POST GRADUATE DIPLOMA IN BIOPROCESS TECHNOLOGY

SYLLABUS

NATIONAL COLLEGE
(Autonomous)
(College with Potential for Excellence)
(Nationally Re-accredited at 'A' Grade by NAAC)
(Affiliated to Bharathidasan University)
Tiruchirappalli - 620 001.

P.G. DIPLOMA IN BIOPROCESS TECHNOLOGY (P.G.D.BP.T)
COURSE STRUCTURE

Course Duration: 1 year (Full Time) (After Post Graduation only)

Semester	Course	Title of the Paper	Credits	Hrs / Week	Internal Mark	External Mark	Max. Mark
I	Core I	Bioprocess Engineering	4	6	25	75	100
	Core II	Bioenergetics & Enzyme Technology	4	6	25	75	100
	Core III	Bioreactor Design and Analysis	4	6	25	75	100
	Core IV	Transfer Phenomena in Bioprocess	4	6	25	75	100
	Core V	Lab in Bioprocess I	4	6	40	60	100
TOTAL			**20**	**30**	**140**	**360**	**500**
II	Core VI	Downstream and Bioseparation Process	4	6	25	75	100
	Core VII	Animal and Plant Cell Bioprocess	4	6	25	75	100
	Core VIII	Biotechnological Processes and Products	4	6	25	75	100
	Core IX	Lab in Bioprocess II	4	6	40	60	100
	Core X	In-plant Training	4	6	40	60	100
TOTAL			**20**	**30**	**155**	**345**	**500**
GRAND TOTAL			**40**	**60**	**295**	**705**	**1000**

SEMESTER I
CORE COURSE I – BIOPROCESS ENGINEERING

Hours: 6 **Credits: 4**

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Unit 1 Introduction to Biomolecules, Identification of Microorganisms - Structure, properties and classification - carbohydrates, lipids, proteins and nucleic acids; Prokaryotes & Eukaryotes; Bacterial Taxonomy, Microscopy, general structural organization of bacteria and other microorganisms.

Unit 2 Upstream Processing - Isolation, Preservation and Improvement of Industrial Micro-Organisms; Medium requirements for fermentation process; Criteria for good medium; Sterilization - batch and continuous heat sterilization of liquid media, filter sterilization of liquid media and Air. Design of sterilization equipment

Unit 3 Principles of enzyme catalysis - Proteins as enzymes; Classification of Enzymes; Mechanism of Enzyme Action; Determination of elementary step rate kinetics, patterns of substrate concentration dependence, modulation and regulation of enzyme activity

Unit 4 Kinetics of substrate utilization, product formation and biomass production - Phases of cell growth in batch cultures - transient growth kinetics, Simple unstructured kinetic models for microbial growth, Growth of filamentous organisms; Environmental conditions affecting growth kinetics, substrate and product inhibition on cell growth and product formation; structured kinetic models, segregated kinetic models of growth.

Unit 5 Energy and Material Balances - Introduction to Engineering Calculations, Material-Balance calculations, Stoichiometry of microbial growth and Product formation, Energy – Balance Calculations with and Without Reactions

Reference books:

1. Principles of Biochemistry by A.L. Lehninger, D.L.Nelson and M.M Cox (2006) Worth publishers, New York.
2. Cruger.W and A.Cruger, *A Textbook of Industrial Microbiology* (*2e)*, Sinauer Associates, Sunderland,US, 2004.
3. Stryer.L, *Biochemistry (4e)*, Freeman, 2002.
4. Textbook of Biochemistry by Thomas Devlin (2002), John publishers.
5. Michael Shuler and Fikret Kargi, *Bioprocess Engineering: Basic Concepts (2e)*, Prentice Hall, Englewood Cliffs, NJ, 2002.
6. Bailey .J.E and D. F. Ollis, *Biochemical Engineering Fundamentals (2e),* Mc-Graw Hill, Inc., 1986.
7. Pauline M Doran, *Bioprocess engineering principles (1e),* Academic Press, 1995.

SEMESTER I

CORE COURSE II – BIOENERGETICS AND ENZYME TECHNOLOGY

Hours: 6 **Credits: 4**

Unit 1 Frontier of Biological Thermodynamics - Energy conservation in living organism, Irreversibility and life, third law and biology, entropy and protein stability, Energy, information processing and life, second law and evolution, Gibbs free energy, Equilibrium concepts for biological thermodynamics.

Unit 2 Fundamental concepts of Thermodynamics - System and Surroundings, First law of thermodynamics -Internal energy, enthalpy, Heat capacity, applied examples from biochemistry. Second law – Entropy and universe, Concept of heat engines, protein stability and calorimetric measurements, Fundamentals of Differential scanning calorimeter and Isothermal calorimeter in biological property measurements, Third law of thermodynamics, Maxwell equations, Gibbs-Duhem Equation and the Phase Rule, Legendre Transforms.

Unit 3 Gibbs free energy and its Applications - Gibbs free energy and equilibrium, Chemical potential, ionic solutions, Equilibrium constant, standard state in biochemistry, Acid and bases, chemical coupling and redox reactions, Gibbs free energy in photosynthesis, glycolysis citric acid cycle, Oxidative phosphorylation and ATP hydrolysis, substrate cycling, Membrane transport, Enzyme substrate interaction, Haemoglobin, Protien solubility, stability and dynamics.

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Unit 4 Reaction Kinetics - Rate of a reaction, rate constant and order of the reaction, effect of temperature, collision and transition state theory, Electron transfer kinetics, Enzyme kinetics and inhibition, Reaction mechanism of lysozyme, protein folding and pathological misfolding, polymerisation, muscle contraction and the molecular motors.

Unit 5 Mechanism of enzyme action – Energy mechanics. Enzyme Kinetics – MM hypothesis, Significance of Km and Vm values, Modifiers of Enzyme activity – Reversible and Irreversible modifications.

Reference books:

1. Donald T. Haynie, *Biological Thermodynamics*, Cambridge press, 2008.
2. Enzyme structure and Mechanisms (1995). Alan Fersht W.H.Freeman and Company New York.
3. Principles of Biochemisty by A.L. Lehninger, D.L.Nelson and M.M Cox (2006) Worth publishers, New York.
4. Biochemistry by L.Stryer, (2002) W.H. Freeman & Co., New York.
5. Introduction to protein structure by C.Branden J.Tooze. (2006) Publishing Inc.
6. Textbook of Biochemistry by Thomas Devlin (2002), John publishers.
7. Robert A. Alberty, *Thermodynamics of Biochemical Reactions*, John willy publications, 2003.

SEMESTER I
CORE COURSE III - BIOREACTOR DESIGN AND ANALYSIS

Hours: 6 **Credits: 4**

Unit 1 Introduction and Review of Bio-reaction engineering concepts, Mass transfer effects in heterogeneous reaction. Stirred tank batch bioreactor: stirred batch bio reactor for enzymes, cell cultures. Computers in fermentation, modeling, software sensors, control and supervision of fermentation processes. – off-line / online measurements – PID

Unit 2 Continuous Stirred Tank Bioreactor : Continuous operation of mixed reactor, enzyme reactions in a mixed reactor, performance equation for M-M kinetics, substrate inhibition kinetics and product inhibition kinetics, chemostat with cell cultures –steady state cell and substrate concentrations and productivity as a function of dilution rate, CSTR with immobilized enzymes, operation of CSTR in a constant feed rate policy-simulation for conversions with and without diffusion limitations, chemostat in series, Graphical design

Unit 3 Plug Flow and Packed Bed Bioreactor: Performance equation with Michelin-Menten kinetics, substrate inhibition and product inhibition, plug flow reactor for immobilized enzymes, operation of plug flow reactor in constant feed rate policy, simulation for conversion with and without diffusion limitations. Fed–batch reactor: Applications of fed reactor, Fed batch operation of mixed reactor, material balance on cell and substrate

Unit 4 Recycle system: Chemostat with recycle, Biological waste water treatment, Feed forward control of the activated sludge process. The Transient Behavior of Bioreactors: Stability analysis, Stability of the chemostat, Stability of chemostat with substrate inhibition, Operating diagram, Transient responses of the chemostat, control of the chemostat, Turbidostat operation, Nutristat operation

Unit 5 Design of a fermenter: Basic function of a fermenter for microbial or animal cell culture, basic bioreactor design criteria, overview of bioreactor types-stirred tank bioreactor, bubble column bioreactor, air-lift reactor, propeller loop reactor, jet loop reactor, schematic overview of a fermenter with control system, operating issues that affect reactor design, aeration and oxygen mass transfer in bioreactor system, design of chemostat. Instrumentation and control: Methods of measuring process variables, measurement and control of dissolved oxygen, pH measurements and Non-ideal flow: Non-ideal flow, RTD, E,C,F-curves

Reference books:

1. Blanch H.W and Douglas S. Clark, *Biochemical Engineering*, CRC Press, 1997.
2. Michael L Shuler and Fikret Kargi, *Bioprocess Engineering: Basic Concepts*, Prentice-Hall of India Pvt Ltd, 2008.
3. Stanbury P.F., Whitaker A. and Hall S.J, *Principles of Fermentation Technology*. Elsevier India Pvt Ltd, 2007.

4. Arthur T. Johnson, *Biological Process Engineering: An Analogical Approach to Fluid Flow, Heat Transfer, and Mass Transfer Applied to Biological Systems,* John Wiley and Sons, 1998.
5. Pauline M. Doran, *Bioprocess Engineering Principles*. Academic Press, 1995.
6. Rao D.G., *Introduction to Biochemical Engineering.* Tata McGraw-Hill, 2005.

SEMESTER I

CORE COURSE IV – TRANSFER PHENOMENA IN BIOPROCESS

Hours: 6 Credits: 4

Unit 1 Introduction to Transport Phenomena – momentum, heat and mass transfer in bioprocessing. Momentum transfer Review of basic concepts – Conservation of Mass, Conservation of Energy, Momentum Balance – Momentum Balance in a Circular Pipe, Flow Velocity Profile. Fermentation Broth Rheology – Viscosity, Rheological Properties of Fermentation Broths, Factors affecting broth viscosity.

Unit 2 Mixing in a Bioreactor – Flow regimes with and without baffles, various types of impellers and mixing equipment. Power Requirements for Mixing, Ungassed Newtonian Fluids, Gassed Fluids, Improving Mixing in Fermenters, Effect of Rheological Properties on Mixing, Role of Shear in Stirred Fermenters.

Unit 3 Heat Transfer - Review of basic concepts – Various modes of heat transfer, viz., conduction convection and radiation. Design Equations for Heat Transfer Systems – Energy Balance, Calculation of Heat-Transfer Coefficients. Application of heat transfer in bioprocessing, Heat Management in Bioreactors, Relationship between heat transfer, cell concentration and stirring conditions

Unit 4 Mass transfer - Review of basic concepts – Diffusivity, theory of diffusion, analogy between mass, heat and momentum transfer, role of diffusion in bioprocessing. Definition of binary mass transfer coefficients, transfer coefficients at high mass transfer rates- boundary layer theory, penetration theory. Convective mass transfer – Liquid-solid mass transfer, liquid-liquid mass transfer, gas liquid mass transfer.

Unit 5 Oxygen transport to microbial cultures – Gas liquid mass transfer fundamentals, oxygen requirement of microbial cultures. Oxygen requirements of microbial cultures oxygen mass transfer fundamentals. oxygen transfer and oxygen demand. Oxygen transfer by aeration and agitation. Determination of oxygen mass transfer coefficient by various methods including dynamic gassing out and oxygen balance methods. Design considerations & Scale-up of fermentors. Design criteria for fermentor, scale up criteria and examples.

Reference books:

1. Arthur T. Johnson, Biological Process Engineering: An Analogical Approach to Fluid Flow, Heat Transfer, and Mass Transfer Applied to Biological Systems, John Wiley and Sons, 1998.
2. Pauline M. Doran, Bioprocess Engineering Principles, Academic Press, 1995.
3. Blanch H.W and Douglas S. C, Biochemical Engineering, CRC Press, 1997.
4. Michael L Shuler and Fikret Kargi, Bioprocess Engineering: Basic Concepts, Prentice-Hall of India Pvt Ltd, 2008.

SEMESTER I
CORE COURSE V - LAB IN BIOPROCESS I

Hours: 6 Credits: 4

1. Media preparation, Sterilization.
2. Culture transfer techniques, Isolation of pure cultures.
3. Microbial isolation and screening.
4. Bacterial staining
5. Bacterial growth curve studies
6. Isolation of Antibiotic producing organism
7. Extracellular activities of micro organisms- amylase, gelatinase, lipase, caseinase
8. Qualitative study of enzyme activity
9. Effect of pH, Temperature, Substrates, Inhibitor on enzyme activity
10. Enzyme kinetics – Km, Vmax, Specific activity and activity determination
11. Anatomy of Fermentor, cleaning of Fermentor, Assembling and final pre-sterilization of Fermentor, Anatomy and calibration of fermentor electrodes / probes, Post – sterilization procedures, Aseptic techniques in inoculation of fermentors
12. Aseptic sampling from fermentors
13. Techniques to determine microbial contaminations
14. Trouble shooting and diagnostics

Reference books:

1. An Introduction to Practical Biochemistry by Rodney Boyer (2003). Pearson Education.
2. Microbiology. A laboratory manual by J. G. Cappuccino and N. Sherman (2004). Pearson Education.
3. Molecular Cloning by J. Sambrook and D. W. Russell (2001). Cold Spring Harbour Lab. Press.
4. Laboratory Manual of Biochemistry by J.Jayaraman (1988) Wiley Eastern
5. . Practical Biochemistry by Wilson and Walker (1994). Cambridge University Press
6. A short course in Bacterial Genetics by J.H. Miller (1992) Cold Spring Harbor Laboratory.
7. Methods for Genetics and molecular Bacteriology by Ed. RGF Murray, WA. Wood & NB krieg (1994) American society for Microbiology.
8. Handbook of Laboratory culture media, Reagents, Stains and Buffers by N. Kannan (2003), Panima Publishers, New Delhi.
9. A short course in Bacterial Genetics by J.H. Miller (1992) Cold Spring Harbor Laboratory.
10. Plant Molecular Biology by Grierson and S.N. Covey (1988) Blackie
11. Applied Plant Biotechnology. S.Ignacimuthu S.J. (1996) - Me Graw Hill publications Co. Ltd., New Delhi.

SEMESTER II

CORE COURSE VI- DOWNSTREAM AND BIOSEPARATION PROCESS

Hours: 6 Credits: 4

Unit 1 Role of Downstream Processing in Biotechnology - Role and importance of downstream processing in biotechnological processes. Problems and requirements of bioproduct purification. Economics and downstream processing in Biotechnology. Cost cutting strategies, characterstics of biological mixtures, process design criteria for various classes of bioproducts (high volume-low value products and low volume- high value products), physicochemical basis of bio-separation processes..

Unit 2 Primary Separation and Recovery Processes - Cell disruption methods for intracellular products, removal of insolubles, biomass (and particulate debris) separation techniques; flocculation and sedimentation, centrifugation and filtration methods. Precipitation methods - Precipitation with salts, organic solvents & polymers

Unit 3 Extraction - Batch extractions, staged extractions-cross current, co current, counter current extractions. Differential extractions, fractional extractions with a stationary phase, fractional extractions with two moving phases. Aqueous two-phase extraction - reverse micelle extraction, supercritical fluid extraction, in-situ product removal/integrated bioprocessing

Unit 4 Membrane-based separations (micro- & ultra-filtration) - Theory; design & configuration of membrane separation equipment; applications; reverse osmosis, dialysis, electro dialysis, Isoelectric focusing. Adsorption - Adsorption isotherms, industrial adsorbents, adsorption equipments for batch and continuous operations (co current and counter current), adsorption in fixed beds.

Unit 5 Chromatography - Principles of chromatographic separation – gel filtration, reversed phase, hydrophobic interaction, ion-exchange, expanded bed adsorption, bio affinity and IMAC, supercritical fluid chromatography.

Reference books:

1. Belter P.A, Cussler E and Wei Shan Hu, *Bioseparation – Downstream Processing for Biotechnology*, Wiley Interscience, 1988.
2. Asenjo and Juan A. Asenjo, *Separation Processes in Biotechnology*, CRC Press, 1990.
3. Wankat P.C, *Rate Controlled Separation*, Kluwer Publishers, 1990.
4. Wang D.I.C, Cooney C.L, Demain A.L, Dunnil.P, Humphery A.E. and Lilly M.D. *Fermentation and Enzyme Technology*, John Wiley and Sons, 1979.
5. Industrial Microbiology & Biotechnology by Arnold L. demain & Julian E. Davis. (2004) ASM Press.

SEMESTER II

CORE COURSE VII - ANIMAL AND PLANT CELL BIOPROCESS

Hours: 6 Credits: 4

Unit 1 Introduction to mammalian cell culture – mammalian cell characteristics, growth kinetics, metabolism, bioreactors for mammalian cell culture, process monitoring and control. Equipments and requirements for animal cell culture technology, Introduction to balanced salt solution, and simple growth medium, chemical, physical and metabolic functions of different constituents of culture medium. Role of CO2 and supplements, serum and protein free defined media.

Unit 2 Plant cell culture – Introduction, culture media – micronutrients, carbon sources, vitamins, pH, plant growth regulators. medium preparation, Facilities – sterile transfer facilities, temperature, light, aeration. culture initiation, - sterile explants, callus culture intiation, suspension culture, bioreactors and scale – up. Growth quantitation – fresh weight, dry weight, packed cell volume, indirect measurement, viabilitiy assays, secondary metabolite production, Regeneration, micropropagation, and transformation.

Unit 3 Insect cell culture, culture techniques – media preparation, Flasks and roller bottles, shakers and spinner flasks, stirred tank reactors, airlift fermentors, fed batch culture, MOI and infectivity, recovery of insect cells, protein expression using stable cell lines. Process issues in large – scale mammalian and insect cell culture, tissue engineering and cell therapy.

Unit 4 Plant secondary metabolites production: cell culture, hairy root culture, Ri plasmid, control mechanism and maintenance of phenyl propanoid pathway, alkaloids, flavonoids, phenols.

Unit 5 Nuclear transplantation, therapeutic transplantation, transfection methods-lipofection, electroporation, microinjection, embryonic stem cell transfer, targeted gene transfer, hybridoma technology and production of monoclonal antibodies, stem cells – embryonic & adult stem cells, and potent uses of human stem cells.

Reference Books:

1. Animal Cell culture by J.R.W. Masters (2000) Oxford University Press.
2. Animal Biotechnology by M.M. Ranga (2003) Student Edition, Jodhpur.
3. Molecular Biotechnology by Bernard R. Glick and Jack J. Pasternak (2002). Panima Publishing House, New Delhi.
4. Monoclonal Antibodies: Principles and Practice by J.W. Goding (1983) Academic Press.
5. Hybridoma Technology in Biosciences and Medicine by T. A. Springer (1985) Plenum Press, New York.
6. Plant cell culture by R.A Dixon And R.A. Gonzales (2004) IRL press.
7. Genetic Engineering of crop plants-by (Eds) G.W. Lycett and D. grierson (1990).
8. Plant Tissue culture: theory and practice a revised edition by S.S. Bhojwani and M.K. Razdan (2004) Elsevier science.

SEMESTER II

CORE COURSE VIII - BIOTECHNOLOGICAL PROCESSES AND PRODUCTS

Hours: 6 Credits: 4

Unit 1 Primary and secondary metabolites – Organic feed stocks, organic acids, amino acids, enzymes, nucleosides, nucleotides and related compounds, vitamins and antibiotics

Unit 2 Vitamins & Antibiotics – vitamin B12, riboflavin, β carotene, β –lactam antibiotics, amino acids and peptide antibiotics, carbohydrate antibiotics, macro lactone antibiotics, tetracyclines and anthracyclines, nucleoside antibiotics & aromatic antibiotics.

Unit 3 Organic acids & Feed stocks – citric acids, gluconic acids, acetic acids, lactic acids, kojic acids, Itaconic acids – ethanol, glycerol, butanol, acetone, fermentation.

Unit 4 Amino acids – glutamic acid, lysine, tryptophan, structure and biosynthesis of nucleotides, nucleosides and related compounds. Enzyme production – amylase, glucose isomerases, asparaginase, proteases, rennin, pectinases, lipases, penicillin acylase. Enzyme & cell immobilization.

Unit 5 Ergot alkaloids – significance and occurrence, structure, biosynthesis, strain development, production. Microbial transformations – types, applications - antibiotics, pesticides, non-steroid compounds, sterols and steroids.

Reference books:

1. Industrial Microbiology & Biotechnology by Arnold L. demain & Julian E. Davis. (2004) ASM Press.
2. Fermentation Microbiology & Biotechnology by Emt.el-Mansi & CFA. Bryce (2004). Taylor & Francis Ltd.
3. Principles of fermentation technology by P.F. Stanbury, A. Whitaker & S.J. Hall(1997). Oxford.
4. The Bacterial Vol. Ill by Gungalus, I.C. and stainer. RY. (Eds.) Academic press. New York.
5. Bacterial physiology and metabolism by Sala Teh JR - Academic press, New York..
6. Chemical Engineering by J.M. Coulson and J.F. Richardson (1984) Pergamon Press.

SEMESTER II

CORE COURSE IX - LAB IN BIOPROCESSES II

Hours: 6 Credits: 4

1. Introduction to bioprocess technology parts and designs of bioreators;
2. Production of biomass; batch and continuous fed batch fermentation,
3. Analysis and recovery of products- Qualitative, quantitative- enzymes, secondary metabolites, by chromatography, spectrophotometry etc.,
4. Laboratory scale fermentation of antibiotics, immobilization of cells and enzymes.
5. Down Stream Processing-Enzyme/Proteins, Secondary metabolites
6. Beer or Wine Production and Quality Assessment
7. Citric Acid Production and Quantification.

Reference books:

1. Industrial Microbiology & Biotechnology by Arnold L. demain & Julian E. Davis. (2004) ASM Press.
2. Fermentation Microbiology & Biotechnology by Emt.el-Mansi & CFA. Bryce (2004). Taylor & Francis Ltd.
3. Principles of fermentation technology by P.F. Stanbury, A. Whitaker & S.J. Hall(1997). Oxford.
4. The Bacterial Vol. Ill by Gungalus, I.C. and stainer. RY. (Eds.) Academic press. New York.
5. Bacterial physiology and metabolism by Sala Teh JR - Academic press, New York..
6. Chemical Engineering by J.M. Coulson and J.F. Richardson (1984) Pergamon Press.

SEMESTER II
CORE COURSE X – IN PLANT TRAINING
Credits : 4

The students (individually) in Second Semester will be assigned project work / In plant Training in an Industry/Institute under the supervision of a guide. Report of the project / In plant Training should be completed and submitted for evaluation at the end of the Second Semester.

GENERAL INSTRUCTIONS

SEMINAR / ASSIGNMENT
This course is designed for the students to develop skills in searching technical literature, coordinating it and making a good presentation. Presentation of a good written report is also part of exercise (Assignment). The students will be given the seminar on a topic assigned to them, on soft skills or technical topics.