BIOREACTORS

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Contents

Summary

A review of recent advances in aerobic bioreactor design and view of strategic development of bioreactors in the last decades is presented. Various types of bioreactors are described from the energy input as well as mechanically, circulation pump and compressed gas mixed bioreactors. Large scale production and waste water treatment

bioreactors are also presented. Based on economic strategy of biosynthesis of fine chemicals, the design of fluidized bed, perfusion airlift, membrane, hollow fibre and ultrafermentation reactors are discussed.

1. Introduction

Bioreactors are the core of any bioprocess. In principle, bioreactor design does not differ from normal gas-liquid reactor design. Bioreactors generally represent special forms of gas-liquid reactors. The whole reaction mechanism is complicated by the inclusion of the mass transfer step that gives the possibility for the reaction to be mass transfer controlled when the mass transfer rate is slow relative to the reaction rate, and kinetically controlled when the reaction rate is much slower than the mass transfer rate. The majority of bioreactors have the limitation of gas-liquid mass transfer, and growth and/or production rates are often the rates at which oxygen can be transferred into the liquid. Bioreactors are in general reactors without geometrical shape, their type and design is highly dependent of the kind microorganism, organic tissues or cell segments used in the process of biosynthesis.

In analogy with old nomenclature that named enzymes ferments [see also – *Enzyme Production*], the reactors where the processes with enzymes catalysis proceed were named fermentors. Both terms were changed to biocatalysis and bioreactors although in some literature fermentors means – bioreactors.

Gas-liquid or gas-slurry reactors are used in aerobic fermentations. Many fermentation processes such as production of acetic acid, wine, yeast etc. [see also – *Production of Alcoholic Beverages*; – *Production of Organic Acids*], have been known in home production or small scale operations in the past. Higher demands for various fermentation products in time influenced large scale production with various trays or vessels. This interest led to the art of creating bioprocess reaction vessels, bioreactors or bioreactors, known in general as bioreactor design.

The fermentation industry is now over its first centennial, having envolved from the first step in industrial fermentation plants and the first bioreactor design to contemporary plants. The first industrial plant for citric acid biosynthesis with strain *Penicillium cytromices* was built in 1893. It was based on a surface production using as bioreactors large and flat trays. At its early beginning of aerobic bioreactor design was based mostly on experience and manufacturing art criteria. Early aerobic bioreactors were based on the bubble column principle. But aeration with the simple bottom nozzle was less effective in the sense of heat and mass transfer, therefore the most common reactors used in commercial productive fermentations become stirred tank reactors variety and the design of these dates back to 1940's when they were used for the first modern industrial fermentation of antibiotic Penicillin [see also – *Production of Antibiotics*]. Little literature appeared before 1972 although an air-lift bioreactor was already patented by Le François 1955. This is not surprising since applications to biotechnology did not receive much attention before about 1968, but in the same year ICI started with laboratory work on single cell protein production possibilities (Pruteen process).

As pneumatic dispersion of the gas phase was less effective in the sense of heat and mass transfer it was not surprise that further development led to mechanical mixing as a solution of this problem. Energy costs by power input were neglected at that time. In further development the Stirred Tank Reactor (STR) was popularized as a universal bioreactor and it is elsewhere still the most widely used type of bioreactor in fermentation technology.

Many actors have led to bioreactor design in recent years. In a survey K. Schügerl in 1982 cited the following driving forces:

- Need to reduce capital costs.
- Need to reduce energy input costs.
- Need to reduce substrate evaporative losses.
- Need for very large reactors (especially for single cell production and waste water treatment), leading to additional design problems in the area of increased power requirements.
- Need for low shear reactors in the case of shear sensitive cultures.
- Need for increased substrate conversion.

To systematize design approaches to these problems bioreactors are classified into three groups.

- Bioreactors with mechanically moved internal parts to provide agitation and mixing energy input.
- Bioreactors with a circulation pump for liquid phase movement.
- Bioreactors mixed by compressed gas sparging.

These three main groups are comprehensively presented in Figures. 1, 10 and 15.

2. Bioreactors with Mechanically Moved Internal Part

Mechanically mixed bioreactors use different impellers, motor driven from the top or the bottom, or some other means, for e.g. vibration of the impeller or the whole reactor. Basical problems in this type of bioreactors are mechanical seals, the motor drive and the type of impeller. The most used types of impellers in mechanically mixed bioreactor are usually Ruston type, curved blade and six blades turbines or marine impeller. Various hard metals, ceramics and carbon seals are used in bottom drive systems, silicon or special double seals are popular in the top drive systems .

The conventional single and multiple blade impellers in wall baffled reactors (Figures. 1.1, 1.4) are combined with internally immerged tubes which provide bulk mixing with more modest power inputs (Figures. 1.2, 1.3, 1.5, 1.6), a tubular recirculating loop reactor for more complete substrate utilization with rotating impeller (Figure 1.7) or perforated plate (Figure 1.9). A Short Loop Reactor for high oxygen transfer and perfect mixing is presented in Figure 1.14. The only non steady mode is a pulsative operation used in the pulsation cascade bioreactors (Figure 1.10).

Figure 1.8 presents a cascade reactor with mixing elements and Figure 1.11 a horizontal tubular reactor with a rotating drum. The configuration of waste treatment processes

includes a rotating wheel mixer (Figure 1.12) and biodisc reactor (Figure 1.13).

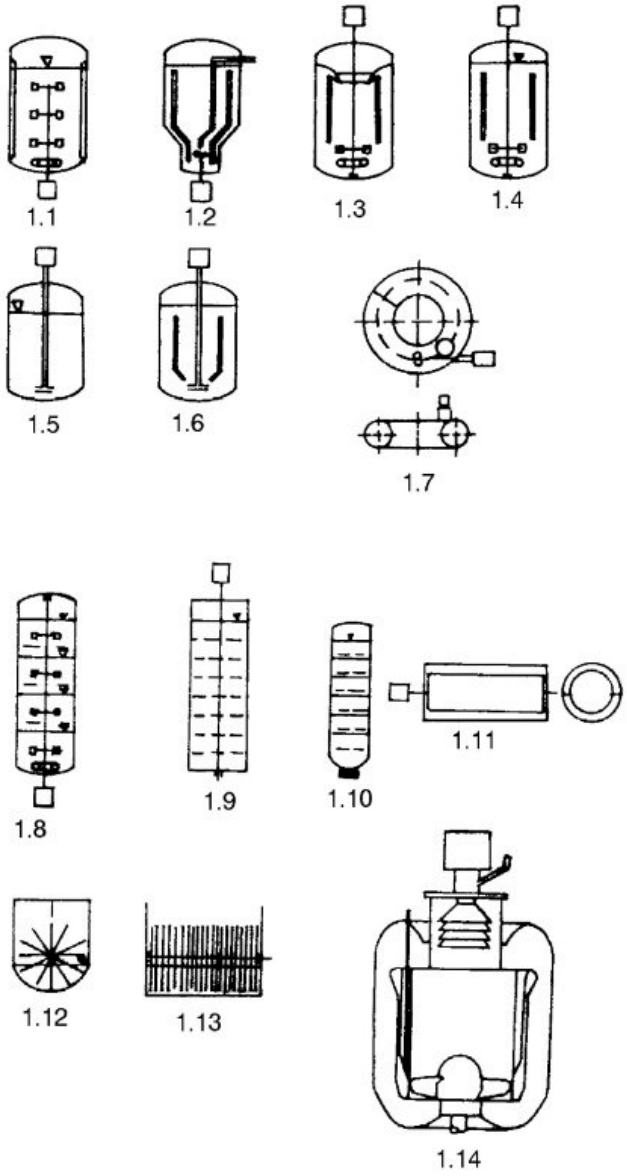

Figure 1. Bioreactors with mechanically moved internal part

A quite different design of horizontal bioreactors with biofilms (the biodisc) was developed for the treatment of waste water . The device consists of a series of closely spaced discs anchored to a shaft supported just above the surface of the liquid. Thus a unit area of biological slime is alternately submerged to absorb food and then raised out of the liquid to oxidize the absorbed components. A comparable design, called the multiple blade horizontal reactor (MBHR), was presented by Means and coworkers for the handling of mycelial fermentations without the formation of a biofilm. The tube consists of nine cylindrical compartments, joined end to end, where each part is sealed off from its neighbouring compartment by a separating plate having an overflow hole in

the upper half. The combined splashing of the bioreactor walls and the shearing action between the agitator blades and comb-shaped baffle plates installed vertically at the bottom of each compartment in the bioreactor increased mixing and suppressed the formation of mycelial deposits. Similar horizontal cylindrical chambers with several rotating discs are known in the literature for different technologies , hidrocarbon fermentation , continuous cultivation of microbes - gas-liquid contacting paddle-wheel reactor. Another design shown in Figure 2c is the horizontal rotary reactor (HRR) with an unbaffled rotating drum, originally constructed for the accurate measurement of oxygen transfer rates and subsequently used for carrying out several fermentations . The HRR was constructed by Bioengineering AG, Switzerland and is also called the rotaschön-reactor.

Furthermore, a type of annular reactor, the thin-layer tubular reactor (ThLTR; Figure 2d**),** was designed by Gorbach , and used for the verification of Danckwerts' renewal theory of mass transfer . It has also found application in biotechnology in which less foaming was observed . In order to increase the oxygen transfer rate in this reactor type, the mechanically agitated and aerated tubular reactor (MATR) (Figure 2d) was further developed and characterized by Moser for yeast production. Thin-layer reactors including HRR, TLR and MATR were summarized in a recent article.

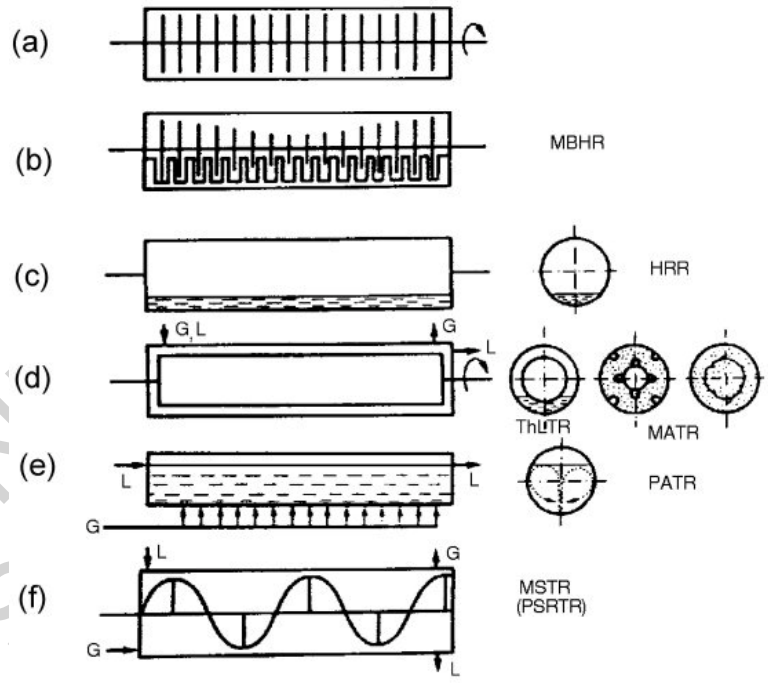

Figure 2. Horizontal tubular reactors

A pneumatically aerated tubular reactor (PATR) Figure 2e) has been designed for biological waste water treatment . The criteria for the choice of continuous reactors with long residence times have been reviewed by Langensiepen. A special feature of the PATR, apart from the absence of any mechanical devices is the fact that air or O_2 is introduced over the entire lenght of the reactor. Consequently oxygen supply can be adapted to oxygen consumption, thereby avoiding oxygen limitation.

With regard to the oxygen transfer rate, following correlations have been reported in the literature :

$$\text{For MATR : } k_L a = c\,(P/V)^{0.5 - 1.2} \qquad (1)$$

$$\text{For TLR : } k_L a = c\,(P/V)^{0.4 - 0.9}\,(vs,g)^{0.4-0.2} \qquad (2)$$

Last but not least, a series of scraped tubular reactors agitated either by mechanical means (MSPFR) or pneumatically with gas jets (PSPFR) was designed by Moo-Young and coworkers . One of these designs is schematically shown in Figure 4h. Wall growth is minimized by using rotating internal coils, a moving belt of internal discs, or helical ribbons and orifices directly in the tube. These scrapers partially segregate the liquid into moving compartments, where cross flow aeration, effected by orifices at the bottom is realized as in the case of the PATR. These devices have been used for the production of several materials, including lipase by yeast and cellulase by fungi. Since the production of both lipase and cellulase is object to catabolite repression, better performance may be expected in CPFRs.

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