Model Curriculum for
Postgraduate Degree Course
M.Sc. (Industrial Biotechnology)

June 2021

SCHOOL OF APPLIED SCIENCES AND TECHNOLOGY

GUJARAT TECHNOLOGICAL UNIVERSITY
AHMEDABAD-382424

PREFACE

Introduction

Promotion of Indian Biotechnology sector is high on policy agenda of Government of India. Biotechnology has also been recognized as one of the key priority sectors under 'Make in India', 'Skill India' and 'Startup India' initiatives of Government of India, as it is one of sectors expected to contribute towards enterprise creation, innovation and economic growth.

Gujarat Technological University (GTU) is a premier academic and research institution which has driven new ways of thinking since its 2007 founding, established by the Government of Gujarat vide Gujarat Act No. 20 of 2007. Today, GTU is an intellectual destination that draws inspired scholars to its campus, keeping GTU at the nexus of ideas that challenge and change the world. GTU has immensely contributed to the dynamism through various policies and initiatives, establishment of innovation clusters, academia-industry partnerships, increasing capabilities for technology development, etc. Keeping in mind requirement for trained manpower in various industries of Biotechnology, GTU initiated Post-Graduate Program, M.Sc. Industrial Biotechnology to select best students and train them to join research or industry workforce contributing significantly to biotechnology workforce.

Course work & Project

The course curriculum of M.Sc. Industrial Biotechnology aims to address mismatch between 'knowledge' gained by students and appropriate skill set required for technology development and implementation including present contemporary needs of economy.

Over the first three semesters, M.Sc. Students are required to do substantial amount of course work and Laboratory experiments along with industry visit. The fourth semester is devoted mostly to the Project work in collaboration with industry. The curriculum has been designed to provide all students with a general background in Biotechnology followed by more specific knowledge in the area of Industrial Biotechnology. Electives will be taken during the third semester which will provide specialized knowledge in the area of the individual interest.

Eligibility for Admission

Minimum 50% (45% for SC/ST/SEBC/EWS) or equivalent marks in the qualifying examinations:

B.Sc. or equivalent in Biotechnology, Biochemistry, Microbiology, Bioinformatics, Genetics, Molecular Biology OR any branch of Life Sciences.

Student Intake

30 per year

Fee Structure

12,500/- (Per Semester, As per GTU norms)

M.Sc. Industrial Biotechnology

S.No.	Title	Credits
	SEMESTER ONE	
1	Microbial Biochemistry	3
2	Industrial Microbiology	3
3	Genetic Engineering	3
4	Bioinformatics	3
5	Statistics	3
6	Industrial Visit	0
7	Laboratory I: Microbial Biochemistry	2
8	Laboratory II: Molecular Biology and Genetic Engineering	4
9	Laboratory III: Bioinformatics and Statistics	4
	TOTAL	25
	SEMESTER TWO	
1	Fermentation Technology	3
2	Downstream Processing	3
3	Enzyme Engineering	3
4	Immunotechnology	3
5	Bioentrepreneurship	2
6	Intellectual Property Rights, Biosafety and Bioethics	2
7	Laboratory IV: Fermentation Technology	4
8	Laboratory V: Downstream Processing	4
9	Laboratory VI: Enzyme Engineering	2
	TOTAL	26
	SEMESTER THREE	
1	Animal and Plant Biotechnology	3
2	Environmental Biotechnology	3
3	Biomanufacturing Principles and Practice	3
4	Metabolic Engineering	3
5	Elective	3
6	Seminar/Journal Club/ Communication Skills	2
7	Laboratory VII: Cell Culture	4
8	Laboratory VIII: Environmental Biotechnology	4
	TOTAL	25
	SEMESTER FOUR	
1	Project in Collaboration with Industry	22
2	Presentation of Project Completion	2
	TOTAL	24
	TOTAL CREDITS	**100**

Recommended Electives:

1. Advanced Biomanufacturing | 2. Computational Biology | 3. Fundamentals of Technology Transfer | 4. Introduction to Omics Technologies

Semester One

Microbial Biochemistry

Credits

3

Course Objectives

The objective of this course is to give an insight in applicability of microbial biochemistry in different fields of industry.

Student Learning Outcomes

On completion of this course, students should be able to:

- Discuss microbial signal transduction and homeostasis;
- Describe microbial genome;
- Describe mutation, mutagenesis, mutants and mutation analysis;
- Discuss molecular basis of mutations;
- Compare prokaryotic and eukaryotic genomes.

Unit I **Microbial diversity** 5 lectures	Structural/physiological/biochemical differences between different basic microbial cell types, Biochemical/microscopic/molecular methods used to differentiate between archae, eubacteria and eukaryotes, Estimation of microbial biodiversity, Diversity in some ecosystems.
Unit II **Introduction to biomolecules** 3 lectures	Sugars - mono, di, and polysaccharides with specific reference to glycogen, amylose and cellulose, glycosylation of other biomolecules - glycoproteins and glycolipids; amino acids – structure and functional group properties, peptides and covalent structure of proteins, nucleosides, nucleotides, nucleic acids - structure, a historical perspective leading up to proposition of DNA double helical structure.
Unit III **Microbial nutrition** 3 lectures	Microbial nutrition, Different types of culture medium, C/N/P balance and making of culture medium.
Unit IV **Cell membranes** 4 lectures	Outer membrane of Gram –ve bacteria and control of its synthesis (potential targets for drug design), Different types of transport within the cell.
Unit V **Bio-energetic principles** 4 lectures	Oxidation-reduction reactions, Electron carriers and cellular metabolism, High energy compounds and their role in microbial fermentation, Enzymes as catalysts.
Unit VI **Major catabolic pathways** 4 lectures	Glycolysis, Pentose Phosphate Pathway, Citric Acid cycle, Oxidative Phosphorylation; Cellular metabolites and interconnectivity in biochemical pathways, Respiration and electron transport.
Unit VII **Metabolic diversity** 5 lectures	Energy from oxidation of inorganic electron donors, Methanotrophy and methylotrophy, Nitrate and Sulfate reduction, Acetogenesis, Methanogenesis, Fermentations-energetics and redox constraints, Anaerobic respiration.
Unit VIII **Microbial photosynthesis** 4 lectures	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 IX
Microbial genetics
4 lectures

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

Unit X
Applications of genetic engineering
6 lectures

Vectors and Expression systems (only bacteria and fungi), Case studies in microbial derived products.

Recommended Textbooks and References:

1. M.T. Madigan and J.M. Martinko, (2006), *Brock Biology of Microorganisms*, 11th Ed, Pearson Prentice-Hall.
2. Voet, D., & Voet, J. G. (2016). *Biochemistry* (5th ed.). Hoboken, NJ: J. Wiley & Sons.

Industrial Microbiology

Credits
3

Course Objectives

The objectives of this course are-

- Equip students with theoretical and practical understanding of industrial microbiology;
- Encourage students to appreciate exploitation of microorganisms in industries as a viable alternative to use of chemicals to production of useful products.

Student Learning Outcomes

On completion of this course, students should be able to:

- Describe the main steps and processes used to produce biological products in industry;
- Discover new useful microorganisms and store them reliably for later use;
- Evaluate which molecular techniques are applicable to improve production.

Unit I
Characteristics of microbes
4 lectures

Introduction to Microbiology and Microbes, Morphology, Structure and Growth, Bacterial and other Microbial growth curves.

Unit II
Isolation of microbes from nature and screening of biological activities
4 lectures

Actinomycetes, Bacteria, Fungi, Developing and Semi-automating Screening Tests.

Unit III
Culture preservation and inoculum development
4 lectures

Culture Preservation, Cryopreservation, Inoculum Development.

Unit IV
Small scale liquid fermentation
5 lectures

Introduction and Scope, Fermentation Vessels, Shakers, Media /Composition and Gas Exchange, Sampling and Analysis.

Unit V
Small scale solid state fermentation
4 lectures

Advantages/Disadvantages of Solid State Fermentation, Growth and Production of Enzymes, Small Scale Process Control.

Unit VI
Experimental designs for improvement of fermentation
4 lectures

Sequential Nature of Design Experiments, Screening Designs, Optimization Designs and Verification of Models.

Unit VII
Cell and enzyme immobilization
4 lectures

Different types of Immobilizations (entrapment, cross linking, covalent *etc.*), Performance and case studies.

Unit VIII
Strain improvements by recombinant and non-recombinant methods
5 lectures

Recombinant Methods, Non recombinant (Mutagenesis, fusion, recombination *etc.*), Operational Conditions, Statistical analysis.

Unit IX
Culture and analysis using gel microdrops
4 lectures

GMD's for Culture and Assays, Open GMD's, Closed GMD's.

Unit X
Culture of extremophiles
4 lectures

Culture strategies and Challenges, Preservation, Batch and Continuous cultivation *etc.*

Recommended Textbooks and References:

1. M.T. Madigan and J.M. Martinko, (2006), *Brock Biology of Microorganisms*, 11th Ed, Pearson Prentice-Hall.
2. J. M. Willey, L. Sherwood, C.J. Woolverton, L.M. Prescott, (2011), *Prescott's Microbiology*, McGraw Hill, New-york.
3. A.L. Demain and J. Davies, (2004), *Manual of Industrial Microbiology and Biotechnology*, 2nd Ed.ASM Press.

Genetic Engineering

Credits
3

Course Objectives

The objectives of this course are to teach various approaches to conducting genetic engineering and its applications in biological research as well as in biotechnology industries.

Student Learning Outcomes

Given the impact of genetic engineering in modern society, students should be endowed with strong theoretical knowledge of this technology. In conjunction with the practicals in molecular biology & genetic engineering, the students should be able to take up biological research as well as placement in the relevant biotech industry.

Unit I
Introduction and tools for genetic engineering
6 lectures

Impact of genetic engineering in modern society; general requirements for performing a genetic engineering experiment; restriction endonucleases and methylases; DNA ligase, Klenow enzyme, T4 DNA polymerase, polynucleotide kinase, alkaline phosphatase; cohesive and blunt end ligation; linkers; adaptors; homopolymer tailing; labelling of DNA: nick translation, random priming, radioactive and non-radioactive probes,

hybridization techniques: northern, southern, south-western and far-western and colony hybridization, fluorescence *in situ* hybridization.

Unit II
Different types of vectors
7 lectures

Plasmids; Bacteriophages; M13mp vectors; pUC19 and pBluescript vectors, phagemids; Lambda vectors; Insertion and Replacement vectors; Cosmids; Artificial chromosome vectors (YACs; BACs); Principles for maximizing gene expression vectors; pMal; GST; pET-based vectors; Protein purification; His-tag; GST-tag; MBP-tag *etc.*; Intein-based vectors; Inclusion bodies; methodologies to reduce formation of inclusion bodies; mammalian expression and replicating vectors; Baculovirus and *Pichia* vectors system, plant based vectors, Ti and Ri as vectors, yeast vectors, shuttle vectors.

Unit III
Different types of PCR techniques
7 lectures

Principles of PCR: primer design; fidelity of thermostable enzymes; DNA polymerases; types of PCR – multiplex, nested; reverse-transcription PCR, real time PCR, touchdown PCR, hot start PCR, colony PCR, asymmetric PCR, cloning of PCR products; TA cloning vectors; proof reading enzymes; PCR based site specific mutagenesis; PCR in molecular diagnostics; viral and bacterial detection; sequencing methods; enzymatic DNA sequencing; chemical sequencing of DNA; automated DNA sequencing; RNA sequencing; chemical synthesis of oligonucleotides; mutation detection: SSCP, DGGE, RFLP.

Unit IV
cDNA analysis
7 lectures

Insertion of foreign DNA into host cells; transformation, electroporation, transfection; construction of libraries; isolation of mRNA and total RNA; reverse transcriptase and cDNA synthesis; cDNA and genomic libraries; construction of microarrays – genomic arrays, cDNA arrays and oligo arrays; study of protein-DNA interactions: electrophoretic mobility shift assay; DNase footprinting; methyl interference assay, chromatin immunoprecipitation; protein-protein interactions using yeast two-hybrid system; phage display.

Unit V
Gene silencing and genome editing technologies
13 lectures

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 transgenic plants; debate over GM crops; introduction to methods of genetic manipulation in different model systems *e.g.* fruit flies (*Drosophila*), worms (*C. elegans*), frogs (*Xenopus*), fish (zebra fish) and chick; Transgenics - gene replacement; gene targeting; creation of transgenic and knock-out mice; disease model; introduction to genome editing by CRISPR-CAS with specific emphasis on Chinese and American clinical trials; Cloning genomic targets into CRISPR/Cas9 plasmids; electroporation of Cas9 plasmids into cells; purification of DNA from Cas9 treated cells and evaluation of Cas9 gene editing; *in vitro* synthesis of single guide RNA (sgRNA); using Cas9/sgRNA complexes to test for activity on DNA substrates; evaluate Cas9 activity by T7E1 assays and DNA sequence analysis; Applications of CRISPR/cas9 technology. Applications gene therapy/gene editing - antiviral strategies, cancer immunotherapy, hematologic disorders, liver-targeted gene editing, neuromuscular disorders, ocular disorders *etc.*, examples of Chinese and American clinical trials.

Recommended Textbooks and References:

1. Old, R. W., Primrose, S. B., & Twyman, R. M. (2001). *Principles of Gene Manipulation and Genomics*, 7th Edition: Oxford: Blackwell Scientific Publications.
2. Green, M. R., & Sambrook, J. (2012). *Molecular Cloning: a Laboratory Manual.* Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press.
3. Brown, T. A. (2006). *Genomes* (3rd ed.). New York: Garland Science Pub.
4. Selected Papers from Scientific Journals, particularly Nature & Science.
5. Technical Literature from Stratagene, Promega, Novagen, New England Biolabs

Statistics

Credits

3

Course Objectives

The objective of this course is to introduce students to statistical methods and to understand underlying principles, as well as practical guidelines of "how to do it" and "how to interpret it" statistical data.

Student Learning Outcomes

On completion of this course, students should be able to:

- Understand how to summarise statistical data;
- Apply appropriate statistical tests based on an understanding of the study question, type of study and type of data;
- Interpret results of statistical tests.

Unit I
Introduction
5 lectures

Types of biological data (ordinal scale, nominal scale, continuous and discrete data), frequency distribution and graphical representations (bar graph, histogram, box plot and frequency polygon), cumulative frequency distribution, populations, samples, simple random, stratified and systematic sampling.

Unit II
Descriptive statistics
5 lectures

Measures of Location, Properties of Arithmetic Mean, median, mode, range, Properties of Variance and Standard Deviation, Coefficient of Variation, Grouped Data, Graphic Methods, Obtaining Descriptive Statistics on Computer, Case study.

Unit III
Probability and distribution
4 lectures

Introduction to probability and laws of probability, Random Events, Events-exhaustive, Mutually exclusive and equally likely (with simple exercises), Definition and properties of binomial distribution, poisson distribution and normal distribution.

Unit IV
Correlation and regression analysis
6 lectures

Correlation, Covariance, calculation of covariance and correlation, Correlation coefficient from ungrouped data Spearson's Rank Correlation Coefficient, scatter and dot diagram, General Concepts of regression, Fitting Regression Lines, regression coefficient, properties of Regression Coefficients, Standard error of estimate.

Unit V
Statistical hypothesis testing
4 lectures

Making assumption, Null and alternate hypothesis, error in hypothesis testing, confidence interval, one-tailed and two-tailed testing, decision making.

Unit VI
Tests of significance
8 lectures

Steps in testing statistical significance, selection and computation of test of significance and interpretation of results; Sampling distribution of mean and standard error, Large sample tests (test for an assumed mean and equality of two population means with known S.D.), z-test; Small sample tests (t-test for an assumed mean and equality of means of two populations when sample observations are independent); Parametric and Non parametric tests (Mann-Whitney test); paired and unpaired t-test, chi square test.

Unit VII
Experimental designs
8 lectures

Introduction to study designs: Longitudinal, cross-sectional, retrospective and prospective study, Principles of experimental designs, Randomized block, and Simple factorial designs, Analysis of variance (ANOVA) and its use in analysis of RBD, introduction to meta-analysis and systematic reviews, ethics in statistics.

Recommended Textbooks and References:

1. Jaype Brothers, (2011), *Methods in Biostatistics for Medical Students and Research Workers* (English), 7th Edition
2. Norman T.J. Bailey, (1995), *Statistical Methods in Biology,* 3rd Edition,

Cambridge University Press.
3. P. N. Arora and P. K. Malhan, (2006), *Biostatistics,* 2nd Edition, Himalaya Publishing House.
4. Jerold Zar, *Biostatistical Analysis,* 4th Edition. Pearson Education.
5. *Biostatistics: A Foundation for Analysis in the Health Sciences*, 7th Edition, Wiley.
6. ML Samuels, JA Witmer (2003) *Statistics for the Life Sciences,* 3rd edition. Prentice Hall.

Bioinformatics

Credits

3

Course Objectives

The objectives of this course are to provide students with theory and practical experience of use of common computational tools and databases which facilitate investigation of molecular biology and evolution-related concepts.

Student Learning Outcomes

Student should be able to:

- Develop an understanding of basic theory of these computational tools.
- Gain working knowledge of these computational tools and methods.
- Appreciate their relevance for investigating specific contemporary biological questions.

Unit I
Biological databases
5 lectures

Introduction, Primary & Secondary database, Sequence file formats, Introduction to structures, Protein Data Bank (PDb), Molecular Modelling Database (MMDb), Structure file formats, Visualizing structural information, Database of structure viewers, Collection of sequences, sequence annotation, sequence description.

Unit II
Sequence alignment and database searching
5 lectures

Evolutionary basis of sequence alignment, Optimal alignment methods, Substitution scores & gap penalties, Statistical significance of alignments, Database similarity searching, FASTA, BLAST, Low complexity regions, Repetitive elements, Multiple Sequence Alignment: Progressive alignment methods, Motifs and patterns, Clustral, Muscle; Scoring matrices, Distance matrices.

Unit III
Phylogenetic analysis
5 lectures

Alignment, tree building and tree evaluation, Comparison and application of Unweighted Pair Group Method with Arithmetic Mean (UPGMA), Neighbour Joining (NJ), Maximum Parsimony (MP), Maximum Likelihood (ML) methods, Bootstrapping, Jackknife; Software for Phylogenetic analysis. DNA barcoding: Methods tools and databases for barcoding across all species, Applications and limitations of barcoding, Consortium for Barcode of Life (CBOL) recommendations, Barcode of Life Database (BOLD).

Unit IV
Structural biology
5 lectures

3-D structure visualization and simulation, Basic concepts in molecular modeling: different types of computer representations of molecules; External coordinates and Internal Coordinates, Molecular Mechanics, Force fields *etc.* Secondary structure elucidation using Peptide bond, phi, psi and chi torsion angles, Ramachandran map, anatomy of proteins – Hierarchical organization of protein structure –like CATH (class, architecture, topology, homology), SCOP (Structural Classification of Proteins), FSSP (families of structurally similar proteins).

Unit V
Classification and comparison of 3D structures
5 lectures

DNA & RNA secondary and tertiary structures, t-RNA tertiary structure; Protein Secondary structure prediction: Algorithms viz. Chou Fasman, GOR methods, Tertiary Structure prediction: Fundamentals of the methods for 3D structure prediction (sequence similarity/identity of target proteins of known structure, fundamental principles of protein folding *etc.*) Homology/comparative modeling, fold recognition, threading approaches, and ab initio structure prediction methods; CASP (Critical Assessment of protein Structure Prediction); Computational design of promoters, proteins & enzymes.

Unit VI
Applications in drug design
5 lectures

Chemical databases like NCI/PUBCHEM; Fundamentals of Receptor-ligand interactions; Structure-based drug design: Identification and Analysis of Binding sites and virtual screening; Ligand based drug design: Structure Activity Relationship – QSARs & Pharmacophore; *In silico* predictions of drug activity and ADMET.

Unit VII
Analysis of microarray data
5 lectures

Designing of oligo probes; Image processing and normalization; Microarray data variability (measurement ad quantification); Analysis of differentially expressed genes; Experimental designs.

Unit VIII
Biological algorithms
2 lectures

Comparison with computer algorithms, string structures, Introduction to programming in computational biology through C/ Perl / Java.

Unit IX
Systems biology
3 lectures

System-level understanding of biological systems, use and integration of data from transcriptomics, proteomics and metabolomics; concepts in glycomics, interactomics and fluxomics.

Recommended Textbooks and References:

1. A.D. Baxevanis and B.F.F. Ouellette (Eds). (2002), *Bioinformatics: a Practical Guide to the Analysis of Genes and Proteins*, John Wiley and Sons.
2. D.W. Mount, (2001), *Bioinformatics: Sequence and Genome Analysis*, Cold Spring Harbor Laboratory Press.
3. Jones & Peuzner, (2004); *Introduction to Bioinformatics Algorithms*; Ane Books, India.
4. Dov Stekel, (2003); *Microarray Bioinformatics*; Cambridge University Press.
5. Web-resources and suggested reviews/ research papers.

Laboratory I: Microbial Biochemistry

Credits 2

Course Objectives

The objective of this laboratory course is to learn how to handle cells, culture them, prepare mutants, do biochemical analysis of proteins, primary and secondary metabolites.

Student Learning Outcomes

On completion of this course, students should be able to:

- Isolate, characterize, and classify microorganisms;
- Discuss microbial signal transduction and homeostasis;
- Identify various microbes;
- Estimate amount of various biochemical contents in the microbes.

Syllabus

1. Identify Bacteria, Yeasts, Filamentous fungi, Actinomycetes by Microscopy, Cultivate Bacteria and Other Microbes in Liquid Culture and Solid Media
2. Isolation of Pure Cultures by Streaking
3. Isolation of Auxotropic Mutants of Bacteria, Replica Plating
4. Antimicrobial Sensitivity and Demonstration of Drug Resistance
5. Estimation of Lipids
6. Estimation of Carbohydrates
7. Estimation of Proteins (Bradford, Lowry's Method)
8. Estimation of alcohol, Acetic Acid by Gas chromatography
9. Isolation of Carotenoids (and lipids) and Analysis by Thin Layer Chromatography (TLC)
10. Isolation of Secondary Metabolites and analysis by TLC
11. Maintenance of Stock Cultures: slants, stabs, glycerol stocks.

Recommended Textbooks and References:

1. Cappuccino JG and Welsh C (2016) *Microbiology: a Lab Manual.* Benjamin Cummins Publishing Co.
2. Plummer DT (1971). *An Introduction to Practical Biochemistry*. McGraw-Hill, NY

Laboratory II: Molecular Biology and Genetic Engineering

Credits

4

Course Objectives

The objectives of this course are to provide students with the experimental knowledge of molecular biology and genetic engineering.

Student Learning Outcomes

Students should be able to gain hands-on experience on gene cloning, protein expression and purification. This experience would enable them to begin a career in industry.

Syllabus

1. Concept of lac-operon:
   a) lactose induction of β-galactosidase.
   b) Glucose Repression.
   c) Diauxic growth curve of *E. coli*.
2. UV mutagenesis to isolate amino acid auxotroph.
3. Phage titre with λ phage/M13.
4. Genetic Transfer-Conjugation, gene mapping.
5. Plasmid DNA isolation and DNA quantitation.
6. Restriction Enzyme digestion of plasmid DNA.
7. Agarose gel electrophoresis.
8. Polymerase Chain reaction.
9. DNA Ligation.
10. Preparation of competent cells.
11. Transformation of *E.coli* with standard plasmids, Calculation of transformation efficiency.
12. Confirmation of the insert by Colony PCR and Restriction mapping
13. Expression of recombinant protein, concept of soluble proteins and inclusion body formation in *E.coli,* SDS-PAGE analysis
14. Purification of His-Tagged protein on Ni-NTA columns
    a) Random Primer labeling
    b) Southern hybridization.

Recommended Textbooks and References:

1. Green, M. R., & Sambrook, J. (2012). *Molecular Cloning: a Laboratory Manual.* Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press.

Laboratory III: Bioinformatics and Statistics

Credits

4

Course Objectives

The aim is to provide practical training in bioinformatics and statistical methods including accessing major public sequence databases.

Student Learning Outcomes

On completion of this course, students should be able to:

- Describe contents and properties of important bioinformatics databases, perform text- and sequence-based searches and analyse and discuss results in light of molecular biological knowledge;
- Explain major steps in pairwise and multiple sequence alignment, explain its principles and execute pairwise sequence alignment by dynamic programming;
- Predict secondary and tertiary structures of protein sequences;
- Perform and analyse various statistical tools available to analyse data.

Syllabus

1. Using NCBI and Uniprot web resources.
2. Introduction and use of various genome databases.
3. Sequence information resource: Using NCBI, EMBL, Genbank, Entrez, Swissprot/ TrEMBL, UniProt.
4. Similarity searches using tools like BLAST and interpretation of results.
5. Multiple sequence alignment using ClustalW.
6. Phylogenetic analysis of protein and nucleotide sequences.
7. Use of gene prediction methods (GRAIL, Genscan, Glimmer).
8. Using RNA structure prediction tools.
9. Use of various primer designing and restriction site prediction tools.
10. Use of different protein structure prediction databases (PDB, SCOP, CATH).
11. Construction and study of protein structures using Deepview/PyMol.
12. Homology modelling of proteins.
13. Use of tools for mutation and analysis of energy minimization of protein structures.
14. Use of miRNA prediction, designing and target prediction tools.
15. Use of Statistical packages like SPSS (Statistical Package for Social Sciences)/ SAS (Statistical Analysis System) & Maple.
16. MATLAB (Matrix Laboratory).
17. Performing various statistical analysis like T-test, ANOVA, Regression, Chi-square, PLS (Partial Least Squares) and PCA (Principle Component Analysis).

Semester Two

Fermentation Technology

Credits

3

Course Objectives

This course provides an understanding of exploitation of microorganisms and other cell lines in manufacture of therapeutic, diagnostic and bulk commodity biological products.

Student Learning Outcomes

On successful completion of this course, students should able to:

- Gain understanding of variety of fermentation and subsequent processing approaches available for manufacture of biological products and design and operation of these systems;
- Appreciate regulatory framework of biopharmaceutical industry.

Unit I
Reaction engineering
5 lectures

Homogeneous reactions Basic reaction theory, calculation of reaction rates, general reaction kinetics for biological systems, yields in cell culture, cell growth kinetics, production kinetics, kinetics of cell death; Continuous stirred tank reactor as a tool for calculating kinetic parameters of growth and product formation; Concept of maintenance and calculation of maintenance coefficient.

Unit II
Process initialization
5 lectures

Types of sterilization, thermal death kinetics of microorganism; Heat sterilization of liquid medium in batch and continuous mode; Air sterilization; Inoculum development; Various types of fermentation, submerged and solid state fermentation, aerobic and anaerobic fermentation; Overview of biosynthetic mechanisms; Metabolic stoichiometry.

Unit III
Reactor engineering
5 lectures

Bioreactor configurations, practical considerations for bioreactor construction, monitoring and control of bioreactors, ideal reactor operations, batch operation of a mixed reactor.

Unit IV
Bioprocess scale up
5 lectures

Heat and mass transfer issues in bioreactors, Estimation of KLa, Scale up with constant parameters like oxygen transfer rate, mixing, shear stress, flow regime, Reactor volume, *etc.* Scale-up methods by currently used rules-of-thumb *viz.* constant P/V, kLa, Various approaches to scale-up including regime analysis and scale-down; Analysis of alternate bioreactor configurations including cell-recycle, air-lift and immobilized-cell bioreactors, Problems on scale-up methods.

Unit V
Commercial product processing
5 lectures

Bulk organics (ethanol), Biomass (Bakers Yeast), Organic acids (Citric Acid), Amino Acids (L-Lysine), Microbial Transformations (Steroids), Antibiotics (Penicillin), Extra Cellular Polysaccharides (Xanthan Gum), Nucleotides (5-GMP), Vitamins (B12), Pigments (Shikonin).

Unit VI
Process technology
5 lectures

Production of cell biomass and some primary metabolites, *e.g.* ethanol, acetone-butanol, citric acid, dextran and amino acids; Microbial production of industrial enzymes-glucose isomerase, cellulase & lipases.

Unit VII
Bioconversions
5 lectures

Applications of bioconversion, transformation of steroids and sterols; Transformation of non-steroidal compounds, antibiotics and pesticides; Bioenergy-fuel from biomass, production and economics of biofuels.

Unit VIII
Biosafety and Biosecurity
5 lectures

Biological Risk Assessment, Laboratory Biosafety Level 1 to 4, Animal Biosafety for recombinant research, Biosecurity, development of biosecurity program, Containment for biohazards.

Recommended Textbooks and References:

1. M. L. Schuler, F. Kargi & M. DeLisa, (2017), *Bioprocess Engineering - Basic Concepts*, 3rd Ed., Prentice Hall.
2. Pauline M. Doran, (2012), *Bioprocess Engineering Principles*, 2nd Edition Academic Press.
3. C. Ratledge & B. Kristiansen, (2008). *Basic Biotechnology*, 3rd Ed., Cambridge University Press.
4. Peter F. Stanbury, Stephen J. Hall & A. Whitaker, (2007), *Principles of Fermentation Technology,* Elsevier India Pvt Ltd.

Downstream Processing

Credits

3

Course Objectives

The objective of this course is to provide an overview of various aspects of recovery and processing of biological products.

Student Learning Outcomes

Students should be able to identify and design relevant unit operations for recovery of biological products.

Unit I

Screening and design purification strategies

5 lectures

Overview of down-stream processing, Establishment of design space for biopharmaceutical process, High-throughput process development, Media selection in ion-exchange chromatography in single microplate, high-throughput screening of dye-ligand for chromatography.

Unit II

Low-resolution protein purification methods

7 lectures

Aqueous two phase partitioning systems, A platform for isolation of process related impurities from therapeutic proteins, Simultaneous purification refolding of protein by affinity precipitation and macro (Affinity ligand)-facilitated three-phase partitioning (MLFTPP), Co-expression and co-purification of antigen-antibody complexes in bacterial cytoplasm and periplasm, immunoglobulin purification by caprylic acid; Filtration, chromatography (comparison), rationale of choosing between quality and cost of different products.

Unit III

Protein purification and characterization

6 lectures

Introduction, initial recovery of proteins, removal of whole cells and cell debris, concentration and primary purification, protein inactivation and stabilization, protein characterization.

Unit IV

Large scale protein purification

3 lectures

Some general principles, range and medical significance of impurities potentially present in protein based therapeutic products, labeling and packing of finished products.

Unit V

Animal based products

4 lectures

General DSP, Case studies of: monoclonal antibodies, Tissue plasminogen activator, insulin, erythropoietin.

Unit VI

Plant based products

3 lectures

General DSP, Case studies of: shikonin, Protein extracts from Seed material and green tissues.

Unit VII

Microbial based products

3 lectures

General DSP, Case studies of: lipase, cellulose, amylase, horse radish peroxidase, subtilisin, ethanol, citric acid, xanthan gum.

Recommended Textbooks and References:

1. Nikolaos E. Labrou, (2014), *Protein Downstream Processing: Design, Development and Application of High and Low Resolution Methods in Molecular Biology*, Springer protocols, Humana Press.
2. Gary Walsh, (2002), *Proteins: Biochemistry and Biotechnology,* 2nd Edition, Wiley Blackwell.

Enzyme Engineering

Credits

3

Course Objectives

This course will enable students to understand concepts in enzymology and enzyme techniques.

Student Learning Outcomes

On completion of this course, students should be able to:

- Gain clear understanding in isolation, purification and characterization of enzymes;
- Understand enzyme engineering technologies.

Unit I
Introduction to enzymes
4 lectures

What are enzymes, Brief history of enzymes, Nomenclature and classification of enzymes, Properties of enzymes, Structure of enzymes, Active site of enzymes, Factors influencing enzyme activity, Enzyme assays.

Unit II
Specificity and mechanism of enzyme action
6 lectures

Types of specificity, Koshland "induced fit" hypothesis, Strain or transition – state stabilization hypothesis; Mechanism of catalysis, Mechanism of reaction catalyzed by enzyme without cofactors, Metal-activated enzyme and metalloenzyme, Coenzymes in enzyme catalyzed reactions.

Unit III
Enzyme kinetics
5 lectures

Kinetics of enzyme-catalyzed reaction, Methods for investigating kinetics of enzyme-catalyzed reactions, Interpretation of Km, Vmax, Turnover number and Kcat, Specific activity of enzymes, Enzyme units, Inhibition of enzyme activity, Regulation of enzyme activity.

Unit IV
Immobilization of enzymes
4 lectures

Concept, Methods of immobilization, Kinetics of immobilized enzymes, Effects of immobilization on enzymes, Use of immobilized enzymes, Bioreactors using immobilized enzyme.

Unit V
Industrial applications of enzymes
4 lectures

Industrial enzymes: Sales value of industrial enzymes, Traditional (non-recombinant) sources of industrial enzymes, Impact of genetic engineering on enzyme production, Engineered enzymes, Extremophiles: hyperthermophiles, Enzymes from hyperthermophiles, Enzymes from additional extremophiles, Enzymes in organic solvents.

Unit VI
Industrial enzymes
6 lectures

Proteases and Carbohydrases, Proteolytic enzymes: Carbohydrases, Lignocellulose degrading enzymes, Pectin and Pectic enzymes.

Unit VII
Additional industrial enzymes
5 lectures

Lipases, Penicillin acylase, Amino acylase and Amino acid production, Cyclodextrins and cyclodextrin glycosyl transferase, Enzymes in animal nutrition, Enzymes in molecular biology; Clinical applications of enzymes.

Unit VIII
Enzyme Engineering
5 lectures

Prediction of enzyme structure, Design and construction of novel enzymes.

Recommended Textbooks and References:

1. T. Palmer and P.L. Bonner, (2007), *Enzymes: Biochemistry, Biotechnology and Clinical Chemistry*, Woodhead publishing limited.

2. N.C. Price and L. Stevens, (2002), *Fundamentals of Enzymology*, Oxford University Press.
3. Wolfgang Aehle, (2004), *Enzymes in Industry: Production and Applications* (Ed.) Wiley-VCH Verlag GmbH & Co. KGaA.
4. Branden and Tooze, (1999), *Introduction to Proteins Structure*, Garland Publishing Group
5. Gary Walsh, (2014), *Proteins: Biochemistry and Biotechnology*, John Wiley & Sons Ltd.

Immuno-technology

Credits

3

Course Objectives

The objectives of this course are to learn about structural features of components of immune system as well as their function. The major emphasis of this course will be on development of immune system and mechanisms by which our body elicit the immune response. This will be imperative for students as it will help them to think like an immunologist and predict about nature of immune response that develops against bacterial, viral or parasitic infection, and prove it by designing new experiments.

Student Learning Outcomes

On completion of this course, students should be able to:

- Evaluate the usefulness of immunology in different pharmaceutical companies;
- Identify the proper research lab working in the area of their own interests;
- Apply their knowledge and design immunological experiments to demonstrate innate, humoral or cytotoxic T lymphocyte responses and figure out the kind of immune responses in the setting of infection (viral or bacterial) by looking at cytokine profile.

Unit I

Lymphocyte maturation and cell-mediated immune response

9 lectures

Components of innate and acquired immunity; Important organs and cells of immune responses, complement and inflammatory responses; pathogen recognition receptors (PRR) and pathogen associated molecular pattern (PAMP); innate immune response; mucosal immunity; antigens - immunogens, haptens; Major histocompatibility complex (MHC) genes, Role of MHC in infectious diseases and disease susceptibility, HLA typing; Immunoglobulins-basic structure, classes & subclasses of immunoglobulins, antigenic determinants; multigene organization of immunoglobulin genes; B-cell receptor; Immunoglobulin superfamily; principles of cell signaling; 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.

Unit II

Antigen-antibody interactions

8 lectures

Precipitation, agglutination and complement mediated immune reactions; advanced immunological techniques - RIA, ELISA, Western blotting, T cell epitope prediction and 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, Hybridoma and monoclonal antibodies, Applications of monoclonal antibodies; HLA-tetramer complex, Application of HLA-tetramer complex in analyzing antigen/peptide –specific T cell responses using flow cytometer.

Unit III

Vaccinology

7 lectures

Active and passive immunization; live, killed, attenuated, subunit vaccines; vaccine technology- role and properties of adjuvants, recombinant DNA and protein based vaccines, reverse vaccinology; peptide vaccines, conjugate vaccines; antibody genes and antibody engineering- chimeric, hybrid monoclonal antibodies; catalytic antibodies and

generation of immunoglobulin gene libraries, idiotypic vaccines and marker vaccines, viral-like particles (VLPs), dendritic cell based vaccines, vaccine against cancer, T cell based vaccine, edible vaccine and therapeutic vaccine; Success stories in vaccinology *e.g.* Hepatitis, Polio, Small pox, DPT.

Unit IV

Clinical immunology

10 lectures

Immunity to infection: bacteria, viral, fungal and parasitic infections (Tuberculosis, HIV/AIDS, Schistosomiasis, Kala Azar, Chickungunya, Dengue); hypersensitivity reactions–Type I-IV; autoimmunity; types of autoimmune diseases; mechanism and role of CD4+ T cells; MHC and TCR in autoimmunity; 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, anaphylactic shock; immunosenescence: a challenge for an aging population; Immune exhaustion in the setting of chronic infections and malignancies; chronic Inflammation (Inflammaging) and immune activation; mucosal immunity and Gut Associated Lymphoid Tissue (GALT) in various gastrointestinal (GI) infections; complement deficiencies and human health;role of regulatory B cells (Bregs) in human disease. Monoclonal antibodies and their therapeutic role in reversing T cell functionality, Fab, F(ab)2 fragments; single-chain variable fragment (scFv), A trifunctional antibody; Bi-specific T-cell engagers (BiTEs) as artificial bispecific monoclonal antibodies for the use as anti-cancer drug.

Recommended Textbooks and References:

1. Kindt, T. J., Goldsby, R. A., Osborne, B. A., & Kuby, J. (2006). *Kuby Immunology*. New York: W.H. Freeman.
2. Brostoff, J., Seaddin, J. K., Male, D., & Roitt, I. M. (2002). *Clinical Immunology.* London: Gower Medical Pub.
3. Murphy, K., Travers, P., Walport, M., & Janeway, C. (2012). *Janeway's Immunobiology.* New York: Garland Science.
4. Paul, W. E. (1993). *Fundamental Immunology.* New York: Raven Press.

Bioentrepreneurship

Credits

3

Course Objectives

Research and business belong together and both are needed. In a rapidly developing life science industry, there is an urgent need for people who combine business knowledge with the understanding of science & technology. Bio-entrepreneurship, an interdisciplinary course, revolves around the central theme of how to manage and develop life science companies and projects. The objectives of this course are to teach students about concepts of entrepreneurship including identifying a winning business opportunity, gathering funding and launching a business, growing and nurturing the organization and harvesting the rewards.

Student Learning Outcomes

Students should be able to gain entrepreneurial skills, understand the various operations involved in venture creation, identify scope for entrepreneurship in biosciences and utilize the schemes promoted through knowledge centres and various agencies. The knowledge pertaining to management should also help students to be able to build up a strong network within the industry.

Unit I

Innovation and entrepreneurship in bio-business

8 lectures

Introduction and scope in Bio-entrepreneurship, Types of bio-industries and competitive dynamics between the sub-industries of the bio-sector (*e.g.* pharmaceuticals *vs.* Industrial biotech), Strategy and operations of bio-sector firms: Factors shaping opportunities for innovation and entrepreneurship in bio-sectors, and the business implications of those opportunities, Alternatives faced by emerging bio-firms and the relevant tools for strategic decision, Entrepreneurship development programs of public and private agencies (MSME, DBT, BIRAC, Make In India), strategic dimensions of patenting & commercialization strategies.

Unit II

Bio markets: business strategy and marketing

8 lectures

Negotiating the road from lab to the market (strategies and processes of negotiation with financers, government and regulatory authorities), Pricing strategy, Challenges in marketing in bio business (market conditions & segments; developing distribution channels, the nature, analysis and management of customer needs), Basic contract principles, different types of agreement and contract terms typically found in joint venture and development agreements, Dispute resolution skills.

Unit III

Finance and accounting

8 lectures

Business plan preparation including statutory and legal requirements, Business feasibility study, financial management issues of procurement of capital and management of costs, Collaborations & partnership, Information technology.

Unit IV

Technology management

8 lectures

Technology – assessment, development & upgradation, Managing technology transfer, Quality control & transfer of foreign technologies, Knowledge centers and Technology transfer agencies, Understanding of regulatory compliances and procedures (CDSCO, NBA, GCP, GLA, GMP).

Recommended Textbooks and References:

1. Adams, D. J., & Sparrow, J. C. (2008). *Enterprise for Life Scientists: Developing Innovation and Entrepreneurship in the Biosciences*. Bloxham: Scion.
2. Shimasaki, C. D. (2014). *Biotechnology Entrepreneurship: Starting, Managing, and Leading Biotech Companies*. Amsterdam: Elsevier. Academic Press is an imprint of Elsevier.
3. Onetti, A., & Zucchella, A. *Business Modeling for Life Science and Biotech Companies: Creating Value and Competitive Advantage with the Milestone Bridge*. Routledge.
4. Jordan, J. F. (2014). *Innovation, Commercialization, and Start-Ups in Life Sciences*. London: CRC Press.
5. Desai, V. (2009). *The Dynamics of Entrepreneurial Development and Management*. New Delhi: Himalaya Pub. House.

Intellectual Property Rights, Biosafety and Bioethics

Credits

3

Course Objectives

The objectives of this course are:

- To provide basic knowledge on intellectual property rights and their implications in biological research and product development;
- To become familiar with India's IPR Policy;
- To learn biosafety and risk assessment of products derived from biotechnology and regulation of such products;
- To become familiar with ethical issues in biological research.

Student Learning Outcomes

On completion of this course, students should be able to:

- Understand the rationale for and against IPR and especially patents;
- Understand why India has adopted an IPR Policy and be familiar with broad outline of patent regulations;
- Understand different types of intellectual property rights in general and protection of products derived from biotechnology research and issues related to application and obtaining patents;
- Gain knowledge of biosafety and risk assessment of products derived from recombinant DNA research and environmental release of genetically modified organisms, national and international regulations;
- Understand ethical aspects related to biological, biomedical, health care and biotechnology research.

Unit I
Introduction to IPR
5 lectures

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; plant variety protection and farmers rights act; concept of 'prior art': invention in context of "prior art"; patent databases - country-wise patent searches (USPTO, EPO, India); analysis and report formation.

Unit II
Patenting
5 lectures

Basics of patents: types of patents; Indian Patent Act 1970; recent amendments; WIPO Treaties; Budapest Treaty; Patent Cooperation Treaty (PCT) and implications; procedure for filing a PCT application; role of a Country Patent Office; filing of a patent application; precautions before patenting-disclosure/non-disclosure - patent application- forms and guidelines including those of National Bio-diversity Authority (NBA) and other regulatory bodies, fee structure, time frames; types of patent applications: provisional and complete specifications; PCT and conventional 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; patent infringement- meaning, scope, litigation, case studies and examples; commercialization of patented innovations; licensing – outright sale, licensing, royalty; patenting by research students and scientists-university/organizational rules in India and abroad, collaborative research - backward and forward IP; benefit/credit sharing among parties/community, commercial (financial) and non-commercial incentives.

Unit III
Biosafety
5 lectures

Biosafety and Biosecurity - introduction; historical background; introduction to biological safety cabinets; primary containment for biohazards; biosafety levels; GRAS organisms, biosafety levels of specific microorganisms; recommended biosafety levels for infectious agents and infected animals; definition of GMOs & LMOs; principles of safety assessment of transgenic plants – sequential steps in risk assessment; concepts of familiarity and substantial equivalence; risk – environmental risk assessment and

food and feed safety assessment; problem formulation – protection goals, compilation of relevant information, risk characterization and development of analysis plan; risk assessment of transgenic crops *vs* cisgenic plants or products derived from RNAi, genome editing tools.

Unit IV
National and international regulations
5 lectures

International regulations – Cartagena protocol, OECD consensus documents and Codex Alimentarius; Indian regulations – EPA act and rules, guidance documents, regulatory framework – RCGM, GEAC, IBSC and other regulatory bodies; Draft bill of Biotechnology Regulatory authority of India - containments – biosafety levels and category of rDNA experiments; field trails – biosafety research trials – standard operating procedures - guidelines of state governments; GM labeling – Food Safety and Standards Authority of India (FSSAI).

Unit V
Bioethics
5 lectures

Introduction, ethical conflicts in biological sciences - interference with nature, bioethics in health care - patient confidentiality, informed consent, euthanasia, artificial reproductive technologies, prenatal diagnosis, genetic screening, gene therapy, transplantation. Bioethics in research – cloning and stem cell research, Human and animal experimentation, animal rights/welfare, Agricultural biotechnology - Genetically engineered food, environmental risk, labeling and public opinion. Sharing benefits and protecting future generations - Protection of environment and biodiversity – biopiracy.

Recommended Textbooks and References:

1. Ganguli, P. (2001). *Intellectual Property Rights: Unleashing the Knowledge Economy.* New Delhi: Tata McGraw-Hill Pub.
2. *National IPR Policy*, Department of Industrial Policy & Promotion, Ministry of Commerce, GoI
3. *Complete Reference to Intellectual Property Rights Laws*. (2007). Snow White Publication Oct.
4. Kuhse, H. (2010). *Bioethics: an Anthology*. Malden, MA: Blackwell.
5. Office of the Controller General of Patents, Design & Trademarks; Department of Industrial Policy & Promotion; Ministry of Commerce & Industry; Government of India. http://www.ipindia.nic.in/
6. Karen F. Greif and Jon F. Merz, *Current Controversies in the Biological Sciences -Case Studies of Policy Challenges from New Technologies*, MIT Press
7. World Trade Organisation. http://www.wto.org
8. World Intellectual Property Organisation. http://www.wipo.int
9. International Union for the Protection of New Varieties of Plants. http://www.upov.int
10. National Portal of India. http://www.archive.india.gov.in
11. National Biodiversity Authority. http://www.nbaindia.org
12. Recombinant DNA Safety Guidelines, 1990 Department of Biotechnology, Ministry of Science and Technology, Govt. of India. Retrieved from http://www.envfor.nic.in/divisions/csurv/geac/annex-5.pdf
13. Wolt, J. D., Keese, P., Raybould, A., Fitzpatrick, J. W., Burachik, M., Gray, A., Wu, F. (2009). *Problem Formulation in the Environmental Risk Assessment for Genetically Modified Plants*. Transgenic Research, 19(3), 425-436. doi:10.1007/s11248-009-9321-9
14. Craig, W., Tepfer, M., Degrassi, G., & Ripandelli, D. (2008). *An Overview of General Features of Risk Assessments of Genetically Modified Crops*. Euphytica, 164(3), 853-880. doi:10.1007/s10681-007-9643-8
15. Guidelines for Safety Assessment of Foods Derived from Genetically Engineered Plants. 2008.
16. Guidelines and Standard Operating Procedures for Confined Field Trials of Regulated Genetically Engineered Plants. 2008. Retrieved from http://www.igmoris.nic.in/guidelines1.asp

17. Alonso, G. M. (2013). *Safety Assessment of Food and Feed Derived from GM Crops: Using Problem Formulation to Ensure "Fit for Purpose" Risk Assessments.* Retrieved from http://biosafety.icgeb.org/inhousepublicationscollectionbiosafetyreviews.

Laboratory IV: Fermentation Technology

Credits

Course Objectives

This laboratory course provides students with opportunity to gain hands on wine making experience that expands on areas of fermentation technology.

Student Learning Outcomes

On successful completion of this course, students should:

- Become familiar with operation of fermentation machinery;
- Develop understanding of necessity for routine chemical, sensory and microbiological analyses during the wine making process.

Syllabus

1. Assembly of bioreactors
2. Sterilization
3. Calibration of Probes (pH and Dissolved Oxygen)
4. Understanding control
5. Controller tuning
6. Cascade control of Dissolved Oxygen
7. Growth of control
8. Batch/Fed batch with concentrated feed
9. Continuous Stirred Tank Reactor running at different dilution rates
10. Estimation of Growth/Product formation & Substrate utilization kinetics
11. Estimation of Kla by dynamic gasing out and gas balancing.

Laboratory V: Downstream Processing

Credits

Course Objectives

The objectives of this course are to provide students with hands on knowledge of the primary unit operations involved in downstream processing.

Student Learning Outcomes

Students should be able to gain hands-on experience on approaches to cell disruption, centrifugation, filtration, and precipitation.

Syllabus

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.

Recommended Textbooks and References:

1. Desai, M. (2000) *Downstream Processing of Proteins: Methods and Protocols,* Humana Press.

Laboratory VI: Enzyme Engineering

Credits

2

Course Objectives

This course will provide hands on experience of various enzyme purification techniques along with enzyme quantification techniques.

Student Learning Outcomes

On completion of this course, students should be able to:

- Understand the underlying principles of enzyme purification;
- Purify an enzyme using various chromatography techniques;
- Estimate the purity of enzymes.

Syllabus

1. Purification of enzyme by Ion Exchange (anion and cation), gel filtration and Hydrophobic Interaction Chromatography
2. Immobilization by entrapment and surface immobilization
3. Running of immobilization energy column
4. Estimation of mass transfer effect (diffusion control reaction, Enzyme pellet efficiency, comparison with free enzyme system)
5. Estimation of stability of enzyme (thermal, operational and pH).

Semester Three

Animal and Plant Biotechnology

Credits

3

Course Objectives

The objective of this course is to educate students about fundamental concepts of animal and plant cell system, bioprocess technology using eukaryotic system and their related applications, thus, preparing them to meet challenges of new and emerging areas of biotechnology industry.

Student Learning Outcomes

On completion of this course, students should be able to:

- Demonstrate knowledge of techniques related to basic cell culture, cloning and hybridoma production;
- Differentiate and describe establishment of primary cell culture and cell lines and enlist methods for quantitation and validation. Applications of various techniques of animal biotechnology in medical, farmland, industrial research and assessment of its social and ethical concerns;
- Recognize and assess need for ethical standards and professional codes of conduct in animal and plant biotechnology research, Intellectual property rights.

Unit I

Culture media for animal cell culture

3 lectures

Introduction and history; Media and supplements, serum, serum free media, natural media, feeder layer on substrate, Gas Phase for tissue culture, source of tissue, primary culture; Stages of commitment and differentiation, proliferation and malignancy.

Unit II

Subculture and cell lines

3 lectures

Cross contamination, terminology, naming and choosing cell line and its maintenance. Criteria for subculture, growth cycle and split ratio, propagation in suspension and attached culture.

Unit III
Cloning and hybridoma technology
3 lectures

Vectors and cloning, somatic cell fusion, hybridomas, HAT selection, Medium suspension fusion, selection of hybrid clones, organ culture, tumorigenesis.

Unit IV
Cell separation and quantitation
3 lectures

Separation techniques based on density, size, sedimentation velocity, antibody based techniques- immuno panning, magnetic sorting, fluroscence activated cell sorting; Quantitation-cell counting, cell weight, DNA content, protein, rate of synthesis, measurement of cell proliferation.

Unit V
Cell characterization and differentiation
4 lectures

Authentication, record keeping, provenance, parameters of characterization, lineage and tissue markers, cell morphology, karyotyping, chromosome banding; Differentiation-commitment, terminal differentiation; Lineage selection, proliferation and differentiation, commitment and lineage, markers of differentiation, induction of differentiation, cell interaction-homotypic and heterotypic; Cell-matrix interaction.

Unit VI
Application of animal biotechnology and related problems
3 lectures

Artificial animal breeding, cloning and transgenic animals, medicines, vaccines, diagnosis of diseases and disorders, gene therapy, forensic application.

Unit VII
Cell and tissue culture in plants
7 lectures

Callus cultures; *in vitro* morphogenesis-organogenesis and embryogenesis; Artificial seeds, Micropropagation (clonal propagation); Haploidy; anther and ovule culture, Embryo culture; Protoplast isolation, culture protoplast fusion and somatic hybridization, cybrids, somaclonal variation; *in-vitro* mutation methods; virus elimination, pathogen indexing; cryopreservation; production of secondary metabolites; sources of plant secondary metabolites; criteria for cell selection, factors affecting culture of cells; different bioreactors and their use in secondary metabolite production; biochemical pathways for production of different secondary metabolites; and biotransformation.

Unit VIII
Genetic engineering and applications
6 lectures

Principles and methods of genetic engineering and its applications in agriculture especially transgenic plants; Molecular markers-hybridization and PCR based markers, RFLC, RAPD, STS, SSR, AFLP, SNP markers; DNA fingerprinting- Principles and applications, introduction to mapping of genes/QTLS, marker assisted selection-Strategies for introducing genes of biotic and abiotic stress resistance in plants; Molecular diagnosis of pathogens in plants.

Unit IX
Plant and animal genomics
4 lectures

Overview of genomics- definition, complexity and classification, need for genomic level analysis, methods of analyzing genome at various levels- DNA, RNA, Protein, metabolites and phenotype, genome projects and bioinformatics- sources for genome research- database overview of forward and reverse genetics for assigning function of gene; Social, cultural, economic, legal problems; bioethics.

Recommended Textbooks and References:

1. Freshney, I., (2010), *Cultures of Animal Cells,* John Wiley and Sons Inc.
2. Cibelli, J., Robert P., Keith L.H.S., Campbell H., and West M. D. (Editors), (2002) *Principles of Cloning*, St. Diego academic press.
3. J Hammond, *et al., Plant Biotechnology,* Springer Verlag.
4. R J Henry, *Practical Application of Plant Molecular Biology,* Champman and Hall
5. Brun T.A. (2006). *Gene Cloning and DNA Analysis. An Introduction*, Oxford, Blackwell Pub.

6. Primrose S.B and Twyman R.M. (2006). *Principles of Gene Manipulation and Genomics*, Maldem M.A Blackwell Pub.
7. Gordon T, (2005), *Reference Technique in Farm Animals*. Oxford. CAB International.
8. Porter R., Totowa N.J, (2007), *Animal Cell Biotechnology: Methods and Protocols*, Humana press.

Environmental Biotechnology

Credits

3

Course Objectives

The course describes role of microorganisms in recycling soil nutrients, biodegradation of complex plant polymer, sustaining and improving plant growth through improving nutrient availability, production of plant growth promoting substances and inhibiting pathogens. This course also deals with various aspects and impact of our interactions with environment, waste treatment technologies, kinetics and reactors. The biodegradation and bioremediation mechanisms provided by plants and microbes are dealt in detail.

Student Learning Outcomes

On completion of this course, students should gain understanding of the basic microbiological, molecular and analytical methods extensively used in environmental biotechnology.

Unit I
Biological nitrogen fixation
4 lectures

Physiology and biochemistry of nitrogen fixing organisms, genetics and regulation of gene expression, signaling factors and molecular interaction in establishing rhizobia legume symbiosis.

Unit II
Biofertilizers
4 lectures

Phosphate Solubilizing Microorganisms, inorganic phosphate solubilization and its mechanisms, phosphate mineralizers-phytate and organic phosphate hydrolyzing bacteria, Ecto- and Endo- Mycorrhizae.

Unit III
Plant growth promoting rhizobacteria(PGPR)
4 lectures

PGPR in improving plant growth, mechanism in plant growth promotion, factors affecting rhizosphere colonization.

Unit IV
Environmental problems and monitoring
5 lectures

Pollution and its classification; Effluent standards- examination of waste water, characteristics, municipal and industrial waste water; Global environmental problems, global warming, acid rain, ozone depletion; Sampling and analysis; Environmental monitoring and audit; Environmental laws and policies in India.

Unit V
Biotreatment, kinetics and reactor design
6 lectures

Principles of biological treatments; Biological treatment- composting, suspended growth systems, attached growth systems; Bioreactor design- activated sludge process, trickling filters, fluidized bed and packed bed reactor, rotating biological contactors, oxidation ponds and ditches, lagoons, anaerobic reactors.

Unit VI
Bioremediation and biodegradation
6 lectures

Bioremediation principles and processes, Biosorption, bioaccumulation, bioconversion, biotransformation, bioleaching, biodegradation, detoxification, activation, accumulation and co-metabolism; Strategies and techniques of bioremediation *in situ* and *ex situ* of hydrocarbons, pesticides and dyes; GMOs in bioremediation and

biodegradation, Microbial enhanced oil recovery.

Unit VII
Principles of microbial diversity
6 lectures

Evolution of life, principles and concept of microbial diversity, ecological diversity, structural and functional diversity; Methods of studying microbial diversity- Morphological, biochemical/physiological and molecular techniques; Microbial classification and taxonomy; Phenetic, phylogenetic, and genotypic classification, numerical taxonomy, taxonomic ranks, phylogenetic tree, techniques for determining microbial taxonomy and phylogeny- classical and molecular characteristics.

Unit VIII
Fundamental of ecology
5 lectures

Ecosystem, energy in ecological systems, energy participating in food chains and food webs; Interactions among microbial populations, interaction between microbes and plants and between microbes and animals.

Recommended Textbooks and References:

1. Atlas R.M and Bertha, R. (2009). *Microbial Ecology*, 4th Ed, Pearson Education.
2. Maier, R.M., Peppler I.L and Gertha C.P. *Environmental Microbiology*, 2nd Ed, Academic press.
3. Olum E.P and Barrett G.W. (2005). *Fundamental of Ecology*, 5th Ed, Cenegage learning.
4. Wiley J.M., Sherwood, L.M and Woolverton C.J. Prescott, Harley and Klein, (2005), *Microbiology*, 7th Edition, McGraw Hill.
5. Garrity, G.M, Brenner, D.J, Kreig M.R. and Statey J.T. (2005), *Bergey's Manual of Systematic Bacteriology*, 2nd ed, Vol II Springer.
6. Lawrence K. W, Volodymyr Ivanov, Joo-Hwa Tay, Yung-Tse Hung, (2010), *Environmental Biotechnology*, Vol 10, Handbook of Environmental Engineering, Springer.
7. Hans-Joachim Jordening, Josef Winter, (2005), *Environmental Biotechnology: Concepts and Application*, Wliey-vch.
8. Christon Hurst, Ronald L.C, Guy R. K, Miachael J.M, Linda D. S, (2002) *Manual of Environmental Microbiology*, 2nd edition, ASM press.

Biomanufacturing Principles and Practice

Credits
3

Course Objectives

This course will help students to develop conceptual clarity and knowledge about systems which brings and guarantee quality in products (Biopharmaceuticals, diagnostics and foods) manufactured for human use. The knowledge of GMP and GLP requirements is critical for students who opt for careers in biomanufacturing.

Student Learning Outcomes

On completion of this course, students should:

- Understand basics of biomanufacturing, GMP and GLP requirements;
- Understanding quality control measurements taken for biomanufacturing in industries.

Unit I
Biomanufacturing principles
6 lectures

Overview and design of biomanufacturing, quality by design approach, technical considerations, phases and scale up: life cycle of manufacturing, raw material considerations, compliance and quality in biomanufacturing, lean biomanufacturing; Process analytical technology (PAT) during biomanufacturing: background and need tools for data acquisitions (software in fermenters, flow filtrations, chromatography, analysis and design process analyzers, process control tools and continuous improvement and knowledge management; Standard manufacturing operating procedures of

biotechnology, including upstream and downstream processing of proteins, and quality control of protein production, and final fill and finish of product; Case studies to be included at least: therapeutic proteins, monoclonal antibodies, human vaccines.

Unit II
Quality system
4 lectures

Introduction to quality system, main elements of a quality system; Essential of quality system; Practical implementation of a quality system; Structure of quality manual, correlation between GMP requirements (WHO) and ISO 9001:2000.

Unit III
Principles and practice of GMP
10 lectures

Personnel: Principles of human resource management, duties of senior management, organizational structures, qualification and profiles requirement, workplace and job descriptions, health monitoring and occupational health safety, training, function owners subject to public law; Premises: Official requirements, material & personnel flow and layout, air cleanliness classes and grades, construction elements, barrier systems, isolators and safety cabinets, building services, heating ventilation air conditioning (HVAC), process gases, qualification of premises and HVAC systems, pharma monitoring of HVAC systems, particle monitoring.; Facilities and Equipment: Facility planning, materials, hygienic design in solid handling, system controllers and process control systems, technical documentation, calibration, maintenance, cleaning of facilities, containment (personnel protection) in solid handling; Pharmaceutical water: Water qualitiy, generation of pharmaceutical water, distribution and storage of pharmaceutical water, qualification of water supplies, operation of water supplies, pure steam systems; Qualification: Official requirements, preparation of qualification, qualification documentation, design qualification (DQ), Installation qualification (IQ), operational qualification (OQ), Performance qualification (PQ), special cases of qualification; Process Validation: Official requirements, Validation - a key element of quality management, validation planning and procedure, validation documentation, process validation and product lifecycle ; Cleaning Validation: Official requirements, how to validate cleaning procedures, cleaning validation master plan, establishing scope of validation, acceptance criteria and limit calculation, sampling procedures, analytical procedure, documentation, maintenance of validated status, cleaning validation documentation; Production: Sanitation, personnel hygiene, production hygiene, sanitation programme, environmental monitoring, GMP in production process, weigh-in, identification, in-process control prevention of cross-contamination, empty chapter, reworking, warehouse and logistics; Sterile Production and Packaging: Introduction, Air lock concepts, manufacture of terminally sterilised products, sterilisation processes, aseptic processing, freeze-drying, testing for sterility, testing for endotoxins, testing for leakage and for particles, microbiological monitoring, packaging materials, packaging process, qualification of a servo-controlled blister packaging line, blow-fill-seal technology (BFS technology); Documentation: Official requirements, GMP-compliant documentation, batch documentation, standard operating procedures (SOPs), site master file, electronic batch recording and batch release, CAPA, document management systems.

Unit IV
GMP in regulation
2 lectures

Information, national bodies and pharmaceutical associations; Pharmacopeia; EU directives and guidelines, USA: CFR and FDA guidelines, ICH-guidelines, PIC/S guidelines, GMP of other regions, WHO guidelines.

Recommended Textbooks and References:

1. *Introduction to Biomanufacturing*, by Northeast Biomanufacturing Center and collaboration, 2012.
2. *Introduction to Biomanufacturing*, by Mark Witcher. In Encyclopedia of Industrial Biotechnology.
3. *Good Manufacturing Practices for Pharmaceuticals (e-resource): A Plan for Total Quality Control.* Sidney Willig and James Stoker.

4. *Biotechnology Operations: Principles and Practices*, by John M. Centanni, Michael J. Roy; CRC press
5. *Learn Biomanufacturing*, 1st Ed.; by Nigel Smart; Woodhead Publishing
6. *GMP Manual*; Publisher Maas & Peither America, Inc. GMP Publishing.

Metabolic Engineering

Credits

3

Course Objectives

The objective of this course is to provide a quantitative basis, based on thermodynamics, enzyme kinetics, metabolic flux analysis and metabolic control analysis, for understanding of metabolic networks in single cells and at organ level.

Student Learning Outcomes

On successful completion of this course, students should be able to:

- Identify the appropriate host and/or metabolic pathways to produce a desired product or remediate a toxin;
- Compare potential metabolic engineering strategies using quantitative metabolic modeling.

Unit I
Introduction
2 lectures

Stoichiometry, kinetics and thermodynamics of cellular reactions.

Unit II
Material balances and data consistency
2 lectures

Material balances on pathways and whole cell balances; Over and under-determined systems; Data consistency for over-determined systems.

Unit III
Regulation of metabolic pathways
2 lectures

Regulation of metabolic pathways; role of enzymes, substrate, product and regulatory molecules; Hierarchical control in cellular systems.

Unit IV
Manipulation of metabolic pathways
5 lectures

Pathway manipulation strategies for overproduction of various metabolites, examples of ethanol overproduction, overproduction of intermediates in main glycolytic pathway and TCA cycle like pyruvate, succinate *etc.*; Need for multiple genomic modifications; Modulating fluxes in desired pathways; Tools for multiple genomic modifications examples- TALENS CRISPR-Cas systems as well as traditional systems of gene knock ins and knock outs and promoter engineering.

Unit V
Synthetic biology
3 lectures

Metabolic pathway synthesis; Relation with bioprocess design; BIOBRICKS approaches; Introduction to tools of synthetic biology.

Unit VI
Metabolic flux analysis
4 lectures

Metabolic flux analysis; Building stoichiometric matrix; Steady state and pseudo steady state assumptions; Using different optimizing functions to solve linear programming problem; FBA, understanding flux cone and constraints; Introducing additional constraints from thermodynamics; Brief introduction to developments in this area; MOMA (Minimization of Metabolic Adjustment), iFBA (Integrated Flux Balance Analysis) *etc.*

Unit VII
Determination of metabolic flux
2 lectures

Experimental determination of metabolic fluxes; C^{13} labeling, NMR and GC-MS based methods for flux determination.

Recommended Textbooks and References:

1. Stephanopoulos, G.N., Aristidou, A.A., Nielsen, J. (1998) *Metabolic Engineering: Principles and Methodologies*. 1st ed. San Diego: Academic Press.
2. Smolke, C.S. (2010) *Metabolic Pathway Engineering Handbook: Fundamentals*. 1st ed. New York: CRC Press.
3. Smolke, C.S. (2010) *Metabolic Pathway Engineering Handbook: Tools and Applications*. 1st ed. New York: CRC Press.

Laboratory VII: Cell Culture

Credits

4

Course Objectives

The objective of this laboratory course is to introduce students to cell culture basics, covering topics such as requirements of a laboratory dedicated to cell culture experiments, laboratory safety, aseptic technique, and microbial contamination of cell cultures, as well as providing basic methods for passaging, freezing, and thawing cultured cells.

Student Learning Outcomes

On completion of this course, student should be able to:

- Gain working knowledge of these techiques and understanding of good cell culture practices for healthcare and biotechnology product development;
- Obtain good biosafety practices and familiarize with basic cell culture laboratory equipment.

Syllabus

1. Orientation to animal mammalian cell culture
2. Aseptic techniques for cell culture
3. Preparation of media and other reagents
4. Establishing primary cell culture
5. Preparation of monolayer and suspension cultures
6. Preparation and thawing cells
7. Checking viability and counting
8. Subculture, feed both adherent and suspension cultures
9. Growth curve analysis and use of fluorescent microscope for identification and analysis of cell cycle
10. Cell line cryopreservation
11. Preparation of cells for microscopy
12. Identification of apoptosis
13. Demonstration of mammalian cell culture in research and towards development of a variety of applications, such as large scale culture, production of monoclonal antibodies, production of viral vaccines and amniocentesis studies
14. Gene transfer experiments
15. Virus infection studies and virus quantification
16. Blood cell preparation such as macrophages, RBC *etc.*

Recommended Textbooks and References:

1. R. Ian Freshney, (2010) *Culture of Animal Cells: a Manual of Basic Technique and Specialized Applications*, 6th Ed, John Wiley & Blackwell
2. J. M. Davis (2002), *Basic Cell Culture (Practical Approach Series)*. 2nd Edition, OUP Oxford.
3. *Current Protocols in Immunology*, Wiley publications
4. *Current Protocols in Cell Biology,* Wiley publications
5. S.J. Higgins and B.D. Hames (2000), *Protein Expression, A Practical Approach*. OUP Oxford.

Laboratory VIII: Environmental Biotechnology

Credits

Course Objectives

This course will give hands on experience of various emerging technologies used for pollution control and bioremediation.

Student Learning Outcomes

On completion of this course, students should be able to:

- Gain basic knowledge of bioremediation techniques;
- Understand procedures involved in water, air and land pollution control.

Syllabus

1. Assay for dissimilatory nitrate reductase activity
2. Estimation of nitrogenase activity of free living bacteria in soils
3. Study of biooxidation of ferrous and sulphur by chemolithotrophic bacteria
4. Adaptation of soil bacteria to metals
5. Biosorption of heavy metals from industrial effluents
6. Enrichment and isolation of Azodye degrading bacteria and their application in treatment of dye containing effluents
7. Enrichment and isolation of 2,4-D degrading bacteria
8. Study of microbial mineral phosphate solubilisation activity
9. Enrichment and isolation of naphthalene degrading bacteria
10. Analysis of biosurfactant production by hydrocarbon degrading organisms
11. Estimation of microbial activity of soil by dehydrogenase assay
12. Waste water treatment:
    a. Biological Oxygen Demand, Chemical Oxygen Demand measurement
    b. Running of anaerobic and aerobic fluidized bed reactors
    c. Upflow Anaerobic Sludge Blanket reactor startup and running
    d. Analysis of reactor operation.

Recommended Electives

Advanced Biomanufacturing

Credits

Course Objectives

The objectives of this course is to introduce students with Bio-manufacturing program. Existing biotechnology degree programs focus on product understanding during research and early development stages but there is need to educate students on the program that will address later stages of development and production process understanding.

Student Learning Outcomes

Student should be able to:

- Understand how a product can be developed;
- Knowledge on regulatory and Quality aspects of product development;
- Demonstrate good laboratory procedures and practices;
- Describe standard operating procedures for biotechnology research and assign Biosafety levels;
- Perform activities in compliance with the cGMP's (Current Good Manufacturing Practices) that are mandated by the FDA (Food & Drug Administration);
- Hands-on training on microbiological

methods, cell biological methods, bioprocess development with industrial oriented approach;
- Become an entry-level biomanufacturing scientist, who can produce new drug discoveries, biologicals, biomedical devices used in surgeries, and food products in a very clean environment.

Unit I
Survey of various microscopic agents of particular importance to humans
4 lectures

Emphasis on those involved in infectious disease, host defenses against disease, and elements of infection chains and means utilized for breaking chains, monoclonal antibodies *etc.*

Unit II
Clean rooms and bio-safety levels
5 lectures

Clean Room classification, gowning, Introduction to clean room gowning, proper sanitation techniques, regulations and recommendations for biosafety, ascending levels of containment, Defining microbiological practices, safety equipment, and facility safeguards for the corresponding level of risk associated with handling a particular agent. Introduction to Safe Laboratory Practices: Guidelines for safe laboratory practices, role of institution's safety committee and local rules and regulations pertaining to laboratory safety.

Unit III
Scientific communication in biomanufacturing
3 lectures

Analysis and preparation of protocols and standard operating procedures (SOPs), report and present data and experimental conclusion, analysis of articles about scientific research and developments in biotechnology.

Unit IV
Biomanufacturing production
8 lectures

Emphasis on growth and monitoring of fermenters and bioreactors, including cleaning, media preparation, aseptic inoculation, cell harvesting, lysis, protein recovery and purification of proteins using centrifugation, ultrafiltration and chromatography techniques.

Unit V
Development, production, recovery and analysis of biotechnology products
8 lectures

Case studies of Vaccine manufacturing process that briefly involves generation of antigen/virus/bacteria/recombinant product, purification, testing product, evaluating efficacy of product, stability of product, formulating product and its stability *etc.*,(Tracing the path of a drug or biologic from cell through production facility, final processing, and in human body), growth characteristics of organisms used to produce pharmaceutical proteins, and techniques used. Fundamentals in biotechnology laboratory techniques: Emphasis on developing skillful use of applicable instruments; protein purification and assays; recombinant DNA work; isolation and tracking techniques; laboratory notebook, spreadsheet data analysis; written protocols and familiarity with standard operating procedures.

Unit VI
Business and regulatory practices
4 lectures

Sound manufacturing procedures and basic business principles: Key concepts for product quality and safety as it moves through a biomanufacturing production pipeline, roles of governmental oversight and regulation during discovery, development and manufacturing of new products for biopharmaceutical industry.

Recommended Textbooks and References:

1. Zhong, Jian-Jiang, (2004), *Biomanufacturing*. Springer.
2. Michael C. Flickinger, Stephen W. Drew, (1999), *The Encyclopedia of Bioprocess Technology: Fermentation, Biocatalysis, and Bioseparation*. Wiley-Blackwell.
3. James E. Bailey , David F. Ollis, (1986), *Biochemical Engineering Fundamentals*, McGraw-Hill
4. Lisa Yount, (2004), *Biotechnology and Genetic Engineering*. Facts on File.
5. Nathan S. Mosier, Michael R. Ladisch, (2009), *Modern Biotechnology: Connecting Innovations in Microbiology and Biochemistry to Engineering Fundamentals*, Wiley-AIChE.

Computational Biology

Credits

3

Course Objectives

The objective of this course is to provide students with theory and practical experience of essentials to aid for genomic, proteomic and metabolomics courses and drug design program.

Student Learning Outcomes

On completion of this course, students are expected to:

- Develop an understanding of basic theory of these computational tools;
- Develop required database extraction, integration, coding for computational tools and methods necessary for all Omics;
- Formation of hypothesis for investigating specific contemporary biological questions, provide help to experiment with or develop appropriate tools;
- Critically analyze and interpret results of their study with respect to whole systems.

Unit I

Introduction to computational biology basics and biological databases

4 lectures

Computers in biology and medicine; Overview of biological databases, nucleic acid & protein databases, primary, secondary, functional, composite, structural classification database, Sequence formats & storage, Access databases, Extract and create sub databases, limitations of existing databases.

Unit II

Pairwise and multiple sequence alignments

5 lectures

Local alignment, Global alignment, Scoring matrices - PAM, BLOSUM, Gaps and penalties, Dot plots. Dynamic programming approach: Needleman and Wunsch Algorithm, Smith and Waterman Algorithm, Hidden Markov Model: Viterbi Algorithm. Heuristic approach: BLAST, FASTA. Building Profiles, Profile based functional identification.

Unit III

Genome analysis

6 lectures

Polymorphisms in DNA sequence, Introduction to Next Generation Sequencing technologies, Whole Genome Assembly and challenges, Sequencing and analysis of large genomes, Gene prediction, Functional annotation, Comparative genomics, Probabilistic functional gene networks, Human genome project, Genomics and crop improvement; Study the available GWAS, ENCODE, HUGO projects, extract and build sub databases; Visualization tools including Artemis and Vista for genome comparison; Functional genomics case studies.

Unit IV
Structure visualization
3 lectures

Retrieving and drawing structures, Macromolecule viewing platforms, Structure validation and correction, Structure optimization, Analysis of ligand-protein interactions; Tools such as PyMol or VMD.

Unit V
Molecular modelling
6 lectures

Significance and need, force field methods, energy, buried and exposed residues; side chains and neighbours; fixed regions; hydrogen bonds; mapping properties onto surfaces; RMS fit of conformers and protein chains, assigning secondary structures; sequence alignment: methods, evaluation, scoring; protein curation: backbone construction and side chain addition; different types of protein chain modeling: ab initio, homology, hybrid, loop; Template recognition and alignments; Modeling parameters and considerations; Model analysis and validation; Model optimization; Substructure manipulations, annealing, protein folding and model generation; loop generating methods; loop analysis; Analysis of active sites using different methods in studying protein–protein interactions.

Unit VI
Structure-based drug development
6 lectures

Molecular docking: Types and principles, Semi-flexible docking: Flexible docking: Ligand and protein preparation, Macromolecule and ligand optimization, Ligand conformations, Clustering, Analysis of docking results and validation with known information. Extra-precision docking platforms, Use of Small-molecule libraries, Natural compound libraries for virtual high throughput screening.

Unit VII
Ligand-based drug development
6 lectures

Quantitative structure activity relationships. Introduction to chemical descriptors like 2D, 3D and Group-based; Radar plots and contribution plots and Activity predictions, Pharmacophore modeling, Pharmacophore-based screenings of compound library, analysis and experimental validation.

Recommended Textbooks and References:

1. Mount, D. W. (2001). *Bioinformatics: Sequence and Genome Analysis*. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press.
2. Bourne, P. E., & Gu, J. (2009). *Structural Bioinformatics*. Hoboken, NJ: Wiley-Liss.
3. Lesk, A. M. (2004). *Introduction to Protein Science: Architecture, Function, and Genomics*. Oxford: Oxford University Press.
4. Campbell, M & Heyer, L. J. (2006), *Discovering Genomics, Proteomics and Bioinformatics*, Pearson Education.
5. Oprea, T. (2005). *Chemoinformatics in Drug Discovery*, Volume 23. Wiley Online Library.
6. Gasteiger, J. & Engel,T. (2003), *Chemoinformatics: a Textbook*, Wiley Online Library.

Fundamentals of Technology Transfer

Credits
3

Course Objectives

The 'Transfer of Technology' (Know how about Processes & material) from one site to other site takes place at some stage of product life-cycle. It may be from Discovery/basic R&D, Process R&D, scale-up, manufacturing, production to launch and approval phase. This course will be beneficial for students and researchers who are interested to working in industries from R&D to commercial manufacturing.

Student Learning Outcomes

On completion of this course, students should:

- Have basic understanding of principles of technology transfer;
- Be aware of process involved in transfer of technology during all the stages of drug development.

	It will also strengthen in additional domains such as project management, Clinical, Regulatory affairs, Quality Control and Quality Assurance.
Unit I **Introduction to tech transfer** 4 lectures	Purpose, Life cycle of product development: Technology Transfer, Drug Discovery and Development Process, Importance of Technology Transfer; Scope and Glossary in Bio-manufacturing.
Unit II **Regulatory and business perspective** 4 lectures	Regulatory Requirements for Technology Transfer, Safety, Health and Environmental (SHE) Regulations, Waste Disposal, Potential Impact of notification of new substances (NONS) regulations, economic factor, Social Aspects and impact, culture and team building.
Unit III **Organization strategy, planning and management** 4 lectures	Stages of the Technology Transfer Process, Management of Change, Organization, Teams Supporting the TT Process, Global Technology Transfer Management Team (GTTMT), Documentation Required to Support TT, Planning, Timings.
Unit IV **Training as essential element** 3 lectures	Learning from Technology Transfer, Developing a Training Strategy, Scope of Training, Prioritization and Context of Training Needs, Detailed Contents of Training Programmes, Methods and Tools for Delivering Training, Management of Training Programmes, Trainers, Templates and Style Guidelines, Training Documentation, Measuring Success and Auditing of Training.
Unit V **Quality control: analytical method transfer** 4 lectures	Analytical T T: Principles, What, when and How? (Objective, Scope, Responsibilities), procedure including Pre-transfer activities, Transfer protocol and Report, Experimental design and Acceptance criteria, Alternate approaches.
Unit VI **Active pharmaceutical/ product ingredients** 4 lectures	Introduction, Synthesis/preparation, route/process and final forms, Developmental data, Stability Data, Raw material, Process information: Process Research and Development, Role of Process R&D, Good Process Design, equipment description, specifications, packaging specifications, facility requirement, Qualification of equipment, validation plan: process, cleaning, computer.
Unit VII **Production: Dosage form (processing, packaging and cleaning)** 4 lectures	Introduction, Stability Data, API, Excipients and Raw material, Process information, equipment description, packaging specification, facility requirement, Qualification and validation.
Unit VIII **Documentation** 1 lectures	Batch manufacturing records (BMR), SOPs for analytical procedure, format COA, format stability data, format for testing of raw material, Validation Plan, Validation report.
Unit IX **Case Studies** 3 lectures	Case Studies and examples.

Recommended Textbooks and References:

1. Mark Gibson, PDA Bethesda, *Technology Transfer: an International Good Practice Guide for Pharmaceuticals and Allied Industries*, DHI Publishing.
2. *Technology Transfer*, Good Practice Guide ISPE
3. WHO Guidelines on Transfer of Technology in Pharmaceutical Manufacturing, (2011), Annex 7 WHO Technical Report Series, No. 961.

Introduction to OMICS Based Technologies

Credits

3

Course Objectives

The objective of this course is to give an introduction to Genomics and other global Omics technologies, theory and practical aspects of these technologies and application of these technologies in biology. The students should be able to gain working knowledge of these technologies and appreciate their ability to impart a global understanding of biological systems and processes in health and disease.

Student Learning Outcomes

On completion of this course, students should have:

- Overview of genome variation in population including technologies to detect these variation;
- Understand how High-throughput DNA sequencing (HTS) can be used to identify disease causing genetic variants in monogenic diseases;
- Understand how Genome Wide Association Studies (GWAS) can detect disease associated markers in multifactorial diseases;
- Understand how HTS technologies can be used to explore changes in gene expression;
- Understand application of various Omics technologies.

Unit I
Genome mapping
6 lectures

Structure and organization of prokaryotic and eukaryotic genomes- nuclear, mitochondrial and chloroplast genomes; Computational analysis, Databases, Finding genes and regulatory regions; Tools for genome analysis– PCR, RFLP, DNA fingerprinting, RAPD, SNP detection, SSCP, FISH to identify chromosome landmarks; Human Genome Project- landmarks on chromosomes generated by various mapping methods, BAC libraries and shotgun libraries preparation, Physical map, Cytogenetic map, Contig map, Restriction map, UCSC browser.

Unit II
Microarray technology
6 lectures

Basic principles and design, cDNA and oligonucleotide arrays, DNA microarray, Instrumentation and structure; Designing a microarray experiment. Comparative Genomic Hybridization (CGH) arrays, Resequencing arrays; Different platforms (Affymetrix, Agilent *etc.*); Data Processing and Normalization - Algorithms of data processing and Normalization; Tools used to normalize; Microarray databases – NCBI; GEO (Gene Expression Omnibus), ArrayExpres (EBI); Functional Analysis: Differential gene expression; Gene Ontology functional enrichment tools, Pathway analysis (KEGG Database); Applications of Microarray technology; Case studies - Application of expression profiling in human disease; Comparison of Microarray technology and High throughput sequencing technology.

Unit III
Sequencing technologies
7 lectures

Introduction to sequencing, Maxam and Gilbert method, Sanger Sequencing techniques and applications; Next Generation sequencing (NGS), quality check, Library Preparations, Platform overview and comparison (Illumina, 454 (Roche), SOLiD (Life technology), Specific Biosciences, Ion Torrent, Nanopore, PacBio; Types of NGS, DNA-sequencing - Whole genome sequencing, exome sequencing, Deep sequencing, ChIP sequencing, RNA-sequencing and types (small RNA sequencing, non coding RNA sequencing),Whole transcriptome sequencing; Data Processing and

Analysis: Data Quality Check, filtering and Genome assembly and mapping to reference genomes, mapping tools (bowtie, maq *etc.*), Sequence Alignment formats: Sequence Alignment/Map (SAM) format, Binary Alignment/Map (BAM) format, Functional Analysis: Pathway analysis, Gene Ontology analysis ; Application of different sequencing technique, methylomics, *in vivo* protein binding, genome wide association studies (GWAS), Histone modification, microbial sequencing.

Unit IV

Proteomics

7 lectures

Relationship between protein structure and function; Outline of a typical proteomics experiment, One- and two-dimensional gel electrophoresis (IEF and 2D electrophoresis), Alternatives to electrophoresis; Multiplexed protein analysis, Spot visualization and picking; Tryptic digestion of protein and peptide fingerprinting, Mass spectrometry : ion source (MALDI, spray sources), analyzer (ToF, quadrupole, quadruple ion trap) and detector; Post translational Modifications: Quantitative proteomics, clinical proteomics and disease biomarkers, mass spectral tissue imaging and profiling; Protein-protein interactions: Surfaceomes and Secretomes, Solid phase ELISA, pull-down assays (using GST-tagged protein) tandem affinity purification, western analysis, surface plasmon resonance technique; Yeast two hybrid system, Phage display, Protein interaction maps, Protein arrays-definition; Types of protein arrays, Applications- diagnostics, expression profiling. Protein databases, Protein databank.

Unit V

Metabolomics

6 lectures

Introduction and overview of metabolites, sample collection and processing, Non tracer and tracer (radio labelled)-based techniques in metabolomics (HPLC, NMR, LC-MS and GC-MS); Metabolome data processing derived by various techniques, analysis of databases (MetaboLight, Meta Cyc, MMCD *etc.*), Analysis tools, Metabolic pathways and network analysis; Metabolic flux analysis (TCA, Amino acids, fatty acids, intermediary metabolites), Stoichiometric metabolic flux analysis, ^{13}C metabolic flux analysis (MFA), Metabolic control analysis (MCA); Applications of metabolomics; Integration of metabolomics data sets with other data (*eg.* Transcriptomics, enzyme activity *etc.*).

Recommended Textbooks and References:

1. Brown TA (2006) *Genomes*, 3rd Edition, Garland Science.
2. Campbell AM and Heyer LJ (2007) *Discovering Genomics, Proteomics and Bioinformatics*. Benjamin Cummings.
3. Primrose S and Twyman R (2006) *Principles of Gene Manipulation and Genomics,* 7th Edition, Blackwell.
4. Rehm H (2006) *Protein Biochemistry and Proteomics*, 4th Edition, Academic Press.
5. Twyman RM., *Principles of Proteomics*, 2nd Edition, Garland Science Taylor & Francis Group New York and London.
6. Liebler DC, *Introduction to Proteomics Tools for the New Biology*, Humana Press, Totowa NJ. USA.
7. Teresa Whei-Mei Fan, Andrew M. Lane, Richard M. Higashi; Eds. (2012) *The Handbook of Metabolomics*. Springer ISBN 978-1-61779-618-0
8. John C. Lindon, Jeremy K. Nicholson, Elaine Holmes, Eds. (2007) *The Handbook of Metabonomics and Metabolomics*. Elsevier ISBN: 978-0-444-52841-4.

Available Resources

Equipment available in Laboratories

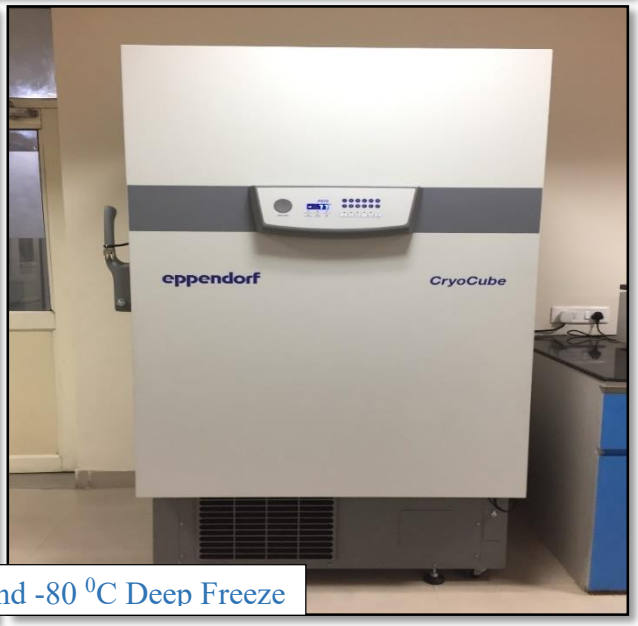
Central Biotechnology Equipment Lab
Deep Freezer (-80ºC)
Ultra-Pure Water Purification System
Gel Documentation System
Gradient PCR
UV-Vis Spectrophotometer
Real Time PCR
Refrigerated Centrifuge
Nano Drop Spectrophotometer
Fluorescence Microscope

Animal Cell Tissue Culture Lab
Bright Field/Phase Contrast / Fluorescence inverted Microscope with Camera
Refrigerated Centrifuge
Cell counter
Biosafety Cabinet Class II
CO_2 Incubator
ELISA plate reader
Deep Freezer (-20ºC)
Liquid Nitrogen Containers

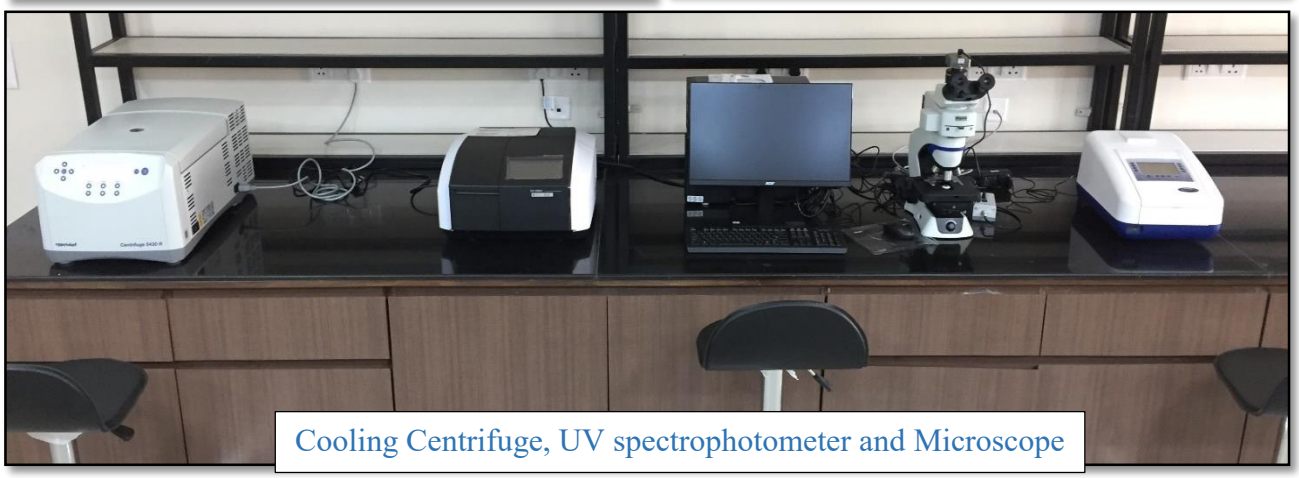
Microbial Biotechnology Lab
Autoclave
Bright Field/Phase Contrast Microscope with Camera
Compound Microscope
Hot Air Oven
Multiple pocket tester
Hot plate Magnetic Stirrer
Digital Dry Bath
Vortex Mixer
Water Bath
Weighing Balance
Micro Centrifuge
Micropipettes
Microwave Oven
pH Meter
Refrigerator
Deep Freezer (-20ºC)
Chiller (Water circular)
Incubator Shaker
Laminar Air Flow

Photographs of Facilities

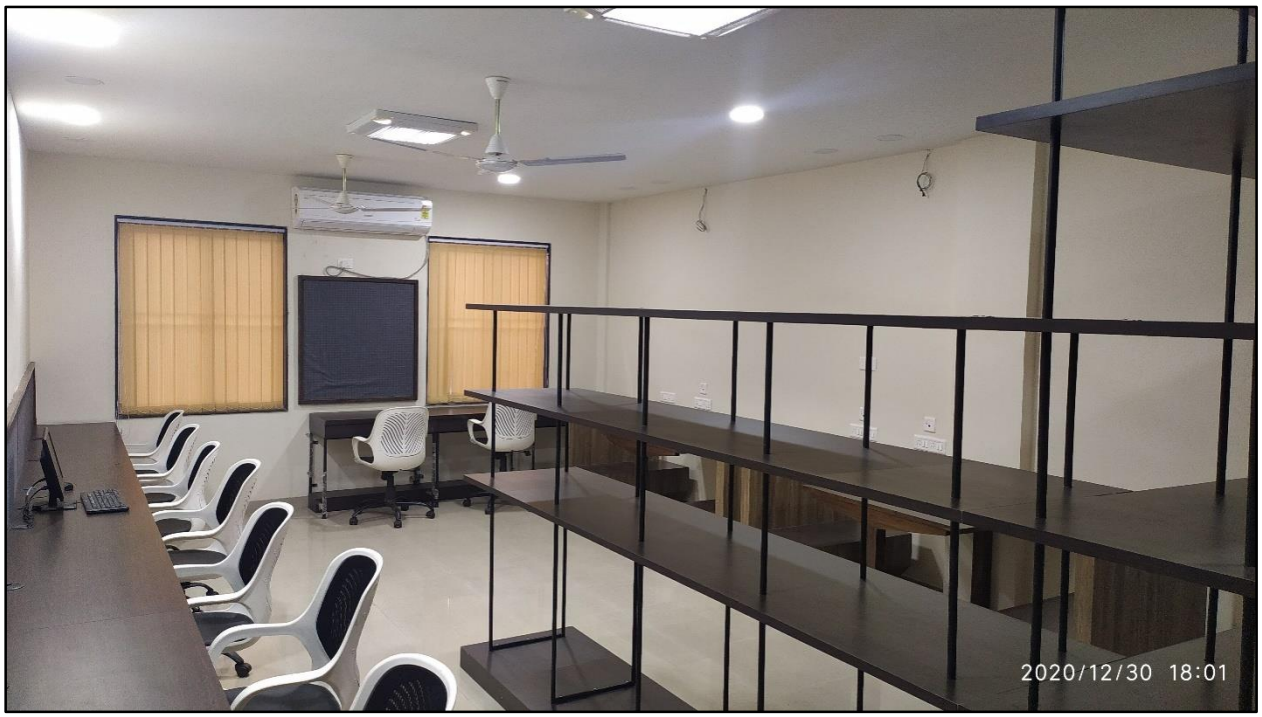
Real-Time PCR & Gradient PCR

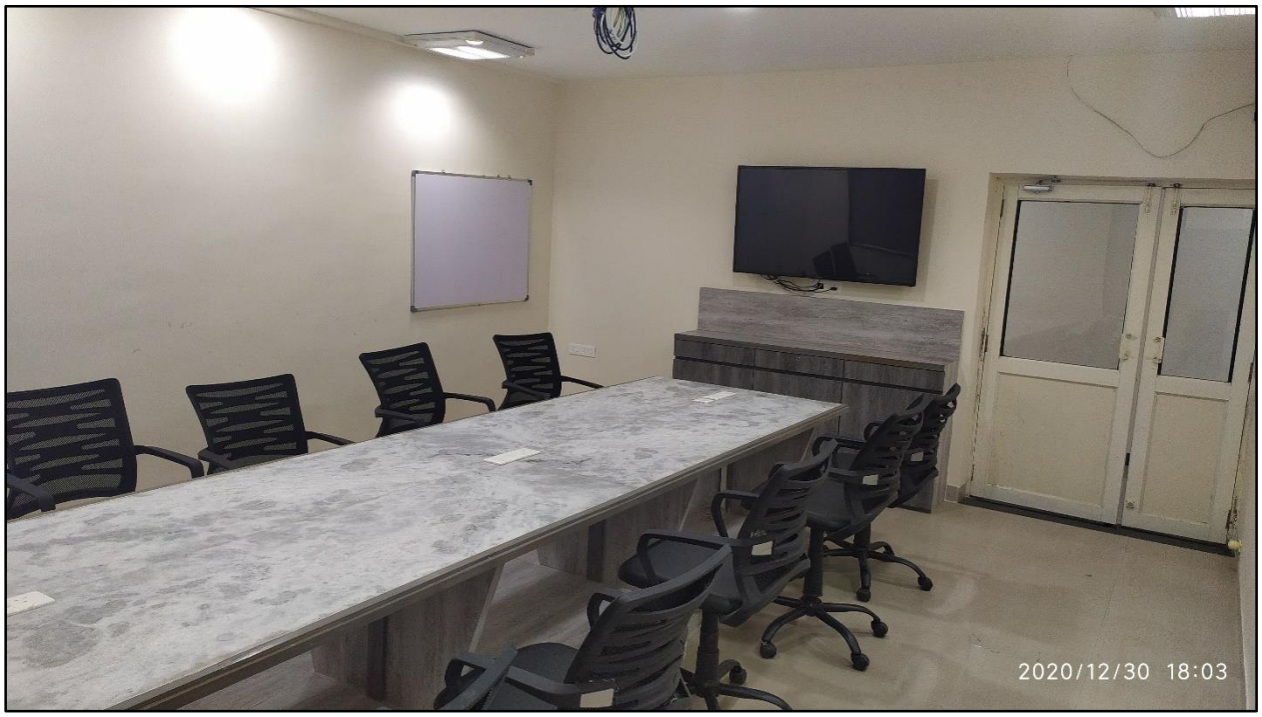


BSC-II facility and -80 ^{0}C Deep Freeze



Cooling Centrifuge, UV spectrophotometer and Microscope





----------*Thank You*----------