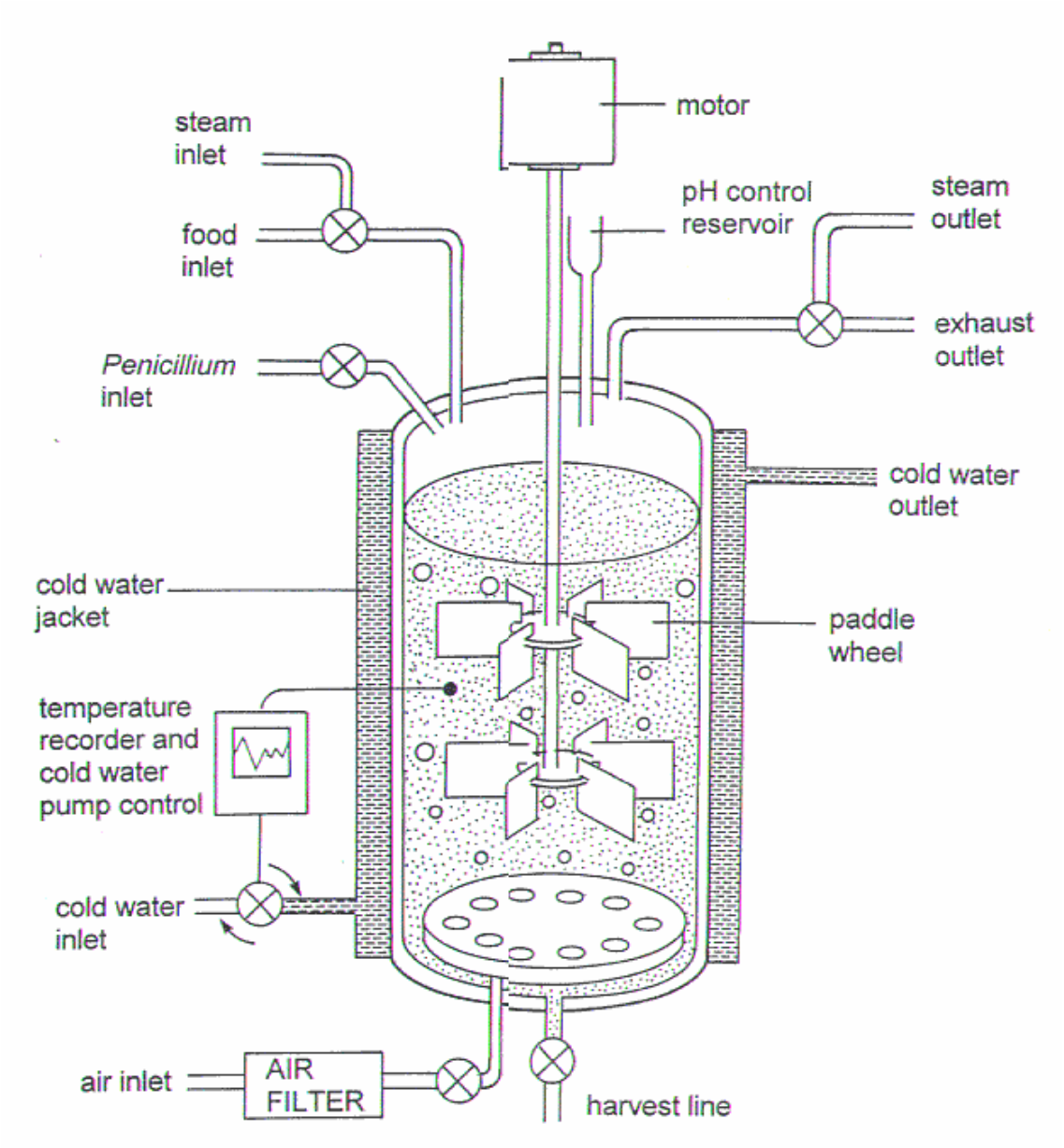
Different Types of Fermentor and Their Design



1 BODY CONSTRUCTION

Construction materials differ with small scale, pilot and large scale. In small scale for vessel construction glass or stainless steel may be used. For pilot and large scale process, stainless steel (>4% chromium), mild steel (coated with glass or epoxy material), wood, plastic or concrete may be used as vessel construction material. Any vessel used should not have any corners and smooth surface is essential. The construction material must be non toxic and corrosion proof.

Glass vessel (borosilicate glass)

Type I – glass vessel round or flat bottom with top plate. It can be sterilized by autoclaving and the largest diameter is 60cm.

Type II – glass vessel flat bottom with top and bottom stainless steel plate. This type is used in *in situ* sterilization process and the largest diameter 30cm.

Stainless steel

Stainless steel is used as vessel construction material with the following modifications,

1. >4% chromium (atleast 10-13%) may be added
2. film of thin hydrous oxide - non-porous, continuous, self healing, corrosion resistance
3. inclusion of nickel - improves engineering
4. presence of molybdenum - resistance to halogen salts, brine, sea water
5. tungsten, silicone - improve resistance

Thickness of vessel should be increased with scale. Side plates have lower thickness than top and bottom plates. Top and bottom plate are hemispherical to withstand pressures.

2.SEALING

Sealing between top plate and vessel is an important criteria to maintain airtight condition, aseptic and containment. Sealing have to be done between three types of surfaces *viz.* between glass-glass, glass- metal and metal-metal. There are three types of sealing. They are gasket, lipseal and 'O' ring. This sealing ensures tight joint in spite of expansion of vessel material during fermentation. The materials used for sealing may be fabric-nitryl or butyl rubbers. The seals should be changed after finite time. There are two way of sealing in O ring type simple sealing and double sealing with steam between two seals.

3. BAFFLES

Baffles are metal strips that prevent vortex formation around the walls of the vessel. These metal strips attached radially to the wall for every 1/10th of vessel diameter. Usually baffles are present but when the vessel diameter is over 3dm3 around 6-8 baffles are used. There should be enough gap between wall and baffle so that scouring action around vessel is facilitated. This movement minimizes microbial growth on baffles and fermentation walls. If needed cooling coils may be attached to baffles.

4. AERATION SYSTEM (SPARGER)

Sparger is a device for introducing air into fermenter. Aeration provides sufficient oxygen for organism in the fermenter. Fine bubble aerators must be used. Large bubbles will have less surface area than smaller bubbles which will facilitate oxygen transfer to a greater extent. Agitation is not required when aeration provides enough agitation which is the case Air lift fermenter. But this is possible with only for medium with low viscosity and low total solids. For aeration to provide agitation the vessel height/diameter ratio (aspect ration) should be 5:1. Air supply to sparger should be supplied through filter. There are three types of sparger *viz.* porous sparger, orifice sparger and nozzle sparger.

1. Porous sparger: made of sintered glass, ceramics or metal. It is used only in lab scale-non agitated vessel. The size of the bubble formed is 10-100 times larger than pore size. There is a pressure drop across the sparger and the holes tend to be blocked by growth which is the limitation of porous sparger.

2. Orifice sparger: used in small stirred fermenter. It is a perforated pipe kept below the impeller in the form of crosses or rings. The size should be ~ ¾ of impeller diameter. Air holes drilled on the under surfaces of the tubes and the holes should be atleast 6mm diameter. This type of sparger is used mostly with agitation. It is also used with out agitation in some cases like yeast manufacture, effluent treatment and production of SCP.

3. Nozzle sparger: Mostly used in large scale. It is single open/partially closed pipe positioned centrally below the impeller. When air is passed through this pipe there is lower pressure loss and does not get blocked.

4. Combined sparger agitator: This is air supply via hallow agitator shaft. The air is emitted through holes in the disc or blades of agitator.

EXIT GAS COOLER

Similar to liebig condenser, condenses the moisture from the exhaust gas in the fermenter. This removes as much moisture as possible from the gas leaving the fermenter and prevent excess fluid loss.

AGITATION

Agitation provides uniform suspension of cells in homogenous nutrient medium. This agitation provides bulk fluid and gas phase mixing, air dispersion, facilitates oxygen transfer and heat transfer and uniform environment through out the vessel. There are four classes, namely Disc turbine, Vaned disc, Open turbine of variable pitch and Marine impeller. Disc turbine prevents flooding by air bubbles. Flooding occurs when the air bubble is not properly dispersed the air pocket is formed one area. Flooded only at 120min/hour of air discharge when disc turbine is used. When open turbine and propeller are used the medium is flooded at 21min per hour of air discharge. Difference between disc turbine and open turbine is as follows:

Disc turbine Open turbine. Prevent flood by air bubbles till 120min/hour. Prevent flooding only till 21min/hour radial flow Axial flow Disc forces air to tip of agitator to be dispersed disc is absent Rushton disc turbine with 1/3 of fermentor diameter has been optimum for some fermentation process. Now recent designs of agitator have been introduced. Scaba is a new design of agitator that can handle high flow rate before flooding and has Radial flow. But this is not ideal for top to bottom mixing. Prochem maxflow agitator has low power conception with high hydrodynamic thrust. This design has increased downward pumping capacity of blades. In this design agitator/ vessel diameter ratio is 0.4. Appoximately 66% less power requirement even when viscous and oxygen transfer efficiency improved. Intermig agitator has two units. Unlike the earlier design agitator/ vessel diameter ratio is 0.6-0.7. For this agitator larger air sparger is used and top to bottom mixing not efficient. New turbine designs with dual impeller have been introduced. One for gas disperser and other for aiding circulation with multirod mixing.

TYPES OF FERMENTERS

The main function of a fermenter is to provide a controlled environment for the growth of microorganisms or animal cells, to obtain a desired product. Few of the bioreactor types are discussed below:

STIRRED TANK FERMENTER

Microbial fermentations received prominence during 1940's namely for the production of life saving antibiotics. Stirred tank reactor is the choice for many (more than 70%) though it is not the best. Stirred tank

reactor's have the following functions: homogenization, suspension of solids, dispersion of gas-liquid mixtures, aeration of liquid and heat exchange.

The Stirred tank reactor is provided with a baffle and a rotating stirrer is attached either at the top or at the bottom of the bioreactor. The typical decision variables are: type, size, location and the number of impellers; sparger size and location. These determine the hydrodynamic pattern in the reactor, which in turn influence mixing times, mass and heat transfer coefficients, shear rates etc. The conventional fermentation is carried out in a batch mode. Since stirred tank reactors are commonly used for batch processes with slight modifications, these reactors are simple in design and easier to operate. Many of the industrial bioprocesses even today are being carried out in batch reactors though significant developments have taken place in the recent years in reactor design, the industry, still prefers stirred tanks because in case of contamination or any other substandard product formation the loss is minimal. The aspect ratio (H/D) of stirred vessel varies over a wide range. When aeration is required, the aspect ratio is usually increased. This provides for longer contact times between the rising bubbles and liquid and produces a greater hydrostatic pressure at the bottom of the vessel.

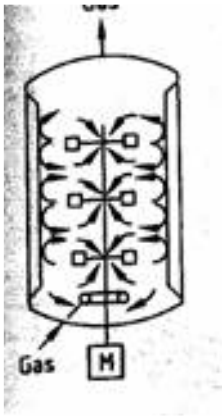


Fig.2 Stirred tank fermenter

The batch stirred tanks generally suffer due to their low volumetric productivity. The downtimes are quite large and unsteady state fermentation imposes stress to the microbial cultures due to nutritional limitations. The fed batch mode adopted in the recent years eliminates this limitation.

The Stirred tank reactor's offer excellent mixing and reasonably good mass transfer rates. The cost of operation is lower and the reactors can be used with a variety of microbial species. Since stirred tank reactor is commonly used in chemical industry the mixing concepts are well developed. Stirred tank reactor with immobilized cells is not favored generally due to attrition problems; however by separating the zone of mixing from the zone of cell culturing one can successfully operate the system. This requires a relatively high input of energy per unit volume. Baffles are used to reduce vortexing.

Airlift Bioreactors:

Airlift reactors are often chosen for culture of plant and animal cells and immobilized catalyst because shear level is low. Gas is sparged into only part of the vessel cross section called the riser. Gas hold-up and decreased liquid fluid density cause liquid in the riser to move upwards. Gas disengages at the top of the vessel leaving heavier bubble-

free liquid to re-circulate through the down comer. Airlift reactors configurations are internal-loop vessels and external-loop vessels. In the internal-loop vessels, the riser and downcomer are separated by an internal baffle or draft tube. Air may be sparged into either the draft tube or the annulus. In the external-loop vessels, separated vertical tubes are connected by short horizontal section at the top and bottom. Fewer bubbles are carried into the downcomer, the density difference between fluids in the riser and downcomer is greater, and circulation of liquid in the vessel is faster . Accordingly, mixing is usually better in external-loop than internal-loop reactors. The riser and downcomer are further apart in external-loop vessels while gas disengagement is more effective than in internal-loop devices.

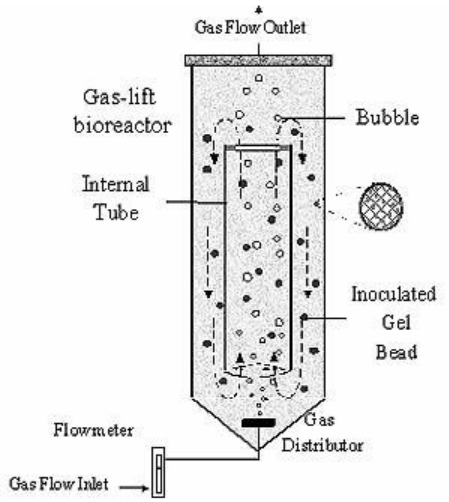
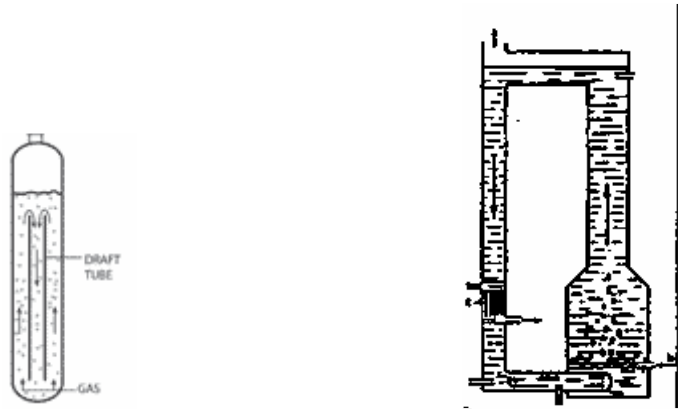


Fig.3 Air-lift fermenter

Air lift bioreactors offers great advantages like there are no moving parts, high gas adsorption efficiency, good heat transfer characteristics and short mixing time. ALR are preferable over CSTR because it provides a low shear environment for microorganisms. ALR do not possess mechanical stirrers so there in reduced risk of contamination. Less energy is required for the ALR and it is of low cost. Airlift bioreactors are of two types: internal loop and external loop airlift bioreactor.



(a) (b)

Fig.4 (a) Inner loop air lift fermenter (b) Outer loop air lift fermenter

FLUIDISED BED BIOREACTOR

Fluidized bed bioreactors (FBB) have received increased attention in the recent years due to their advantages over other types of reactors. Most of the FBBs developed for biological systems involving cells as biocatalysts are three phase systems (solid, liquid & gas). The fundamentals of three phase fluidization phenomena have been comprehensively covered in chemical engineering literature. The FBBs are generally operated in co-current upflow with liquid as continuous phase and other more unusual configurations like the inverse three phase fluidized bed or gas solid fluidized bed are not of much importance. Usually fluidization is obtained either by external liquid re-circulation or by gas fed to the reactor. In the case of immobilized enzymes the usual situation is of two-phase systems involving solid and liquid but the use of aerobic biocatalyst necessitate introduction of gas (air) as the third phase. A differentiation between the three phase fluidized bed and the airlift bioreactor would be made on the basis that the latter have a physical internal arrangement (draft tube), which provides aerating and non-aerating zones. The circulatory motion of the liquid is induced due to the draft tube.Basically the particles used in FBBs can be of three different types: (i) inert core on which the biomass is created by cell attachment. (ii) Porous particles in which the biocatalyst is entrapped.(iii) Cell aggregates/ flocs (self-immobilization). In comparison to conventional mechanically stirred reactors, FBBs provide a much lower attrition of solid particles. The biocatalyst concentration can significantly be higher and washout limitations of free cell systems can be overcome. In comparison to packed bed reactors FBBs can be operated with smaller size particles without the drawbacks of clogging, high liquid pressure drop, channeling and bed compaction. The smaller particle size facilitates higher mass transfer rates and better mixing. The volumetric productivity attained in FBBs is usually higher than in stirred tank and packed bed bioreactors. There are several successful examples of using FBBs in bioprocess development.

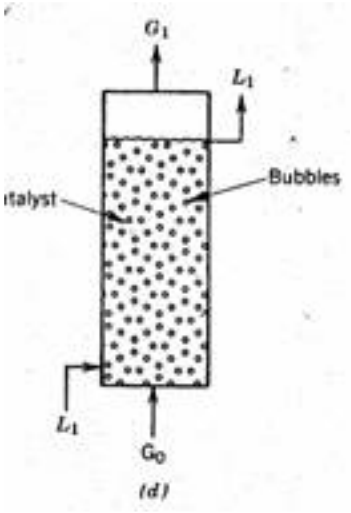


Fig.5 Fluidised bed bioreactor

PACKED BED BIOREACTOR

Packed bed or fixed bed bioreactors are commonly used with attached biofilms especially in wastewater engineering. The use of packed bed reactors gained importance after the potential of whole cell immobilization technique has been demonstrated. The immobilized biocatalyst is packed in the column and fed with nutrients either from top or from bottom. One of the disadvantages of packed beds is the changed flow characteristic due to

alterations in the bed porosity during operation. While working with soft gels like alginates, carragenan etc the bed compaction which generally occurs during fermentation results in high pressure drop across the bed. In many cases the bed compaction was so severe that the gel integrity was severely hampered. In addition channeling may occur due to turbulence in the bed. Though packed beds belong to the class of plug flow reactors in which backmixing is absent in many of the packed beds slight amount of backmixing occurs which changes the characteristics of fermentation. Packed beds arc generally used where substrate inhibition governs the rate of reaction. The packed bed reactors are widely used with immobilized cells. Several modifications such as tapered beds to reduce the pressure drop across the length of the reactor, inclined bed, horizontal bed, rotary horizontal reactors have been tried with limited success.

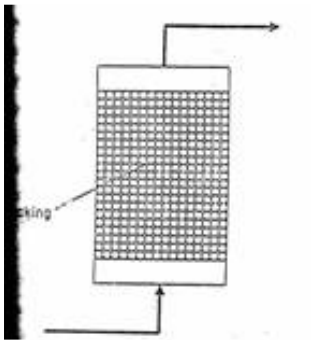


Fig.6 Packed bed bioreactor

BUBBLE COLUMN FERMENTER

Bubble column fermenter is a simplest type of tower fermenter consisting of a tube which is air sparged at the base. It is an elongated non-mechanically stirred fermenter with an aspect ratio of 6:1. This type of fermenter was used for citric acid production.

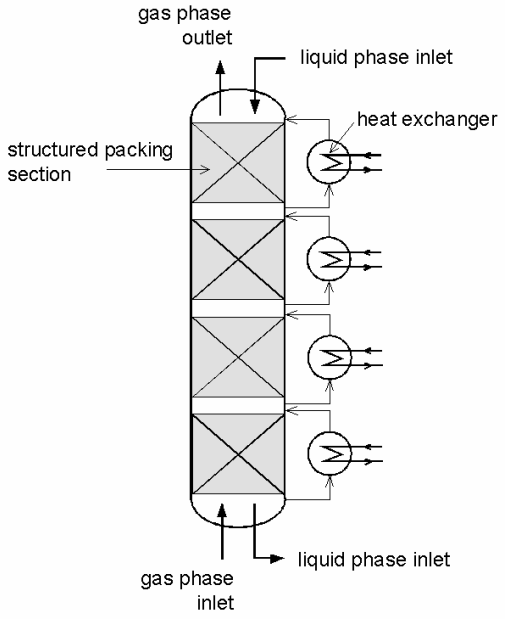


Fig.7 Bubble column fermenter

CONTROL AND MONITORING FERMENTATION SYSTEM

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. There are three types of sensors used in fermenter. They are, In-line sensors form integral part of fermenter. The directly measured value controls the process. Eg. Antifoam probe. On-line sensors form integral part of fermenter. The measured value must be entered into control system to control process. Eg. Ion specific sensors, mass spectrophotometer. Off-line sensors do not form integral part of fermenter. The measured value must be entered into control system for data collection.

TEMPERATURE

Heat is generated from any fermentation process due to microbial activity and agitation. The heat control in small scale is carried out by thermostatically controlled bath, internal heating coils, heating jacket(water),silicon heating jacket ;large scale: inter coils and cold water circulation. Cooling water is required less for bacteria but more for fungi (due to low optimum temperature for growth).

TEMPERATURE CONTROLLING DEVICE

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 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:

1. 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.

2. 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 is 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. Components used for controlling temperature in a fermenter are water inlet, pressure regulator, magnetic inlet valve, heater, circulation pump, jacket, cooling water valve, cold finger,

pt-100 sensor, controller, exit gas cooler and drain to remove overflow.

GAS FLOW RATE

GAS FLOW RATE MEASURING DEVICE

Flow rate can be measured by simple variable area meter.

a) Rotameter: is a vertically mounted glass tube with an increasing bore size and enclosing a free moving float (a ball or a hollow thumble). The position of float indicates the flow rate. This is less accuracy at low flow rate. Since air coming out of it is non-sterilized, it is placed between inlet and filter. Metal tubes can replace glass tubes. Float position determined by magnetic or electrical techniques. This can be used to measure gas and liquid flow rates.

GAS FLOW RATE CONTROLLING DEVICE

Needle valve is used to control the gas flow rate. Piston movement of the valve is controlled by fluctuations in pressure in flow measuring device. This should be placed upstream of supply when regulated air flow rate is required. This should be placed down stream when fluctuates and back pressure is constant.

AGITATION MEASURING AND CONTROLLING DEVICE

Agitation speed can be measured by power consumed by agitator shaft. Wattmeter is usually used in large scale process. It is a measure of power consumed for rotation of agitator shaft. This measure is less accurate because power required to rotate against friction in the bearing is taken into consideration. Torsion dynamometer is used in small scale. This has to be placed outside the vessel and less accurate due to friction. Strain gauges can be mounted on shaft within fermenter from which electric signal is picked up through lead wires passing out of fermenter via an axial hole. Tachometer can be used to control the agitation speed. The rate of rotation is monitored either by electromagnetic induction or voltage generation or light sensing or magnetic force. Final choice is made by the type of signal required to record or monitor the signal. The agitator
speed is also controlled by gear box usage, modifying the size of wheels and drive belts and changing the drive motor.

FOAM SENSING

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:

1. Additional metering of 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.
2. Mechanical metering of foam. For this purpose, an upper drive with a special disktype 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 bioreactors. Foam formation can be sensed by a probe which is a stainless steel rod insulated except at tip and set at a defined level. When foam touches the probe tip current passed through with foam as electrolyte and vessel as earth. This current
actuates a vessel/pump to release antifoam into fermenter. Process timer are also included which ensures time gap for antifoam mixing in the medium and reducing foam before next sensing occurs.

Dissolved oxygen can be measured by Galvanic electrode which consists of KCl or KOH or bicarbonate or acetate as electrolyte. Lead is used as anode and silver acts as cathode. The electrodes measure the partial pressure of the dissolved oxygen concentration. The sensing tip of electrode is a membrane made up of Teflon, polyethylene or polystyrene allows gas phase passage so that an equilibrium is established between the gas phases inside and outside the electrode. Due to slow movement of oxygen the changes are read slowly.

pH MONITORING DEVICES

A pH measurement is a determination of the activity of hydrogen ions in an aqueous solution. Many important properties of a solution can be determined from an accurate measurement of pH, including the acidity of a solution and the extent of a reaction in the solution. Many chemical processes and properties, such as the speed of a reaction and the solubility of a compound, can also depend greatly on the pH of a solution. In applications ranging from industrial operations to biological processes, it is important to have an accurate and precise measurement of pH. Most modern pH electrodes consist of a single combination reference and sensing electrode instead of separate electrodes. This type of pH electrode is much easier to use and less expensive than the electrode pair. A combination electrode is functionally the same as an electrode pair.