

• CREDIT - I

Bioreactor Design and Operation :

(A) Basic Components, Design & Scale-up of fermentors :

(1) Designing of Bioreactors.

(a) Design aspects CSTRs

(b) Dimensional ratios of outer shell.

(c) Operational aspects such as working volume, baffles & impellers.

(2) Configuration (placement) of impellers in a vessel & different types of impellers (types of turbines & propellers and their combinations.)

(3) Immobilized cell reactors & air-lift reactors : Design & operation.

(4) Batch, fed-batch & continuous fermentors: Applications, advantages & limitations of each type.

• CREDIT - II :

Process Variables & Monitoring :

(A) Process variables :

(1) Aeration theory of oxygen transfer in bubble aeration, oxygen transfer kinetics

(Oxygen Uptake Rate - OUR , Oxygen Transfer rate - OTR , C_{crit}), determination of K_La value.

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- (2) Agitation: functions of agitation, flow patterns with different types of impellers: Effect of agitation & microbial biomass on $K_L a$ values.
- (a) fermentation broth rheology & power requirements for agitation concept of Newtonian & non-Newtonian fluids.
 - (b) Effect of broth rheology on heat, nutrient & oxygen transfer.
 - (c) Reynold's number, power number, aeration number: solving examples using different software programs.

(3) Monitoring of Process Variables:

- (1) Use of various types of sensors and biosensors for monitoring environmental parameters (pressure, pH, temperature, DO and DCO_2)

- (2) Basic principles of operation, types of biosensors.

● CREDIT - III :

- Applications of Bioprocess Technology :

- (A) Upstream & Downstream processing for the following microbial metabolites:

- (1) Antibiotics (Rifamycin)
- (2) Microbial Enzymes (Chitinase)
- (3) Exopolysaccharides (Pullulan & Xanthan)
- (4) Immobilized cells/enzymes for bioconversion
- (5) fungi in agriculture & environmental applications
- (6) Bio-mining, Microbial Extraction of Cu, Au & U from ore & their bio-recovery.
- (7) Probiotics & prebiotics: fundamental aspects & health benefits.

• CREDIT - IV :

★ Concepts of IPR, ISO Certification, SOP preparation, validation and Entrepreneurship

(A) Intellectual property rights (IPR) :

(1) Basic Concepts of IPR

(2) Introduction to forms of IPR - patents & Designs.

(3) Patents : Concepts & principles of patenting

(4) Procedure of obtaining patents.

(B) Concepts of ISO certification.

(C) Preparation of SOPs.

(D) Validation protocols for methods (as per WHO names) in :

(1) Quality control

(2) Process validation.

(E) Exercises on preparation of SOPs, operation & validation for analytical methods.

(F) Entrepreneurship :

(1) Concept of entrepreneurship : Scope for entrepreneurship in microbiology / life sciences

(2) Concept of Incubation centre.

(3) Challenges & Considerations for startups & small scale industry.

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* History of Fermentation —

- Louis Pasteur the father of fermentation.
- Is a French chemist & microbiologist.
- Research in various fields like vaccination, pasteurization & fermentation.
- He also proposed a germ theory.
- In 1856 one of Pasteur's students, whose father was a local wine manufacturer, approached him for advice on problems of preventing beetroot alcohol from souring.
- This led Pasteur to begin his work on optimization of fermentation process.
- From his research he found that the process used for fermentation of beer is not good enough & because of this it may lead to contamination of yeast by the environment & wine ~~gets~~ quickly sour & not able to store.
- For that he suggests that making beer in a controlled manner environment with the least possible contact with air during fermentation & pasteurization in bottle to stabilize the drink & prevent fermentation.

that's why
yeast → Replaced by bacteria. → & beetroot becomes sour.

* Upstream & Downstream processing for the microbial metabolite Antibiotic (Rifamycin) —

* Fermentation —

- Fermentation is a biochemical process that involves microorganisms breaking down large organic molecules into simpler ones, without the presence of oxygen.

- It is a enzyme catalyzed, metabolic process whereby organisms convert starch or sugar to alcohol or an acid anaerobically releasing energy.

* Microbial Metabolites —

- are chemical compounds produced by microorganisms during their growth and metabolism, especially under controlled conditions such as fermentation.

- These of two types :

(i) Primary metabolites

(ii) Secondary metabolites.

● Upstream processing deals with screening and identification of microorganisms, media preparation, multiplication of microbes inside bioreactors.

- While the Downstream processing deals with extraction, purification & filtration of the resulting product.

* Upstream processing —

1) Strain Selection

2) Medium Composition

3) Fermentation

4) Induction of Rifamycin production

— Upstream processing refers to initial stages in production process which involves cultivation of microorganisms (usually Amiclatopsis mediterranei, Nocardia sp. species or Streptomyces) that produce rifamycin.

1) Strain Selection —

- This step involves selecting microbial strains that has high rifamycin-producing potential.
- This often requires screening natural isolates or genetically engineered strains to improve yields.

2) Medium Composition —

- The culture medium is optimized to provide the necessary nutrients for microbial growth & antibiotic production.
- This includes carbon sources (such as glucose or starch), nitrogen sources (such as peptone or ammonia salts), minerals, vitamins & trace elements.
- The Composition can be tailored based on the strain & desired yield of rifamycin.

3) Fermentation —

• Fermentation process —

- The microbial strain is inoculated into large fermentors or bioreactors, where it grows under controlled conditions.

(temperature, pH, oxygen & agitation.)

- Typically, the fermentation process is carried out in batch or fed-batch systems.

- The initial phase involves cell growth, & once the cells reach a certain density, the antibiotic production phase begins.

• Optimizing fermentation Conditions —

- Factors like aeration, pH control, temperature & agitation are optimized for maximum antibiotic production.

- Rifamycin production is secondary metabolite, meaning it is produced when the growth phase slows down & cells begin to produce antibiotics as a defence mechanism.

4) Induction of Rifamycin production —

- Rifamycin biosynthesis is often triggered by the depletion of essential nutrients or specific chemical precursors, and certain stress conditions can also enhance production.

- The culture's pH, nutrient concentration & oxygen supply are controlled to induce optimal antibiotic production.

→ to Remove cell debris, toxins & other waste materials.

Recovery of useful product after fermentation

* Downstream processing

1) Harvesting / filtration

2) Extraction

3) Purification

4) Formulation.

Downstream processing refers to the obtaining most purest & effective form of antibiotic rifamycin.

1) Harvesting

After fermentation the microbial culture is harvested by separating the cells & the liquid medium.

This is done using filtration, centrifugation or other methods to separate biomass from the broth.

2) Extraction

Recovery of compound from the mixture.

Separated on solubility in 2 diff. immiscible liquids.

Solvent extraction — (Separates compounds by dissolving them in different liquids.)

Rifamycin is typically extracted from the fermentation broth using organic solvents (eg. ethyl acetate, butyl acetate, chloroform) to separate the antibiotic from the aqueous phase.

The solvent is chosen based on its ability to selectively dissolve rifamycin while behind other undesirable metabolites.

• Liquid-Liquid extraction

In this step, antibiotic is extracted into organic phase & then separated from aqueous phase.

3) Purification —

• Chromatographic Techniques —

- After extraction, rifamycin is further purified through chromatographic methods:

(i) TLC (Thin Layer chromatography) —

- To separate compounds & identify rifamycin.

(ii) HPLC (High performance Liquid chromatography)

- To achieve high purity by separating rifamycin from other by-products & residual culture medium components.

• Crystallization — ^{done for liquified materials / used for low molecular mass compounds.}

- After chromatography, the antibiotic may be crystallized to obtain a solid, pure product.

4) Formulation —

- Once purified, rifamycin is typically formulated into its final dosage forms such as tablets, capsules or injectables.

• Sterilization →

Depending on the form sterilization might be required. (eg. Injectables are sterilized by filtration or autoclaving)

• Lyophilization →

- In some cases, especially for injectable formulations, rifamycin may be lyophilized (freeze-dried) to produce a powder that can be reconstituted with a solvent before use.

* Quality Control & final product Release -

- Quality control testing is performed to ensure that the rifamycin meets the required standards for purity, potency & safety.
- & then the final product is packaged & Released.

1) Define Bioreactors

→ Bioreactor is a vessel in which a biological reaction or change takes place.

- Bioreactor is a equipment used for the process of fermentation which is biochemical process that involves microorganisms breaking down large organic molecules into smaller ones without presence of oxygen.

- Bioreactor is a stainless steel vessel that provides sterile environment for the growth of microbial, plant or animal cells.

- 1) Define Bioreactors (also called fermenters)
- Bioreactor is a vessel in which a biological reaction or change takes place.
 - Bioreactor is a equipment used for the process of fermentation, which is biological process that involves micro-organisms breaking down large organic molecules into smaller ones without presence of oxygen.
 - Bioreactor is a stainless steel vessel that provides sterile environment for the growth of microbial, plant or animal cells.
- 2) Define Downstream process.
- Downstream processing is a series of steps that purify biological products from natural sources.
 - Downstream processing refers to the Recovery & purification of biosynthetic products.
 - Downstream processing includes extraction, purification & filtration steps.
- 3) What is CSTRs?
- CSTRs stands for Continuous Stirred Tank Reactors.
 - Continuous stirred Tank Reactor is a chemical reactor that mixes reactants continuously to produce products.
 - CSTR are well suited for reactions that require high conversion rates.

4) Write down the principle of air-lift fermentor.

→ The principle of air-lift fermentor is that compressed air is injected into a liquid to create gas-liquid mixture that rises to the top.

- This mixing process is called an airlift.

- Low-pressure air-lift fermentors are designed to couple heat & mass transfer processes using a single vehicle, viz. low-pressure air.

5) Define Immobilized cell Reactor.

→ An Immobilized cell Reactor is a bioreactor that confines cells within a matrix to improve their productivity & recovery.

- The cells are immobilized by attaching them to a support material such as a gel, bead or foam.

6) Write down the limitations of continuous fermentors.

→ • Continuous fermentation has several limitations such as:

(i) Equipment → It requires precise feeding equipment & rational equipment.

(ii) Contamination → There is higher risk of bacterial contamination & genetic changes.

(iii) Product quality → The quality of product can be affected by the amount of dead cells & debris, & whether it is genetically stable.

Q.2. Attempt the following questions.

1) Write the Difference between Batch fermentation & continuous fermentation.

Batch fermentation	Continuous fermentation
(i) Batch fermentation is a closed system where all nutrients are added at once.	(i) Continuous fermentation is an open system where nutrients are added continuously.
(ii) It occurs in batches.	(ii) It occurs at periodic intervals.
(iii) Conditions do not remain constant throughout batch fermentation.	(iii) Conditions remain constant throughout continuous fermentation.
(iv) Turnover rate is low.	(iv) Turnover rate is high.
(v) Microorganisms use nutrients slowly.	(v) Microorganisms use nutrients rapidly.
(vi) Log phase is shorter.	(vi) Log phase is longer.
(vii) Product removed when fermentation stops.	(vii) Product continuously removed.
(viii) Easy to set up and maintain.	(viii) Can be difficult to maintain conditions.
(ix) If Contamination occurs only one batch is wasted.	(ix) Contamination can affect a huge volume of product.
(x) Product quality can vary between batches.	(x) Product quality more consistent.
(xi) There is no removal of wastes. takes place.	(xi) There is removal of wastes takes place.
(xii) In batch fermentation minimum chance of contamination.	(xii) In Continuous fermentation maximum chance of contamination.

1) Explain in details CSTRs with diagram.

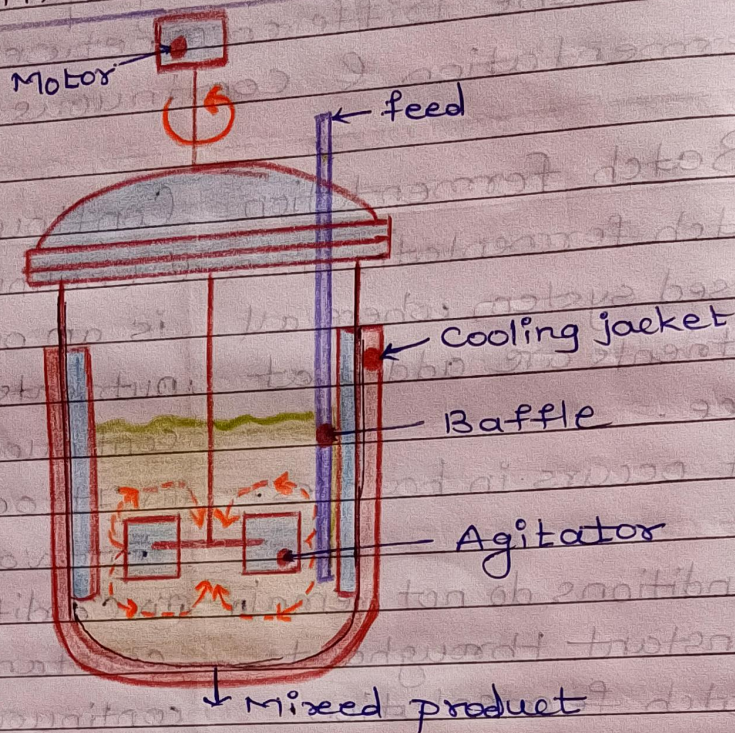


fig. Continuous stirred Tank Reactor.

- CSTR $\rightarrow$ Continuous Stirred Tank Reactor.
- CSTR is a type of chemical reactor where reactants flow into the reactor and products flow out continuously, while the contents inside are kept well mixed.
- CSTR is an open system where nutrients added continuously.
- CSTR is a type of chemical reactor widely used in industrial processes for the continuous production of chemicals, pharmaceuticals & other products.
- It operates by continuously introducing reactants into a well-mixed vessel, where they undergo chemical reactions and

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simultaneously removing the products at same flow rate, maintaining steady-state conditions.

• Different parts of the CSTRs —

• Vessel → main container where reaction occurs, typically made of stainless steel or glass, depending on reaction conditions.

• Agitation system (Impeller) → A Rotating mechanism inside vessel that provides vigorous mixing to maintain a uniform composition throughout reaction mixture.

• Baffles → vertical plates installed within vessel to prevent swirling and promote better mixing.

• Inlet port → The opening where reactants are continuously fed into reactor.

• Outlet port → Opening where reaction mixture (products) is continuously withdrawn from the reactor.

• Jacket → Double walled design around the vessel that allows for circulating coolant or heating fluid to control reaction temperature precisely.

• Temperature Control System → Sensors and controllers to monitor and maintain desired reaction temperature.

• Key features of CSTRs —

(i) Continuous operation —

- Reactants are continuously fed into the reactor, & products are continuously withdrawn, allowing for uninterrupted production.

(i) Efficient Mixing —

- Reactor is equipped with an impeller or other mixing devices to ensure uniform distribution of temperature & concentration throughout vessel, promoting consistent reaction rates.

(ii) Steady-state Conditions —

- By maintaining constant flow rates & mixing, CSTRs achieve steady-state operation where the concentrations of reactants & products remain constant over time.

• Applications —

1) Chemical Engineering —

- commonly used for liquid-phase reactions, polymerizations, & other chemical syntheses.

2) Biochemical processes —

- In bioreactors, CSTRs facilitate continuous fermentation & cell culture processes.

• Advantages —

1) Good Temperature Control.

2) Flexibility

3) Scalability.

4) Efficient mixing

5) Stable performance

6) Versatility

7) Easy control.

• Disadvantages —

1) Residence time distribution.

2) Scale-up challenges.

2) What is OTR and OUR with reference to bioreactor.

→ In context of bioreactors, OTR and OUR are important parameters used to assess the performance of biological systems, especially in processes involving microorganisms or cell cultures.

(A) OTR (Oxygen Transfer Rate) —

- OTR is a critical measurement in operation of bioreactor.
- OTR refers to rate at which oxygen is transferred from the gas phase (air or oxygen supply) into liquid phase (culture medium) where the microorganisms or cells reside.
- OTR measures the rate at which oxygen is transferred into culture medium.
- The OTR is defined by the $K_L a$ and the difference oxygen con. of the introduced gas & oxygen conc. in medium.
- Oxygen can be supply by means of air or pure oxygen bubbles introduced to the water to create additional gas-water interfaces.

• Importance of OTR —

- Oxygen supply is vital for cellular respiration, growth and product formation in aerobic fermentation processes.
- The efficiency of oxygen transfer is crucial for maintaining optimal growth conditions in culture.

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- If OTR is too low microbial growth on cell culture, processes may slow down or even stop.
 - on other hand if it's too high, it can lead to foam formation or increased energy consumption due to need for more aeration.

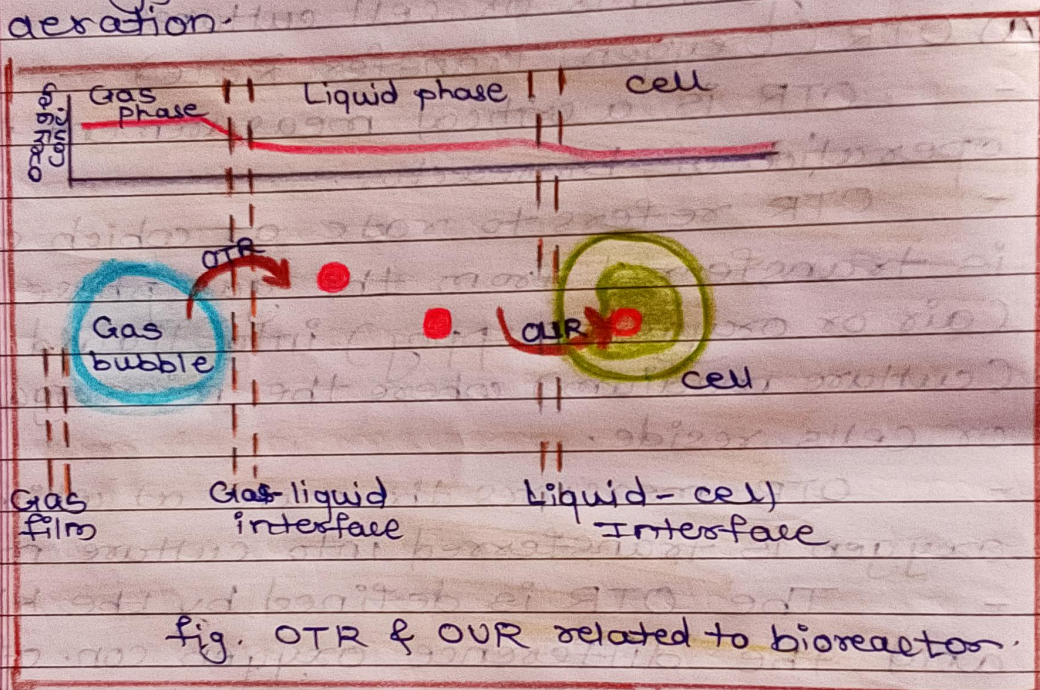


fig. OTR & OUR related to bioreactor.

• Factors Influencing OTR —

- Agitation speed → More agitation increases surface area for oxygen transfer.
- Aeration rate → Higher air flow rates can increase the oxygen transfer but might lead to mechanical stresses.
- Liquid viscosity → Higher viscosity reduces oxygen transfer efficiency.
- Temp. & pressure → Affects solubility of oxygen in medium.

(v) Type of microorganism $\rightarrow$ Some organisms have higher oxygen demands than others.

• Measurement of OTR —

- OTR is typically calculated by measuring DO (dissolved oxygen) conc. in bioreactor & analyzing how it changes over time.

(B) OUR (Oxygen Uptake Rate) —

- OUR refers to the rate at which microorganisms or cells consume oxygen in bioreactor.

- This is an important indicator of metabolic activity of culture.

- It is a measure of metabolic activity of the cells & depends on factors like cell density, growth rate, & specific metabolic pathways of the cells.

• Importance of OUR —

- provides insight into respiratory activity & growth rate of microorganisms or cells.

- High OUR values typically indicate that the organisms are growing rapidly or actively metabolizing.

- Monitoring OUR helps in determining whether culture is healthy, active growth phase or whether its experiencing stress due to nutrient limitation, pH imbalance or oxygen deficiency.

• Factors influencing OUR —

- (i) Cell growth phase $\rightarrow$ In exponential growth phase, OUR is usually high as cells are dividing & metabolizing rapidly.

① Substrate availability $\rightarrow$ High levels of available nutrients can increase the OUR.

② Oxygen availability $\rightarrow$ If oxygen is limited, the OUR will decrease or stabilize, even if the organisms are still active.

• Measurement of OUR —

- OUR is typically determined by measuring change in dissolved oxygen conc. over time.
- It is commonly measured using DO probes that continuously monitor oxygen levels in bioreactor.

• Relationship between OTR & OUR —

- The relationship between OTR & OUR is important for maintaining optimal oxygen levels in bioreactor.

- If OTR is too low, the cells may not have enough oxygen, leading to reduced growth or even cell death.

- Conversely if, OTR is too high compared to OUR, oxygen may accumulate in the medium, which can be detrimental to some cell types.

3) Write Down Commercial production of Chitinase.

$\rightarrow$ Chitinase is an enzyme that breaks down chitin, a biopolymer found in exoskeleton of arthropods, insects & fungi.

- Chitinase has a wide range of industrial applications, including its use in agriculture (as a biocontrol agent), in food industry (as an additive), in biotechnology (as a research tool).

and pharmaceuticals (for potential use in drug delivery & tissue engineering).

- Commercial production of chitinase involves both microbial fermentation & enzymatic extraction.

1) Selection of chitinase producing organisms —

- It is essential to selecting a suitable organism that can produce chitinase enzyme in high quantities.

- Fungi → Trichoderma & Aspergillus are natural producers of chitinase.

- These organisms have ability to grow on low-cost substrates & produce high enzyme yields.

- Bacteria → Bacillus, Pseudomonas, Streptomyces & Aeromonas are also capable of producing chitinase.

- Bacteria can be preferred for their faster growth rates & ease of genetic manipulation.

- Yeasts → Yeasts strains like Saccharomyces cerevisiae can also be engineered for chitinase production.

2) Fermentation Process (Upstream processing) —

a) Culture Media preparation —

- Culture media used for chitinase production can contain essential nutrients (such as carbon sources (e.g. chitin, starch, glucose), nitrogen sources (e.g. ammonium salts, peptone), minerals & vitamins.

- Carbon source can vary depending on the microorganism's preference & the goal of production.

- for fungal organisms like Trichoderma, chitin itself is commonly used as carbon source because it induces chitinase production.

(b) Inoculum preparation —

- A starter culture, or inoculum, is prepared by cultivating selected microorganisms in a small volume of growth medium.

- This culture is then transferred to the larger-scale fermentation vessel.

(c) Fermentation conditions —

• Temperature → around $25 - 30^{\circ}\text{C}$ for fungi & bacteria but vary depending on organism.

• pH → between $5.5 - 7.0$ which favours enzyme production.

• Oxygenation → Aeration necessary to ensure organisms growth efficiently.

- Agitation in bioreactor helps to maintain optimal oxygen supply.

• Time → duration of fermentation can vary but generally lasts between $24 - 72\text{ hrs}$ depending on microorganism.

8) Harvesting the Chitinase (Downstream processing) —

- After fermentation, next step is harvesting chitinase from culture medium.

a) Separation of Biomass —

- In most cases, fermentation medium contains both microorganism's biomass & chitinase enzyme.

- first step of separation involves removing cells by centrifugation or filtration.
- This step isolates clear culture broth which contains chitinase enzyme.

(b) Enzyme purification —

- Chitinase enzyme is often present along with other proteins in culture broth.
- purification techniques used to isolate chitinase from other proteins & impurities. common purification methods are:
 - Precipitation → Using salts (ammonium sulfate) or organic solvents to precipitate enzyme from solution.
 - Chromatography → Techniques like ion-exchange, affinity & size-exclusion chromatography used to separate chitinase based on its charge, size or specific-binding properties.
 - Dialysis → to remove small molecular contaminants that may remain after purification steps.

(c) Concentration —

- After purification chitinase enzyme is often concentrated using tech. like ultra-filtration or evaporation to reduce volume of enzyme solution.

4) Formulation & Stabilization —

- To ensure commercial viability of chitinase it must be formulated in a stable form.
- Lyophilization (freeze-drying) —
 - involves drying chitinase by freezing liquid & then removing water under vacuum.

5) Quality Control and Standardization —

- To ensure consistency & quality in final product, quality control measures are put in place. may include:

- (i) Enzyme Activity Assays
- (ii) Purity Testing
- (iii) Microbial testing

6) Applications —

- 1) Agriculture → as biocontrol
- 2) Food Industry
- 3) Biotechnology
- 4) Pharmaceuticals

4) What is Impellers? Explain their different types

→ • Impellers —

- Impellers are mechanical devices used in bioreactors to mix the contents, promoting uniform distribution of nutrients, gases & cells as well as ensuring proper heat transfer.

- They help to maintain appropriate environment for biochemical reactions such as those used in fermentation or cell culture processes.

- Impellers facilitate fluid flow, ensuring adequate mixing, oxygen transfer & removal of metabolic products.

- The impeller, also known as agitator, is a key component of the bioreactor.

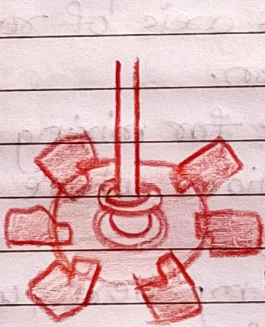
- It performs the important tasks of mixing, aeration, heat & mass transfer within vessel.

• function —

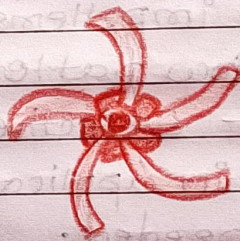
Impellers are crucial for maintaining a homogenous environment within a bioreactor, ensuring that cells have access to nutrients, oxygen & other essential components, while also facilitating removal of waste products.

• Mechanism —

They work by creating a flow pattern within bioreactor, which helps to mix liquid & distribute heat & gases effectively.



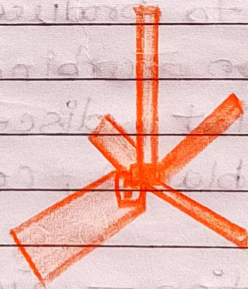
Radial flow
impellers.



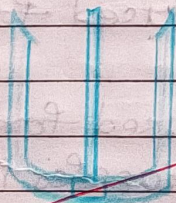
propeller.



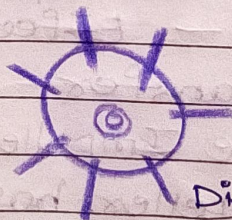
Axial flow
Impellers



pitched blade
turbine



Anchor Impeller



Disc Impeller.

fig. Types of Impellers.

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• Different types of Impellers —

1) Axial flow impellers — (Marine Impeller)

— This causes liquid to flow parallel to the impeller's axis of rotation, creating a strong axial flow pattern.

- Characteristics — Good for large scale bioreactors & applications where strong mixing is required.

- Examples — Marine impellers, which are designed to produce axial flow.

2) Radial flow Impellers —

— These impellers cause the liquid to flow perpendicular to the impeller's axis of rotation, creating a radial flow pattern.

- Characteristics — Effective for mixing & mass transfer, especially in applications where more gentle mixing is needed.

- Examples — Pitched-blade impellers, which are designed to produce both radial & axial flows.

3) Rushton Turbine Impeller —

— A flat, disc-like impeller with series of vertical blades, commonly used for gas-liquid mixing.

- Application — Typically used for aerated bioreactors where oxygen transfer is crucial (e.g. fermentation processes)

- Advantages — Effective for turbulent mixing & oxygen transfer.

4) Marine-style Impeller (Propeller Impeller) —

— This impeller has blades similar to those on a ship's propeller and is typically angled to improve fluid flow.

- Application — Used in applications requiring efficient circulation & mixing of culture medium.

- Advantages — Good for mixing liquids with low viscosity & when gentler mixing is required.

5) Pitched Blade Impeller —

- Features blades angled at a specific pitch, often used for axial & radial flow.

- Application — Used in bioreactors where both mixing & oxygen transfer are needed especially for animal cell culture.

- Advantages — can handle shear-sensitive cells & provides good mixing at moderate speeds.

6) Disc Impeller —

- A flat disc with several blades mounted on it creating a high shear environment.

- Application — Used in mixing operations requiring high shear forces, such as in animal cell culture.

- Advantages — Good for homogeneous mixing in smaller vessels.

7) Anchor Impeller —

- A large, flat impeller that moves fluid radially, typically used in tall, narrow reactors.

- Applications — often used in processes involving highly viscous fluids, such as production of certain biomolecules.

- Advantages — Ensures the smooth flow of high-viscosity cultures with minimal shear stress.

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5) What is Agitation? Explain its functions with different types of agitators.

→ • Agitation —

- Agitation refers to controlled mixing or stirring of the contents within bioreactors to maintain homogeneity of the culture environment.

- This process is crucial for various biochemical & biological processes occurring within bioreactors, such as microbial fermentations, cell culture or enzyme reactions.

- Agitation helps to ensure that the cells or microorganisms receive the required nutrients, oxygen & pH balance, while also facilitating the removal of metabolic waste products.

• Functions of Agitator in a bioreactor —

1) Oxygen transfer —

- one of the critical functions of agitation is enhancing OTR.

- Agitation helps disperse oxygen more efficiently by increasing surface area for oxygen transfer between air & liquid phase.

- Agitation helps to break up air bubbles allowing for larger surface area for oxygen to dissolve into liquid.

2) Mixing of Nutrients and Cells —

- Agitation ensures uniform distribution of nutrients, cells & other components throughout bioreactor.

- Without proper mixing, nutrients might settle or accumulate in certain regions leading to localized depletion, which can limit growth or productivity.

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3) Enhancing Heat Transfer —

— Agitation promotes efficient heat transfer from the bioreactor vessel to the cooling system, helping to maintain the desired temperature.

4) Maintaining Homogeneous Conditions —

— By ensuring uniform mixing, agitation helps maintain a consistent temperature, pH, & other crucial parameters throughout the bioreactor.

5) Preventing Cell Clumping —

— Agitation helps keep cells in suspension, preventing them from settling to the bottom of bioreactor or forming clumps, which can hinder growth & product formation.

6) Waste Removal —

— During biological processes, microorganisms or cells produce metabolites, byproducts, & waste materials.

— Agitation helps in removal of these byproducts, ensuring that their accumulation does not inhibit cell growth or product formation.

7) Prevention of Sedimentation —

— proper agitation prevents cells from settling, ensuring a consistent & effective growth environment, thereby preventing clumping or aggregation.

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Types of Agitation Systems in bioreactors.

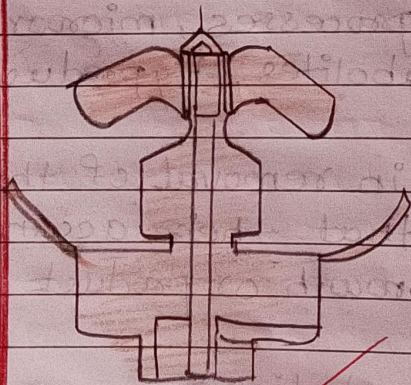
1) Mechanical Agitation —

• Impellers —

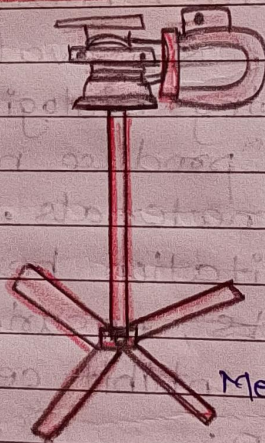
- These are most common type of agitators used in bioreactors.
- design of impeller can vary, including types such as Rushton turbines, pitched-blade turbines or marine propellers, depending on desired flow & shear characteristics.

• functions —

- Impellers physically stir the medium, generating shear & turbulence.
- Choice of impeller depends on types on type of cells, desired shear stress, & mixing efficiency.



Magnetic stirrer.
(agitation)



Mechanical Agitator

