REVISED CURRICULUM

M. Tech

BIOTECHNOLOGY & BIOCHEMICAL ENGINEERING

सत्यमेव जयते

Department of Biotechnology
Ministry of Science & Technology,
Government of India

REVISED CURRICULUM

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CONTENTS

LIST OF ELECTIVES

1. Protein Engineering
2. Nanobiotechnology
3. Metabolic Engineering
4. Process Control & Instrumentation
5. Food Process & Biotechnology
6. Animal Biotechnology
7. Plant Biotechnology
8. Environmental Biotechnology
9. Pharmaceutical Biotechnology
10. Genomics & Proteomics
11. Bioentrepreneurship
12. Bioreaction Engineering

Contents for electives are given separately.

SEMESTER - I

Introductory Biology - 3 Credits

Unit I

Introduction to Macromolecules

Introduction to Biology; Macromolecules; Carbon chemistry; Proteins: Structure, folding, catalysis; Nucleic acids: storage and transfer of genetic information; Lipids: membranes, energy storage; Carbohydrates: energy storage, building blocks

Unit II

Molecular genetics

Genes; Basics of DNA replication, transcription, translation, Genome organization; Mutations; Gene technology

Unit III

Cell biology and energetics

Cell structure; Membranes; Function of cell organelles; Energetics; ATP and glycolysis; Respiration; Photosynthesis

Unit IV

Reproduction, Heredity, Evolution

Reproduction and Heredity; Cell division: mitosis, meiosis, gamete formation, pollination; Mendelian genetics; Evolution; Gene variation (Hardy-Weinberg principle); Darwin's theory of evolution.

Unit V

Principles of Classification

Viruses, bacteria, protists, fungi; Physiology aspects of Plants & Animals; Regulatory systems (nervous, endocrine, immune systems); Ecology; Populations and communities; Biosphere; Conservation

Texts/References

1. W. K. Purves et al. Life, The Science of Biology, 7th Edition, W. H. Freeman and Co., 2003. http://www.whfreeman.com/thelifewirebridge2/
2. Peter H. Raven et al., Biology, 6th Edition, McGraw Hill, 2007. http://www.ravenbiology.com

Introductory Mathematics - 3 Credits

Unit I

Calculus review

Calculus (Quick review of concepts): Review of limits, continuity, differentiability; Mean value theorem,

Taylor's Theorem, Maxima and Minima; Fundamental theorem of Calculus; Improper integrals; Applications to area, volume; Convergence of sequences and series; Power series; Partial Derivatives; Gradient and Directional derivatives; Chain rule; Maxima and Minima.

Unit II

Ordinary Differential Equations

First order differential equations: Exact equations, Integrating factors and Bernoulli equations.

Unit III

Second and higher order differential equations

Linear ODEs with constant coefficients: the characteristic equations; Cauchy-Euler equations; Linear dependence and Wronskians; Method of undetermined coefficients; Method of variation of parameters; Laplace transforms: Inverse theorem, shifting theorems, partial fractions.

Unit IV

Linear Algebra

Basics: Vectors, matrices, determinants; Matrix addition and multiplication; Systems of equations: Gauss elimination, Matrix rank, Linear independence, Cramer's rule; Inverse of a matrix: Gauss-Jordan elimination; Eigenvalues and Eigenvectors: characteristic polynomials, eigenvalues of special matrices(orthogonal, unitary, hermitian, symmetric, skew-symmetric, normal).

Unit V

Numerical methods

Solution of equations by iteration; Interpolation by polynomials; Piecewise linear and cubic splines; Numeric integration and differentiation; Linear systems: Gauss elimination, Gauss-Siedel, matrix inversion; LU factorization; Matrix eigenvalues; Numerical solution of ODEs: Euler and Runge-Kutta methods, Predictor-Corrector methods; Exposure to software packages like Matlab or Scilab.

Texts/References

1. G. B. Thomas and R. L. Finney, Calculus and Analytic Geometry, 9th Edition, ISE Reprint, Addison-Wesley, 1998.
2. E. Kreyszig, Advanced engineering mathematics, 8th Edition, John Wiley, 1999.
3. W. E. Boyce and R. DiPrima, Elementary Differential Equations, 8th Edition, John Wiley, 2005.

Engineering Principles - 3 Credits

Unit I

Energy and Material Balances

Unit operations and unit processes: historical and more recent developments in chemical engineering; Process variables and degrees of freedom; Differential and integral balances; Lumped and distributed balances; Balances in systems involving physical changes.

Unit II

Steady state energy and material balances
Balances in reacting systems; Balances in systems involving recycle, purge, and bypass; Computer aided calculations; Generalization to unsteady state balances

Unit III

Properties of substances
Single component and multicomponent systems; Single and multiphase systems.

Unit IV

Introduction to transport phenomena: Momentum transfer
Viscosity; Molecular theory of Gases and Liquids; Shell balance: Falling film, Circular tube; Equations of Change for isothermal systems: Continuity, Motion, Energy, Substantial derivatives; Unidirectional flows: Pipe flow, Variable viscosity falling film, Couette viscometer, Rotating Sphere; Unsteady flows: Startup Plate flow, Parallel plates etc.

Unit V

Introduction to transport phenomena: Heat & Mass transfer
Thermal conductivity and mechanism of energy transport; Shell energy balances and temperature distributions in solids and laminar flow; Diffusivity and the mechanisms of mass transport; Concentration distributions in solids and laminar flow; Equations of change for multicomponent systems; Introduction to the concept of heat and mass transfer coefficients; Dimensional Analysis (Buckingham Pi theorem).

Texts/References

1. R.M. Felder and R.W. Rousseau, Elementary Principles of Chemical Processes, 3rd Edition, J. Wiley, New York, 2000.
2. D.M.Himmelblau, Basic Principles and Calculations in Chemical Engineering, 6th Edition, Prentice Hall of India. New Delhi, 1996.
3. B.I.Bhatt and S.M.Vora, Stoichiometry, 3rd Edition, Tata McGraw Hill. New Delhi. 1996.
4. R. B. Bird et al., Transport Phenomena, 2nd Edition, Wiley, 2006.

Molecular Biology - 3 Credits

Unit I

Genome organization
Organization of bacterial genome; Structure of eukaryotic chromosomes; Role of nuclear matrix in chromosome organization and function; Matrix binding proteins; Heterochromatin and Euchromatin; DNA reassociation kinetics (Cot curve analysis); Repetitive and unique sequences; Satellite DNA; DNA melting and buoyant density; Nucleosome phasing; DNase I hypersensitive regions; DNA methylation & Imprinting

Unit II

DNA Structure; Replication; Repair & Recombination
Structure of DNA - A-,B-, Z- and triplex DNA; Measurement of properties-Spectrophotometric, CD, AFM

and Electron microscope analysis of DNA structure; Replication initiation, elongation and termination in prokaryotes and eukaryotes; Enzymes and accessory proteins; Fidelity; Replication of single stranded circular DNA; Gene stability and DNA repair- enzymes; Photoreactivation; Nucleotide excision repair; Mismatch correction; SOS repair; Recombination: Homologous and non-homologous; Site specific recombination; Chi sequences in prokaryotes; Gene targeting; Gene disruption; FLP/FRT and Cre/ Lox recombination.

Unit III

Prokaryotic & Eukaryotic Transcription

Prokaryotic Transcription; Transcription unit; Promoters- Constitutive and Inducible; Operators; Regulatory elements; Initiation; Attenuation; Termination-Rho-dependent and independent; Anti-termination; Transcriptional regulation-Positive and negative; Operon concept-lac, trp, ara, his, and gal operons; Transcriptional control in lambda phage; Transcript processing; Processing of tRNA and rRNA

Eukaryotic transcription and regulation; RNA polymerase structure and assembly; RNA polymerase I, II, III; Eukaryotic promoters and enhancers; General Transcription factors; TATA binding proteins (TBP) and TBP associated factors (TAF); Activators and repressors; Transcriptional and post-transcriptional gene silencing

Unit IV

Post Transcriptional Modifications

Processing of hnRNA, tRNA, rRNA; 5'-Cap formation; 3'-end processing and polyadenylation; Splicing; RNA editing; Nuclear export of mRNA; mRNA stability; Catalytic RNA.

Translation & Transport

Translation machinery; Ribosomes; Composition and assembly; Universal genetic code; Degeneracy of codons; Termination codons; Isoaccepting tRNA; Wobble hypothesis; Mechanism of initiation, elongation and termination; Co- and post-translational modifications; Genetic code in mitochondria; Transport of proteins and molecular chaperones; Protein stability; Protein turnover and degradation

Unit V

Mutations; Oncogenes and Tumor suppressor genes

Nonsense, missense and point mutations; Intragenic and Intergenic suppression; Frameshift mutations; Physical, chemical and biological mutagens; Transposition - Transposable genetic elements in prokaryotes and eukaryotes; Mechanisms of transposition; Role of transposons in mutation; Viral and cellular oncogenes; Tumor suppressor genes from humans; Structure, function and mechanism of action of pRB and p53 tumor suppressor proteins; Activation of oncogenes and dominant negative effect; Suppression of tumor suppressor genes; Oncogenes as transcriptional activators.

Text/References

1. Benjamin Lewin, Gene IX, 9th Edition, Jones and Barlett Publishers, 2007.
2. J.D. Watson, N.H. Hopkins, J.W Roberts, J. A. Seitz & A.M. Weiner; Molecular Biology of the Gene, 6th Edition, Benjamin Cummings Publishing Company Inc, 2007.
3. Alberts et al; Molecular Biology of the Cell, 4th edition, Garland, 2002.

Microbial Biochemistry - 3 Credits

Unit I

Cell Structure (Special emphasis on Cell Wall & Membrane) and Microbial Diversity

Structural differences between different microbial cell types and cellular organelles; Biochemical/Microscopic/ Molecular methods used to differentiate between archae, eubacteria and eukaryotes; Cell wall of prokaryotes; Outer membrane of Gram –ve bacteria and control of its synthesis; Potential targets for drug design.

Unit II

Biomolecules and Principles of Microbial Nutrition

Importance of non-covalent interactions in biological systems; Non-informational and Informational Macromolecules and their organization; Microbial nutrition; Different types of culture medium; C/N/P balance and making of culture medium.

Unit III

Bioenergetics and Catabolic Pathways

Oxidation-reduction reactions; Electron carriers and cellular metabolism; High energy compounds and their role in microbial fermentations; Enzymes as catalysts; Cellular metabolites and interconnectivity in biochemical pathways; Respiration and Electron Transport.

Unit IV

Metabolic diversity

Energy from oxidation of inorganic electron donors; Iron oxidation; Methanotrophy and methylotrophy; Nitrate and Sulfate reduction; Acetogenesis; Methanogenesis; Fermentation-energetics and redox constraints; Anaerobic respiration; Chlorophylls and other pigments involved in microbial photosynthesis; Anoxygenic and oxygenic photosynthesis; Autotrophic CO_2 Fixation: Calvin cycle, Reverse Citric Acid cycle, Hydroxy-propionate cycle.

Unit V

Microbial Genetics and Genomics

Mutations and their chemical basis; Mutagens and their use in Biotechnology; Modes of recombination; Comparative prokaryotic genomics

Texts/References

1. M.T. Madigan and J.M. Martinko, Brock Biology of Microorganisms, 11th Edition, Pearson Prentice-Hall, 2006.
2. L. Stryer, Biochemistry, 4th Edition, Freeman, 2002.
3. G. Gottschalk, Bacterial Metabolism, 2nd Edition, Springer-Verlag, New-York, Berlin. 1986.

Immunology - 3 Credits

Unit I

Immunology- fundamental concepts and anatomy of the immune system

Components of innate and acquired immunity; Phagocytosis; Complement and Inflammatory responses; Haematopoesis; Organs and cells of the immune system- primary and secondary lymphoid organs; Lymphatic system; Lymphocyte circulation; Lymphocyte homing; Mucosal and Cutaneous associated Lymphoid tissue.(MALT&CALT); Mucosal Immunity; Antigens - immunogens, haptens; Major Histocompatibility Complex - MHC genes, MHC and immune responsiveness and disease susceptibility, HLA typing

Unit II

Immune responses generated by B and T lymphocytes

Immunoglobulins-basic structure, classes and subclasses of immunoglobulins, antigenic determinants; Multigene organization of immunoglobulin genes; B-cell receptor; Immunoglobulin superfamily; Principles of cell signaling; Immunological basis of self –non-self discrimination; Kinetics of immune response, memory; B cell maturation, activation and differentiation; Generation of antibody diversity; T-cell maturation, activation and differentiation and T-cell receptors; Functional T Cell Subsets; Cell-mediated immune responses, ADCC; Cytokines-properties, receptors and therapeutic uses; Antigen processing and presentation- endogenous antigens, exogenous antigens, non-peptide bacterial antigens and super-antigens; Cell-cell co-operation, Hapten-carrier system

Unit III

Antigen-antibody interactions

Precipitation, agglutination and complement mediated immune reactions; Advanced immunological techniques - RIA, ELISA, Western blotting, ELISPOT assay, immunofluorescence, flow cytometry and immunoelectron microscopy; Surface plasmon resonance, Biosenor assays for assessing ligand –receptor interaction, CMI techniques- lymphoproliferation assay, Mixed lymphocyte reaction, Cell Cytotoxicity assays, Apoptosis, Microarrays, Transgenic mice, Gene knock outs

Unit IV

Vaccinology

Active and passive immunization; Live, killed, attenuated, sub unit vaccines; Vaccine technology- Role and properties of adjuvants, recombinant DNA and protein based vaccines, plant-based vaccines, reverse vaccinology; Peptide vaccines, conjugate vaccines; Antibody genes and antibody engineering- chimeric and hybrid monoclonal antibodies; Catalytic antibodies and generation of immunoglobulin gene libraries.

Unit V

Clinical Immunology

Immunity to Infection : Bacteria, viral, fungal and parasitic infections (with examples from each group); Hypersensitivity – Type I-IV; Autoimmunity; Types of autoimmune diseases; Mechanism and role of CD4+ T cells; MHC and TCR in autoimmunity; Treatment of autoimmune diseases; Transplantation – Immunological basis of graft rejection; Clinical transplantation and immunosuppressive therapy; Tumor immunology – Tumor antigens; Immune response to tumors and tumor evasion of the immune system, Cancer immunotherapy; Immunodeficiency-Primary immunodeficiencies, Acquired or secondary immunodeficiencies.

Texts/References

1. Kuby, RA Goldsby, Thomas J. Kindt, Barbara, A. Osborne Immunology, 6th Edition, Freeman, 2002.
2. Brostoff J, Seaddin JK, Male D, Roitt IM., Clinical Immunology, 6th Edition, Gower Medical Publishing, 2002.
3. Janeway et al., Immunobiology, 4th Edition, Current Biology publications., 1999.
4. Paul, Fundamental of Immunology, 4th edition, Lippencott Raven, 1999.

Lab on Biochemistry & Analytical Techniques - 3 Credits

1. To prepare an Acetic - Na Acetate Buffer system and validate the Henderson-Hasselbach equation.
2. To determine an unknown protein concentration by plotting a standard graph of BSA using UV-Vis Spectrophotometer and validating the Beer- Lambert's Law.
3. Titration of Amino Acids and separation of aliphatic, aromatic and polar amino acids by TLC.
4. AN ENZYME PURIFICATION THEME (such as *E.coli* Alkaline phosphatase or any enzyme of the institutions choice).

   (a) Preparation of cell-free lysates
   (b) Ammonium Sulfate precipitation
   (c) Ion-exchange Chromatography
   (d) Gel Filtration
   (e) Affinity Chromatography
   (f) Generating a Purification Table
   (g) Assessing purity by SDS-PAGE Gel Electrophoresis
   (h) Assessing purity by 2-D gel Electrophoresis
   (i) Enzyme Kinetic Parameters: Km, Vmax and Kcat.
5. Biophysical methods (Circular dichroism spectroscopy, fluorescence spectroscopy).
6. Determination of mass of small molecules and fragmentation patterns by Mass Spectrometry

Lab on Microbiology - 3 Credits

1. Sterilization, disinfection, safety in microbiological laboratory.
2. Preparation of media for growth of various microorganisms.
3. Identification and culturing of various microorganisms.
4. Staining and enumeration of microorganisms.
5. Growth curve, measure of bacterial population by turbidometry and studying the effect of temperature, pH, carbon and nitrogen.
6. Assay of antibiotics production and demonstration of antibiotic resistance.
7. Isolation and screening of industrially important microorganisms.
8. Determination of thermal death point and thermal death time of microorganisms.

Lab on Immunology - 2 Credits

1. Selection of animals, Preparation of antigens, Immunization and methods of bleeding, Serum separation, Storage.
2. Antibody titre by ELISA method.
3. Double diffusion, Immuno-electrophoresis and Radial Immuno diffusion.
4. Complement fixation test.
5. Isolation and purification of IgG from serum or IgY from chicken egg.
6. SDS-PAGE, Immunoblotting, Dot blot assays
7. Blood smear identification of leucocytes by Giemsa stain
8. Separation of leucocytes by dextran method
9. Demonstration of Phagocytosis of latex beads
10. Separation of mononuclear cells by Ficoll-Hypaque
11. Flowcytometry, identification of T cells and their subsets
12. Lymphoproliferation by mitogen / antigen induced
13. Lymphnode Immunohistochemistry (direct and indirect peroxidase assay)
14. Hybridoma technology and monoclonal antibody production.
15. Immunodiagnostics using commercial kits

Communication Skills

Process of communication

Concept of effective communication- Setting clear goals for communication; Determining outcomes and results; Initiating communication; Avoiding breakdowns while communicating; Creating value in conversation; Barriers to effective communication; Non verbal communication- Interpreting non verbal cues; Importance of body language, Power of effective listening; recognizing cultural differences

Presentation skills

Formal presentation skills; Preparing and presenting using Over Head Projector, Power Point; Defending Interrogation; Scientific poster preparation & presentation; Participating in group discussions

Technical Writing Skills

Types of reports; Layout of a formal report; Scientific writing skills: Importance of communicating Science; Problems while writing a scientific document; Plagiarism; Scientific Publication Writing: Elements of a Scientific paper including Abstract, Introduction, Materials & Methods, Results, Discussion, References; Drafting titles and framing abstracts

Computing Skills for Scientific Research

Web browsing for information search; search engines and their mechanism of searching; Hidden Web and its importance in Scientific research; Internet as a medium of interaction between scientists; Effective email strategy using the right tone and conciseness

Texts/References

1. Mohan Krishna and N.P. Singh, Speaking English effectively, Macmillan, 2003.

SEMESTER - II

Genetic Engineering - 3 Credits

Unit I

Basics Concepts

DNA Structure and properties; Restriction Enzymes; DNA ligase, Klenow enzyme, T4 DNA polymerase, Polynucleotide kinase, Alkaline phosphatase; Cohesive and blunt end ligation; Linkers; Adaptors; Homopolymeric tailing; Labeling of DNA: Nick translation, Random priming, Radioactive and non-radioactive probes, Hybridization techniques: Northern, Southern and Colony hybridization, Fluorescence in situ hybridization; Chromatin Immunoprecipitation; DNA-Protein Interactions-Electromobility shift assay; DNaseI footprinting; Methyl interference assay

Unit II

Cloning Vectors

Plasmids; Bacteriophages; M13 mp vectors; PUC19 and Bluescript vectors, Phagemids; Lambda vectors; Insertion and Replacement vectors; Cosmids; Artificial chromosome vectors (YACs; BACs); Animal Virus derived vectors-SV-40; vaccinia/bacculo & retroviral vectors; Expression vectors; pMal; GST; pET-can be omitted vectors; Protein purification; His-tag; GST-tag; MBP-tag etc.; Intein-based vectors; Inclusion bodies; Methodologies to reduce formation of inclusion bodies; Baculovirus and pichia vectors system, Plant based vectors, Ti and Ri as vectors, Yeast vectors, Shuttle vectors

Unit III

Cloning Methodologies

Insertion of Foreign DNA into Host Cells; Transformation; Construction of libraries; Isolation of mRNA and total RNA; cDNA and genomic libraries; cDNA and genomic cloning; Expression cloning; Jumping and hopping libraries; Southwestern and Far-western cloning; Protein-protein interactive cloning and Yeast two hybrid system; Phage display; Principles in maximizing gene expression

Unit IV

PCR and Its Applications

Primer design; Fidelity of thermostable enzymes; DNA polymerases; Types of PCR – multiplex, nested, reverse transcriptase, real time PCR, touchdown PCR, hot start PCR, colony PCR, cloning of PCR products; T-vectors; Proof reading enzymes; PCR in gene recombination; Deletion; addition; Overlap extension; and SOEing; Site specific mutagenesis; PCR in molecular diagnostics; Viral and bacterial detection; PCR based mutagenesis, Mutation detection: SSCP, DGGE, RFLP, Oligo Ligation Assay (OLA), MCC (Mismatch Chemical Cleavage, ASA (Allele-Specific Amplification), PTT (Protein Truncation Test)

Unit V

Sequencing methods; Enzymatic DNA sequencing; Chemical sequencing of DNA; Automated DNA sequencing; RNA sequencing; Chemical Synthesis of oligonucleotides; Introduction of DNA into mammalian

cells; Transfection techniques; Gene silencing techniques; Introduction to siRNA; siRNA technology; Micro RNA; Construction of siRNA vectors; Principle and application of gene silencing; Gene knockouts and Gene Therapy; Creation of knock out mice; Disease model; Somatic and germ-line therapy- in vivo and ex-vivo; Suicide gene therapy; Gene replacement; Gene targeting; Transgenics; cDNA and intragenic arrays; Differential gene expression and protein array.

Text/References

1. S.B. Primrose, R.M. Twyman and R.W.Old; Principles of Gene Manipulation. 6th Edition, S.B.University Press, 2001.
2. J. Sambrook and D.W. Russel; Molecular Cloning: A Laboratory Manual, Vols 1-3, CSHL, 2001.
3. Brown TA, Genomes, 3rd ed. Garland Science 2006
4. Selected papers from scientific journals.
5. Technical Literature from Stratagene, Promega, Novagen, New England Biolab etc.

Bioprocess Engineering & Technology - 3 Credits

Unit I

Principles of enzyme catalysis

Proteins as enzymes; Michaelis-Menten kinetics; Kinetics and Statistics; Inhibition; Effect of pH and temperature; Enzymology; Immobilized enzymes: methods, mass transfer considerations; Industrial enzymes

Unit II

Microbial growth

Introduction to metabolism; Nutrient transport; Glycolysis; TCA cycle and other pathways; Control of metabolism; Factors affecting microbial growth; Stoichiometry: mass balances; Stoichiometry: energy balances; Growth kinetics; Measurement of growth.

Unit III

Bioreactors

Introduction to bioreactors; Batch and Fed-batch bioreactors, Continuous bioreactors; Immobilized cells; Bioreactor operation; Sterilization; Aeration; Sensors; Instrumentation; Culture-specific design aspects: plant/ mammalian cell culture reactors.

Unit IV

Bioseparations

Biomass removal; Biomass disruption; Membrane-based techniques; Extraction; Adsorption and Chromatography

Unit V

Industrial Processes and Process economics

Description of industrial processes; Process flow sheeting; Process economics

Texts/References

1. Michael Shuler and Fikret Kargi, Bioprocess Engineering: Basic Concepts, 2nd Edition, Prentice Hall, Englewood Cliffs, NJ, 2002.
2. Pauline Doran, Bioprocess engineering principles, 1 Edition, Academic Press, 1995.
3. Colin Ratledge, Bjorn Kristiansen, Basic Biotechnology, 2nd Edition, Cambridge University Press, 2001.
4. Roger Harrison et al., Bioseparations Science and Engineering, Oxford University Press, 2003.

Biostatistics - 3 Credits

Unit I

Probability and Descriptive Statistics

Scientific notation: significant digits, rounding off, scientific notation, Error analysis; Counting and Probability: Addition rules; Permutations; Combinations; Inclusion-exclusion rule; Sampling with and without replacement; Conditional probability: Bayes' theorem; Independence; Descriptive statistics and Random variables; Measures of central tendency: mean, median, mode; Expectation; Measures of spread: range, percentile, standard deviation; Higher moments: kurtosis, skew, Displaying data: Histograms, stem-and-leaf plots, box plots, frequency distributions; Discrete random variables: Bernoulli, Binomial, Poisson; Geometric distributions; Continuous random variables: Normal; Exponential distributions; Standard normal distribution.

Unit II

Inferential statistics and one sample hypothesis testing

Samples and populations: Random, stratified and cluster sampling; Single- and Double-blind experiments; Point and interval estimates; Sampling distributions: *t*, chi-square, F distributions; Hypothesis testing: null and alternative hypotheses, decision criteria, critical values, type I and type II errors, Meaning of statistical significance; Power of a test; One sample hypothesis testing: Normally distributed data: *z*, *t* and chi-square tests; Binomial proportion testing.

Unit III

Multi-sample and nonparametric hypothesis testing

Two sample hypothesis testing; Nonparametric methods: signed rank test, rank sum test; Kruskal-Wallis test; Analysis of variance: One-way ANOVA.

Unit IV

Curve fitting

Regression and correlation: simple linear regression; Least squares method; Analysis of enzyme kinetic data; Michaelis-Menten; Lineweaver-Burk and the direct linear plot; Logistic Regression; Polynomial curve fitting.

Unit V

Design of Experiments

Single factor experiments; Randomized block design; Lackett-Burman Design; Comparison of *k* treatment means; Factorial designs; Blocking and confounding; Response surface methodology.

Texts/References

1. Bernard Rosner, Fundamentals of Biostatistics, 5th Edition, Thomson Brooks/Cole, 2000.
2. Richard A. Johnson, Probability and Statistics for Engineers, 6th Edition, Prentice Hall, 2000.
3. Morris H. DeGroot, Mark J. Schervish, Probability and Statistics, 3rd Rev. Edition, Addison-Wesley, 2002.
4. E. Kreyszig, Advanced Engineering Mathematics, 9th Edition, John Wiley, 2006.

Downstream Processing in Biotechnology - 3 Credits

Unit I

Biomass removal and disruption: Centrifugation; Sedimentation; Flocculation; Microfiltration; Sonication; Bead mills; Homogenizers; Chemical lysis; Enzymatic lysis

Unit II

Membrane based purification: Ultrafiltration ; Reverse osmosis; Dialysis ; Diafiltration ; Pervaporation; Perstraction

Unit III

Adsorption and chromatography: size, charge, shape, hydrophobic interactions, Biological affinity; Process configurations (packed bed, expanded bed, simulated moving beds)

Unit IV

Precipitation (Ammonium Sulfate, solvent); Electrophoresis(capillary); Crystallization; Extraction(solvent, aqueous two phase, super critical), Drying

Unit V

Case studies

Texts/References

1. E L V Harris and S. Angal, Protein Purification Methods, Ed. IRL Press at Oxford University Press, 1989.
2. P.A. Belter, E.L. Cussler and Wei-Shou Hu., Bioseparations-Downstream Processing for Biotechnology, Wiley-Interscience Publication, 1988.
3. J. E. Bailey and D. F. Ollis, Biochemical Engineering Fundamentals, 2nd Edition, Mc-Graw Hill, Inc., 1986.
4. R. K. Scopes, Berlin, Protein Purification: Principles and Practice, Springer, 1982.

IPR & Biosafety - 3 Credits

Unit I

Introduction to Intellectual Property

Types of IP: Patents, Trademarks, Copyright & Related Rights, Industrial Design, Traditional Knowledge, Geographical Indications, Protection of New GMOs; International framework for the protection of IP

IP as a factor in R&D; IPs of relevance to Biotechnology and few Case Studies; Introduction to History of GATT, WTO, WIPO and TRIPS

Unit II

Concept of 'prior art'

Invention in context of "prior art"; Patent databases; Searching International Databases; Country-wise patent searches (USPTO, EPO, India etc.); Analysis and report formation

Unit III

Basics of Patents

Types of patents; Indian Patent Act 1970; Recent Amendments; Filing of a patent application; Precautions before patenting-disclosure/non-disclosure; WIPO Treaties; Budapest Treaty; PCT and Implications; Role of a Country Patent Office; Procedure for filing a PCT application

Unit IV

Patent filing and Infringement

Patent application- forms and guidelines, fee structure, time frames; Types of patent applications: provisional and complete specifications; PCT and convention patent applications; International patenting-requirement, procedures and costs; Financial assistance for patenting-introduction to existing schemes; Publication of patents-gazette of India, status in Europe and US

Patenting by research students, lecturers and scientists-University/organizational rules in India and abroad, credit sharing by workers, financial incentives

Patent infringement- meaning, scope, litigation, case studies and examples

Unit V

Biosafety

Introduction; Historical Backround; Introduction to Biological Safety Cabinets; Primary Containment for Biohazards; Biosafety Levels; Biosafety Levels of Specific Microorganisms; Recommended Biosafety Levels for Infectious Agents and Infected Animals; Biosafety guidelines - Government of India; Definition of GMOs & LMOs; Roles of Institutional Biosafety Committee, RCGM, GEAC etc. for GMO applications in food and agriculture; Environmental release of GMOs; Risk Analysis; Risk Assessment; Risk management and communication; Overview of National Regulations and relevant International Agreements including Cartagena Protocol.

Important Links

http://www.w3.org/IPR/

http://www.wipo.int/portal/index.html.en

http://www.ipr.co.uk/IP_conventions/patent_cooperation_treaty.html

www.patentoffice.nic.in

www.iprlawindia.org/ - 31k - Cached - Similar page

http://www.cbd.int/biosafety/background.shtml

http://www.cdc.gov/OD/ohs/symp5/jyrtext.htm

http://web.princeton.edu/sites/ehs/biosafety/biosafetypage/section3.html

Lab on Genetic Engineering - 4 Credits

1. Isolation of genomic DNA from *Bacillus subtilis** genome.
2. PCR amplification of *scoC* gene and analysis by agarose gel electrophoresis
3. Preparation of plasmid, pET-28a from *E.coli* DH5α and gel analysis.
4. Restriction digestion of vector (gel analysis) and insert with NcoI and XhoI
5. a. Vector and Insert ligation

   b. Transformation in E.coli DH5α.
6. Plasmid isolation and confirming recombinant by PCR and RE digestion.
7. Transformation of recombinant plasmid in *E.coli* BL21 (DE3) strain.
8. Induction of ScoC protein with IPTG and analysis on SDS-PAGE
9. Purification of protein on Ni-NTA column and analysis of purification by SDS-PAGE
10. a. Random Primer labeling of scoC with Dig-11-dUTP

    b. Southern hybridization of *B. subtilis* genome with probe and non-radioactive detection.

*Any other bacterial strain can be used.

Lab on Downstream Processing - 4 Credits

1. Conventional filtration
2. Centrifugation in batch and continuous centrifuge
3. Cell disruption
4. Protein precipitation and its recovery
5. Ion-exchange chromatography
6. Membrane based filtration-ultra filtration in cross flow modules and micro filtration
7. Adsorption process in batch and continuous mode.

Applied Bioinformatics - 3 Credits

Unit I

Sequence-alignment related problems.

Sequence databases; Similarity matrices; Pairwise alignment; BLAST; Statistical significance of alignment; Sequence assembly; Multiple sequence alignment; Clustal; Phylogenetics: distance based approaches, maximum parsimony.

Unit II

Pattern analysis in sequences

Motif representation: consensus, regular expressions; PSSMs; Markov models; Regulatory sequence identification using Meme; Gene finding: composition based finding, sequence motif-based finding.

Units III and IV

Structure-related problems

Representation of molecular structures (DNA, mRNA, protein), secondary structures, domains and motifs; Structure classification (SCOP, CATH); Visualization software (Pymol, Rasmol etc.); Experimental determination of structures (X-ray crystallography, NMR); Structure databases; Secondary structure prediction; RNA structure prediction; Mfold; Protein structure prediction by comparative modelling approaches(homology modelling, threading); Ab initio structure prediction: force fields, backbone conformer generation by Monte Carlo approaches, side-chain packing; Energy minimization; Molecular dynamics; Rosetta; Structure comparison (DALI, VAST etc.); CASP; Protein-ligand docking; Computer-aided drug design (pharmacophore identification); QSAR; Protein-Protein interactions

Unit V

System-wide analyses

Transcriptomics: Microarray technology, expression profiles, data analysis; SAGE; Proteomics: 2D gel electrophoresis; Mass Spectrometry; Protein arrays; Metabolomics: 13C NMR based metabolic flux analysis

Texts/References

1. David W. Mount. Bioinformatics: Sequence and Genome Analysis 2nd Edition, CSHL Press, 2004.
2. A. Baxevanis and F. B. F. Ouellette, Bioinformatics: a practical guide to the analysis of genes and proteins, 2nd Edition, John Wiley, 2001.
3. Jonathan Pevsner, Bioinformatics and Functional Genomics, 1st Edition, Wiley-Liss, 2003.
4. P. E. Bourne and H. Weissig. Structural Bioinformatics. Wiley. 2003.
5. C. Branden and J. Tooze, Introduction to Protein Structure, 2nd Edition, Garland Publishing, 1999.

Bioprocess Plant Design - 3 Credits

Unit I

Introduction; General design information; Material and energy balance calculations; Process Flowsheeting.

Unit II

Scale up and scale down issues: Effect of scale on oxygenation, mixing, sterilization, pH, temperature, inoculum development, nutrient availability and supply; Bioreactor scale-up based on constant power consumption per volume, mixing time, impeller tip speed (shear), mass transfer coefficients.

Scale up of downstream processes: Adsorption (LUB method); Chromatography (constant resolution etc.); Filtration (constant resistance etc.); Centrifugation (equivalent times etc.); Extractors (geometry based rules).

Scale-down related aspects.

Unit III

Selection of bioprocess equipment (upstream and downstream); Specifications of bioprocess equipment; Mechanical design of reactors, heat transfer and mass transfer equipment; Design considerations for maintaining sterility of process streams and process equipment; Piping and instrumentation; Materials of construction for bioprocess plants.

Unit IV

Facility design aspects; Utility supply aspects; Equipment cleaning aspects; Culture cell banks; cGMP guidelines; Validation; Safety.

Unit V

Process economics; Case studies.

Texts/References

1. Robert H. Perry and Don W. Green (eds.), Perry's Chemical Engineers' Handbook, 7th Edition, McGraw Hill Book Co., 1997.
2. Michael Shuler and Fikret Kargi, Bioprocess Engineering: Basic Concepts, 2nd Edition, Prentice Hall, Englewood Cliffs, NJ, 2002.
3. Roger Harrison et al., Bioseparations Science and Engineering, Oxford University Press, 2003.
4. J. M. Coulson and J. F. Richardson (Eds.) R.K.Sinnott, Chemical Engineering Volume 6: An introduction to Chemical Engineering Design, 2nd Edition, Butterworth-Heinemann Ltd., UK. (Indian Edition: Asian Books Private Limited, New Delhi)
5. Max S. Peters and Klaus, D. Timmerhaus, Plant Design and Economics for Chemical Engineers, 4th Edition, McGrawHill Book Co., 1991.
6. M. V. Joshi and V.V.Mahajani, Process Equipment Design, 3rd Edition, Macmillan India Ltd., 2000.
7. Michael R. Ladisch, Bioseparations Engineering: Principles, Practice and Economics, 1st Edition, Wiley, 2001.
8. Relevant articles from Bioprocess journals.

Lab on Bioreactor Operations - 4 Credits

1. Microbial growth and product formation kinetics
2. Enzyme kinetics
3. Effects of inhibitor on microbial growth
4. Enzyme immobilization techniques
5. Bioconversion using immobilized enzyme preparation
6. Bioconversion in batch
7. Fedbatch and continuous bioreactors
8. Oxygen transfer studies in fermentation
9. Mixing and agitation in fermenters
10. RTD studies
11. Mass transfer in immobilized cell/enzyme reactor