

FERMENTATION & BIOPROCESSING
(Syllabus of the theory papers)

BiSEP1: UPSTREAM PROCESS

Total Hours: 52

Unit- I:

(8 hours)

Bioprocess development: An interdisciplinary challenge, Biotechnology & Bioprocess Engineering, steps in bioprocess development, Microbial culture, Screening and selection for fermentation processes; Preservation and improvement of industrially important microorganisms, Strain development.

Unit-II:

(8 hours)

Media for industrial fermentations: Media ingredients, medium formulation, oxygen requirements, antifoams, medium optimization, Ingredients for mammalian cell culture and plant cell culture. Inoculum production for bacterial and fungal processes. Media sterilization, Batch Process (thermal death kinetics), continuous sterilization process; sterilization of fermenter and other ancillaries, filter sterilization of air and media.

Unit- III:

(8 hours)

Inoculum development for industrial fermentation & Microbial Kinetics:

Introduction, Criteria for transfer of inoculum, development of inocula for bacterial processes, yeast processes and mycelial processes. Inoculum development for plant fermenter, aseptic method of inoculation, achievement and maintenance of aseptic conditions.

Fermentation Material and Energy balance, Microbial growth kinetics: Microbial growth cycle, measurement of growth, Batch culture, continuous culture, fed-batch culture, applications and examples.

Unit- IV:

(8 hours)

Design of bioreactors: Basic objective of fermenter design, aseptic operation & containment, body construction, agitator and sparger design, baffles, stirrer glands and bearings. Process parameters and measurement techniques: measurement of temperature, pressure and pH, DO, foam etc.; flow rate of liquid and gases; Automation (processes computerization). Validation of Fermentor

Unit- V:

(10 hours)

Bioreactor configurations and types: Bubble column, airlift reactor, packed bed, fluidized bed, trickle bed, Membrane reactor, Photobioreactor, Solid state fermenter, Animal and plant cell bioreactors. Scale up and Scale down studies of bioreactors.

Heat and Mass transfer in Bioprocess, Relationship in between heat transfer, cell concentrations and stirring conditions, Measurement of K_La , Rheological properties of fermentation broths, Factors affecting broth viscosity, Mixing in Fermenters.

Unit- VI:

(10 hours)

Animal cell culture: Cell culture practices, nutritional requirement of cultured cell, cell growth and propagation, prevention and eradication of contamination, Cell synchronization; Cell cloning. Measurement of cell death, Apoptosis. Cryopreservation and Cell banking - transport of animal germplasm (i.e. semen, ovum and embryos).

Scaling-up of animal cell culture. PAT (Process Analytical Technologies) for Control of large scale Cell culture. Application of animal cell culture: Stem cell cultures, embryonic stem cells and their applications, Hybridoma technology, Cell culture based vaccines

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3. Bioprocess Engineering, Basic Concepts, II Ed. Michael L Shuler, FikretKargi, Prentice Hall of India pvt. Ltd. 2002.
4. Pauline M. Doran, Bioprocess Engineering Principles, Academic Press an Imprint of Elsevier.
5. Coulson & Richardson's Chemical Engineering, R.K. Sinnottl, III Ed. Vol 6 Butterworth-Heinemann-Elsevier Pub, 1999.
6. Coulson & Richardson's Chemical Engineering, J F Richardson & J H Harker, 5th Ed, Vol 2, Butterworth- Heinemann-Elsevier Pub, 2003.
7. Manual of Industrial Microbiology & biotechnology, Arnold Demain& Julian E. Davis, II Ed, ASM Press. Washington DC, 1999.
8. Current developments in Solid Substrate fermentation, Ashok Pandey, Carlos Ricardo Soccol, Christian Larroche – 2008.
9. Industrial Biotechnology by Rita Singh, S. Ghosh, Global Vision Publishing Ho, 2004
10. Industrial Biotechnology: Sustainable Growth and Economic success by WimSoetaert, Erick J. Vandamme,
11. Basic Cell Culture: A Practical Approach by J.M. Davis, 2nd ed. 2002 Oxford University press, oxford
12. Culture of Animal Cells: A Manual of Basic Technique 4th ed. By R. Ian Freshney Wiley-Liss, 2000
13. Animal Cell Culture Third Edition A Practical Approach Edited by John R. W. Masters Oxford University Press Great Clarendon Street, Oxford OX2 6DP 2000.
14. Animal Cell Technology: From Biopharmaceuticals to Gene TherapyEdited by Leda R. Castilho A^ngela Maria Moraes, Elisabeth F.P. Augusto and Michael Butler. Taylor & Francis group 2008.
15. Pharmaceutical Biotechnology Concepts and Applications Gary Walsh John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex PO19 8SQ, England 2007
16. Cell and Tissue Culture: Laboratory procedures in Biotechnology Edited by Alan Doyle and J. Bryan Griffiths Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex PO19 8SQ, England 1998.

BiSEP2: DOWNSTREAM PROCESSING

Total Hours: 52

Unit- I:

(6 hours)

Basic concepts of Bio-separation Technology: Separation characteristics of proteins and enzymes – size, stability, properties; purification methodologies, Characteristics of bio products; Flocculation and conditioning of broth, overview of reaction processes involved in separation

Unit- II:

(8 hours)

Methods for extraction of proteins -Cell disruption methods for intracellular products Osmotic shock, Homogenization, various types of homogenizers, Sonication, Enzyme digestion. Centrifugation: basic principles, design characteristics; ultracentrifuges; principles and applications.

Unit- III:

(8 hours)

Filtration (batch and continuous filtration). Membrane based separation processes, Micro-filtration; Reverse osmosis, Nanofiltration, Ultrafiltration and Affinity ultrafiltration, Membrane modules. Liquid-liquid extraction, Supercritical fluid extraction, precipitation, distillation, drying of product.

Unit- IV:

(10 hours)

Product Resolution/Fractionation - Chromatography: Gel filtration chromatography, Ion-exchange chromatography (IEC), Chromatofocusing. Affinity chromatography: Immunoaffinity purification, Immunoaffinity matrices, ligand affinity, hydrophobic interaction chromatography (HIC), HPLC, RP – HPLC.

Unit- V:

(8 Hours)

Electrophoresis – Theory and factors affecting. Polyacrylamide and Agarose gel electrophoresis; Capillary electrophoresis; 2 D- Electrophoresis; isoelectric focusing; Pulsed field gel electrophoresis. Western blotting, staining techniques.

Unit- VI:

(12 Hours)

Analysis of the final product - Protein-based contaminants, Removal of altered forms of the protein of interest from the product stream, Product potency, Determination of protein concentration (all the major protein assays – principles). Amino acid analysis, Peptide mapping, N-terminal sequencing, Analysis of secondary and tertiary structure. Detection of protein-based product impurities: rapid methods for detection of specific organisms and toxins (immunological/molecular methods).

REFERENCES:

1. Basic Principles of Membrane technology, 2nd edition, Marcel Mulder. Springer, 2007.
2. Biocatalytic Membrane reactors, Enrico Drioli & Lidietta Gicorna. Taylor Francis Group, 2004.
3. Biochemical Engineering Fundamentals, 2nd Edition, James E. Bailey, David F. Ollis. McGraw Hill International Editions, 1986.
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5. Bioprocess Engineering, Basic Concepts, 2nd Edition, Michael L. Schuler, Fikret Kargi. Prentice Hall of India Pvt. Ltd., 2002.
6. Bioseparations Principles and Techniques, B. Sivasankar. Prentice hall of India Pvt. Ltd., 2007.
7. Fermentation - A Practical Approach, B. Mc Neil and L. M Harvey, Oxford University Press, 1990.
8. Fermentation Microbiology and Biotechnology, Bryce C.F and El Mansi. Taylor and Francis, London, 2002.
9. Handbook of Bioseparations, Volume 2, Edited by Satinder Ahuja. Academic Press, 2000.
10. Introduction to Biochemical Engineering, 2nd Edition, D.G Rao. Tata McGraw Hill International Editions, 1986.
11. Manual of Industrial Microbiology & biotechnology, 2nd Edition, Arnold Demain & Julian E. Davis, ASM Press, Washington DC, 1999.
12. Membrane Technology and applications, 2nd Edition, Richard W Baker. John Wiley & Sons Ltd, 2004.
13. Prescott and Dunn's Industrial Microbiology, 4th Edition, Edited by Gerald Reed, CBS Publishers and Distributors, New Delhi, 1999.
14. Principles and techniques of practical biochemistry, 6th Edition, Keith Wilson and John M Walker, Cambridge University press, Cambridge. 1995.
15. Principles of Fermentation technology, 2nd Edition, Stranburry P.F and Whittaker, Pergamon press, 2004
16. Techniques used in Bio product analysis, Butterworth Heinemann Ltd, 1992.

BiSEP3: FACILITY MANAGEMENT AND APPLICATIONS OF FERMENTATION

Total Hours: 52

Unit- I: (8 hours)

Cleanroom - What is a Cleanroom? The Need for Cleanrooms, Types of Cleanrooms, Basis of Cleanroom Standards, Federal Standard 209E/ISO standards- ISO14000-1, Pharmaceutical Cleanroom Classification, Sources of clean room documents and standards - The International Confederation of Contamination Control Societies (ICCCS). Recommended Practices and Guides of the Institute of Environmental Sciences and Technology (IEST), International Clean room Forum.

Unit -II: (10 hours)

The Design of Turbulently Ventilated and Ancillary Cleanrooms- Air supply, High efficiency air filters, Air movement within a turbulently ventilated Cleanroom, Room pressurization and air movement control between rooms, Construction materials and finishes. Ancillary Clean Rooms – Clothing change area, Material transfer area, Containment Rooms. Design of Unidirectional Cleanrooms and Clean Air Devices. Cleanroom Testing and monitoring Airborne Particle Counters, Continuous Monitoring Apparatus for Airborne Particles, Microbial Sampling of the Air. Cleanroom Clothing, Operating a Cleanroom, Cleanroom Disciplines, Methods to Monitor Hazards and Control Methods.

Unit- III: (8 hours)

Microbial primary and secondary metabolites: Aminoacids (glutamic acid, lysine) by modified strains, Vitamins (A and C) and Recombinant protein production insulin. Organic acids (citric acid). Production of Antibiotics (penicillin).

Unit- IV: (8 hours)

Microbial Enzymes: Microbial production and purification of lipase. Immobilization of enzymes. Microbial exopolysaccharides (EPS): classification and applications of cyclodextrin, alginate, chitosan.

Unit- V: (8 hours)

Plant Cell Suspension Culture and Secondary Metabolites: Establishing cell cultures, Types of suspension culture. Production of secondary Metabolites – Immobilized cell culture system, Hairy root cultures. Role of elicitors and precursor feeding on stimulation of chemical production, Biotransformation and methods of biotransformation, transformation of steroids.

Unit- VI: (10 hours)

Microbial food: miso, tofu, cheese-cheddar, sauerkraut. Probiotics, Microbial Biomass- Baker's yeast, SCP. Mushroom cultivation. **Microbial beverages:** Production of wine and beer. **Microalgal culture and its industrial application:** omega 3- fatty acids, β -carotene, biodiesel production.

REFERENCE:

1. Cleanroom Technology: Fundamentals of Design, Testing and Operation William Whyte, Second edition, John Wiley & Sons, UK, 2010
1. Clean room Technology - W. Whyte
2. Clean room Design-Technology and Engineering-W. Whyte
3. Introduction to Contamination Control and Cleanroom Technology: Author: Matts Ramstorp.
4. Cleanrooms: facilities and practices: Michael Kozicki, Stuart A. Hoenig, Patrick J. Robinson
5. Clean Room Design: Minimizing Contamination Through Proper Design:: Bengt Ljungqvist, Berit Reinmüller
6. Encyclopedia of Cleanrooms, Bio-Cleanrooms, and Aseptic Areas Dr. Philip R. Austin, P.E.
7. Comprehensive Biotechnology, vol 1,2,3 & 4 Murray Moo Young, Pergamon Press, 2004
8. Industrial microbiology, Cassida, Wiley Eastern Ltd, 1993
9. Industrial biotechnology, Cruger & Cruger 2nd Ed, Sutherland MA Sinauer Associates 1990
10. Manual of Industrial Microbiology & biotechnology, Arnold Demain & Julian E. Davis, II Ed, ASM Press. Washington DC, 1999.
11. Microbial biotechnology, Fundamental of Applied Microbiology Alexander, G, WH Freeman and com. 1993
12. Industrial Microbiology, Ed 4. Prescott & Dunn, 2004, McGraw Hill Book Pub.
13. Microbial Technology : Fermentation Technology , 2nd Edition, Vol. II Pepler, H.J. and D. Perlman, (2004), Academic Press / Elsevier.
14. Fermentation Microbiology and Biotechnology 2nd Edition El-Mansi, E.M.T. (2007)., CRC/Taylor & Francis.

BiSEP4: Syllabus of the Elective theory papers

(Choose any one from the following)

BiSEP4a: PRODUCTION/ MANUFACTURING BIOLOGIST

Total Hours: 52

Unit- I:

Supervision of bio pharmaceutical production process: Supervise bio pharmaceutical production activities: Bio pharmaceutical production schedule and guidelines to production operators to handle production activities, Directions for junior biologists/ production operators - proper ingredients, temperatures, pressure and mixing times, etc.

Unit – II:

Documentation and Reporting: Documentation - Documentation of activities in the production process, Record of production output for each shift operation in the Batch Process.

Reporting – Following of approved guidelines of respective Drug Administration Body (MHRA, USFDA, CDSCO, etc.), Standard Operating Procedures and other statutory requirements, Reporting of breakdowns, Maintenance of GMP standards at shop floor and conditions suitable for production of quality products.

Unit – III:

Manage staff and inventory: Staff - Procedures to be followed in Managing staff details at production site. Role of production staff during audit

Inventory - Stock of raw materials and chemicals for production activities, Requirement and source materials as per daily production schedule, labeling, raw material conditions, batch no., shelf life and quantities, etc.

Unit – IV:

Maintain a healthy, safe and secure working environment in the life sciences facility: Self monitor and safety principles and standards, behavioural safety of workmen to current Good Manufacturing Practices (cGMP). Shop floor standards. Reporting of health issues, safety and security policies and procedures.

Managing emergency procedures: illness, accidents, fires, evacuation of worker/s during emergency.

Unit – V:

Coordination with Shift Supervisor: Work instructions from reporting supervisor, Reporting to supervisor - process-flow improvements and production defects received from previous process, potential hazards or expected process disruptions, maintenance and repair schedule proactively, handover of completed work.

Unit – VI:

Coordination within the team and with cross functional teams: Team player: Working with colleagues and sharing of work, work flow related difficulties. Interact with colleagues from cross functional teams: Feedback from Quality Control and Quality Assurance, Completion of work on time, support to Quality Assurance team during audits, coordination during breakdowns and for preventive and corrective maintenance, Coordination with Stores.

BiSEP4b: QUALITY CONTROL/QUALITY ASSURANCE BIOLOGIST

Total Hours: 52

Unit-I:

16 hours

Essentials of quality control: Preparations - buffer, solvents, solutions and microbial media for running bio-analytical quality tests, assays to carry out quality control procedures on biopharmaceutical products.

Concepts of pharmacopeia like BP, USP, EP and other applicable guidelines such as WHO, ICH and EMEA, etc., statistical tools and software like combistats, safe handling of infectious materials like cultures, strains and seed strains, procedures for handling infectious spillage control, GLP/GMP, biochemical analysis of proteins, bio analytical and microbiological methods, working of instruments/apparatus/equipment, biological assays, application of various analytical techniques such as HPLC, capillary electrophoresis including icIEF, FTIR, Circular Dichroism, UV and Fluorescence spectroscopy, ELISAs, enzyme assays and other applicable methods for the testing of biopharmaceuticals, application of microbiological techniques such as air monitoring, water testing, surface monitoring, microbial monitoring, biosafety levels and biosafety hazards

Unit-II:

10 hours

Quality Assurance: Quality checks - quality assurance samples, master sample, internal controls, statistical analysis of test data, techniques and concepts of statistical quality control and statistical process control, non-conformities. Operational aspects – calibration, accuracy checks of quality control equipments like stability chambers and BOD incubators, HPLC, gas chromatography, photofluorometer, etc., application softwares used in quality analysis

Unit-III:

6 hours

Safety and Security at workplace: Different types of occupational health hazards, knowledge of chemical substances, characteristics & safety measures, use of safety gears, masks, gloves & accessories, evacuation procedures for workers & visitors. Health, safety & security issues – types (illness, fire accidents), company policies and procedures, When and how to report, summon medical assistance & emergency services

Unit-IV:

6 hours

Interpersonal Skills: Understand work output requirements, company rules, guidelines & policies related to the process flow, identifying and reporting issues requiring intervention, delivery of quality work on time & report any anticipated reasons for the delay, importance of team work, resolution of conflicts, multi-tasking, training the team members, knowledge of project management

Unit-V:

6 hours

Clean work station: Cleaning the work area and equipments, materials and equipments required for cleaning, adequate ventilation for the work area, personal protective equipments, dealing with accidental damage, procuring and storing housekeeping equipment and supplies, disposal of wastes, maintain schedules and records for housekeeping

Unit-IV:**8 hours**

Reporting and documentation in quality: Reporting – company procedures, escalation matrix for reporting identified issues - defects, problem, incidents, quality issues and test results, feedback to production manager and R&D staff. Documentation – procedures and good documentation practices, offline and online mode, accuracy, details, controlled document files and test records, regulatory and compliance requirements, inspection - procedures, protocols and checklists, inspection reports.

Syllabus of the practical papers

BiSEP5: Lab- I: UPSTREAM PROCESSING AND APPLICATIONS OF FERMENTATION

- Isolation of industrially important microorganisms
- Production of Industrially important Enzyme by submerged fermentation (Lab scale)
- Shake flask to lab scale fermenter studies
- Production of Industrially important Enzyme by solid state fermentation
- Production of Organic acids
- Production of Antibiotics
- Wine preparation
- Production of alcohol by microbes.
- Beer production, sampling and total and viable yeast cells
- Study of Microbial Growth Kinetics
- Production of biofuel by microorganism

BiSEP6: Lab-II: DOWNSTREAM PROCESSING

- Cell disruption by ultrasonication.
- Soxhlet extraction of plant metabolites and usage of flash evaporator.
- Partial purification of industrial important enzymes by ammonium sulphate precipitation.
- Partial purification of industrial important enzymes by dialysis and reverse osmosis.
- Chromatography of Industrial Important Enzymes.
- SDS-Polyacrylamide gel electrophoresis (SDS-PAGE)- Molecular weight
- Cell Separation by Centrifugation
- Purification and estimation of Organic Acid
- Purification of antibiotics and antibiotic assay
- Estimation of alcohol