing by stirred speed, efficient gas dispersion by stirrer and easy control of the gas dispersion. But the foremost problem with this type of reactor is the high shearing which becomes the limiting factor in the use of this reactor. The high shearing leads to the damage of the shear sensitive cells mainly in the case of plants. The power consumption of this type of reactor is also quiet high which makes the scientist to develop a new type of reactor that is the pneumatically agitated reactor. First step towards the designing of this type of reactor is the Bubble column reactor.

A multiphase reactor has been divided into three categories: the trickle bed reactor (fixed or packed bed), fluidized column reactor and the bubble column reactor.

This bubble column reactor is basically a cylindrical vessel with a gas distributor at the bottom with a gas sparger used for the aeration in the liquid or liquid-solid interface. This type of bubble column reactor with solid-liquid interface is called slurry type bubble column reactor. A wide application area of such reactor provides a lot of advantages. First of all, they have high mass and heat transfer coefficient that means high heat and mass transfer characteristics. Low maintenance cost and compactness provide it with the greater durability [3].These attractive advantages make their use in industry quiet high. These advantages promote their use in many chemical, petrochemical, biochemical and metallurgy industries. Some very well uses of this bubble column reactor are the famous Fischer-Tropsch process which is the indirect method for the liquefaction of the coal to produce transportation fuel and many other gaseous fuels [3].

Other uses of the bubble column in the biochemical industries are:

Bioproducts	Biocatalyst
Thienamycin	Streptomyces cattleya[4]
Glucoamylase	Aureobasidium pullulans [5]
Acetic acid	Acetobacter aceti[6]
Taxol	Taxus cuspidate[7]
Oragnic acids	Eubacterium limosum[8]
Ethanol fermentation	Saccharomyces cerevisiae[9]
Monoclonal antibody	Hybridoma cells[10]

TABLE 1: Bioproducts & Biocatalyst

Beside all these advantages, bubble column lacks the advantages of the low shearing to the plant cells or some shear sensitive cells. So, this leads the researcher to go for the more improved version of the bubble column that is the airlift bioreactor. According to the IUPAC definition, it is defined as the bioreactor in which the reaction medium is kept fixed mixed and gassed by the introduction of gas or any other gas at the base of the column base equipped with either a draft tube or other device (external device) through which the reaction mixture is kept separated into the gassed and ungassed region [11]. It carries no moving parts with it so increases the durability and ease to handle. These pneumatically agitated airlift reactors provides a more improved shearing of the cells which makes its use for the shear sensitive cells more popular.The main advantage of airlift over bubble column are improved mixing and actually higher mass transfer coefficient in some instances. This latter is possible because of the very high gas velocities which may be used in airlifts. These airlift reactors are also having much more improved liquid circulation. And the most important factor is the low power consumption as compared to the bubble column.

Bubble column vs. Airlift bioreactor

Bubble column reactor	Airlift reactor
Gas flow rate is not the deciding factor in the liquid flow circulation.	Gas flow rate is the deciding factor in the liquid flow circulation.
Large liquid throughputs not possible.	Large liquid throughputs possible.
External recycle mechanisms required for high liquid velocities.	**No** external recycle mechanisms required for high liquid velocities.
Gas velocities for liquid blown out condition are low.	Gas velocities for liquid blown out condition are high.
Draft tube absent.	Draft tube present.
High power consumption.	Low power consumption.

TABLE2: Bubble column vs. Airlift bioreactor

Working of Airlift Bioreactor:

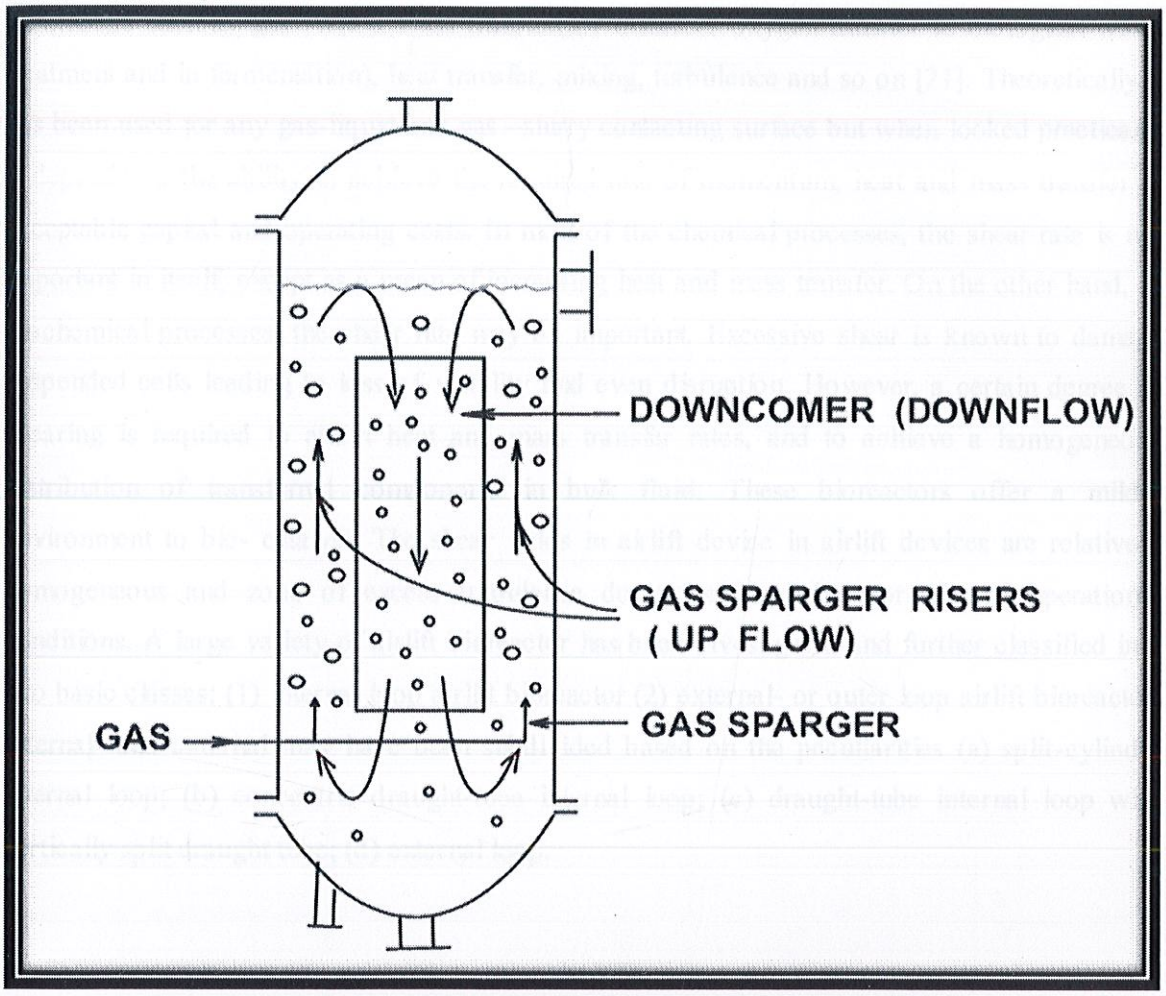


Figure 11: Basic Design Air Lift Bioreactor

As it has been previously described by the IUPAC definition but in 1988, Chisti et al, described it as a pool of liquid divided into two vertical zones connected at the bottom and top where on eof the zones (the riser) is sparged by a gas and the resulting gas holdup difference between the gas sparged riser and the ungassed downcomer leads to a difference in the bulk densities of the fluid in the two zones and hence an induced fluid circulation – upflow in the riser and the downflow in the downcomer-is set up. Further it is the coming years; it has been divided into five parts –a gas-liquid separator, two risers, a downcomer and a bottom section. This induced

fluid circulation is the design characteristic of airlift bioreactor. It determines the residence time of the liquid in the various zones of the reactor and controls important reactor performance parameters such as gas –liquid mass transfer(for instance, oxygen transfer in biological waste treatment and in fermentation), heat transfer, mixing, turbulence and so on [21]. Theoretically it has been used for any gas-liquid and gas –slurry contacting surface but when looked practically it depends on the ability to achieve the required rate of momentum, heat and mass transfer at acceptable capital and operating costs. In most of the chemical processes, the shear rate is not important in itself, except as a mean of increasing heat and mass transfer. On the other hand, in biochemical processes, the shear rate may be important. Excessive shear is known to damage suspended cells leading to loss of viability and even disruption. However, a certain degree of shearing is required to attain heat and mass transfer rates, and to achieve a homogeneous distribution of transferred components in bulk fluid. These bioreactors offer a milder environment to bio- catalyst. The shear fields in airlift device in airlift devices are relatively homogeneous and zone of excess turbulence do not exist under normal and operational conditions. A large variety of airlift bioreactor has been investigated and further classified into two basic classes: (1) internal loop airlift bioreactor (2) external- or outer loop airlift bioreactor. Internal- and external may have been subdivided based on the peculiarities (a) split-cylinder internal loop; (b) concentric draught-tube internal loop; (c) draught-tube internal loop with vertically split draught tube; (d) external loop.

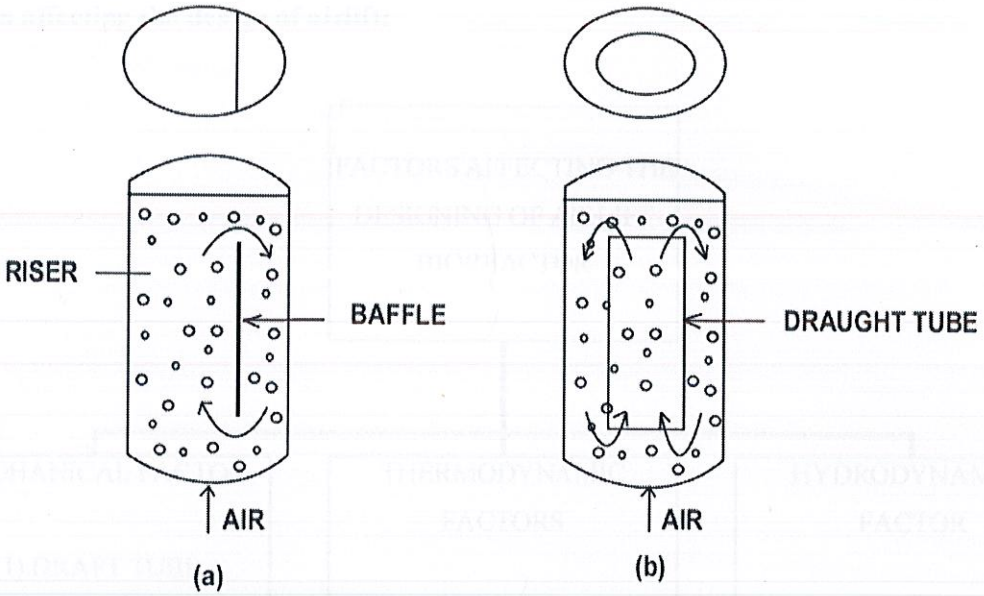


Figure 12: Internal Loop Draught Tube Types

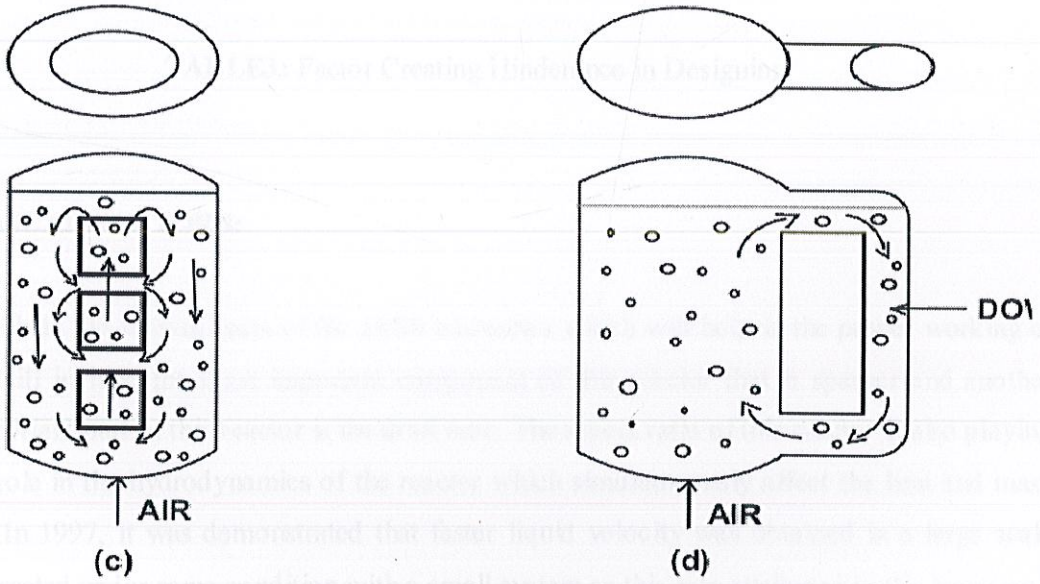


Figure 13: External Loop Draught Tube Types

Factors affecting the design of airlift:

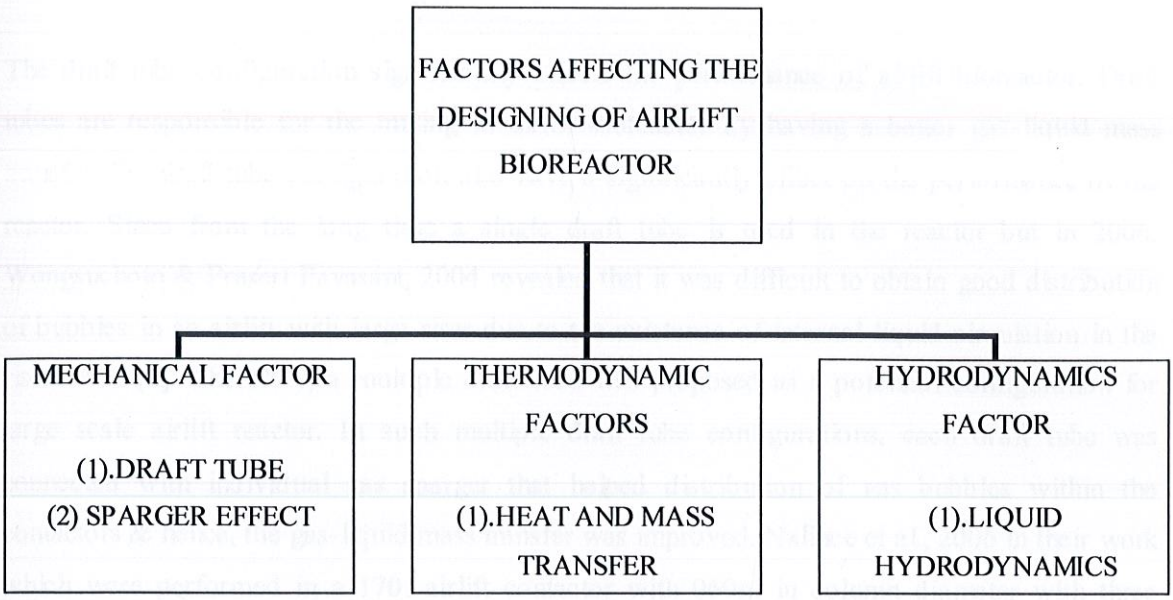


TABLE3: Factor Creating Hinderance in Designing

MECHNICAL FACTORS:

It will include the various parts of the airlift bioreactor which will help in the proper working of it. This will include the most important component of this reactor that is sparger and another most important part of this reactor is the draft tube. The aspect ratio of this reactor is also playing a major role in the hydrodynamics of the reactor which simultaneously affect the heat and mass transfer. In 1997, it was demonstrated that faster liquid velocity was obtained in a large scale airlift operated under same condition with a small system as this was attributed to the lower wall friction generated in the larger scale airlift contactor than the smaller system [13]. Similarly in 2004, Blazej et al stated that gas holdup increased with an increase in reactor scale under the same operating condition [7].

I.Draft tube

ii.Sparger design and location

I.Draft tube configuration

The draft tube configuration significantly affects the performance of airlift bioreactor. Draft tubes are responsible for the mixing in airlift bioreactor by having a better gas-liquid mass transfer. So, draft tube configuration also have a significantly effect on the performance of the reactor. Since from the long time a single draft tube is used in the reactor but in 2006, Wongsuchoto & Prasert Pavasant, 2004 revealed that it was difficult to obtain good distribution of bubbles in an airlift with large riser due to the existence of internal liquid circulation in the riser itself [6]. Therefore, a multiple draft tube was proposed as a potential configuration for large scale airlift reactor. In such multiple draft tube configurations, each draft tube was connected with individual gas sparger that helped distribution of gas bubbles within the contactors & hence, the gas-liquid mass transfer was improved. Nalinee et al., 2006 in their work which were performed in a 1701 airlift contactor with 069m in column diameter with three different configuration of draft tube (Fig.5) with different u_{sg}, A_d/A_r, and salinity level and compared it with the conventional single draft tube system. Increasing the number of draft tube enhanced the contacting area between riser and downcomer leading to a better circulation of fluid inside the airlift system. This is also resulted in a higher gas liquid interfacial area for better mass transfer.

Effect of geometry on the sparger geometry and its location

As we know that in airlift bioreactor, the bubbles which are the carriers of oxygen inside the reactor plays a crucial role in the overall performance of the reactor.The ERT is used to analyze the flow regime by the use of different spargers. The ERT (electrical resistance tomography) gives quantitative information such as a characteristic time and a characteristic frequency of void fraction waves, which are closely related to flow structure in the prevailing regime. But the question is that what are these void fractions and void fraction waves? In general, the bubble column gas bubbles are generated using the gas sparger and this gas bubble fraction is called void fraction. Due to the chaotic behavior of collision and coalition of bubble, disturbance waves are generated in the bubble column and this is known as void fraction waves or kinematic waves. These waves play an important role in identifying the flow regime of the bubble column

hydrodynamics. Void fraction waves are detected by measuring the mean void fraction of the flow pipe. Based on the void fraction properties and wall pressure fluctuation, the flow regimes are classified into three parts (discrete bubbly flow, cluster bubbly flow and churn turbulent flow).This ERT distinguishes the void fraction disturbance in different flow regime with great clarity. These three different flow patterns throw some lights on the gas-liquid interfacial behavior in the bubble column.

Discrete bubbly flow

The gas phase is uniformly distributed in the liquid as discrete bubble. Here the bubble numbers density gradually increases as the gas flow is increased. The bubbles are characterized by uniform size and uniform void fraction. The bubble generated at the sparger rise undistributed, a small transverse axial oscillations occur. The extend of the bubble coalescence and break up is almost negligible and there is no large scale liquid circulation in the column.

Cluster bubbly flow

In the cluster bubbly flow regime, bubble coalesces or agglomerate churns together and consequently form cluster. As they travel through the column than the bubble cluster larger and coalesces with each other. This creates the bubble fluctuation. The time record of the flow shows the apparent random fluctuation with increase in the calculated void fractions values. This type of flow is also called as the transition flow between the homogeneous and heterogeneous regimes. This results in the hydrodynamic instability.

Churn turbulent flow

In churn-turbulent regime, abrupt coalescence of the packed bubbles appears with re-distribution of bubbles to form and distorted structure of gas phase which shows the characteristics of churn type flow. Large-scale repeated re-circulation of liquid is induced by the voidage profile with higher order of gas velocities. The unstable structures are suddenly developed with slight increase in the gas flow rate. The flow pattern observed to be irregular structure. Localized recirculation takes place. The turbulent characteristics are assumed to be isotropic and scale of turbulence is directly proportional to the column diameter.

Gas sparger location:

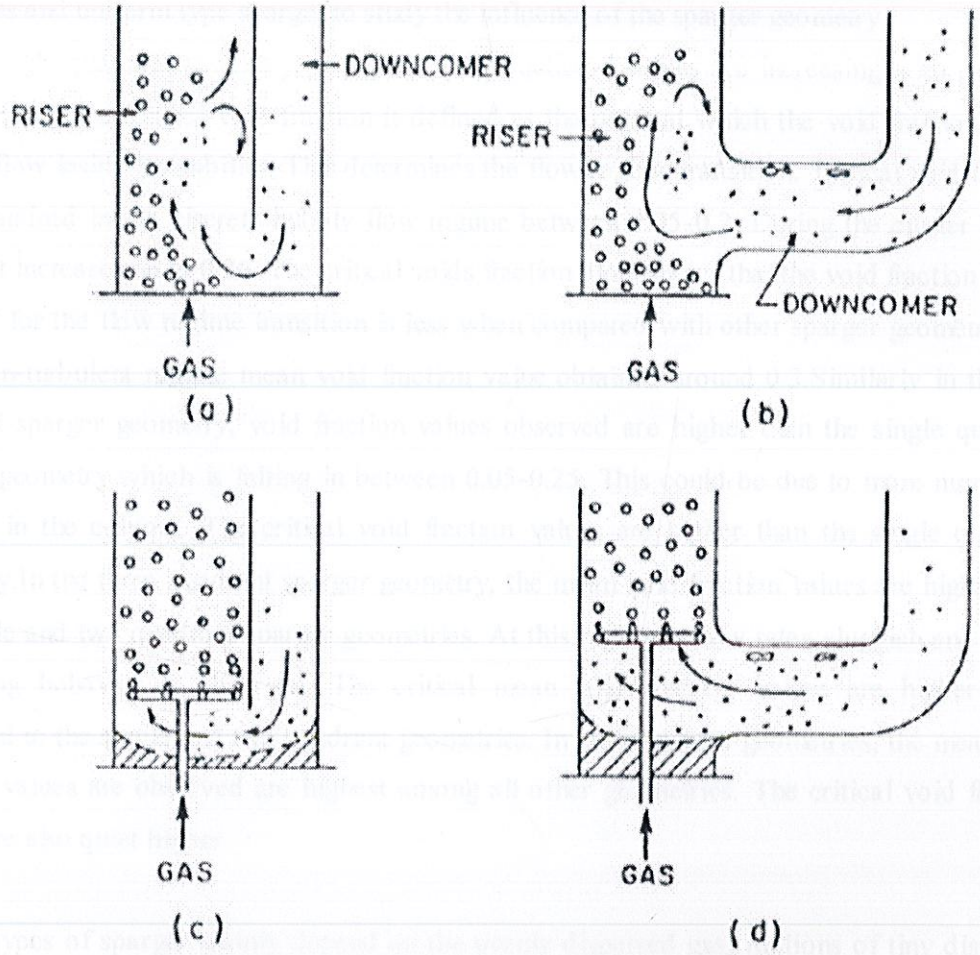


Figure 5.1: The influence of sparger location on gas distribution in airlifts. Poor distribution of gas in (a) internal- and (b) external-loops. Proper sparger positioning (c and d) for improved gas distribution. Hatched areas indicate the filled-in zones to improve liquid flow and to prevent any biomass settling.

Figure 14: Influence of Sparger Location

Quicker & Deckwar [10] & Kuo [26] have studied the effect of sparger geometry on the void fraction wave. In their work, the sparger was designed with 184 holes with 1mm diameter of each. The sparger has four sections of 46 holes present in each section with a separate control vale or each section. They conducted the experiment with single quadrant, two quadrant, three quadrants and uniform type sparger to study the influence of the sparger geometry.

In the single quadrant geometry, the mean void fractional values are increasing with gas flow rate. Actually the critical void fraction is defined as the point at which the void fraction of the bubbly flow losing its stability. This determines the flow regime transition. Typical void fraction value obtained in the discrete bubbly flow regime between 0.05-0.2. During the cluster bubbly regime it increases up to 0.26. The critical voids fraction plots shows that the void fraction values required for the flow regime transition is less when compared with other sparger geometries. In the churn-turbulent regime mean void fraction value obtained around 0.3.Similarly in the two quadrant sparger geometry, void fraction values observed are higher than the single quadrant sparger geometry which is falling in between 0.05-0.25. This could be due to more number of bubbles in the column. The critical void fraction values are higher than the single quadrant geometry.In the three quadrant sparger geometry, the mean void fraction values are higher than the single and two quadrant sparger geometries. At this high gas flow rates sluggish and highly oscillating behavior is observed. The critical mean void fraction values are higher when compared to the single and two quadrant geometries. In uniform type geometries, the mean void fraction values are observed are highest among all other geometries. The critical void fraction values are also quiet higher.

So, the types of sparger mainly depend on the evenly dispersed gas, millions of tiny dispersed gas, millions of tiny bubble and on the high surface area. Higher efficiency in sparging can be achieved by tiny bubble propagation. This bubble propagation will provide maximum surface area for the mass transfer. Let's first consider about two broad classifications (perforated and porous) which are generally explained in many literatures. It was seen that the porous types with smaller diameter develop smaller bubbles as compared with the perforated ones and the benefit of smaller bubbles in the gas holdup in the reactors already explained. Therefore the gas holdup in system that equipped with porous plate at high superficial gas velocity is app. 40 per cent higher than the system equipped with perforated plate. Krishna et al. shows that V_b is directly proportional to d_B [42]. So, concluding it with this statement that the initial size of the bubble is

dependent on the sparger type and larger bubbles have higher rise velocity and lower gas holdup. Among all the correlations in the literature, Hikita's correlation better describe this dependence [4].

Method to determine the bubble diameter and the efficiency of the sparger [38].
*1.Calculate Weber's number of the gas [45]. $W_e = \frac{\sigma_G U^2_{G,0} D_C^4}{N_0^2 d_0 \sigma}$ $W_e = \frac{\sigma_g U_{G,0} d_0}{\sigma}$
2. Calculate Sauter's mean diameter[-] $\frac{\sum_i^N d_i^3}{\sum_{i=1}^N d_i^2}$
3. Use Krishna et al. theory to determine the performance[42]

TABLE4: Determine Bubble Diameter and Efficacy of Sparger

*According to Mersmann, a Weber number more than 2 is necessary for the breakage and axial mixing of liquid.

Sparger location: Since in 1970's very little concern was given to the location of the sparger in the reactor. In1970's the location of sparger is generally at the bottom. But as the flow visualization studies suggested that it was not the best position as the recirculating fluids flowing from the downcomer over the gas stream emerging from the sparger caused a maldistribution of gas to the far wall of the riser. The gases get concentrated on the wall for some distance before it was dispersed by the turbulent forces. So, the sparger should be kept just inside the riser above a point at which the downcomer joins the riser. But the problem was the dead area in the reactor. A good solution to this problem is to cover that area with the plastic. This will also removes the problem of settling down.

THERMODYNAMIC FACTORs

It generally includes the heat and the mass transfer effects governing the thermodynamic conditions in the reactor.

Heat Transfer

In commercial reactor design, the two main limitations on size are the abilities of the design to provide an adequate supply of oxygen and to remove the metabolic heat efficiently. Airlift vessels are found to produce heat transfer coefficients than bubble columns under identical conditions. Removal of heat can be difficult particularly in large bioreactors and for satisfactory reactor design, the knowledge of heat-transport in these devices are essential. Actually higher heat loads occur when highly reduced substrate such as hydrocarbons are oxidized. Lewis et al. made two contributions to heat transfer process [14].

i. Heat transfer by steady state condition in a stagnant liquid film adjacent to the heating surface.

ii. Heat transfer from the liquid film to bulk dispersion via packet of liquid which are continually brought to the surface of the film from the bulk and are mixed again with the bulk fluid due to induced agitation.

$$h \propto \left(\frac{k_L \rho_L C_p}{\pi t}\right)^{1/2}$$

Large reactors generally uses internal coils for heat removal as compared over the cooling jackets because in most of the cases it increases the surface area for heat transfer. But in some cases the coils get foiled by the microbial culture decreasing the heat transfer and adversely effecting the mixing. Heating surface to fluid heat transfer coefficient is theoretically and experimentally shown to increase with the gas velocity raised to ¼ powers. Within airlift bioreactor, the riser is the best possible location for heating and cooling. If any how we select the downcomer as the location of heating zones than the downcomer entrance will be the best possible location. However, in all cases heat transfer coefficient increases with increasing gas input. As for the most productive fermentation typical metabolic heat generation is of order 3 to 15kw/m^3.

$$Q_H = U_H A_H \Delta T$$

$$P_T = P_h + \rho_L g(h_L - h_p)$$

Only two correlations for film heat transfer coefficient in concentric internal loop airlift reactor are available

$$h_f=8.71\left(\frac{A_r}{A_d}\right)^{0.25}\left(\frac{C_{P\mu L}}{k_t}\right)^{-0.5}U_{Gr}^{0.22}$$

$$h_f = 13.34\left(1+\frac{A_r}{A_d}\right)^{-0.7}U_G^{0.275}$$

(Ouyoung et al, 1988)

Higher heat transfer coefficient was found in the work of Ouyoung than the Chakravarty, it might be due to sparger effect or geometric configuration of the bottom part of reactor.

Mass transfer

In general for mass transfer the following equation is used,

$$\frac{dC_L}{dt} = k_L a_L(C^* - C_L)$$

When integrated between $C_L=C_O$ at t=0 and $C_L=C_L$ at t=t, it yields:

$$ln\frac{(C^* - C^0)}{(C^* - C^L)} = k_L a_L t$$

This equation can be used for the determination of k_La_L based on the transient gassing in method when the reactor is fully back mixed. (For point measurement)

$$a_L = \frac{6}{d_B}\frac{\epsilon}{1-\epsilon}$$

$$t_G = \left(\frac{V_L}{Q_G}\right)\frac{\epsilon}{1-\epsilon}$$

Multiplying the a_L by the true mass transfer coefficient, k_L we obtain:-

(a)

$$k_L a_L = \frac{6kL}{dB}\frac{\epsilon}{(1-\epsilon)}$$

And taking log we get;

(b)

$$ln k_L a_L = \ln\left(\frac{6k_L}{d_B}\right) + ln\frac{\epsilon}{1-\epsilon}$$

It is purely theoretically derived, relationship and it suggests that a log-log plot of $k_L a_L$,As ε/(1-ε) should have a unite slope. So the equation (a) can be arranged to

$$\frac{k_L}{d_B} = \frac{k_L a_L (1-\epsilon)}{6\epsilon}$$

Equation can be correlated with the gas holdups based on the above described hydrodynamics considerations model of gas holdup by:-

$$k_L a_L = a\left(\frac{P_G}{V_L}\right)^b$$

Now, looking into the correlation between mass transfer and mixing:-

The steady state dissolved oxygen concentration (C^*) is the function of pressure which changes with the depth. Therefore: -

$$C* = \frac{Y_A P_T}{H'}$$

Where

$$P_T = P_h + \rho_L g(h_L - h_p)$$

Here h_p is the height at which dissolved oxygen electrode is placed.

In many literatures it was seen that $k_L a_L$ was effected by [19]:

1) DO electrode location- here electrode where located at the column axis of 5.752 and 0.635m, respectively above the bubble column .despite the highly viscous fluid (2 dry wt/vol. % SF in 0.15M NACL, the DO electrode location did not affect the $k_L a_L$.

2) Solid concentration:-the $k_L a_L$. Value decreased with increasing solids concentration but it was not effected either by the liquid height (h_L) in the reactor or by the cross sectional shape of the reactor.

3) Power input:-no effect on the liquid height (h_L) on the mass transfer is seen in air-water.

HYDRODYNAMIC FACTORS:

For the proper understanding of the designing and working of the airlift bioreactor we must have to be clear about the hydrodynamic behavior of the fluids in the reactor and also their measuring parameters in order to scale up the productivity of the reactor. Young et al. (1991) are among the first investigators to study the local two phase hydrodynamics in a external loop airlift column reactor [49]. Vial et al. (2002) investigated the global and local hydrodynamics in the riser of an external airlift column [43]. They measured the overall gas holdup and bulk liquid circulation by conventional techniques, the bubble size distribution by photographic techniques, the local gas holdup by the optical fiber probe technique, the gas velocity by the ultrasound Doppler techniques, and the local liquid velocity and thus root mean square (RMS) velocities by the laser Doppler anemometer techniques. Lo and Hwang (2003) further investigated the bubble dynamics in an internal loop airlift column, i.e., local and overall gas holdups, local gas velocity , bubble size distribution , by using the dual electrical resistivity probe technique [22]. Wu and Merchuk (2003) used PIV (Particle Image Velocimetry) technique to measure the liquid flow map in the wall vicinity of the downcomer in an internal loop reactor [47]. Bulk liquid circulation velocities can be measured by Pilot tube, magnetic tracer method, and liquid solution tracer techniques [1, 2, 3, 5, 25, 51]. Luo and Al-Dahhan (2008) studied the macro mixing in a draft tube airlift bioreactor using the computer automated radioactive particle tracking (CARPT) techniques where it was shown that the flow structure in the top and the bottom region have significant effect on the macro mixing in the reactor and very different from the flow structure in the riser and the downcomer regions [21]. So, in order to properly understand the designing and the scale up of the airlift reactor these flow phenomena understanding is of great importance. Another techniques which are giving good results is the CFD (computational fluid dynamics) which could be extremely cost- and time-effective in reactor design, scale- up, and performance assessment, operation and process intensification of such reactors.

TABLE 5: Techniques Used In Variable Measurement in Different Reactor Type

Reference	Reactor type	Variable measured	Techniques used
Merchuk and Stein (1981)	External loop column	Liquid circulation velocity Gas holdup	Magnetic flow meter Differential Pressure
Bello et al. (1984,1985)	External loop column Internal loop column	Liquid circulation velocity Gas holdup	Tracer techniques Differential pressure
Chisti and Moo-Young (1988)	Internal loop column Split cylinder	Liquid circulation velocity	Tracer techniques
Young et al.(1991)	External loop column	Local liquid velocity Local gas velocity Local gas holdup	Hot-film anemometry Resistivity Probe Gamma densitometry
Merchuk et al. (1998)	Internal loop column	Liquid circulation velocity Overall gas velocity	Pulse-injection resonance Differential Pressure
Vial et al. (2002)	External loop column	Liquid circulation velocity Overall gas velocity Rms velocity Local gas velocity Local gas holdup	Pulse-injection resonance Differential Pressure Anemometer Aerometric Laser Doppler Optical fiber probe

(2) **Gas hold-up**

Gas holdup can be defined as the percentage by volume of the gas in the two or three phase mix in the column. As this is the pneumatically agitated reactor so it is very important to see the bas holdup in this reactor as this would be the only source of gas in such reactors. So, it is very essential to know about the various parameters of the gas hold up in the reactor. The volume fraction of gas in the gas-liquid dispersion or the gas holdup has a strong influence on the performance of these reactors. Actually, the resistance time of the gas in the liquid, the gas-liquid contact area for mass transfer and gas holdup which occurs under a given operating conditions. Gas holdup depends on the superficial gas velocity. Actually the superficial gas velocity depends on the flow rate divided by the cross-sectional area. Other physical factors such as viscosity and density of the liquid, surface tension of solution, and the presence of solids, electrolytes, and surfactants affect the gas holdup.

The difference in the gas holdup between the riser and the downcomer in an airlift reactor determines the magnitude of the induced liquid circulation velocity which in turn influences the bubble rise velocity and the gas holdup. So, the liquid velocity affects the gas holdup which together affects the mixing behavior, mass and heat transfer, the shear rate and the ability of the reactor to suspended solids. The basic equation which shows the dependence of gas holdup on the superficial gas velocity is given below

$\varepsilon_G = aU_{sg}^{b}$

In which 'a' is the function of the reactor geometry and of the properties of the liquid and 'b' is determined by the flow regime as well as the reactor geometry and also on operating variables and on the physical properties of the system. Further in 1986, M.Y. Chisti & Moo-young, in their literature signifies that bubble flow rate changes to a coalesced bubble flow. But some of the disperities in literature were found in Siegel et al., 1986, to the fact that gas velocity U_{Gr} doesn't take into account the recirculating gas [40]. So, he introduced the term that was true superficial gas velocity which takes into account the recirculating velocity. The value of 'b' for this was taken to be 0.4 which was same as that has been used by the other correlation in different literatures. But Verlaan et al in his work showed that the consideration of recirculating gas contributes about only 10 per cent, so it is unnecessary to account the recirculating gas [44].

The volumetric flow rate of liquid in the riser of an airlift reactor can be expressed in terms of the superficial liquid velocity in the riser and it is the cross sectional area;

$Q_{Lr} = U_{Lr} A_r$ (i)

Where Q_{Lr} is the liquid flow rate, U_{Lr} is the superficial liquid velocity in the riser and A_r is the riser cross sectional area.

For the downcomer we have

$Q_{Ld} = U_{Ld} A_d$ (ii)

Where Q_{Ld} is the liquid flow in the downcomer, U_{Ld} is the superficial liquid velocity in the downcomer and A_d is the downcomer cross sectional area.

$Q_{Lr} = Q_{Ld}$

From equation (i) and (ii) we get: $U_{Lr} A_r = U_{Ld} A_d$ (iii)

In terms of liquid velocities in various zones: $V_{Lr} A_r(1- \varepsilon_r) = V_{Ld} A_d(1- \varepsilon_d)$ (iv)

Where V_{Lr} and V_{Ld} are the linear velocities in the riser and downcomer respectively.

ε_r and ε_d are the gas holdup in the riser an downcomer respectively.

Rearrangement of equation (iv) gives:

$$\epsilon_d = \frac{V_{Lr} A_r}{V_{Ld} A_d} \epsilon_r - \left(\frac{V_{Lr} A_r}{V_{Ld} A_d} - 1\right) \text{(v)}$$

which would be the form:

$\varepsilon_d = \alpha \varepsilon_r - \beta$ (vi)

$\beta = \alpha - 1$ (vii)

In the previous years it has been simplified into

$\varepsilon_d = \alpha \varepsilon_r$

Which has been proved to be impossible by some of the researchers .The first person to initiate in this process was the Bakker et al, (1993).Later on Miyahara et al.(1986) reduced it into a more correct form i.e.

$\varepsilon_d = \chi \varepsilon_r^n$

Where ' χ' depend on the fluid and the geometry of the reactor and ' n' value ranges from0.8-4.2.

The parameter α and β depends supposedly on the geometry of the reactor, the gas and liquid phase used and the regime of the operation. The 'α' value generally ranged over 0.8-0.9[5]. Thus, by the continuity equation it can be seen that the gas holdup in the riser and the downcomer are related by equation (vi). In many cases the α and β value do not vary with the gas flow rate. Hence a linear dependence is observed.

Liquid Hydrodynamics

As previously discussed these reactors are made up of pool of liquid divided into two vertical zones connected at the top and bottom where one of these zones is sparged by a gas and the resulting gas holdup difference due to difference in the bulk densities in the fluid in the two zones results in the induced liquid circulation. This liquid circulation determines the gas holdup, the prevailing flow regime, heat and mass transfer coefficient and the extent of the mixing in the reactor. The magnitude of liquid circulation is the most important factor for the designing and the scale up of the airlift bioreactor. As there are many shortcomings in the theory about the liquid circulation but with the concept of energy balance model given by M.Y.Chisti, 1986 everything become clear and can be successfully implemented for all types of airlift bioreactor [6]. As from the theory about the circulation the energy input into the riser occurs mainly due to the isothermal expansion of the gas as it moves up the riser but the kinetic energy component of the jet from the gas sparger is unusually small, so can be ignored .Energy is dissipated because of the wall friction in the riser and downcomer along with the friction and drag as the fluid reverses its direction of the fluid on the top and bottom zones connecting the riser and any gas bubbles in the downcomer that are pushed along against the buoyant force. So, here we are considering another most important parameter for the scale up and the designing of airlift bioreactor. A combination of momentum balance over the circulation loop with empirical gas holdup and two phase pressure drop correlation is another approach for the determination of the liquid circulation [36].Taking into accounts the major energy losses the equation for the calculation of the liquid circulation velocity can be shown by [5,7].

$$U_{Lr}=\left(\frac{(2ghD(\epsilon_r-\epsilon_d)}{\frac{K_T}{(1-\epsilon_r)^2}+K_B\left(\frac{A_r}{A_d}\right)^2\frac{1}{(1-\epsilon_d)^2}}\right)^{0.5} \quad \text{(viii)}$$

Where U_{Lr} is the superficial liquid velocity in the riser, g is the acceleration due to gravity, h_d is the gas-liquid dispersion height in the reactor, A_r and A_d are the cross sectional area of the riser and the downcomer respectively, ε_d and ε_r are the fractional gas holdup in the downcomer and the riser respectively, K_T and K_B are the fractional loss coefficient for the top and the bottom zones respectively. As for the internal loop $K_T \ll K_B$ because the energy dissipated in the head

region is negligible as compared to the bottom region. So K_T can be disregarded. Above equation can be simplified to

$$U_{Lr}=\left(\frac{2gh_D(\epsilon_d-\epsilon_r)}{k_B\left(\frac{A_r}{A_d}\right)\frac{1}{(1-\epsilon_d)^2}}\right)^{0.5} \quad \text{(ix)}$$

Where K_B is given by [5,7].

$$K_B = 11.402\left(\frac{A_c}{A_r}\right)^{0.789} \quad \text{(x)}$$

In the external loop airlift bioreactor, the value of $K_T = K_B$ approximately as the top and the bottom riser-downcomer connecting zones often have similar geometries.

$$U_{Lr}=\left(\frac{2gh_D(\epsilon_d-\epsilon_r)}{k_B\left(\frac{A_r}{A_d}\right)\frac{1}{(1-\epsilon_d)^2}}\right)^{0.5}$$

Equation (viii) is dimensionless and clearly shows the dependence on fundamental principles, liquid circulation on such design variables as reactor height, riser to downcomer cross sectional area ratio and the geometries of the top and the bottom zones. But one of the drawback of this eqation is that it doesn't explicitly correlate liquid circulation with the principal operational variables i.e. gas flow rate. It also disregards the wall-friction associated losses, which are small in comparison with the source of energy dissipation [5, 7].

By using the Stoke's law:

drag force= buoyant force [M.Y. Chisti & M.Moo –Young, 1987]

$F_B=(\rho_L-\rho_G)\Pi/6\ d_B^3 g$ ([Buoyancy force] $F_D= (C_D\ U_T^2 A_P\ \rho_L)/2$ [Drag force]

As here bubble was considered as a rigid particle and an approximation is made A_P and C_D are the projected area of the bubble and a dimensionless drag coefficient respectively.

$A_P=\Pi d_B^2/4$.Substitute this value in drag force.

Rearranging equation for buoyancy force and the substituted drag force we get,

$$U_T^2 = \frac{4(\rho_L-\rho_G)gd_B}{3\rho_L C_D}$$

Dependence of the drag coefficient on the Reynolds's number is given by: $C_D = \frac{1}{Re_p^j}$

Reynolds's number: $Re_p = \frac{(\rho_L-\rho_G)U_T d_B}{\mu_L}$

Substituting the value of Reynolds's no. in drag coefficient we get:

$$U_T = \left\{ \frac{4(\rho_L - \rho_G)^{1+j} g d_B^{1+j}}{3\rho_L i \mu_L^{j}} \right\}^{1/(2-j)}$$

So it can be written as: $U_T = Cd_b^x$ where C and x are the functions only of the two phase flow regime.

Further here bubble diameter can be found by using Kolmogoroff's theory.

$$d_B = \phi \frac{\sigma^{0.6}}{(P_G/V_L)^{0.4} \rho_L^{0.2}}$$

Where $\frac{P_G}{V_L} = \rho_L g U_{sg}$

$$a = \left[\frac{4g}{3\rho_L \mu_L^{j} i} \left\{ \frac{(\rho_L - \rho_G)\sigma^{0.6}\phi}{\rho_L^{0.2}} \right\}^{1+j} \right]^{1/(j-2)}$$

Where i and j are empirically dependent.

But (2009, Behnoosh moshtari) as 'x'dependent on flow regime so in homogeneous regime value is between 0.7 -1.2 and in churn turbulent regime ε_G is a weak function of U_g. And n varies from 0.4-0.7. Beside all these correlations (Hikita et al, Hugmark et al, Kumar et al, Reily et al), Haikita's correlation is considered better for estimating gas holdup [14, 15, 16, 17, 18].

Apart from superficial velocity and gas holdup correlation, the bubble size has also an effect in the gas holdup. Through the bubble hydrodynamics it was considered that larger bubbles move faster in the fluid as compared with the smaller bubble. This can be explained by the fact that buoyancy force is directly proportional to its volume but the drag force is directly proportional to its surface area. The ratio of volume to its surface area is 4/3*pi*r^3 / 4*pi*r^2 = r/3 so a larger bubble will move faster in the fluid. So a larger bubble has low residence time as compared to smaller bubble due to which gas holdup of the larger bubble is quiet low as compared to the smaller bubble.

Calculation of liquid velocity:

Here various undefined parameters are defined by

$\epsilon_r = \frac{U_{Gr}}{0.24+1.35(U_{Gr}+U_{Gr})}$ [13]. This equation is satisfied for vertical, independently controlled flow of air and water for ($U_{Lr} + U_{Gr}$) less than 1.3 ms^{-1}.So. this applies only to vertical two phase flow.

$$h_D=\frac{h_L}{1-\epsilon}$$

$$\epsilon=\frac{\epsilon_r A_r+\epsilon_d A_d}{A_r+A_d}$$

It depends in whether the reactor employs a gas-liquid separation device. When the rector do not have this separation than for riser and the downcomer are linearly related [5] where k is approximately 0.7.

$$\varepsilon_d = k\,\varepsilon_r$$

Here gas holdup is generally a few percent lower than that in the gas –injected riser over most of the operational ranges. A gas free downcomer can be obtained only at very low value of the riser gas holdup corresponding to low gas injection rates at which the superficial downcomer liquid velocity is less than about 0.15 ms^{-1}.

Once the riser and the downcomer gas hold up have been calculated and, the gas-liquid dispersion height is determined:

$$h_D=\frac{h_L}{1-\epsilon}$$

where h_L is the ungassed liquid height , h_D is the gas-quid dispersion height and ε is calculated by :

$$\epsilon=\frac{\epsilon_r A_r+\epsilon_d A_d}{A_r+A_d}$$

Relation Between Riser And Downcomer:

The difference in gas holdup between riser and downcomer in an airlift reactor determines the magnitude of the induced liquid circulation velocity which in turn influences the bubble rise and gas holdup which together effect the mixing behavior, mass & heat transfer. So, all aspect of airlift is influenced by gas holdup and liquid circulation.

In Elsevier science, Y. Chisti 1998, in a (shorter communication) literature it was shown the relationship between riser and downcomer velocity. $$\varepsilon_d=\frac{V_{Lr}A_r}{V_{Ld}A_d}\varepsilon_r-\left(\frac{V_{Lr}A_r}{V_{Ld}A_d}-1\right)$$ (This equation is quiet general and can be used for any airlift.)

So it can be written as

1) $\varepsilon_d = \alpha\varepsilon_r - \beta$ 2) $\alpha = V_{Lr} A_r / V_{Ld} A_d$ 3) $\beta = \alpha - 1$

4) $\varepsilon_d = \alpha \varepsilon_r$.

Here if we look into eq.1 we see that in some literatures β has been neglected, zero value of β implies α value of unity. These will the impossible situation because in that situation liquid will cease to circulate and downcomer air will disappear. So all these data confirms that value of β will never be zero.So the equation was modified in the form $\varepsilon_d = \chi\varepsilon_r^n$ 'n' varied from 0.8-4.2; χ depends on the geometry of the reactor and properties of fluid. α and β depends on the geometry of the reactor , the liquid and gas phase used and the regime of operation. α value generally range over 0.8-0.9(Chisti,1989). Generally values of α equal to 1 or more than it are accepted

Bubble Hydrodynamics:

After formation, a bubble rapidly accelerates to its terminal velocity, V_B. The value of V_B is determined by the balance between the buoyant rise force, and the drag force. While it is easy to calculate the buoyancy force for a bubble, the drag force varies with bubble size. For small, spherical bubbles, the drag force can be calculated, and when combined with the buoyancy force, yielding Stoke's Law:

$$V_{St} = \frac{2gr^2}{9\nu}$$

Stoke's Law is only applicable to small bubbles with an immobile surface. An extension of Stoke's Law for a bubble with a mobile surface was derived by Hadamard-Rybczynski and is

$$V_B = \frac{2}{3}\frac{g\Delta\rho}{r^2\mu}\frac{(1+\kappa)}{(2+3\kappa)} \quad \begin{Bmatrix} \kappa = 0 \; clean \\ \kappa = \infty \; dirty \end{Bmatrix}$$

where the dirty case reduces, of course, to Stoke's Law. Additionally, Hadamard-Rybcszynski is only applicable to spherical bubbles (Reynolds number < 1).

As the bubble rises, new interface is created at the upstream hemisphere and *flows* down towards the bottom stream hemisphere where it disappears. It is important for the proper conceptual model to correctly describe the bubble interface. Specifically, the interface is a curved region with water molecules on one side, air molecules on the other, and, if present in the water, surfactant molecules. The water molecules at the interface are continually exchanging with water

molecules in the bulk fluid, and also with water vapor molecules in the gas (according to the equilibrium vapor pressure). Thus to create fresh interface, water molecules at the upstream hemisphere from the bulk fluid arrive at the interface.

This process is shown schematically to the right. The schematic is not to any scale, nor does it show the correct orientation of water molecules on the interface (a result of the dipole moment). Water vapor molecules can be seen in the bubble, and dissolved Nitrogen gas molecules in the water.

Schematic of Bubble Interface

The no slip condition means that the motion of molecules on both sides of the interface must match. Water molecules will exchange with the water molecules in the bulk fluid, Gas molecules with gas in the bubble, and water and gas molecules are continually *creating* interface at the upstream pole, which is also known as the stagnation point, since the flow velocity at the pole itself must be zero. An animation of the flow around a clean bubble is compared with the flow around a contaminated bubble in the Surfactant section.

Larger bubbles deform from sphericity, into ellipsoidal shapes. For bubbles larger than a critical radius, bubbles oscillate both in shape and trajectory. Numerical techniques have been used to solve for V_B for some non-oscillating bubbles; however, only empirical parameterizations are available for larger laminar flow bubbles and oscillating bubbles.

Fluid motions

As the bubble rises, if there are motions in the fluid, it's trajectory, behavior, and evolution will be different from the stagnant fluid assumption inherent in the parameterization of V_B. For example, a stream of bubbles causes an upwelling flow which causes bubbles in the bubble stream to rise faster than if they were alone.

If the fluid is sheared, the bubbles will experience a "lift" force similar to that of an airplane wing and move perpendicular to the velocity shear.

And turbulence motions in the fluid will affect the bubble trajectory, with the affect being strongest for bubbles whose rise is less than the turbulence velocity scale.

Another factor affecting bubble hydrodynamics is the fluid properties. The fluid viscosity, and density, both of which very with temperature, affect the drag force.

Surfactant and Bubble

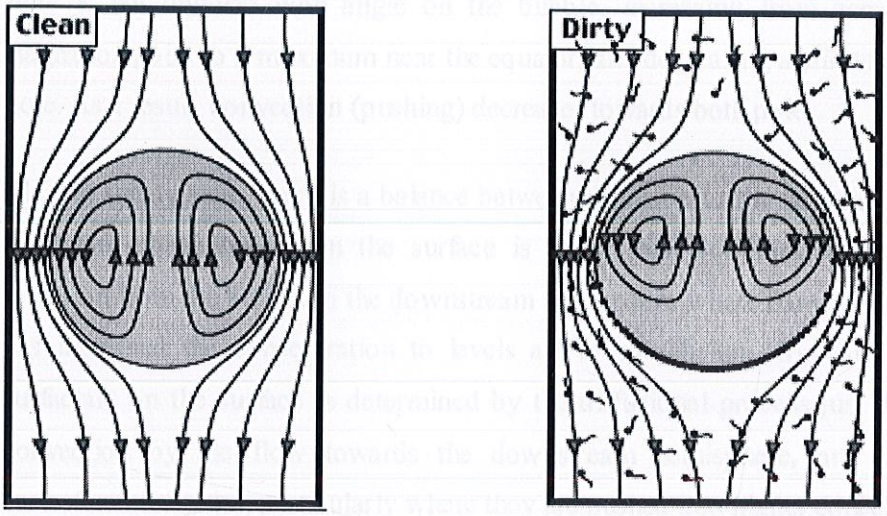


Figure 9: Surfacent And Bubble

Interface creation causes the upstream hemisphere to be clean.

-Surfactants diffuse to the upstream hemisphere.

-Surfactants diffuse from the downstream hemisphere.

-Surfactant gradients cause a surface tension gradient.

-Surface tension gradients decrease surface mobility.

-Bubbles in contaminated water rise slower.

Surfactants are surface active substances whose molecules have a hydrophobic and hydrophilic part. The hydrophobic part tends to align itself in the air, while the hydrophilic part aligns itself in the water, thus surfactants tend to be found at interfaces. Dish washing soap is a familiar surfactant, but many substances, including salt and fatty acids are surfactants. An important effect of surfactants is that they alter the surface tension, which alters the hydrodynamcis of the

interface. Another effect of surfactants is to increase the longevity of bubbles on the surface, and alter the size distribution of bubbles produced in a breaking wave or jet of water.
The clean bubble rises faster because its entire surface is mobile. However, for a bubble in surfactant contaminated water, the situation is very different. Surfactant molecules (black circles) diffuse to the bubble where they accumulate at the interface and are pushed downstream (convection) by the flow. Repulsion between surfactant molecules primarily in the downstream hemisphere (high surfactant concentration) counters the squeezing by the flow. Additionally, the flow is not uniform with angle on the bubble, increasing from zero at the upstream pole stagnation point to a maximum near the equator, and decreasing again to zero at the downstream pole. As a result, convection (pushing) decreases towards both poles.

Thus in steady state, there is a balance between diffusion to the upstream hemisphere where the surfactant concentration on the surface is lower than equilibrium with the bulk fluid, and diffusion from the bubble in the downstream hemisphere where convection (pushing) by the flow has increased the concentration to levels above equilibrium. Similarly, the concentration of surfactant on the surface is determined by the diffusional process just described, the effect of convection by the flow towards the downstream hemisphere, and the repulsion between surfactant molecules, particularly where they are pushed into higher concentration.

As a result, the surfactant concentration on the downstream hemisphere is elevated, and because of convection, most of the gradient occurs in the downstream hemisphere. The surfactant concentration gradient causes a gradient in the surface tension. And this gradient of surface tension has the important effect of decreasing surface mobility. As a result, the internal circulation to the rear of the bubble is supressed, and the flow at the interface is deceased (or stopped) and the bubble experiences a higher drag. The angle from the downstream pole to which the interface is immobilized is called the stagnant cap angle from the stagnant cap model.

Oscillation and Bubble:

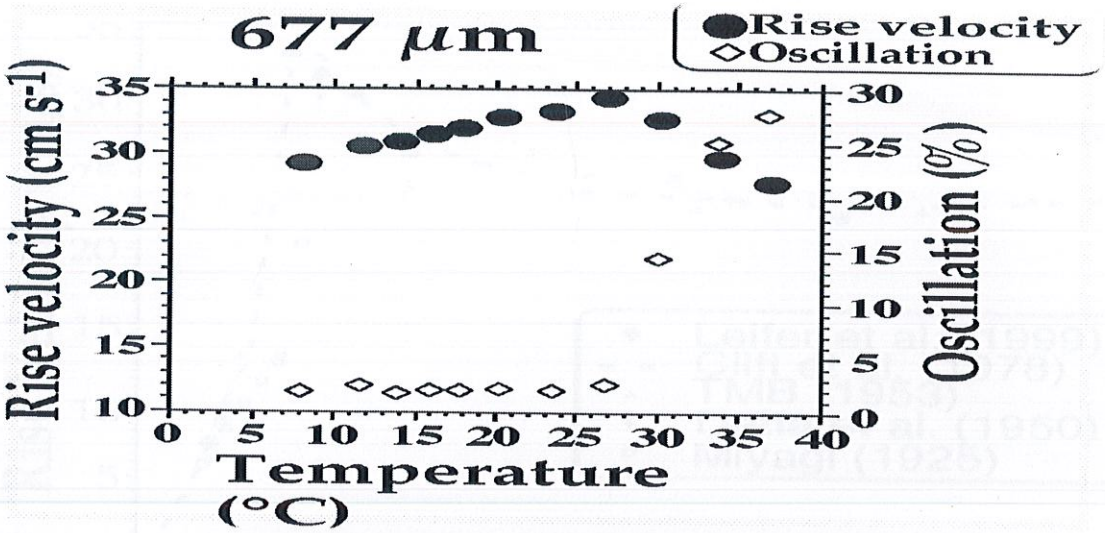


Figure 10: Oscillation And Bubble:

For clean bubbles larger than about 700 microns radius at 20C, oscillations are very important to understanding the hydrodynamics of bubbles. Oscillations are thought to begin from instabilities in the bubble wake, and are observable in both the trajectory and shape. Because of oscillations, the bubble rise speed is affected, as is mass transfer. Additionally, the turbulence created by the rising bubbles will affect other bubbles, and mass transfer in the fluid. Additionally, bubble oscillations are sensitive to the presence of surfactants.

The importance of oscillations is shown in the figure to the left which demonstrates that very small changes in the density and viscosity of water are able to change the trajectory of a 677 micron bubble from linear (T>27C) to oscillatory. With the onset of oscillations, the rise velocity begins to decrease. The experiment was conducted in millipore distilled water. With increasing size, the bubble surface oscillations change from a simple sinusoidal oscillation to higher order modes, the trajectory changes from a simple helix to more complex trajectories. With these changes, the rise velocity becomes less dependant upon temperature.

Temperature and Bubble:

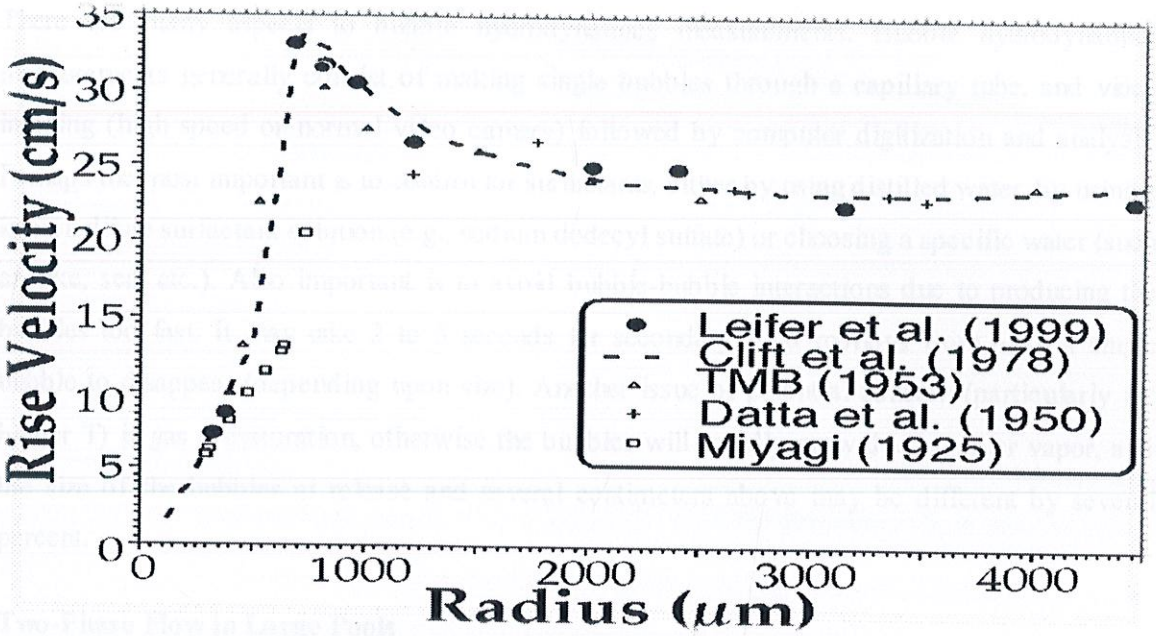


Figure11: Temperature and Bubble

Temperature affects bubble hydrodynamics in several ways. By altering the fluids viscosity and density, the friction force on the bubble is changed and as a result, bubbles rise faster with increasing temperature. However, bubbles larger than approximately 750 microns in radius oscillate as they rise. Because of the oscillations, the bubbles oscillate faster, and move faster but rise slower with increasing temperature. This is in direct contradiction with the prediction of the wave analogy of bubble motion.

A plot of the variation of rise speed with radius for a clean bubble at 20C is shown at the right. Bubbles larger than the peak in the figure to the right oscillate, while bubbles smaller than the peak do not. The oscillations are also accompanied by shape oscillations. Initially, the shape oscillations are simple harmonics, but become multimodal and more complex with increasing size. For bubbles larger than approximately 2000 microns radius, the trajectory oscillations are relatively unimportant while shape oscillations are very complex. As a result, bubble rise velocity becomes independant of temperature. This figure is an adaptation of data from Clift et al., 1978, Leifer et al., 1999 and others.

Measurement Techniques

There are many aspects to bubble hydrodynamics measurements. Bubble hydrodynamics measurements generally consist of making single bubbles through a capillary tube, and video imaging (high speed or normal video camera) followed by computer digitization and analysis. Perhaps the most important is to control for surfactants, either by using distilled water, by using a known dilute surfactant solution (e.g., sodium dodecyl sulfate) or choosing a specific water (such as lake, sea, etc.). Also important is to avoid bubble-bubble interactions due to producing the bubbles too fast. It may take 2 to 5 seconds for secondary fluid motions from even a single bubble to disappear (depending upon size). Another issue of potential concern (particularly for higher T) is gas presaturation, otherwise the bubbles will rapidly grow due to water vapor, and the size of the bubbles at release and several centimeters above may be different by several percent.

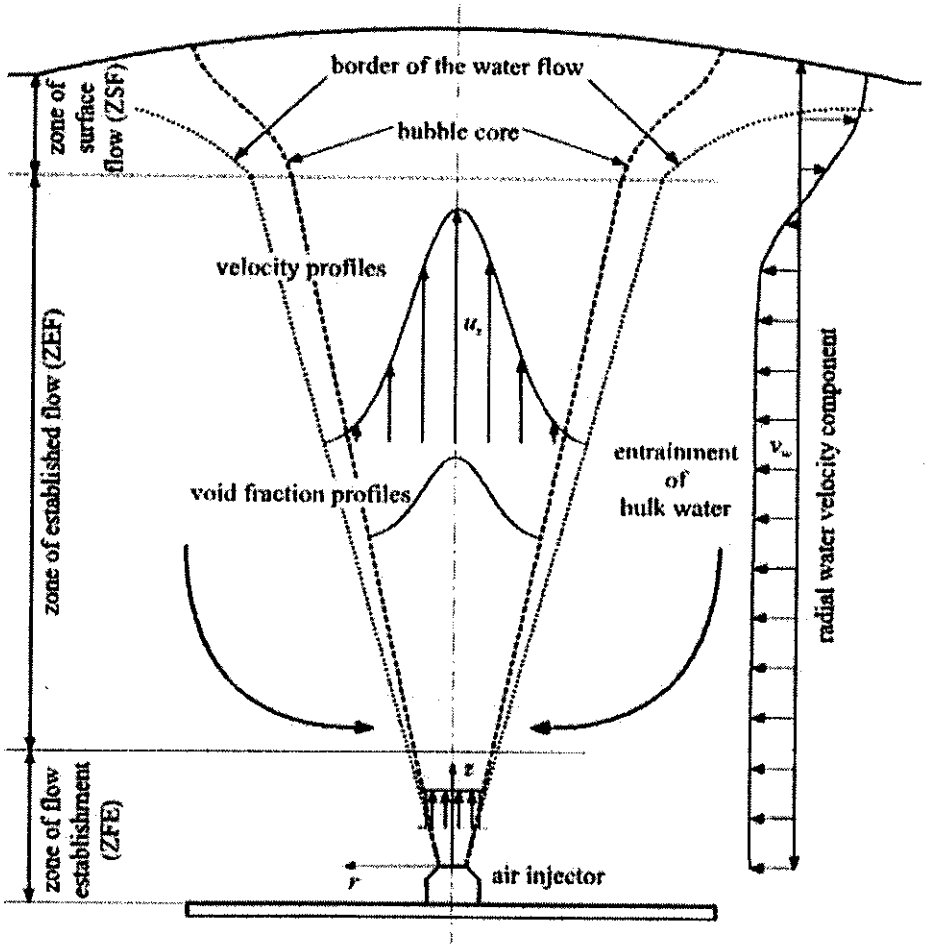
Two-Phase Flow in Large Pools

Two-phase flows in large pools are of importance for several industrial applications. Typical examples include: (1) venting of steam, non-condensable gases, and aerosol mixtures into water pools in nuclear power plants and chemical reactors, (2) gas stirring of liquid metal ladles, (3) aeration in water purification and waste treatment plants, (4) and producing barriers against crude oil spreading across a water surface. The background of the present study falls within the context of pool scrubbing experiments and modeling efforts at the Paul Scherrer Institute (PSI). During a hypothetical severe accident in a nuclear power plant, the large pools available in the containment are foreseen to retain radioactive fission products in the form of aerosol particles and gaseous iodine species. Starting in 1988, an experimental program was carried out at PSI in the POSEIDON facility to assess aerosol and iodine retention models in integral computer codes. The aim of the dissertation is to create a data base for a more complete modeling of the two-phase flow under pool scrubbing conditions.

The main characteristics of the two-phase are illustrated in figure1. Three zones are identified in the pool: The zone of flow establishment (ZFE, movie1), the zone of established flow (ZFE, movie2), and the zone of surface flow (ZSF). A so-called bubble plume is produced in the ZEF,

which consists of a bubble core and a surrounding upward water flow. The bubble plume spreads while it is rising due to water entrainment from the bulk.

A sophisticated large-scale test facility was build at PSI to carry out a test series. The pool is 1 m in diameter and the maximum depth is 4.4 m (figure2). Local void fraction, bubble and water velocities, bubble size distributions and interfacial area concentration are measured with double optical sensors and a hot-film anemometer within the pool (figure3). Typical radial void fraction and water velocity profiles are shown in figure4 together with gaussian error curve fits to describe the variation of the flow parameters. The spreading of the bubble plume and the decrease of void fraction and water velocity with distance from the air injector are illustrated by the graphs. Empirical parameters for a bubble plume model are determined from the measurements and the model computations are compared with the experiment. The comprehensive measurements permit a detailed analysis of the two-phase flow and provide a data base for more complete modeling in a future project.



Fluid Dynamics:

Typical aerodynamic teardrop shape, showing the pressure distribution as the thickness of the black line and showing the velocity in the boundary layer as the violet triangles. The green vortex generators prompt the transition to turbulent flow and prevent back-flow also called flow separation from the high pressure region in the back. The surface in front is as smooth as possible or even employs shark like skin, as any turbulence here will reduce the energy of the airflow. The Kammback also prevents back flow from the high pressure region in the back across the spoilers to the convergent part. Putting stuff inside out results in tubes; they also face the problem of flow separation in their divergent parts, so called diffusers. Cutting the shape into halves results in an aerofoil with the low pressure region on top leading to lift (force)

In physics, **fluid dynamics** is a sub-discipline of fluid mechanics that deals with **fluid flow**—the natural science of fluids (liquids and gases) in motion. It has several subdisciplines itself, including aerodynamics (the study of air and other gases in motion) and hydrodynamics (the study of liquids in motion). Fluid dynamics has a wide range of applications, including calculating forces and moments on aircraft, determining the mass flow rate of petroleum through pipelines, predicting weather patterns, understanding nebulae in interstellar space and reportedly modeling fission weapon detonation. Some of its principles are even used in traffic engineering, where traffic is treated as a continuous fluid.

Fluid dynamics offers a systematic structure that underlies these practical disciplines, that embraces empirical and semi-empirical laws derived from flow measurement and used to solve practical problems. The solution to a fluid dynamics problem typically involves calculating various properties of the fluid, such as velocity, pressure, density, and temperature, as functions of space and time.

Historically hydrodynamics meant something different than it does today. Before the twentieth century hydrodynamics was synonymous with fluid dynamics. This is still reflected in names of some fluid dynamics topics, like magneto hydrodynamics and hydrodynamic stability — both also applicable in, as well as being applied to, gases [1].

Equations of fluid dynamics

The foundational axioms of fluid dynamics are the conservation laws, specifically, conservation of mass, conservation of linear momentum (also known as Newton's Second Law of Motion), and conservation of energy (also known as First Law of Thermodynamics). These are based on classical mechanics and are modified in quantum mechanics and general relativity. They are expressed using the Reynolds Transport Theorem.

In addition to the above, fluids are assumed to obey the *continuum assumption*. Fluids are composed of molecules that collide with one another and solid objects. However, the continuum assumption considers fluids to be continuous, rather than discrete. Consequently, properties such as density, pressure, temperature, and velocity are taken to be well-defined at infinitesimally small points, and are assumed to vary continuously from one point to another. The fact that the fluid is made up of discrete molecules is ignored.

For fluids which are sufficiently dense to be a continuum, do not contain ionized species, and have velocities small in relation to the speed of light, the momentum equations for Newtonian fluids are the Navier-Stokes equations, which is a non-linear set of differential equations that describes the flow of a fluid whose stress depends linearly on velocity gradients and pressure. The unsimplified equations do not have a general closed-form solution, so they are primarily of use in Computational Fluid Dynamics. The equations can be simplified in a number of ways, all of which make them easier to solve. Some of them allow appropriate fluid dynamics problems to be solved in closed form.

In addition to the mass, momentum, and energy conservation equations, a thermodynamical equation of state giving the pressure as a function of other thermodynamic variables for the fluid is required to completely specify the problem. An example of this would be the perfect gas equation of state:

$$p = \frac{\rho R_u T}{M}$$

Where p is pressure, ρ is density, R_u is the gas constant, M is the molar mass and T is temperature.

Compressible vs incompressible flow

All fluids are compressible to some extent, that is changes in pressure or temperature will result in changes in density. However, in many situations the changes in pressure and temperature are sufficiently small that the changes in density are negligible. In this case the flow can be modeled as an incompressible flow. Otherwise the more general compressible flow equations must be used.

Mathematically, incompressibility is expressed by saying that the density ρ of a fluid parcel does not change as it moves in the flow field, i.e.,

$$\frac{D\rho}{Dt} = 0,$$

Where D / Dt is the substantial derivative, which is the sum of local and convective derivatives. This additional constraint simplifies the governing equations, especially in the case when the fluid has a uniform density.

For flow of gases, to determine whether to use compressible or incompressible fluid dynamics, the Mach number of the flow is to be evaluated. As a rough guide, compressible effects can be ignored at Mach numbers below approximately 0.3. For liquids, whether the incompressible assumption is valid depends on the fluid properties (specifically the critical pressure and temperature of the fluid) and the flow conditions (how close to the critical pressure the actual flow pressure becomes). Acoustic problems always require allowing compressibility, since sound waves are compression waves involving changes in pressure and density of the medium through which they propagate.

Viscous vs inviscid flow

Viscous problems are those in which fluid friction has significant effects on the fluid motion.

The Reynolds number, which is a ratio between inertial and viscous forces, can be used to evaluate whether viscous or inviscid equations are appropriate to the problem.

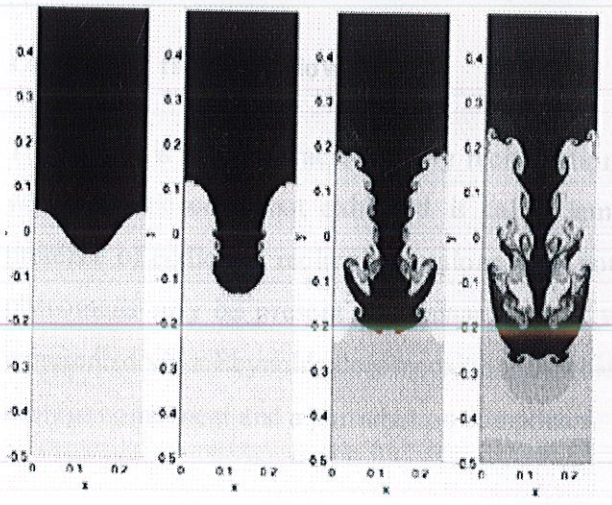
Stokes flow is flow at very low Reynolds numbers, $Re \ll 1$, such that inertial forces can be neglected compared to viscous forces.

On the contrary, high Reynolds numbers indicate that the inertial forces are more significant than the viscous (friction) forces. Therefore, we may assume the flow to be an inviscid flow, an approximation in which we neglect viscosity completely, compared to inertial terms.

This idea can work fairly well when the Reynolds number is high. However, certain problems such as those involving solid boundaries may require that the viscosity be included. Viscosity often cannot be neglected near solid boundaries because the no-slip condition can generate a thin region of large strain rate (known as Boundary layer) which enhances the effect of even a small amount of viscosity, and thus generating vorticity. Therefore, to calculate net forces on bodies (such as wings) we should use viscous flow equations. As illustrated by d'Alembert's paradox, a body in an inviscid fluid will experience no drag force. The standard equations of inviscid flow are the Euler equations. Another often used model, especially in computational fluid dynamics, is to use the Euler equations away from the body and the boundary layer equations, which incorporates viscosity, in a region close to the body.

The Euler equations can be integrated along a streamline to get Bernoulli's equation. When the flow is everywhere irrotational and inviscid, Bernoulli's equation can be used throughout the flow field. Such flows are called potential flows.

Steady vs unsteady flow



Hydrodynamics simulation of the Rayleigh–Taylor instability [2]

When all the time derivatives of a flow field vanish, the flow is considered to be a **steady flow**. Steady-state flow refers to the condition where the fluid properties at a point in the system do not change over time. Otherwise, flow is called unsteady. Whether a particular flow is steady or unsteady, can depend on the chosen frame of reference. For instance, laminar flow over a sphere is steady in the frame of reference that is stationary with respect to the sphere. In a frame of reference that is stationary with respect to a background flow, the flow is unsteady.

Turbulent flows are unsteady by definition. A turbulent flow can, however, be statistically stationary. According to Pope: [3]

The random field $U(x,t)$ is statistically stationary if all statistics are invariant under a shift in time.

This roughly means that all statistical properties are constant in time. Often, the mean field is the object of interest, and this is constant too in a statistically stationary flow.

Steady flows are often more tractable than otherwise similar unsteady flows. The governing equations of a steady problem have one dimension less (time) than the governing equations of the same problem without taking advantage of the steadiness of the flow field.

Laminar vs turbulent flow

Turbulence is flow characterized by recirculation, eddies, and apparent randomness. Flow in which turbulence is not exhibited is called laminar. It should be noted, however, that the presence of eddies or recirculation alone does not necessarily indicate turbulent flow — these phenomena may be present in laminar flow as well. Mathematically, turbulent flow is often represented via a Reynolds decomposition, in which the flow is broken down into the sum of an average component and a perturbation component.

It is believed that turbulent flows can be described well through the use of the Navier–Stokes equations. Direct numerical simulation (DNS), based on the Navier–Stokes equations, makes it possible to simulate turbulent flows at moderate Reynolds numbers. Restrictions depend on the power of the computer used and the efficiency of the solution algorithm. The results of DNS agree with the experimental data.

Most flows of interest have Reynolds numbers much too high for DNS to be a viable option [4], given the state of computational power for the next few decades. Any flight vehicle large enough to carry a human (L > 3 m), moving faster than 72 km/h (20 m/s) is well beyond the limit of DNS simulation (Re = 4 million). Transport aircraft wings (such as on an Airbus A300 or Boeing 747) have Reynolds numbers of 40 million (based on the wing chord). In order to solve these real-life flow problems, turbulence models will be a necessity for the foreseeable future. Reynolds-averaged Navier–Stokes equations (RANS) combined with turbulence modeling provides a model of the effects of the turbulent flow. Such a modeling mainly provides the additional momentum transfer by the Reynolds stresses, although the turbulence also enhances the heat and mass transfer. Another promising methodology is large eddy simulation (LES), especially in the guise of detached eddy simulation (DES)—which is a combination of RANS turbulence modeling and large eddy simulation.

Newtonian vs non-Newtonian fluids

Sir Isaac Newton showed how stress and the rate of strain are very close to linearly related for many familiar fluids, such as water and air. These Newtonian fluids are modeled by a coefficient called viscosity, which depends on the specific fluid.

However, some of the other materials, such as emulsions and slurries and some visco-elastic materials (e.g. blood, some polymers), have more complicated *non-Newtonian* stress-strain behaviours. These materials include *sticky liquids* such as latex, honey, and lubricants which are studied in the sub-discipline of rheology.

Subsonic vs transonic, supersonic and hypersonic flows

While many terrestrial flows (e.g. flow of water through a pipe) occur at low mach numbers, many flows of practical interest (e.g. in aerodynamics) occur at high fractions of the Mach

Number M=1 or in excess of it (supersonic flows). New phenomena occur at these Mach number regimes (e.g. shock waves for supersonic flow, transonic instability in a regime of flows with M nearly equal to 1, non-equilibrium chemical behavior due to ionization in hypersonic flows) and it is necessary to treat each of these flow regimes separately.

Non-relativistic vs relativistic flows

Classical fluid dynamics is derived based on Newtonian mechanics, which is adequate for most applications. However, at speeds comparable to the speed of light, c, Newtonian mechanics is inaccurate and a relativistic framework has to be used instead.

Magneto hydrodynamics

Magneto hydrodynamics is the multi-disciplinary study of the flow of electrically conducting fluids in electromagnetic fields. Examples of such fluids include plasmas, liquid metals, and salt water. The fluid flow equations are solved simultaneously with Maxwell's equations of electromagnetism.

CHAPTER 3

LATEST HAPPENINGS

1. Production of ε-polylysine in an Airlift bioreactor [34].

In this development, the possibilities of the energy saving production of ε-polylysine using Streptomyces albulus strain no.410 in an ABR are evaluated and compared with the production of ε-polylysine in a jar fermentor. It was proved that although the productivity of the ABR is lower than that in the jar fermentor under high P_g/V (700 rpm, 80 kW/m^3), it has advantage both in the ease of scale up to production scale and also in the low overall cost for the production of ε-polylysine with high purity.

2. Photoautotrophic high density cultivation of vegetative cells of Haematococcus Pluvialis in airlift bioreactor

Here an airlift bioreactor was used for the cultivation of H. Pluvialis, one of the most effective microorganism that could produce high potential antioxidant carotenoid, astaxanthin which has been employed as an antioxidant, effective in immune response enhancement and cancer protection. This has been also used in other applications such as aquacultures, food, pharmaceutical and neutraceuticals industries. Not only the use of batch culture was illustrated but also the airlift system was also proven to determine average high productivity of such algae over use in semi-continuous culture.

3. Application of airlift bioreactor in waste water treatment.

Since, due to the various properties of airlift bioreactor such as scaling up and the relatively low power consumption for agitation and oxygenation has made the use of such reactor in the waste treatment as an efficient method. Jin et al. used an airlift reactor in a comprehensive pilot plant system for the starch processing wastewater reclamation. The important part of this paper is the dependence of the fungal morphology in the ALR fluids. As these mycelial growth increases strongly the viscosity which greatly reduce the oxygen transfer rate from the gas to the culture. As a result of which the role of airlift bioreactor came into the picture.

4. Continuous alcoholic fermentation in high call density airlift bioreactor using flocculating yeast.

The main goal of this research is to investigate the feasibility of the utilization of a genetically modified flocculating strain for ethanol production from lactose by the use of a continuous airlift bioreactor due to its advantageous combination of sufficient mixing, low shear stress and low power input.

5. The Aeration of Catharanthus roseus L. G. Don Suspension Cultures in Airlift Bioreactors: The Inhibitory Effect at High Aeration Rates on Culture Growth [16].

This was the research done to evaluate the effect of aeration and the CO_2 level in the growth of Catharanthus roseus L. G. Don Suspension Cultures in airlift bioreactor where it was shown that A high aeration rate (0·86 v.v.m.) was found to inhibit the growth of cultures. Venting cultures at a high rate with low oxygen content gas mixtures was equally inhibitory to culture growth, showing that high aeration was not inhibitory as a result of oxygen toxicity. The dissolved carbon dioxide tension was found to be lower in cultures operated at high aeration than those operated at low aeration. Supplying exogenous CO_2 to cultures at high aeration restored the CO_2 tension to values normally encountered at a low aeration rate, and was found to alleviate the inhibitory effects at high aeration. However, further increasing the CO_2 supply to cultures was found to be severely inhibitory to growth. Therefore, the growth of C. roseus cultures is very sensitive to dissolved CO_2 concentration; growth being inhibited at values either higher or lower than an optimum.

6. Kojic acid production in an airlift bioreactor using partially hydrolyzed raw corn starch [11].

In 3-litres of airlift bioreactor, kojic acid is not produced when the medium used is glucose/germ wheat germ medium (GM1). As compared to this the production given by the jar fermentor is far better but it is not economical in any way .So, for the airlift bioreactor a medium containing the partially hydrolyzed corn starch and a small amount of corn steep liquor (CSL) (SM1) was selected for the use and this has given a good result such that the cost of production of SM1 is reduced by 40 percent than that of the jar fermentor. Furthermore, the energy cost of kojic acid production using SM1 in the airlift bioreactor was less than one-fourth of that for the jar fermentor using GM1.

7. Production of Coenzyme Q_{10} by Rhodobacter sphaeroides in stirred tank and in airlift bioreactor [50].

This Coenzyme Q_{10} is a naturally occurring oil soluble material found abundantly in animals, microorganism and plants as a coenzyme in many electron transfer related reactions. It is also an essential component of the electron transfer system in the plasma membrane of prokaryotes and the inner mitochondrial membrane of eukaryotes, where it plays a key role of an electron donor/acceptor between complex i/ii and complex iii. This study indicated that the fed batch operation accompanying an aeration change-strategy in airlift bioreactor would be useful to have the maximum Coenzyme Q_{10} concentration obtained. This also suggests that airlift type reactor is a suitable bioreactor than traditional stirred tank for Coenzyme Q_{10} production.

8. Production of adventitious root biomass and caffeine derivatives of Echinacea purpurea through the Application of airlift bioreactor

Echinacea purpurea is an important medicinal plant native to N.America that is grown worldwide for commercial purposes. The purple coneflower has gained international importance because of its immune affecting property. The most important potential active component this purple coneflower are caffeic acid derivative,polysaccarids,alkamide and glycoproteins.Of this caffeic acid derivative ,cichoric acid has been found to have immunostimulatory, antiviral and antihyaluronidase activity. In this a bioreactor technology that enabled the mass cultivation of adventitious root of Echinacea purpurea for the production of phenolics and flavonoids derivatives, was derived. The amounts of phenolics flavinoids produced by this type of reactor were found to be higher than the natural strands. Here an inoculums density of 7g/L FW and aeration rate of 0.1 vvm were found to be suitable for the accumulation of biomass and the production of caffeic acid derivatives.

9. Microbial biomass production from rice straw hydrolysate in airlift bioreactors [53].

Rice straw is a rich source of protein for the animal feedstock produced during the rice production.In the present work rice straw hydrolysate as a substrate for microbial biomass was investigated in the external airlift bioreactor of about 11.5 l. The influences of gas flow rate, initial liquid volume, hole diameter of gas sparger and numbers of sieve plates on microbial biomass production were examined. The best results in the external-loop airlift bioreactor were obtained under 9.0 L initial liquid volume, 1.1 (v/v)/min gas flow rate during culture time of 0-24 h and 1.4 (v/v)/min gas flow rate of 24-48 h at 29+/-1 degrees C. The addition of the sieve plates in the riser of the external-loop airlift bioreactor increased productivity. After 48 h, under

optimized operation conditions, crude protein productivity with one sieve and two sieves were 13.6 mg/mL and 13.7 mg/mL, respectively, comparing 12.7 mg/mL without sieves in the airlift bioreactor and 11.7 mg/mL in the in the 10-L mechanically stirred tank bioreactor.

10. Treatment of phenolics containing synthetic wastewater in an internal loop airlift bioreactor (ILALR) using indigenous mixed strain of Pseudomonas sp. under continuous mode of operation [30].

11. Modeling of batch phenol biodegradation in internal loop airlift bioreactor with gas recirculation by *Candida tropicalis* [17].

12. External-loop fluidized bed airlift bioreactor (EFBAB) for the cometabolic biotransformation of 4-chlorophenol (4-cp) in the presence of phenol [23].

13. Semicontinuous cultivation of photoautotropic cell suspension culture in 20L airlift bioreactor.

14. Preparation of photoairlift bioreactor.

15. Microbubble generator enhances performance of airlift bioreactor [29].

16. Airlift bioreactor uses oscillating microbubbles to boost algae yields by 30 percent [29]

UK's University of Sheffield and the Czech Republic's Academy of Sciences (Prague) filled a patent for a microbubble generator that is driven by a fluidic-oscillator and uses up to 18 percent less energy than standard sparging systems. The generator improves the performance of air-lift loop bioreactors (ALBs) by producing smaller bubbles, around 20 micrometers versus 1–3-mm diameter for sparging, thus increasing mass-transfer rates fifty-fold.

17. Removal of hexavalent chromium by *Trichoderma viride* in an airlift bioreactor [28].

18. Itaconic acid production in an air-lift bioreactor using a modified draft tube [30].

Upcoming Research Technologies:

Device for monitoring of local viscosity during the technological processes

A characteristic indicator of many technologic processes is medium viscosity or other rheological properties changes during the process.

For example, in the fermentations by the growth of microorganisms the viscosity of cultivation media changes. In the process of lacquer production various resins are synthesized. By the end of the process of synthesis viscosity starts rapid increase. However, in milk production kefir, curdled milk and yoghurt are produced with the fermentation technologies. As the milk mass curdles, its solidity changes which is characterized also with increase of viscosity. In all of the mentioned cases change of the technological medium viscosity "informs" about the end of the process or about the need to perform influence on the process. In addition to the given examples one can find comparatively many examples where the characteristic parameter of a process would be viscosity.

Currently the described processes cannot be yet directly controlled depending on their viscosity because there are no devices with the help of which it would be possible to comparatively easily on-line measures the viscosity in various technologic processes. The given device should be convenient, robust, not complicated, with comparatively small dimensions (at least the transmitter part which is immersed in technologic environment) and with an economic price. The available systems are expensive, complicated and require auxiliary equipment. For this purpose in 2006 in Latvian State Wood chemistry institute a project of European Structure Fund Development (ERAF) "Indicator of rheological characteristics as a tool for control of biomass and other production processes" was commenced. Now the project is in the final phase and Latvian (P-08-92 from 26.05.2008) and European patents (Priority Nr. 08010576.0/EPO8010576 from 11.06.2008) are pended.

Taking into consideration the above mentioned principles and conditions the viscosity controlling device prototype was developed.

The given device (see block scheme) consists of a transmitter which is made on the basis of a bimorph piezoelectric multi-layer element (1), which is connected to a bimorph element signal processing block (2) and signal generating device (3). The output signal generated by the block (2), then transformed into 4-20 mA or 0-10V signal form, is transferred to the process logical controller PLC or another control device (4). The transmitter is initiated with 30 V impulses which are generated in the signal generating device (3) and from the moment of initiation of signal the damping oscillations in the block (2) are analyzed. PLC or another control device (4) by analyzing the signal of viscosity changes issues control signal to executive mechanisms of

production for regulation of technological process in accordance with the given algorithm. The given algorithm foresees actions which are needed when reaching a value of specified for viscosity. The algorithm depends on character of technological process.

Block schema of viscosity control device

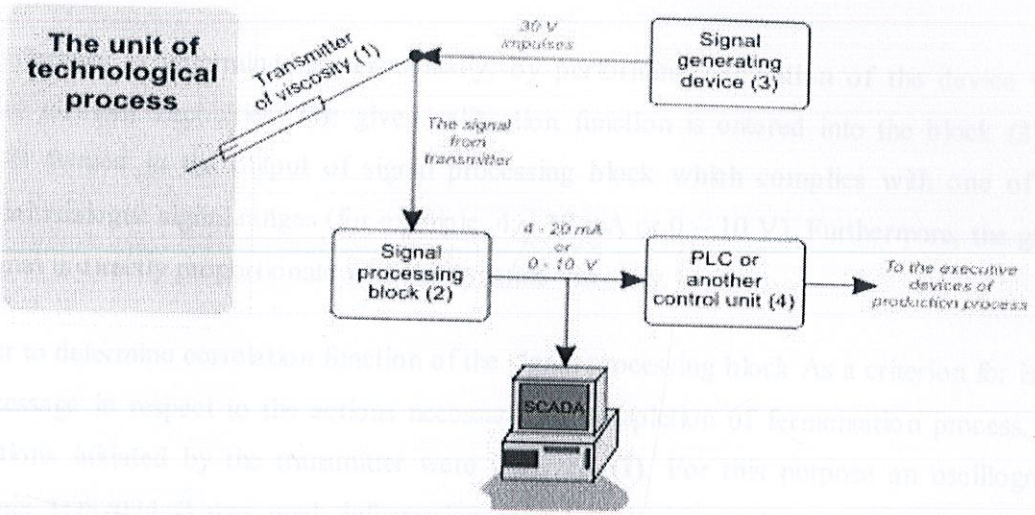


Figure 12: Viscosity Control Device

Transmitter's **(1)** construction is supplemented with elements which significantly increase oscillations amplitude initiated in the bimorph piezoelectric element and the damping time of oscillations, thus increasing sensitivity of the transmitter and thus also the viscosity limits foreseen for control.Transmitter's signal in the signal block **(2)** is processed with analogue to digital converter. Further the amplitude of each oscillation period is defined and on the basis of the given information a logarithmic fluctuation damping decrement d is determined in accordance with the following formula:

$$\delta = \frac{1}{n}\sum_{i=1}^{n} \ln \frac{x_o}{x_n}$$

d – logarithmic damping decrement of oscillations

n – number of oscillations

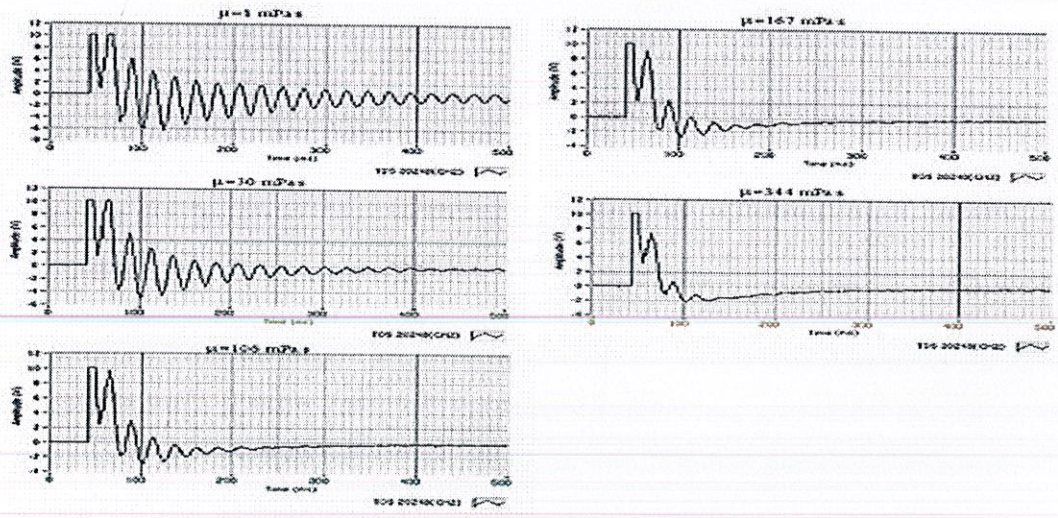
x_o – reference oscillation range

x_n – n oscillation amplitude

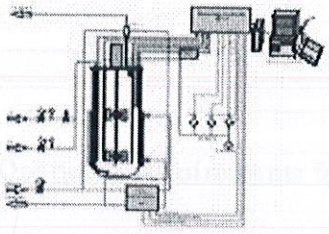
Between the damping decrement and dynamic viscosity there is an increasing functional coherence: $\mu = f(\delta)$

This coherence is determined experimentally, by performing calibration of the device with different medium viscosities. The given calibration function is entered into the block **(2)**. A signal is formed in the output of signal processing block which complies with one of the industrial analogue signal ranges (for example, 4 – 20 mA or 0 – 10 V). Furthermore, the given exit signal is directly proportionate with the dynamic viscosity.

In order to determine correlation function of the signal processing block As a criterion for issue of a message in respect to the actions necessary for completion of fermentation process. the fluctuations initiated by the transmitter were analyzed **(1)**. For this purpose an oscillograph Textronix TDS2024 B was used; information gained by it was analyzed and processed with computer software in graphical and tabular form. Viscosity was modeled by the means of various concentration CMC (carboxymethyl cellulose) solutions. Dynamic viscosity was determined with the help of the viscosimeter SV-10 (A&D Company, Limited). In such manner the damping curves of the transmitter **(1)** in viscosity range from 1 mPas to 344 mPas with optimal viscosity transmitter.onstruction



Application of the given transmitter is realized for control of fermentation process by connecting it as transmitter to the bioprocess controller BIO-3 in the following manner:



Viscosity control in the fermentation process can be applied, for example:

In order to determine the type of control of partial pressure pO2 of the dissolved oxygen (i.e. with the mixer rotation speed change, oxygen enrichment, substrate adding or otherwise);
As a criterion for issue of a message in respect to the actions necessary for completion of fermentation process.

The process control strategies for other processes can be developed based on analysis of on-line viscosity measurements.

Co-current type draft tube for the airlift bioreactor: an innovative mode for the better hydrodynamic and mass transfer in the airlift bioreactor, especially for the shear sensitive plant cultures [54].

CHAPTER 4

CONSTRUCTION PROCEDURE

Operation requirements for bioreactors

The main requirements to be observed for bioreactors can be conventionally divided into 3 groups:

1. Sterility
2. Mixing/aeration as an essential mass exchange factor
3. Process monitoring and control.

To meet these requirements, the bioreactor design should be executed with the corresponding professionalism, and its technical realisability (surface treatment, welds) should be of high quality.

Sterility

One of the major quality comparative characteristics of different bioreactors is the ability to secure sterile fermentations. These requirements are determined to a great extent by the bioreactor's construction and the surface treatment quality. All the further regarded non-sterility risk factors are mainly connected with securing of hermetic sealing at different stages of the process and surface treatment quality. The most characteristic possible non-sterility risk factors from the viewpoint of the construction are as follows:

Mixer's stuffing-boxes, sealing of the sensors' and other devices' inserting ports

One of the most typical pathways of penetrating infectious diseases is the mixer's stuffing-boxes. It is not always easy to secure the effective sealing and unhindered rotation of the drive. Apart from this, the regular servicing of the driver's stuffing-box should be secured to avoid the accumulation of infection there. To prevent the stuffing-box connected problems, bioreactor

drives are constructed on the principle of magnetic drives. In this case, the torque is transferred with the help of the magnetic field. As a result, the bioreactor vessel can be fully sealed.

As regards the sensors and other devices (supply of the titrated and feeded up components, sampling, chemostate realisation, etc.), port sealing should be taken into account, so that the ports could be sealed with the force of the operator's hand, and so that the sealing properties would not change as a result of the sterilisation temperature.

"Pockets", unevennesses and other bottle-necks for the accumulation of infection inside the bioreactor vessel

Inside the bioreactor, infection can be accumulated in places of irregularities and unevennesses. In such places, infectious microorganisms can "hide themselves". Therefore, the bottom inside the reactor should be rounded off, there should not be acute angles, and the surfaces should be polished.

"Unreasoned" sampling, procedure and construction

When sampling, the emergence of steam or flame and other conditions should be predicted, so that, after the termination of the sample spurt, the infection "would not manage" to get into the fermentation solution.

Filtration of the inlet and outlet air flows.

Air should be supplied into the bioreactor through the corresponding porosity air filter so that to hold up the possible infection source. The inlet air flow can be also passed through the pipes, which are being heated. Thereby, by the thermal action, an attempt is made to combat the possible infection at least partially.

Maintenance of overpressure

It is important to maintain the overpressure (0.2-0.5 bar) in the bioreactor's upper space (i.e. between the fermentation solution and the bioreactor jacket) to ensure the protection against the income of infection. The infection income through the outlet air line is hampered by using the outlet air filter.

Even and effective heat transfer

It is necessary to secure the sterilisation temperature, where possible, by the even energy consumption, and heating would be even. If the heating inside the bioreactor is not even, there can be a risk that there will be zones inside the vessel with insufficient sterilisation temperature.

Apart from this, during the sterilisation process, the sensors, devices, connections and other units should not loose their properties. It means that only sterilisable sensors (i.e. those which do not change their properties after the effect of sterilisation) and rubber or other materials, whose working temperature does not exceed 150°C should be used in sealing.

Mixing/Aeration As An Essential Mass Transfer Factor

Mixing and aeration are not the only factors that determine what mass exchange there will be in the bioreactor or how the microorganisms will grow. It is determined both by the properties of the microorganism strain and the choice of the balanced nutrient, process regime, etc. Let these factors remain for technologists; we will discuss what will be profitable for the bioreactor in this respect.

As regards the evaluation of the role of mixing, the 2 extreme points of view are rather widespread:

Microbiologists often say: "What can be the crucial role of mixing if the partial pressure of the dissolved oxygen (Oh, what a long explanation, but it is necessary to be exact!) pO_2 is too low, then more intensive mixing is required. And if the mixer's revolutions are such when we cannot cope with foam and other disorders, then we simply do not increase them and consider pO_2 as insufficient".

In its turn, "mixing people" say: "Oh, the matter is not so simple with mixing! Firstly, it is not correct to choose the mixing and aeration regime - the mass exchange at the same input power is decreased dramatically. Secondly, the choice of the incorrect mixing system already at a minor input power ("mixing people", in contrast to microbiologists, commonly do not say "mixer revolutions" to characterise mixing, but rather "introduced power with mixer") can cause irreversible mechanical damages in the sensitive microorganisms. Thirdly, the senseless increase

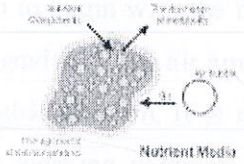
of air consumption causes even the worsening of mass exchange". And there are at least 6 another arguments, how important mixing is in microorganisms' cultivation.

But what is true?

To elucidate it, first of all, let us enumerate the results of mixing:

Air bubble dispersion;
Mass transfer from air bubbles (i.e. oxygen supply) to the liquid and then to cells;
Supply of the nutrient components to cells (more precisely, cell agglomerates);
Prevention of sedimentation;
Securing of heat transfer;
Solubility of the nutrient's components which are less soluble.

The mass transfer process during the cultivations of microorganisms explains the following picture:



As has been already mentioned in the division "Construction of the laboratory bioreactor", the most widespread are standard Ruchton turbine type mixers. At a constant rotational speed of the mixer, they secure the highest input power. This is practically from the viewpoint of the choice of the cultivation regime. Further it will be shown that there are, however, fermentations, in which the standard turbine is not the best solution any more. Certainly, there is a fermentation in which the role of mixing is relatively trivial. However, also in these cases, different mixing/aeration regularities should be taken into account:

Minimal and maximal limit of the mixer rotation

Irrespective of the pO_2 values (or other alternative growth or respiration parameters), it is not recommended to choose a mixer rotation speed lower than the empirically determined critical limit nmin. This limit, nmin, is chosen so that the following would not appear:

Sedimentation;

"Died" zones

In its turn, the choice of the critical limit nmax of the mixer's maximal rotational speed is determined by the following phenomena:

Foaming

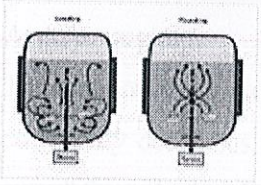
Liquid surface fluctuations, i.e. "waving", hence, also the liquid's evaporation.

Mixing/aeration relationships

When choosing the mixing and aeration intensity values and their relative mutual interactions, the following should be taken into account:

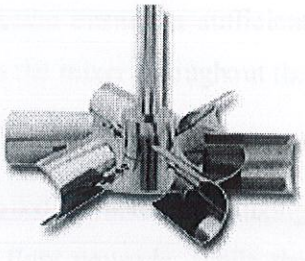
To increase the intensity of oxygen and other components' transfer intensity, first of all, we recommend to begin with the mixer rotational speed increase, and, only with $n > n_{max}$, to begin increasing gradually the air amount Q that is necessary for aeration. Before this, Q is chosen to secure a stable aeration. It is normally 1 vvm (vvm - amount of the introduced air versus the bioreactor's working volume). It means that, if we define air consumption in l/min, then the amount of the introduced air Q will be the same as the bioreactor's working volume.

At relatively low rotational speed values of the mixer, the increase in the amount of the introduced air should be avoided as far as the "flooding" effect begins. What the "flooding" effect is and how the transfer in it from the "loading" state occurs will be explained by the following illustrations:



It can be seen that, as the "flooding" regime sets in, air bubbles are concentrated only in the middle part of the reactor, and they are poorly dispersed. Hence, such a mixing/aeration state is very undesirable for the microorganism growth.

It should be noted that the transfer from "loading" to "flooding" has a hysteresis nature. It means that, as the amount of the introduced air Q decreases, the "flooding" effect will be lost at an air consumption, which is lower than that when it begins.



To continue the review of these problems, it should be noted that, as the "flooding" effect begins, the standard Rushton turbine is not the most suitable mixer's variant any more. In these cases, the most appropriate mixing systems are Chemineer CD-6 or BT-6, as well as Scaba AB 6SRGT (is called also the Smith mixer). Thereby, the mixer construction ensures an intensive grabbing of air bubbles in the radial direction also at minor rotational speed values of the mixer. As a result, the air bubbles have nothing to do but to obey the dispersion. Using such a mixer, its air amount Q, at which the "flooding" effect sets in, can be essentially increased.

Mechanical cultivation of sensitive microorganisms (the case in point here will be the cultivation of mycelial microorganisms, as the mixing of more sensitive cultures has other aspects, i.e. the cultivation of these cultures even in the minimal turbulent regime is not permitted).

In the case of mixing mycelial fungi microorganisms with a standard Rushton turbine, the mass exchange in the cultivation process increases only up to a definite rotational speed of the mixer, and, with the further increase in the mixer's rotational speed, the mass exchange parameters even begin to be impaired. The reason for such a phenomenon is the irreversible mechanical damage of the cells. Certainly, this critical rotation of the mixer is not strictly fixed and depends on different factors:

The variety of microorganisms' strains;
Nutrient's composition;
Aeration regime;
The amount of the grown biomass (at a greater biomass, the critical rotational speed of the mixer commonly decreases, as, in this case, it is more difficult for mycelial microorganisms to "run away" from the locally intensive mixing zones);
And other factors that determine the medium's rheological properties and cell condition.

Ekato Intermig is one of the most widespread mixers for mycelial cultures. Thus, the mixer consists of two mixers, i.e, the lower and upper ones. In this combination, axial

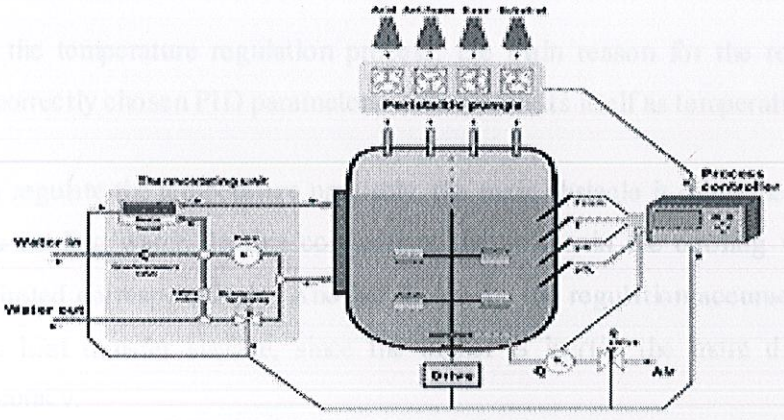
flows are generated in the mixer, and the mixer's radial end construction ensures a sufficient radial mixing. Thereby, an even distribution of the energy introduced in the mixer throughout the reactor's volume is ensured, resulting in the decrease of the maximal shear forces.

Another construction solution for mixing mycelial cultures is the so-called "counterflow mixing system". In this mixing system, the lower mixer generates an axial flow upwards, while the upper mixer downwards. The form of the mixer's blades ensures a sufficient flow eddy, i.e., as a result of tangential components, the given mixing system ensures both even distribution of the mechanically introduced energy (i.e. low shear stresses), and also a sufficient dispersion degree.

Process Monitoring and Control

The integral part of a high-quality bioreactor is a process controller. Such a controller is commonly specially formed for a definite bioreactor brand. This is rather connected with the fact that microorganism cultivation processes have relatively high requirements in respect to precision and sophistication. All this is despite the fact that almost all bioreactors monitor and regulate the same values actually invariably.

The monitoring and control scheme of a typical fermentation process looks like that:



Usually, the following parameters are monitored and controlled in bioreactors:

Temperature

Temperature is an important parameter of fermentation, since, in the cultivation of many microorganisms, the temperature deviation by a couple of degrees can diminish dramatically the growth and biosynthesis productivity. The cultivation temperature is commonly monitored with an accuracy not less than ± 0.5°C. For temperature measurements, stainless steel Pt100 sensors are normally used. The temperature in laboratory bioreactors is controlled by one of the following ways:

A heater is located inside the bioreactor vessel, and cooling is ensured by thin-wall pipes located in the upper cover, which are connected with an electromagnetic valve with the cooling water. Heating and cooling proceed in a thermostat, and this thermostatted water, with the help of a pump, circulates through the bioreactor jacket.

Variant 1 is less complicated, and it ensures a more economic constructive solution. This variant works very well for small bioreactors with the volume up to about 5 litres. Variant 2 ensures a more even distribution of heat throughout the bioreactor volume, which is essential in microorganisms' cultivation.

In the temperature regulation process, the main reason for the regulation inaccuracy are the incorrectly chosen PID parameters. This manifests itself as temperature oscillations.

To regulate the temperature precisely, the main obstacle is often the too high minimal portion of the cooling water. In this connection, the valves in the cooling water supply line should be adjusted correspondingly. Another factor for the regulation accuracy is the area and density of the heat transfer surface, since the higher is inertia, the more difficult is to reach a higher accuracy.

pH

pH control is based on the comparison of the adjusted "set point" and pH real values. For pH measurement, practically only sterilisable electrodes (most often, "Mettler-Tolede" electrodes)

are used. The control of pH values is ensured with the help of peristaltic pumps (silicone tubes are commonly used), correspondingly metering out the acid and the alkali. Normally, the "set point" adjustment consists of the lower pHmin and higher pHmax values. If pH is between these values, then no influence occurs. Such an adjustment of the pH "set point" is applied to prevent the overdose of the titration solution. On the other hand, the "narrow" regulation limits of pH are not necessary for the successful course of the cultivation process. It should be mentioned that pH measurements should be accurate (± 0.02 pH units), since the dynamics of pH values' changes provides valuable information on the process kinetics.

pO_2 (partial pressure of dissolved oxygen)

One of the most specific aspects of the fermentation monitoring is pO_2 measurement and control. pO_2 control is characteristic only for fermentation processes. There are different pO_2 control principles:

Varying the mixer's rotational speed n, assuming that $pO_2 \sim n$.

Combining the change of the mixer's rotation speed n and the amount of the inlet compressed air Q. It is assumed that $pO_2 \sim n$, $pO_2 \sim Q$. First of all, n is usually regulated until it reaches one of the limiting values - nmin or nmax, and its regulation is realised by varying Q. If n and Q have reached the limiting values, but pO2 is not within the necessary limits, then the regulating effect does not occur.

Feeding up the substrate or its any component. It is assumed that pO_2 is proportional to the feeding up intensity. Feeding up is normally realised with controlled peristaltic pumps. This way is sometimes combined with the regulation of the mixer's rotational speed n and the oxygen or air supply flow Q.

In pO_2 regulation, when adjusting the parameters, the following should be taken into account:

pO_2 is commonly adjusted in % from the fixed one. The adjusted pO_2 value has a lower and upper limit. The difference between both these limits is usually 10% - 20%.

Important parameters in pO_2 control are the control limits of the mixer's rotational speed n: n_{min} and n_{max}. It means that, when controlling pO_2, n will vary only within this range. These limits are determined in connection with eliminating of different undesirable phenomena:

n_{min} choice is determined:

to secure the minimal partly turbulent mixing level;by the guaranteed bubble dispersion; by the prevented sedimentation. n_{max} choice is determined by:

Setting in of the intensive foaming regime;

Irreversible mechanical damages of cells;

Liquid surface fluctuation and evaporation.

Foam

The appearance of foam is a very undesirable phenomenon, since, in the course of its appearance, there is a risk to loose an essential part of the fermentation broth. During the foaming, it is not possible to perform high-quality analyses and measurements. For elimination of foam, 2 methods or their combinations are commonly used:

Additional metering of an antifoam, based on the information provided by the foam sensor. The given impulses are relatively low, with long pauses and a limited metering time. This additional control is necessary to avoid the possible overdose, since, in this case, the mass exchange parameters can decrease dramatically.

Mechanical metering of foam. For this purpose, an upper drive with a special disk-type or other type of the mechanical foam breaking mixer is installed in the bioreactor's upper cover. If an intensive foaming begins, then the mechanical breaking of foam will not help any more.

An optimal solution is the combination of both the parameters. The application of Variant 1 is more widely used in laboratory bioreactor.

Construction of the laboratory bioreactor

In terms of the construction, the following variants of the laboratory bioreactor can be made:

Glass bioreactor (without the jacket) with an upper stainless steel lid.

Glass bioreactor (with the jacket) with an upper stainless steel lid.

Glass bioreactor (without the jacket) with the upper and lower stainless steel lids.

Two-part bioreactor - glass/stainless steel.The stainless steel part has a jacket and ports for electrodes installation.

Stainless steel bioreactor with peepholes.

Upper cover

The bioreactor's upper part has:

Ports for electrodes (pH, pO_2, T, p).
Ports for the supply of the titration and feeding medium.
Pipes for sampling and chemostate.
Ports for the connection of the outlet air condenser and filter.
Drive sealing (if the mixer's upper drive is used).
Air sparger mounting (if there is no lower lid).

The lid's ports, connections and mountings should ensure the air-tightness and leak- proofness, sterility, convenient removal and installation of the sensors and other elements. The lid is usually connected with the reactor's rest part employing special screws with a circumference diameter (4-8pieces) and a flat or "0" ring silicone rubber sealing.

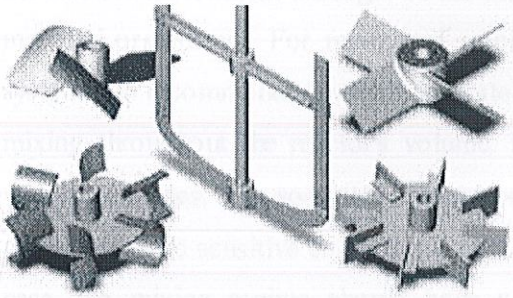
Lid (lower)

If the bioreactor has a lower cover, then the following ports and elements should be placed and fastened there:

Discharge valve;
Sampling device;
Sparger
Mixer's lower drive;
Heaters.

All these connections should secure air-tightness and leak-proofness and should prevent the conditions for infection agents' reproduction ("pockets", unevennesses, etc.).

Mixers



The mixer is mechanically "put on" the mixer's axis. The mixer's diameter is normally 1/3 - 1/2 from the diameter of the reactor vessel. The location of the mixer's axis depends on the fact whether the bioreactor has the upper or lower drive. The upper drive is realisable more easily from the constructive viewpoint. In this case, the construction of the sealing is also easier than in the case of the lower drive. In this case, the servicing of the bioreactor is also simple: the motor is disconnected from the sealing connection places, and then the lid, together with the mixer axis and the mixers, is taken off. In its turn, the lower drive provides a whole range of attractions connected with the operation regimes. In this case, mixing can be ensured in the bioreactor at the removed upper lid. This is important when modelling mixing as well as when cleaning and washing the bioreactor. In this case, it is easier to optimise dispersion, as the mixer can be close to the bioreactor's bottom. *The standard Rushton turbine is most popular*

The standard Rushton turbine is the most widespread mixer's construction. Its diameter d is 1/2 - 1/3 (most typically, 1/3) from the vessel's diameter. The Rushton turbine is a typical radial flow generating mixer. For the mixer axis, there are commonly 2-3 standard turbine mixers. The given mixer ensures the highest input power at fixed rotational speed values of the mixer (power index K_N = 5-7). This mixing system secures a sufficient course of mixing intensity, bubble dispersion and other mixing operations. This mixing system ensures the highest introduced power by constant rotations speed, comparing with other mixers. Therefore, the most part of bioreactors is equipped with such a mixing system. *The mixing of mechanical sensitive microorganisms* However, in the microorganism cultivation practice, there are fermentations in which the

application of the standard turbine mixer does not provide the optimal cultivation result, as irreversible mechanical damages of the microorganisms' cells are caused (this applies mainly to mycelial organisms). For mixing of mechanically sensitive mycelial microorganisms, mixing systems are recommended, which generate dominating axial flows, thereby ensuring a more even mixing throughout the reactor's volume. Ekato Intermig mixing systems are among the most widespread ones. The so-called "Counter-flow mixing system" is known. The approach to the mixing of more sensitive cells (tissue culture, animal cell, etc.) should be different, since; in this case, the mixing regime should have a laminar character. *The mixing by great air flows* Another case when the standard turbine is not effective enough it the dispersion of a great air flow at relatively low rotational speed values of the mixer. With increasing the inlet air amount, it is not dispersed any more, as the "flooding" regime sets in. In this case, to increase the dispersion efficiency, it is recommended to apply SCABA AB 6 SRGT, Chemineer Inc. CD6 or BT6 mixers. The efficiency of these mixers, in comparison with the standard turbine mixer, becomes even more pronounced in the cases of three-phase flows (intensive aeration and the presence of dispersive particles in the medium).

Baffles

Baffles are vertical radially located plates (their width is about 10% from the bioreactor vessel diameter). There are normally 3-4 such plates in the reactor. Baffles are necessary to prevent the formation of a funnel. As a result of funnel formation, the maximally possible rotational speed of the mixer can be essentially limited. Employing baffles, the consumed electric power of the mixer increases by about 20% at the same rotational speed.

Sparger

The supply of compressed air is realised through a sparger. The most widespread constructive solution is a loop pipe with small holes in the lower part (d = 0.05 - 0.15 mm). For mycelial culture fermentations, also loop spargers with a conical air outlet channel are employed. This construction prevents the possible overgrowing of cracks, since, in this case, the outlet diameter is greater, as well as pressure, because it is not distributed among the several pipes.

Bioreactor vessel

Depending on the construction type, the bioreactor vessel is made of steel, metal or their combination. The relation between the height H and diameter D of the bioreactor is within 1.5-2.5. The bioreactors produced in Europe are commonly more "stately" than those produced in the U.S.A. The reactor filling is about 70%. Thus, it is also the part of the working volume in the reactor vessel. There are high requirements for the reactor vessel materials to prevent the inhibition of the microorganism growth. The same applies also to any other part (sensors, pipes, etc.), which are installed inside the bioreactor vessel. The glass should be 100% borosilicate, e.g Pyrex® and Kimax®. All the metal parts should be made from stainless steel. The most widespread brand of the stainless steel applied in bioreactors is 316L. The letter L indicates that this steel is with a low composition of carbon. The inner surface of the stainless steel bioreactor should be polished to about a mirror surface quality to facilitate the washing and sterilisation process. Welding should be carried out in a fully inert gas medium. The inert gas should be argon, which fully replaces the air. With time, the application of the welding technology not corresponding to the requirements can cause the corrosion of the welds.

Condenser, outlet valve and filter

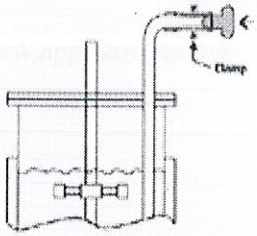
The task of the condenser is to cool the liquid in the air outlet, resulting in the separation of the foam and other liquid particles.For this purpose, a pipe is wound inside the condenser (or another solution that ensures, as possible, a longer air pathway); outside, there are two ports for cold water supply. The condenser is usually connected to the port located in the cover's centre. The condenser outlet is connected with the outlet valve. With the outlet valve, it is possible to regulate the necessary overpressure in the bioreactor's vessel. The valve outlet can be connected with a porous microbiological filter.

Sampling

On the one hand, sampling may seem to be a simple procedure - just open the manual valve in the inlet of the bioreactor vessel, supply as much fermentation broth as required for the sample, and close the tap! In this sampling, we can quite easily guarantee that infection will not be avoided.

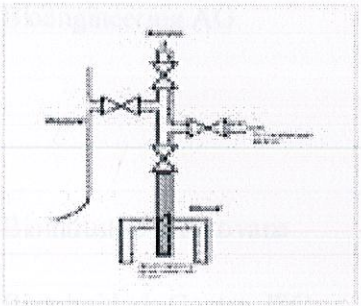
The sampling construction should be such so that measures for preventing non-sterility before and after the sampling be avoided. In the sites of the infection origin, sterilisation should be performed promptly with alcohol or steam. Sampling constructions of different companies are known, which are offered for sale:

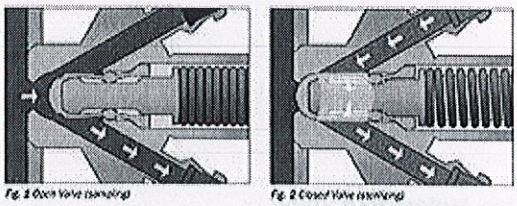
www.keofitt.dk
www.alnab.se
www.strahmanvalves.com
www.schufausa.com



The essence of sampling is based on one of the following principles:

Simple sampling line. A bladder made of silicone or a similar material is placed into the sampling pipe, and its end is stopped with a clamp. Thereby, it is sterilised together with the bioreactor vessel, and it remains in such a state until the sampling. When sampling, the clamp is removed, and the bladder is also pulled down. With the sample's discharge, the pipe's end is immediately washed with alcohol. Then, in a similar way, the sterilised bladder is put on (doing so, sterility should be certainly observed). This method is applicable if the given fermentation has not very high demands on sterility. Another drawback of this method is a hampered possibility of choosing the sample's amount. Keofitt sampling device





in 2 and 3 variants, as can be seen from the Figures, all is clear. In principle, variant 2 can be realised by the laboratory staff. Variant 3 is a compact, as if elegant and simple solution, but high accuracy and professionalism are required for its realising. A whole range of industrial sampling valves operates according to this principle.

All Manufacturers Of Bioreactors:

Company Name	Bioreactor types & Total volumes (l)	Home page
Applikon Dependable Instruments B.V.	G AC 1, 2, 3, 5, 7, 15, 20 SS AC 21.9, 74.2, 110 SS SiP 7, 15, 20, 30	www.applikonbio.com
B. Braun Biotech International	G AC 1, 2, 5, 10 SS-G AC 2, 5 SS SiP 10, 15, 20, 30, 50, 75, 100 Gmini AC 0.5, 1.0	www.bbraunbiotech.com
B. E. Marubishi Co., Ltd.	G AC 1, 2, 3, 5, 7.5, 10 SS SiP 10, 20, 30, 50, 70, 90	www.bemarubishi.co.jp
Bellco Glass, Inc.	Gmulti AC 4 x 3 G AC 3, 5, 8, 15, 36	www.bellcoglass.com/us
Bioengineering AG	G SiS 2.4,3.1,3.7 G AC+SiS 5.5, 7, 9,13,16,19 G+SS AC+SiS 7, 13, 16, 19 G+SS SiS 16, 19, 22 SS SiS 16, 19, 30 SS SiP 42, 50, 75	www.bioengineering.ch
Bioindustrie Mantovane	G+SS SiS	www.biofinlabs.com
Biotehniskais Centrs, JSC	G AC+SiS 6.2 SS SiP 7, 33	www.bioreactors.net
Biotron	G AC 3, 5, 7 SS SiS 5-40	www.ihanil.com
Broadley James	G AC 2, 3, 5, 7, 10, 15	www.broadleyjames.com
DAS GIP	Gmini AC 0.5, 1, 2	www.dasgip.de
Electrolab Ltd.	G AC 1, 2, 5, 10	www.electrolab.co.uk

FairMenTec	G AC 2.7 - 10	www.fairmaintec.com
Heinrich Frings GmbH & Co. KG	SS SiS, SiP 20-400	www.frings.com
	G AC 2.0, 3.6, 7.5, 13	
Infors	Gmulti AC 6 x 0.3, 0.5	www.inford-ht.com
	SS SiP 7-300	
	Gmini AC 0.05, 0.1, 0.25, 0.5,	
Meredos GmbH	1.0	www.meredos.com
	G AC 1-10	
	G AC 1.3, 3, 7.5, 14	
	G+SS AC 1.6, 3.3, 6.6, 14	
New Brunswick Scientific CO., Inc.	SS SiP 20, 30, 40, 80, 100, 120,	www.nbsc.com
	130	
New MBR	G AC 1-6	
(Multiple Bioreactors and Sterile	G SiS 2-5	www.newmbr.ch
Plants AG)	SS SiP 3.5 - 100	
	G AC 1.2, 3.5, 7, 10	
Novaferm AB	SS SiP 7, 15, 25, 40, 75, 140	www.novaferm.se
Pier Guerin Ltd.	G AC 1.9, 4.9, 7.6	www.pierreguerin.com
(Biolafitte & Horitz Division)		
	G AC 1.2	
Scigenics	SS SiS 4.2, 7, 14	www.scigenics.com
	SS SiP 14, 28, 75	
Virtis	G AC	www.virtis.com
Zeta AG	G AC 37	www.bio-t.com

We have used the various equations in order to define the working parameters involved in the reactor:

Gas holdup:

Gas holdup can be defined as the percentage by volume of the gas in the two or three phase mix in the column. The factor effecting liquid circulation is the superficial gas velocity & the cross - section area. $\varepsilon_{G=aUsg}{}^{b}$

In which 'a' is the function of the reactor geometry and of the properties of the liquid and 'b' is determined by the flow regime as well as the reactor geometry and also on operating variables, physical properties of the system

As it is airlift reactor so gas hold up should be the deciding factor for the working of the reactor and its efficiency.

Liquid circulation:

ThE liquid circulation determines the gas holdup, the prevailing flow regime, heat and mass transfer coefficient and the extent of the mixing in the reactor. The magnitude of liquid circulation is the most important factor for the designing and the scale up of the airlift bioreactor.

$$U_{Lr}=\left(\frac{2gh_D(\epsilon_d-\epsilon_r)}{k_B\left(\frac{A_r}{A_d}\right)\frac{1}{(1-\epsilon_d)^2}}\right)^{0.5}$$

Heat transfer:

i. Heat transfer by steady state condition in a stagnant liquid film adjacent to the heating surface.
ii. Heat transfer from the liquid film to bulk dispersion via packet of liquid which are continually brought to the surface of the film from the bulk and are mixed again with the bulk fluid due to induced agitation.

$$Q_H = U_H A_H \Delta T$$

$$P_T = P_h + \rho_L g(h_L - h_p)$$

Only two correlations for film heat transfer coefficient in concentric internal loop airlift reactor are available

$$h_f = 8.71\left(\frac{A_r}{A_d}\right)^{0.25}\left(\frac{C_p\mu_L}{k_t}\right)^{-0.5} U_{Gr}{}^{0.22}$$

$$h_f = 13.34\left(1+\frac{A_r}{A_d}\right)^{-0.7} U_G{}^{0.275}$$

Mass transfer:

k_La_L was effected by [19]:

1) DO electrode location- here electrode where located at the column axis of 5.752 and 0.635m, respectively above the bubble column .despite the highly viscous fluid (2 dry wt/vol. % SF in 0.15M NACL, the DO electrode location did not affect the k_La_L.

2) Solid concentration:-the k_La_L. Value decreased with increasing solids concentration but it was not effected either by the liquid height (h_L) in the reactor or by the cross sectional shape of the reactor. $k_La_L = a\left(\frac{P_g}{V_L}\right)^b$

$$\frac{dC_L}{dt} = k_La_L(C^* - C_L)$$

Considering these basic equation and manipulation of some of them have resulted in the designing process.

CHAPTER 6

RESULTS AND DISCUSSION

Taking above parameters under consideration we came into a design for airlift bioreactor which would really decrease the shear sensitivity for the cell culturing.
Here, we enquired about the various parameters which would affect its working with various equations and theories and came to following conclusions:

Draft tube: Presently, there exist generally two types of draft tube in the market i.e. multiple draft tube and single draft tube for the internal loop airlift bioreactor. But, it was seen that both these types of draft tubes are used in only a few specialized areas of production. For example, multiple draft tubes which was seen as an alternative to the single draft tube are seen to be useful in nitrification industries but it was not well satisfied with other types of processing industries such as with relation with the plant cells which are quiet sensitive and require a better mixing with reduced shearing. So, this co- current type draft tube will provide a better mixing in comparisons with the other draft tube .This will also adjust its length according to the condition in the airlift bioreactor. As the height of the draft tube has a direct relation to the mixing so this co- current draft tube will adjust its height according to its need for the mixing. This will be surely a new innovation in the field of bioreactor as it will provide a better mixing, as a result a better hydrodynamic behavior inside the reactor, resulting in high and improved productivity.

Sparger location: The bottom region is used for the installation of the sparger as this will not affect the hydrodynamics of the fluid inside the reactor.

Sparger efficiency:

Method to determine the bubble diameter and the efficiency of the sparger[38].
*1.Calculate Weber's number of the gas [45]. $W_e = \frac{\sigma_G U^{'2}_{G,0} D_C^*}{N_o^2 d_0 \sigma}$ $W_e = \frac{\sigma_g U_{G,0} d_o}{\sigma}$
2. Calculate Sauter's mean diameter[-] $\frac{\sum_i^N d_i^3}{\sum_{i=1}^N d_i^2}$
3. Use Krishna et al. theory to determine the performance[42]

Through this, we came into a better model for the sparger efficiency calculation.

These all the factors will greatly affect the performance of the reactor resulting in a more uniform hydrodynamic flow inside the reactor.

CHAPTER 7

SOME GREY AREAS

1. A study of the turbulence in the fluid in different zones of airlift reactors with a view to mapping, quantatively, the levels of shear which exist in these systems under various operating conditions.This kind of study would not only provide fundamentally new insight into mass transfer and mixing phenomena, but would be of direct practical use in establishing appropriate reactor designs for the more shear sensitive fermentation.

2. The oscillatory character of liquid circulation and fractional gas holdup needs to be examined in depth for a complete understanding of the relationship between them and also because of the possible impact of these phenomena on mass and heat transfer on mixing.

3. Airlift reactors have potential application in immobilized cell/enzyme processes. Consequently, studies of solid –liquid mass transfer are needed.

4. The design of airlift reactor head-space for gas-liquid separation is a potentially exciting area. In split-sylinder type of airlifts, for example, question of the effect of operation such that the liquid flows into the downcomer just over edge of the baddle, remain to be answered.

CHAPTER 8

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