International Research Journal of Innovations in Engineering and Technology (IRJIET)

ISSN (online): 2581-3048

Volume 9, Issue 7, pp 1-13, July-2025

https://doi.org/10.47001/IRJIET/2025.907001

Fermentation Process and Bioreactor Design: Concepts, Types and Operational Factors

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Abstract **- This comprehensive review addresses the biological processes used in fermentation, with a focus on the design of various bioreactors such as continuous stirred tank reactors (CSTR) and both aerobic and anaerobic reactors. The review explores the history of fermentation, production stages, different types of bioreactors, and their operational characteristics. It highlights the industrial, medical, and environmental applications of these processes, analyzing factors affecting production efficiency, such as oxygen transfer, temperature control, and pH regulation. As the new developments are incorporated into the enhancement of the productions of antibiotics, enzymes, and other pharmaceutical products, the study reinforces the role of biotechnology in the advancement of the pharmaceutical and food industries.**

Keywords: Fermentation, bioreactors, bioreactor design, mass transfer.

I. INTRODUCTION

The combination of biology and the technological domain (technology) is known as biotechnology. It is utilized in a number of industries, chief among them being nutrition, agriculture, and medical. The fermentation process, which has been used for hundreds of years, is the oldest biotechnology method. Fermentation technology refers to the study and use of fermentation [1]. Regarding the idea of fermentation, there are several ways to understand it. For instance, fermentation is today understood to be the process by which different living things, particularly bacteria, produce energy from the perspective of biochemistry and physiology [2]. According to a chemical engineer, fermentation is the process of growing a lot of microorganisms and performing biotransformation within specialised containers known as fermenters or bioreactors [3-4]. Although the words fermenters and bioreactors are similar, they serve different functions. One kind of bioreactor is a fermenter, which has closed containers and a sterile, controlled environment for microbes to grow in an appropriate medium and create a variety of chemicals. Bioreactors closed containers use a living cell as a biocatalyst [5]. The idea of the fermentation process, its stages, types, fermenters, their types and applications will be covered briefly in this article.

II. FERMENTATION

2.1 Concept of fermentation process

The term "fermentation" generally refers to a biochemical process in which sugars are converted into acids, gases, and alcoholic products. This process primarily involves microorganisms, particularly bacteria, which produce energy from a biochemical and physiological perspective. According to a chemical engineer, fermentation is defined as the cultivation of a large number of microorganisms that perform biotransformation within specialized containers known as fermenters or bioreactors. The term fermentation derives from the Latin fervere, meaning to boil. It refers to that type of anaerobic catalysis of carbohydrates, which invariably produces carbon-dioxide bubbles as a product of the phenomenon called fermentation. The fermentation process initiates when the substrate is inoculated with the required microorganisms under optimal environmental conditions, promoting the desired products [6-7].

Fermentation is important for every aspect of our lives on a daily basis:

- Wastewater treatment.
- Environmental management.
- Manufacturing of industrial products (e.g., bread, cheese, coffee).
- Production of industrial and medicinal enzymes.
- Development of vaccines and antibiotics.

2.2 History of fermentation

Although no one understood the origins of fermentation or the relationship between fermentation and microbes at the time, the history of fermentation started around 1200 years ago. The first person to study fermentation was the French microbiologist Louis Pasteur, who demonstrated in 1854 that microbes start the process. In 1907, the German scientist Eduard Buchner was awarded the Nobel Prize for demonstrating that yeast cell enzymes are the source of

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Volume 9, Issue 7, pp 1-13, July-2025
https://doi.org/10.47001/IRJIET/2025.907001

fermentation. For precisely identifying the process by which enzymes are created during fermentation, scientists Arthur Harden and Hans Euler were awarded the Nobel Prize in 1929.The 1940s saw the most significant use of the fermentation process to the manufacture of antibiotics [8].

2.3 Fermentation stages

Two major processing steps of fermentation generally include upstream processing and downstream processing, which transform raw or unprocessed material into the final commodity product.

A. Upstream processing

It consists of three primary sections and involves cultivating microorganisms or cells to generate the desired result. The first section is microorganism production, which includes choosing the right microbes, including fungus and bacteria, which are the most often employed microorganisms in fermentation industries, increasing the strain's yield and productivity, and preserving its purity. The second section is the fermentation medium, which includes the production of the necessary medium as well as the removal of particles and inhibiting substances from the media. The final step is the fermentation process, when the desired product is created as a result of the growth of microorganisms [9].

B. Downstream processing

It includes all the subsequent procedures that take place after fermentation. It consists of several stages, namely (cell harvesting, cell dissociation, cell purification). The process of cell harvesting involves the extraction of solids/cells and insoluble products from the culture broth utilising methods like sedimentation, filtering, centrifugation, etc. Because of their tiny size, stiff walls, and strong internal osmotic pressure, cells often have a hard time dissociating. Therefore, in order to release the products between the cells, some physical treatments might cause the cells to disassociate. High-pressure homogenisation, ultrasonic, thermal shock, osmotic shock, chemical extraction, and enzymatic extraction are some of these methods. Cell purification is crucial as a high degree of purity in the recovered product is required. Typically, methods including liquid extraction, sedimentation, and high-performance liquid chromatography are used to purify the crude product. Additionally, membrane methods like reverse osmosis and ultrafiltration are employed. After drying, the product crystallises [10-11].

2.4 Type of fermentation processes

Different types of fermentation can be classified in the following manner:

1. With respect to variations such as feed substrate to fermenter.
2. With respect to the need for an air supply.
3. With respect to the need for light.

1) The classification of the mode of fermentation is done primarily based on various aspects, such as feeding substrate for the fermenter, which includes batch fermentation, continuous fermentation, and fed-batch fermentation.

- Batch fermentation: The substrate, inoculant, and all other ingredients required for the fermentation process are put into the fermentation vessel, and the process is initiated. The substrate is not added to the fermentation vessel or the product is not taken out of the fermentation vessel until the entire process is complete. This method is attractive for small-scale production because it is relatively inexpensive. Batch fermentation is characterised by four basic phases (lag, exponential, stationary, and death). During the lag phase, cells do not proliferate nor enlarge; rather, they adjust to their new environment. The exponential phase is when cells divide rapidly, the time of fast growth. During this stage, both the cell concentration and product concentration increase exponentially. In the stationary phase, the concentration of cells and the concentration of the product remain constant, with the rate of cell growth equal to the rate of cell death. Finally, in death phase, cells die, and the concentration decreases [12].
- Continuous fermentation: Nutrients are added continuously to the culture, while the products are removed continuously from the culture. with the rationale being the continuous introduction of the fresh medium into the used medium or the harvested cells. This way, a frequent supply of nutrients continues to sustain the exponential growth of microorganisms for a longer time. Thus, harmful metabolites are removed from the culture while deficient nutrients are replenished. There is no change in the volume of culture or medium, as the rate of addition and withdrawal of the medium is equal. Therefore, continuous fermentation is an improvement over batch fermentation since it suffers no downtime for the addition of new media; it is thus an economical process [13].
- Fed-batch fermentation: It includes both batch functioning and continuous fermentation. It is a semi-open fermentation device, wherein the increment of liquid culture is proportional to the addition of culture. The microorganism in the fermenter then grows for a preset period in a batch fashion at a constant inflow rate with an add-as-needed supply of nutrients. At the end of each cycle, the culture suspension gets completely removed. There is one benefit of fed-batch cultures. By

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giving only small amounts of nutrients, yield and productivity can be increased with time. The two types of fed-batch fermentation are solid-state fermentation (SSF) and submerged fermentation (SmF). Solid-state fermentation (SSF) is based on the principle that solid substrates are slowly consumed by bacteria or fungi. Examples include bran, bagasse, paper pulp, wheat bran, rice straw, hay, fruit and vegetable waste, and artificial media. At a constant rate, the nutrients are thus regulated in the gradual release. The advantages of this technique include the reuse of nutrient-rich wastes as fermentation substrate and the commonality of using the same substrate over long periods. Some disadvantages of this way, however, are inability to bacteria with high water activity requirements and very high cost for purification at the end product. Submerged fermentation (SmF) and liquid fermentation (LF) use free-flowing liquids such as broth and molasses. These are for bacteria that require a great deal of water activity. Making it easy for the purification of the desired substances directly into the fermented broth. Yet it demands a continuous flow of substrate supply. The main purpose of using such an advanced technology is to separate the secondary metabolites, which have to be utilised in liquid forms. Some examples of such substrates that are frequently used for SmF or LF are soluble sugars, molasses, liquid media, fruit and vegetable juices, and sewage or wastewater [14-15].

2) With respect to the need for an air supply: There is aerobic fermentation and anaerobic fermentation.

- Aerobic fermentation: Many large-scale fermentation operations are conducted in an aerobic environment, in which sterile air is forced into the fermenter to stir the contents using a motor and sprinklers [16].
- Anaerobic fermentation: The fermenter setup is similar to aerobic fermentation except for the requirement for an agitator and sprinkler to provide aeration. However, the presence of an agitator ensures that the medium in the fermenter has uniform temperature, pH, viscosity, nutrients, etc. Wastewater treatment and ethanol production both employ this kind of fermentation [17].

3) With respect to the need for light: There is light fermentation and dark fermentation [18].

- Light fermentation: When light is present, a certain type of bacteria known as photosynthetic bacteria carry out a series of biochemical events that transform organic molecules into other chemicals that may be used as energy. This process is known Light fermentation.
- Dark fermentation: Dark fermentation is comparable to light fermentation; however, other bacteria are involved in dark fermentation, and it does not require light to start reactions

III. BIOREACTOR AND FERMENTERS

3.1 Bioreactor and Fermenter Concept

The earliest known bioreactors were most likely ceramic jars used by ancient peoples including the Greeks, Romans, Egyptians, and Mesopotamians to ferment bread, wine, beer, and mead. The technology of the fermentation process and the microbial world were unknown at the time. Louis Pasteur's discovery of germs in the 19th century shifted focus to experiments. He used a mixed bacterial culture that contained at least one strain of Clostridium to manufacture microbial butanol. During the First World War in the 20th century, Chaim Weizmann also employed a strain of Clostridium to make acetone, which was then utilised to make artillery projectiles. Later, bioreactors were created for bigger sizes after Alexander Fleming discovered penicillin and the necessity for these medicines to be produced globally. Seven trillion units of penicillin could be produced in industrial bioreactors in 1945.

They are closed systems that allow for the regulated execution of biological processes. The biomechanical and biochemical environment that a bioreactor offers regulates the movement of nutrients, oxygen, and metabolic products into and out of cells. Bioreactors are widely utilised in food processing, fermentation, waste treatment, and the manufacturing of medications from bio-based foods like polylactic acid. Fermenters are a kind of closed-vessel bioreactor that allows microbes to grow in a liquid medium and create a variety of chemicals in a sterile and regulated environment. The metabolic products of sugar, yeast, alcohol, and carbon dioxide are typically handled by fermenters. They can also be used to produce enzymes (lipase, amylase, and cellulase) and hormones and vaccines [5,19].

3.2 Bioreactor and Fermenter Basic Feature, Size and Material

The basic design components of a bioreactor include those related to agitation, foam control, gas exchange in the production organism, headspace volume, sample ports, temperature-pH control, sterilisation system, and charging and discharging lines of the reactor. These are explained in Table 1. The range of bioreactor size begins with some electromagnetic cells, a few mm^3, and includes shake flasks (100-1000 ml), laboratory-scale fermenters (1-50 L), pilot (0.3-10 m^3) and industrial scales (2-500 m^3) when large volumes of industrial applications are concerned [20].

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Materials that can endure several sterilisation cycles on a small scale are crucial when fermentation and strict sterilisation standards are involved. For instance, stainless steel and/or glass can be utilised. Glass has several benefits, including smooth surfaces, non-toxicity, resistance to corrosion, and generally simple inspection of the vessel's inside. Construction materials for pilot and large-scale bioreactors must be resistant to corrosion, pressure sterilisation, possible toxicity, and expense. Since stainless steel satisfies the necessary specifications, it is a good option [1].

Table 1: Different parts of Fermenter and its function [21-22]

Parts of Fermenter	Function
Impellor (agitator)	Continuous stirring of media to ensure distribution of the oxygen throughout the system and prevent cells from settling down.
Sparger (Aerator)	Introduces sterile air or oxygen into media for aerobic fermentation**.**
Baffles (vortex breaker)	Better mixing by disturbing the vortex formation**.**
Temperature probe	Measurement and monitoring of temperature changes of the medium during fermentation.
Cooling Jacket	Maintenance of process temperature.
pH probe	Evaluation and monitoring of the change in pH of the medium.
Level probe	Measurement of medium level.
Foam probe	Detection of the presence of foam.
Acid	Neutralises a basic environment and maintains the pH level.
Base	Neutralises an acidic environment and maintains the required pH.
Antifoam	To break down and prevent foam production in the medium.
Sampling point	For sampling during the process.
Valves	Control and restrict the flow of liquids and gases.

3.3 Types of bioreactors and fermentorse

The most important influencers of the operations of various types of bioreactors utilised in fermentation are the microorganisms involved in the fermentation process and the end products. The different fermenter types listed above are the primary ones being used in the industry; other fermenters are subtypes of these primary fermenters. In general, fermenters can be classified as mechanically agitated fermenters, non-agitated fermenters, and non-mechanically agitated fermenters. Other classifications are as follows: continuous stirred tank reactor, airlift fermenter, tower fermenters, bubble column bioreactor, batch bioreactor, packed bed reactor, membrane bioreactor, photobioreactor, deep jet fermenter, fluidised bed bioreactor, wave bioreactors, sparged tank bioreactor, and microbioreactors.

3.3.1 Continuous stirred tank reactor

Despite not being the greatest kind of fermenter, continuous stirred tank fermenters are still the chosen option for over 70% of fermentation procedures. Because of its numerous benefits, including continuous operation within the tank, temperature control, inexpensive construction costs, easy operation (which lowers labour costs), ease of cleaning, good mixing ability, and high mass transfer rates, this tank type is a common choice for an ideal reactor in chemical engineering [23-24].

These continuous-mode reactors maintain stable nutrient concentrations throughout the process by continuously adding fresh medium and removing products and the culture at the same pace. In CSTR mixing provides a continuous supply of nutrients and oxygen, which are essential for the growth of microorganisms. (CSTR) reactors work at controlled temperature, pressure, and concentration levels, allowing the required chemical changes to occur. In contrast to the old batch reactor tank, the continuous flow tank features high efficiency in mass and heat transfer. The mixing in this case is possible with a mechanical or magnetic stirrer, providing complete concentration and temperature uniformity [25]. The majority of FDA-approved biopharmaceutical manufacturing facilities and procedures employ continuous stirred tank reactors, particularly for producing antibiotics. Additionally, it is used in the treatment of wastewater, vinegar, and baker's

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yeast. This tank has a capacity of 0.05 litres to 100 cubic meters [26-27].

3.3.2 Air lift fermenter

In certain situations, antibiotics are produced in airlift fermentation reactors. This is because, in contrast to stirred tank reactors, air lift fermentation uses less energy because it doesn't require mechanical stirring. In addition, this type is preferred in waste treatment and methanol production because of its good efficiency [28]. Two linked zones created by baffles into which medium is injected are found in these kinds of bioreactors. In one zone, known as the riser, air is pumped, while in the other, known as the descender, no air is introduced. While downhill flow takes place in the down comer, air particle dispersion travels up the riser zone [29]. The central tube plus auxiliary tubes in the reactors improve the mixing and circulation of the medium-fermentation culture. This enhances the mass transfer coefficient mixed with stress balancing, reducing the gas bubble coalescence flying inside the reactor. Important types of airlift bioreactors include internal-loop airlift bioreactors, external-loop airlift bioreactors, and two-stage airlift bioreactors. Internal-loop airlift bioreactors consist of a single vessel with a draft tube along the axis of the vessel, permitting the formation of channels for circulation of liquid within. The design is simple so that they can be used for fermentation, wherein their volume and circulation are maintained at a set rate [30]. External-loop airlift bioreactors possess an external loop to circulate through various channels. These fermenters can be modified in many aspects for varied fermentation purposes. Also, it is probably more correct to refer to airlift bioreactors as some sort of more effective than bubble columns in mixing, especially for more dense microbial suspensions [29]. The production of products in two-stage airlift bioreactors is dependent on temperature. There are two bioreactors on it. Growing cells at a constant temperature of 30ºC are found in this bioreactor. After that, these cells are sent towards a different bioreactor with a temperature of 42ºC.The rapid temperature shift from 30 to 42 degrees Celsius is an issue with this kind of bioreactor. A pump and a transferring tube link the valves in both bioreactors. Its bioreactor grows the cell culture, while the second reactor is used for further processing [30-31].

3.3.3 Tower fermenters

The main function of tower fermenters is continuous fermentation. This was an apparatus that Bass used in the 1870s. It was 8.5 meters high and 1 meter in diameter. The disadvantage of batch fermentation constituted the reason for this fermenter. It is mainly used in the beer-making industry [32-33]. One of the distinguishing features of a typical tower fermenter is the wort gradient and yeast gradient going up the tower. The objective of the multi-stage fermenter is to create the process flow via gravity [34].Without the use of a pump, the bulk of the raw ingredients, water, and malt are first raised to the top of the fermenter before descending. While there is an outlet at the top, there is an intake at the bottom. Additionally, it has insulating jackets, which are designed to keep the temperature at the ideal level for organism growth. Additionally, there are baffles that are intended to cause agitation [35-36].

3.3.4 Bubble Column Bioreactor

Numerous chemical, petrochemical, and biochemical industries make use of bubble column reactors. These reactors have minimal running costs, cheap maintenance, and a straightforward design. They have a cylindrical form and a height: diameter ratio of 4:6. At the base of the column, air or gas is injected via metal microporous spargers or perforated pipes or plates. To accomplish the right O2 transfer or mixing, the air or gas flow rate is precisely maintained [20,37]. To enhance reactor performance, perforated plates are affixed to the fermenter.

3.3.5 Batch bioreactor

The processing industries make extensive use of this kind of bioreactor. It participates in a range of fermentation processes, including batch distillation, liquid extraction, solids dissolving, crystallisation, chemical reactions, and polymerisation. It is made up of an integrated heating and cooling system and a tank with an agitator [38]. They come with different capacities -- less than a litre to more than 15,000 litres. Steel, glass-lined steel, glass alloys, and other materials are used for their construction, and electric connections are used to charge the interior solids and liquids. Fermentation-related gases are released from the top, while liquid products are released from the bottom. The batch reactor's benefits include its adaptability, the ability to perform a wide range of tasks in a single vessel, and its use in the treatment of strong and toxicogenic substances [39-40].

3.3.6 Packed bed reactor

These reactors are also known as fixed-bed reactors. These reactors have many applications in chemical processing, such as catalytic reactions, stripping, distillation, absorption, and separation applications. It's made up of a partition. Such is a tube or channel with catalyst pellets or particles on it, through which liquid passes. When the liquid interacts with the catalyst, the substance's chemical makeup changes. This reactor has many advantages, such as a higher catalyst conversion rate, ease of construction and maintenance,

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improved contact between reactants, cost of maintenance, and works even at high temperatures and pressures [41-42].

3.3.7 Membrane Bioreactor

Since the 1990s, membrane bioreactors (MBR) have been in use. It essentially combines a conventional treatment system with membrane-based filtering to remove organic and suspended solids while also eliminating high amount of nutrients [43]. Membranes are submerged in an aerated vessel known as a biological reactor in an MBR system. The pore size of the membrane would thus range from 0.035 to 0.4 microns. Since the mid-1990s, when the submerged MBR system was developed, its use has expanded greatly and is expanding quickly in both commercial and research applications. MBRs widely used in waste water treatment, include a significant and meritorious drop in the membranes' cost.

3.3.8 Photo bioreactor

These bioreactors are used in fermentation processes that require light, either artificial or sunlight, to be present. The purpose of this bioreactor is to produce light-dependent bacteria, which are known as phototrophs. Similar to green plants, these microorganisms are capable of photosynthesis and can use light to produce biomass. Important byproducts of photobioreactors include p-carotene and asthaxantin. They are often made of clear plastic or glass. They are made out of a variety of tubes or glass that are intended to catch light [44]. These bioreactors can be used to increase the rate of productivity. To carry out the fermentation process, they offer a significant surface to volume ratio. There is a better approach to manage gas transfer. Growth media evaporation is decreased. The batch is safeguarded against contamination. Fouling is kept at a minimum due to self-cleaning ability. Because algae are cultivated under strict supervision, yields are very high. Compared to bag reactors, the yield in this reactor is 10 to 20 times greater. Photo-bioreactors utilise minimal light that increases productivity and yield. Sustained temperature is provided [45-46].

3.3.9 Deep Jet Fermenter

A deep jet fermenter's medium may be circulated with the use of a powerful pump. Compressed air is pumped into a medium jet by an injector nozzle. The gas creates enormous bubbles that are extracted from the top port. After then, the media moves on through the media's degassing ejector nozzle. Finally, the chilled aerated medium is introduced into an air entrainer situated above the reactor [47].

3.3.10 fluidize bed bioreactor

Unlike packed bed reactors, fluidised bed reactors depend on the flow of a fluid for the dispersion of materials. In other words, the biocatalysts are suspended since the fluid flow rate acts like a fluid [48]. The catalysts sit on a porous plate, which permits the flow of fluid just like in a packed bed reactor. The device will work like a packed bed reactor at low fluid flow rates since the force acting on the materials is not sufficient to lift the particles. A stage is therefore reached when an increase in the flow rate causes the particles to be suspended in the fluid. Here, the weight of the particles is suspended in the fluid, and that weight is counterbalanced by the fluid motion. We call this process "incipient fluidisation." The term "fluidized bed reactor" refers to the process by which particles get fluidized and behave like fluid when the fluid flow rate is raised after the initial fluidization. In addition to the fluid flow, aeration can be supplied; however, the particle dispersion is no longer consistent when gases are present. Because of the comparable aspect ratio, the fluidized bed reactor can be categorised as a tower reactor. Because of their superior temperature distribution and notably high particle interaction, certain reactor types improvements in the yield of the product [49]. Numerous chemicals, including vinyl chloride and polypropylene, are produced in the reactor. Additionally, it is employed in the brewing sector to produce beer.

3.3.11 Wave Bioreactors

Comparatively more recent technology for cultivating plant and animal cells is wave bioreactors. The bioreactor system is easy to use and reasonably priced. Polymers can serve the purpose of being used for designing bioreactors while keeping all the attributes of conventional stainless steel. The bioreactor or polymer bag is to be set on a swinging platform. Without sacrificing mixing, the waves produced by the platform's rocking motion offer relatively little shear stress. Additionally, the wave movement stops cells from accumulating. In a polymer bioreactor, it is advantageous to have a pre-sterilized bag; therefore, further sterilisation is not necessary. Because of its less intense wave motion, the wave bioreactor also exhibits comparatively less foaming [50].

3.3.12 Sparged Tank Bioreactor

While the air enters a metal vessel from the bottom, it heats up and agitates the liquid non-mechanically; in doing so, it utilizes a porous plate in a sparged tank bioreactor. A baffle is set up to help scatter the gas bubbles horizontally. The system has relatively less shearing stress and doesn't need an agitator because it is agitated by air. Because there aren't many moving parts in this kind of reactor, it requires a lot less electricity [51].

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3.3.13 Microbioreactors

The innovative concept of microbioreactors enables us to use minuscule amounts of medium and microorganisms to get exact data. Microbioreactors are shaking flask cultures and smaller versions of CSTRs. This kind of bioreactor aids in the screening process for several microbes in a really economical way. When compared to microbial growth medium, the media and other components were found to be costly for animal cell culture experimentation, a microbioreactor is particularly useful. These reactors can be used for phenotyping, media screening, toxicity screening, standardising fermentation parameters, growth profiling, and parallel culture operations. Fluorescence, pH, dissolved oxygen, spectroscopy, and other methods can be used to investigate the aforementioned factors. Only the aforementioned tests require quantities of less than 1 ml. The test may be conducted rapidly on a lab scale after the microbioreactor parameters have been studied, and then it can be scaled up to pilot plants and industrial-scale culture [52]. The commercial microbioreactor is the bioreactor producer that offers multi-parameter testing bioreactors [53].

IV. OPERATING CONDITIONS IN BIOREACTORS

When designing a bioreactor, operating conditions are quite important. This is because the main goal of bioreactor design is to give the cells inside the reactor the best possible environment. The development of microorganisms and their capacity to produce active chemicals are directly impacted by a number of variables, including temperature, pH, mixing, and shear force. Achieving optimal productivity and maintaining the stability of the reactor's internal environment are facilitated by precise management of these factors.

4.1 Temperature

One of the most crucial elements that has to be properly managed in a bioreactor is temperature. Microorganisms are frequently categorised as thermophilic (growing at temperatures above 50°C), mesophilic (growing at temperatures between 20 and 50°C), or climatophilic (growing at temperatures below 20°C) based on their growth temperature [54]. The ideal temperature range for microbe development is always quite limited, regardless of the type of microorganism. Growth will be sluggish if the temperature is below ideal, which will reduce the number of cells produced and the synthesis of products. However, if the growth temperature is too high, metabolite synthesis will be severely impacted, which will lead to a drop in product in addition to mortality in cells.

4.2 PH

Different biological systems present a variety of diverse ideal temperature ranges. The ideal pH range for most microbes is between 5 and 7. For instance, the pH may alter when fermentation is taking place. The medium is exposed to metabolites as cells proliferate, and pH shifts are also brought on by substrate consumption. Thus, it's critical to maintain the proper pH to guarantee a healthy metabolism [55].

4.3 Mixing

A bioreactor would have to be well-mixed to ensure the availability of nutrient nomads in large quantities in the medium and prevent any harmful metabolite accumulation. Mixing is frequently assessed in fermentation or cell culture procedures based on biological performance metrics like productivity and cell growth rate. In a bioreactor, mixing is essential for controlling temperature, pH, and substrate concentration [56]. In a small-scale reactor, maintaining a homogeneous state is simple, but when scaling up, mixing frequently becomes a constraint. Poor mixing frequently results in undesired concentration gradients and decreased mass transfer efficiency in large-scale bioreactors.

4.4 Oxygen transport

An issue in aerobic biological systems is oxygen transport. Water-soluble nutrients are generally required for metabolism and cellular growth. Nutrient supply on an acceptable schedule and in adequate amounts can occur adequately in a well-mixed bioreactor. However, because oxygen is only present in water and is relatively weakly soluble in aqueous solutions, oxygen transport frequently becomes a limiting step for both scaling up and the optimal operation of biological systems. There are certain factors that can significantly influence the product formation and development of a cell, such as oxygen limitation. It has been observed that even a short cessation of aeration in the medium during the penicillin fermentation process has a strong influence on the capacity of cells to produce this antibiotic [57]. When cell density becomes high enough in a particular biological system (bacteria, yeast, animal, or plant cells), it can be expected that there will be a considerable oxygen deficiency. This problem is further aggravated by the fact that most often at high cell densities, the oxygen transfer coefficient deteriorates. Achieving a suitably high oxygen coefficient is a crucial component of bioreactor design because the oxygen transfer coefficient plays a significant role in the oxygen delivery to the medium. Numerous elements influence the mass transfer coefficient, such as the reactor vessel's geometry and operation, agitation speed, aeration rate, fluid dynamics, medium composition, cell type, concentration, and biocatalyst properties. According to estimates, managing

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oxygen transfer accounts for 15–25% of aerobic fermentation's overall expenses.

4.5 Shear force

Shear stress, shear duration, energy dissipation, and cell growth stage are some of the characteristics that are linked to shear-induced cell death. Shear damage from spraying can also happen at several places in the bioreactor, including the suspension surface (either foam-covered or foam-free), the rising zone through the bulk liquid, and the bubble formation zone at the spray device. Bubble-free aeration, which uses membranes for indirect aeration and controls the oxygen supply by diffusion, is one way to get around the issue of rising air bubbles. Reducing the impeller's agitation speed is a typical way to lessen the severity of shear stress in shear-sensitive cell cultures. In very viscous cell culture broths, it may hinder the enhancement of oxygen and heat transfer rates and result in inadequate mixing. Moreover, modest agitation rates can encourage cell agglomeration into clusters of varying sizes at high biomass concentrations. However, damage from agitation and aeration may be reduced with appropriate bioreactor design and management [58].

V. MASS TRANSFER COEFFICIENT

Mass transfer occurs when there are variations in concentrations in the mixtures. Mass transfer processes must ensure that materials move from originally high to low concentration areas. This is perhaps the best example of mass transfer in bioprocessing: the supply of oxygen in aerobic culture fermenters. The concentration of oxygen at the surface of the air bubbles in the liquid is greater than that in the bulk. This concentration gradient moves oxygen from the bubbles into the medium. The volumetric mass transfer coefficient ($K_L a$) is perhaps the most important parameter that describes oxygen mass transfer and regulates unit installations and designs. Its value sets the rate at which oxygen moves from the gas phase into the liquid. The efficiency of oxygen dissipation when delivered into the vessel via a spray device and disseminated throughout the medium by the mixer is demonstrated quantitatively by $K_L a$. As for calculating $K_L a$, it is done in several ways, some experimental and others theoretical.

5.1 Theoretical Evaluation of $K_L a$

One of the most popular empirical correlations linking $K_L a$ to different bioreactor operation modes is van't Riet's 1979 correlation [59]. van't Riet's proposed establishing a correlation between specific power input and surface gas velocity in the stirred tank bioreactor and the $K_L a$.

$$k_L a = C.(P_g/V)^{\propto}.{v_g}^{\beta} \qquad (1)$$

Where:

P_g aerated power input, W/m^3
V working volume, m^3
v_g superficial gas velocity, m/s

C, α, β empirical constants that take into account the vessel's shape (mixer rotors, baffles, etc.), and the coefficients in question are calculated in the following manner per Van't Riet: α = 0.4, β = 0.5, and C = 0.026.

5.2 Experimental Determination Methods of $K_L a$

The main experimental techniques used to determine $K_L a$ are sulphite oxidation methods, the method of oxygen balance, the dynamic gas escaping method, and static gas escaping methods.

The first technique used to determine $K_L a$ was sulphite oxidation [60]. The operation does not involve oxygen-providing equipment; it involves the oxidation of sodium sulphite such that oxygen transfer rates can be established in aerated vessels.

$$Na_2SO_3 + 0.5O_2 = Na_2SO_4$$

The rate of sulphite oxidation is equal to OTR due to the rate of this reaction being such that, as soon as sulphite enters the solution, oxygen is immediately utilised by it for the oxidation reaction. Theoretically, this means that the concentration of dissolved oxygen will be zero, and $K_L a$ may thus be calculated using Eq.2:

$$OTR = k_L a\,.C^* \qquad (2)$$

Chemical analyses of the sulphite solution are conducted throughout the experiment at predetermined intervals while the solution is being stirred at various mixer rotation speeds and air flow rates. Titrating the solution with thiosulphate is the standard method for doing this. This creates a graphical link between time and thiosulphate concentration. The graph has a trend with a linear characteristic, where the slope of the line is equal to OTR. Although the procedure is quite straightforward, it takes a lot of time and is not very precise. Nowadays, this approach is seldom ever applied.

One of the most used experimental techniques for $K_L a$ assessment is the static gassing-out method [61]. The medium in the vessel has first its oxygen removed. The second solubility gas is added; in most cases, nitrogen is preferred. The nitrogen supply is cut once the level of oxygen in the medium gets to zero or a value somewhat close to it. The increase in dissolved oxygen content, as defined by the Eq.3, is then monitored when air is introduced to the medium at a constant flow rate:

International Research Journal of Innovations in Engineering and Technology (IRJIET)

ISSN (online): 2581-3048

Volume 9, Issue 7, pp 1-13, July-2025

https://doi.org/10.47001/IRJIET/2025.907001

$$\frac{dc}{dt} = k_L a.(C^* - C_l) \qquad (3)$$

Integration this equation:

$$ln(C^* - C_l) = -k_L a \qquad (4)$$

Consequently, as seen in Fig. 1, a plot of versus time will produce a straight line of slope.

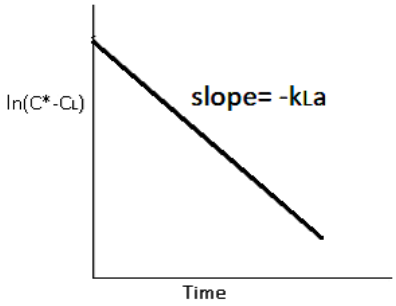

Figure 1: Graph of ln(C*-CL) vs. experimenttime (for determining $K_L a$)

For proper $K_L a$ data, the effects of probe reaction latency on oxygen measurements and the temperature/pressure control during the experiment should be considered; however, the static gassing-out method is relatively easy to perform.

Even while the dynamic gassing-out approach has a few advantages, it is essentially the same as the static method [62]. With dynamic technique for measuring the volumetric oxygen mass transfer coefficient during fermentation operations. Aeration is ceased at point A in Fig. 2 until a certain oxygen concentration is reached at point B in the same figure. Once the aeration is resumed at point B in Fig. 2 data on DO level vs time is collected.

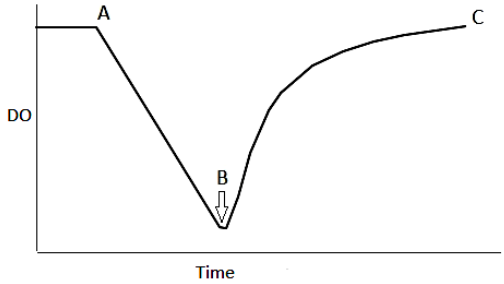

Fig. 2: Dynamic gassing-out experiment time dependent process data.

Eq.5 describes how oxygen moves from the gas phase to the liquid phase.

$$\ln\left(\frac{C^*-C}{C^*-C_0}\right) = -k_L a\,.t \qquad (5)$$

Where:

C_0 concentration of dissolved oxygen prior to resuming the aeration process (refer to point B in Figure 2).

C concentration of dissolved oxygen at time t (in the BC line segment).

The following graph (see Fig. 3) is produced by doing DO measurements and using the data acquired in Equation above.

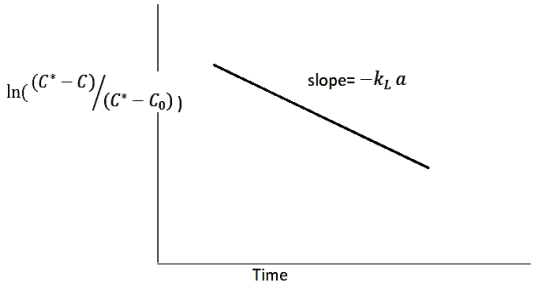

Figure 3: Graphical function to determine $K_L a$

Because the reaction latency of the DO measuring probe may be disregarded, the oxygen balancing technique is thought to be more accurate than the two previously stated methods for determining $K_L a$ [63]. The fundamental concept of the oxygen balance technique is to determine the amount of oxygen entering the fermentation medium, utilise it by microorganisms, and finally, get rid of the exhaust line by gas analyses for oxygen concentration in the gaseous phase. In a steady-state condition, OTR is equal to OUR if you keep the oxygen content in the medium constant. By using this condition, we can establish an oxygen mass balance for calculating $K_L a$.

$$OTR=OUR \qquad (6)$$

$$OTR = Q_{O2-IN} - Q_{O2-OUT} \qquad (7)$$

Where:

Q_{O2-IN} and Q_{O2-OUT} are volumetric oxygen flow rates at the intake and the output.

$$OUR = Q_{O2-V}.V \qquad (8)$$

Where:

Q_{O2-V} rate of volumetric oxygen uptake.
V amount of model media or fermentation volume.

The rate at which oxygen moves from the gas phase to the liquid phase is equal to the rate at which microorganisms consume oxygen in a steady state:

$$k_L a\,.(C^* - C_L) = OUR/V \qquad (9)$$

Combining the equations of the static gassing-out method, the equation for determining $K_L a$ is obtained:

ISSN (online): 2581-3048
Volume 9, Issue 7, pp 1-13, July-2025
https://doi.org/10.47001/IRJIET/2025.907001

$$k_L a = (Q_{O2-IN} - Q_{O2-OUT})/(V.(C^* - C_L) \qquad (10)$$

Considering that gas analysers are needed, the approach is much more costly to execute even if it provides fairly accurate estimations of $K_L a$.

VI. CONCLUSION

Bioreactors are a vital tool in many industries, enabling the efficient production of a wide range of bioproducts. Ongoing advancements in reactor design and control technologies have led to significant improvements in efficiency and quality. Research in this field is expected to continue, driving the development of more sustainable and flexible systems that meet the growing demand for bioproducts in medical, industrial, and environmental applications.

ACKNOWLEDGMENTS

The authors would like to thank the College of Engineering Librarian for his assistance in obtaining some of the resources.

REFERENCES

[1] H. Chandrashekhar and J. V. Rao, "An overview of fermenter and the design considerations to enhance its productivity," Pharmacologyonline, vol. 1, pp. 261–301, 2010.

[2] S. L. Adams and R. E. Hungate, "Continuous Fermentation Cycle Times-Prediction from Growth Curve Analysis," Ind. Eng. Chem., vol. 42, no. 9, pp. 1815–1818, 1950, doi: https://doi.org/10.1021/ie50489a034.

[3] W. B. Altsheler, H. W. Mollet, E. H. C. Brown, W. H. Stark, and L. A. Smith, "Design of a two-bushel per day continuous alcohol unit," Chem. Eng. Prog.;(United States), vol. 43, no. 9, 1947.

[4] V. R. Srinivasan and R. J. Summers, "Continuous culture in the fermentation industry," in Continuous Cultures of Cells, CRC Press, 2020, pp. 97–112.

[5] H. Sheikh, G. G. Anand, and G. B. Shivanna, "Fermentation: A Potential Strategy for Microbial Metabolite Production," 2024, doi: 10.5772/intechopen.114814.

[6] V. Singh, S. Haque, R. Niwas, A. Srivastava, M. Pasupuleti, and C. Tripathi, "Strategies for fermentation medium optimization: an in-depth review," Front. Microbiol., vol. 7, p. 2087, 2017, doi: https://doi.org/10.3389/fmicb.2016.02087.

[7] G. Singhal, V. Verma, S. S. Bhagyawant, and N. Srivastava, "rmentation technology prospecting on bioreactors/fermenters: design and typesFe," Princ. Appl. Ferment. Technol., pp. 65–83, 2018, doi: 10.1002/9781119460381.

[8] Y. Chisti, "Fermentation technology," Ind. Biotechnol. Sustain. growth Econ. success, pp. 149–171, 2010.

[9] M. Rahman, "Medical applications of fermentation technology," Adv. Mater. Res., vol. 810, pp. 127–157, 2013, doi: https://doi.org/10.4028/www.scientific.net/AMR.810.127.

[10] K. K. Prasad and N. K. Prasad, Downstream process technology: a new horizon in biotechnology. PHI Learning Pvt. Ltd., 2010.

[11] B. Kumar, P. Verma, N. Bhardwaj, V. Chaturvedi, and K. Agrawal, "Process optimization, purification and characterization of alkaline stable white laccase from Myrothecium verrucaria ITCC-8447 and its application in delignification of agroresidues," 2018. doi: 10.1016/j.ijbiomac.2018.12.108.

[12] J. I. Betts and F. Baganz, "Miniature bioreactors: current practices and future opportunities," Microb. Cell Fact., vol. 5, pp. 1–14, 2006, doi: 10.1186/1475-2859-5-21.

[13] G. Najafpour, Biochemical engineering and biotechnology. Elsevier, 2015.

[14] R. Subramaniyam and R. Vimala, "Solid state and submerged fermentation for the production of bioactive substances: a comparative study," Int J Sci Nat, vol. 3, no. 3, pp. 480–486, 2012.

[15] A. E. Carnes et al., "Plasmid DNA fermentation strain and process-specific effects on vector yield, quality, and transgene expression," Biotechnol. Bioeng., vol. 108, no. 2, pp. 354–363, 2011, doi: https://doi.org/10.1002/bit.22936.

[16] R. M. Elsayad, S. W. Sharshir, A. Khalil, and A. M. Basha, "Recent advancements in wastewater treatment via anaerobic fermentation process: A systematic review," J. Environ. Manage., vol. 366, p. 121724, 2024, doi: https://doi.org/10.1016/j.jenvman.2024.121724.

[17] G. da P. de Paula et al., "Anaerobide Paula, G. da P., de Lima, R. F. C., Sales, A. L. Â., Alves, E. D., Felício, P. F., Rocha, T. M., & Nunes, L. E. (2025). Anaerobic bacterial fermentation: A strategy for hydrogen production. Research, Society and Development, 14(1), e7814148081–," Res. Soc. Dev., vol. 14, no. 1, pp. e7814148081–e7814148081, 2025, doi: http://dx.doi.org/10.33448/rsd-v14i1.48081.

[18] D. M. Tripathi and S. Tripathi, "Microbial Advancements in Dark Fermentative Biohydrogen Production: Applications and Innovations," in

ISSN (online): 2581-3048
Volume 9, Issue 7, pp 1-13, July-2025
https://doi.org/10.47001/IRJIET/2025.907001

Emerging Trends and Techniques in Biofuel Production from Agricultural Waste, Springer, 2024, pp. 57–80.

[19] T. J. Narendranathan, "Designing Fermentation Equipment.," 1986.

[20] M. R. Spier, L. Vandenberghe, A. B. P. Medeiros, and C. R. Soccol, "Application of different types of bioreactors in bioprocesses," Bioreact. Des. Prop. Appl., no. 978-1-62100-164–5, pp. 53–87, 2011, [Online]. Available: 978-1-62100-164-5

[21] J. Singh, N. Kaushik, and S. Biswas, "Bioreactors – Technology & Design Analysis," Scitech J., vol. I, no. 6, pp. 28–36, 2014.

[22] V. Gaikwad et al., "Designing of Fermenter and its utilization in food industries," Preprints, no. August, pp. 1–24, 2018, doi: 10.20944/preprints201808.0433.v1.

[23] D.-Y. Lee, Y.-Y. Li, Y.-K. Oh, M.-S. Kim, and T. Noike, "Effect of iron concentration on continuous H2 production using membrane bioreactor," Int. J. Hydrogen Energy, vol. 34, no. 3, pp. 1244–1252, 2009, doi: https://doi.org/10.1016/j.ijhydene.2008.11.093.

[24] M. Nehra and V. Nain, Handbook of Industrial Food Microbiology. CRC Press, 2024.

[25] M. Zhu, L. Zhang, B. Cheng, M. Zhang, and Q. Lin, "Synthesis process optimization of 4, 4′-azobis (1, 2, 4-triazole) in a continuous stirred tank reactor (CSTR)," FirePhysChem, vol. 4, no. 1, pp. 48–54, 2024.

[26] Y. Chisti, "Fermentation (industrial): basic considerations. Encyclopedia of food microbiology," 1999, Elsevier.

[27] S. Ali, A. Rafique, M. Ahmed, and S. Sakandar, "Different types of industrial fermentors and their associated operations for the mass production of metbolites," Eur. J. Pharm. Med. Res., vol. 5, no. 5, pp. 109–119, 2018.

[28] N. Taga, K. Tanaka, and A. Ishizaki, "Effects of rheologic conditions in the culture medium on the autotrophic production of poly-(D-3-hydroxybutyric acid) in an air-lift fermentor," 1995, doi: https://doi.org/10.5109/24106.

[29] P. S. Pal, A. Chakraborty, A. Barua, and S. Sinha, "Study of a See-Saw Bioreactor Fluid Dynamics, Shear Force Constraint and Oxygen Absorption Characteristic," 2001.

[30] F. Garcia-Ochoa and E. Gomez, "Bioreactor scale-up and oxygen transfer rate in microbial processes: An overview," Biotechnol. Adv., vol. 27, no. 2, pp. 153–176, 2009.

[31] J. J. Zhong, "Bioreactor engineering," 2019. doi: 10.1016/B978-0-444-64046-8.00077-X.

[32] V. Bellon-Maurel, O. Orliac, and P. Christen, "Sensors and measurements in solid state fermentation: a review," Process Biochem., vol. 38, no. 6, pp. 881–896, 2003, doi: https://doi.org/10.1016/S0032-9592(02)00093-6.

[33] M. Fernandez, J. R. Perez-Correa, I. Solar, and E. Agosin, "Automation of a solid substrate cultivation pilot reactor," Bioprocess Eng., vol. 16, pp. 1–4, 1996.

[34] Z.-Y. Zhang et al., "A biaxial rotating bioreactor for the culture of fetal mesenchymal stem cells for bone tissue engineering," Biomaterials, vol. 30, no. 14, pp. 2694–2704, 2009, doi: https://doi.org/10.1016/j.biomaterials.2009.01.028.

[35] T. Robinson, D. Singh, and P. Nigam, "Solid-state fermentation: a promising microbial technology for secondary metabolite production," Appl. Microbiol. Biotechnol., vol. 55, pp. 284–289, 2001.

[36] C. A. Boulton, W. G. Box, D. E. Quain, and S. W. Molzahn, "Vicinal diketone reduction as a measure of yeast vitality," Tech. quarterly-Master Brew. Assoc. Am., vol. 38, no. 2, pp. 89–94, 2001.

[37] A. Lübbert, "Bubble columns and airlift bioreactors," Encycl. life Support Syst., pp. 1–13, 2009.

[38] M. C. Flickinger and S. W. Drew, Encyclopedia of bioprocess technology. Wiley Online Library, 2009. doi: 10.1002/0471250589.

[39] S. Arora, R. Rani, and S. Ghosh, "Bioreactors in solid state fermentation technology: Design, applications and engineering aspects," J. Biotechnol., vol. 269, pp. 16–34, 2018, doi: https://doi.org/10.1016/j.jbiotec.2018.01.010.

[40] R. Gupta et al., "A comprehensive review on enhanced production of microbial lipids for high-value applications," Biomass Convers. Biorefinery, pp. 1–24, 2021, doi: https://doi.org/10.1007/s13399-021-02008-5.

[41] J. A. C. Leite, B. S. Fernandes, E. Pozzi, M. Barboza, and M. Zaiat, "Application of an anaerobic packed-bed bioreactor for the production of hydrogen and organic acids," Int. J. Hydrogen Energy, vol. 33, no. 2, pp. 579–586, 2008, doi: https://doi.org/10.1016/j.ijhydene.2007.10.009.

[42] S. T. Magar, "Bioreactor—definition, design, principle, parts, types, applications, limitations. Microbe Notes," 2021.

[43] F. Meng, S.-R. Chae, A. Drews, M. Kraume, H.-S. Shin, and F. Yang, "Recent advances in membrane bioreactors (MBRs): membrane fouling and

ISSN (online): 2581-3048
Volume 9, Issue 7, pp 1-13, July-2025
https://doi.org/10.47001/IRJIET/2025.907001

membrane material," Water Res., vol. 43, no. 6, pp. 1489–1512, 2009, doi: 10.1016/j.watres.2008.12.044.

[44] S. Hoekema, M. Bijmans, M. Janssen, J. Tramper, and R. H. Wijffels, "A pneumatically agitated flat-panel photobioreactor with gas re-circulation: anaerobic photoheterotrophic cultivation of a purple non-sulfur bacterium," Int. J. Hydrogen Energy, vol. 27, no. 11–12, pp. 1331–1338, 2002.

[45] Q. Gan, S. J. Allen, and G. Taylor, "Design and operation of an integrated membrane reactor for enzymatic cellulose hydrolysis," Biochem. Eng. J., vol. 12, no. 3, pp. 223–229, 2002, doi: 10.1016/s1369-703x(02)00072-4.

[46] R. N. Singh and S. Sharma, "Development of suitable photobioreactor for algae production - A review," Renew. Sustain. Energy Rev., vol. 16, no. 4, pp. 2347–2353, 2012, doi: 10.1016/j.rser.2012.01.026.

[47] P. Jafari, Z. G. H. MOHAMMAD, F. Almasian, and E. M. TAJABADI, "Optimization of single cell protein (SCP) production in pilot plant scale with a deep jet fermenter of 1000 L capacity," 2012.

[48] G. González, G. Herrera, M. T. García, and M. Peña, "Biodegradation of phenolic industrial wastewater in a fluidized bed bioreactor with immobilized cells of Pseudomonas putida,"Bioresour. Technol., vol. 80, no. 2, pp. 137–142, 2001, doi: 10.1016/S0960-8524(01)00076-1.

[49] B. Özkaya, A. H. Kaksonen, E. Sahinkaya, and J. A. Puhakka, "Fluidized bed bioreactor for multiple environmental engineering solutions," Water Res., vol. 150, pp. 452–465, 2019, doi: 10.1016/j.watres.2018.11.061.

[50] J. J. Zhong, "2.14—Bioreactor Engineering," Compr. Biotechnol. 2nd ed.; Moo-Young, M., Ed, pp. 165–177, 2011.

[51] F. Garcia-Ochoa, E. Gomez, A. Alcon, and V. E. Santos, "The effect of hydrodynamic stress on the growth of Xanthomonas campestris cultures in a stirred and sparged tank bioreactor," Bioprocess Biosyst. Eng., vol. 36, pp. 911–925, 2013, doi: 10.1007/s00449-012-0825-y.

[52] S. Ravindran, P. Singh, S. Nene, V. Rale, N. Mhetras, and A. Vaidya, "Microbioreactors and perfusion bioreactors for microbial and mammalian cell culture," in Biotechnology and Bioengineering, IntechOpen, 2019. doi: 10.5772/intechopen.83825.

[53] C. Toeroek, M. Cserjan-Puschmann, K. Bayer, and G. Striedner, "Fed-batch like cultivation in a micro-bioreactor: screening conditions relevant for Escherichia coli based production processes," Springerplus, vol. 4, pp. 1–10, 2015, doi: 10.1186/s40064-015-1313-z.

[54] S. M. and K. F, "Bioprocess Engineering: Basic Concepts," 2002.

[55] Y. Li, Y. Zhang, and S. Xue, "pH mediated assemblage of carbon, nitrogen, and sulfur related microbial communities in petroleum reservoirs," Front. Microbiol., vol. 13, p. 952285, 2022, doi: https://doi.org/10.3389/fmicb.2022.952285.

[56] C. Oniscu, A.-I. Galaction, D. Cascaval, and F. Ungureanu, "Modeling of mixing in stirred bioreactors: 2. Mixing time for non-aerated broths," Biochem. Eng. J., vol. 12, no. 1, pp. 61–69, 2002, doi: https://doi.org/10.1016/S1369-703X(02)00042-6.

[57] N. J. and V. J, "Bioreaction Engineering Principles.," 1994.

[58] D. Jaros, S. Mende, F. Häffele, C. Nachtigall, H. Nirschl, and H. Rohm, "Shear treatment of starter culture medium improves separation behavior of Streptococcus thermophilus cells," Eng. Life Sci., vol. 18, no. 1, pp. 62–69, 2018, doi: https://doi.org/10.1002/elsc.201700121.

[59] Van't Riet, K, "Review of Measuring Methods and Results in Nonviscous Gas–Liquid Mass Transfer in Stirred Vessels," Ind Eng Chem Process Des Dev., vol. 18, pp. 357–364, 1979.

[60] Cooper, C.M., Fernstrom, G.A., & Millers, S.A, "Performance of Agitated of Gas-Liquid Contactors," Ind. Eng. Chem., vol. 36, pp. 504–509, 1944.

[61] Wise, W.S, "The Measurement of the Aeration of Culture Media," J. Gen. Micro., vol. 5, pp. 167–177, 1951.

[62] Taguchi, H., & Humphrey, A.E, "Dynamic Measurement of the Volumetric Oxygen Transfer Coefficient in Fermentation," Systems. J. Ferm. Technol., vol. 44, n. 12, pp. 881–889, 1966.

[63] Casas, L, "Simultaneous Determination of Oxygen Consumption Rate and Volumetric Oxygen Transfer Coefficient in Pneumatically Agitated Bioreactors," Industrial & Engineering Chemistry Research, vol. 45, n. 3, pp. 1167–1171, 2006.

International Research Journal of Innovations in Engineering and Technology (IRJIET)

ISSN (online): 2581-3048

Volume 9, Issue 7, pp 1-13, July-2025

https://doi.org/10.47001/IRJIET/2025.907001

Citation of this Article:

Duaa Al-Rekabi, & Salih Rushdi. (2025). Fermentation Process and Bioreactor Design: Concepts, Types and Operational Factors. *International Research Journal of Innovations in Engineering and Technology - IRJIET*, 9(7), 1-13. Article DOI https://doi.org/10.47001/IRJIET/2025.907001

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