St Joseph's University, Bengaluru

St. Joseph's Research Institute

School of Life Sciences

Department of Biotechnology

PhD Entrance Examination Syllabus

Unit – 1 : Biomolecules and metabolism

A. Carbohydrates, Proteins, Lipids, Vitamins and Nucleic Acids – Composition & Types, Structure and function, Classification, Metabolisms, Biosynthesis; Diseases and disorders associated with the biomolecular defects.

B. Biomolecular interactions, principles of biophysical chemistry such as pH, buffer, - Computations, reaction kinetics, thermodynamics.

C. Bioenergetics, Glycolysis, Oxidative Phosphorylation, Energy coupled reactions, group transfer, biological energy transducers.

D. Enzymology – Types of enzymes, Classification, Principles of catalysis, enzymes and enzyme kinetics, enzyme regulation, mechanism of enzyme catalysis, isozymes

E. Conformation of proteins (Ramachandran plot, secondary structure, domains, motif and folds).

F. Conformation of nucleic acids (helix (A, B, Z), r-RNA, t-RNA, small RNAs – siRNA, micro-RNA, piwi-RNA.

Unit – 2: Biophysical Techniques

A. Chromatography – Types, Principles and Biological Applications

B. Centrifugation –Theory, Types, Applications,

C. Cellular biophysical methods - Flow cytometry, Patch Clamp.

D. Spectroscopy – Principles, Types – UV Vis, IR, Raman, CD, ICP-OES, Fluorescence, Mass Spectrophotometry – MALDI, ESI-MS MS, GC-MS, LC-MS.

E. Electrophoresis – Agarose, Polyacrylamide gels, 2D gels, Capillary gels and sequencing

F. Microscopy – Light, Electron microscopy – SEM, TEM, STEM, Fluorescence, Phase contrast, Confocal, Atomic Force, Cryo EM

G. Radioisotope methods – Types of isotopes used in biology, Units of Radioactivity, GM Counting, Liquid scintillation counting, Autoradiography.

Unit – 3: Microbes and Molecular Genetics

A. Microbial world – General characteristics of – Bacteria, Algae, Fungi, Protozoa and Viruses.

B. Molecular Microbial taxonomy –16srRNA,ITS, 18s based typing of microbes, Baltimore classification of viruses, Serological typing, Fatty acid profiling, DNA fingerprinting, Nucleic acid hybridization, Chemotaxonomy etc.,

C. Microbial interactions – Normal microbial flora, concepts of Microbiome, Epidemiological approaches.

D. Antimicrobial agents – Types – Antibacterials, Antifungals, Antivirals, mode of action, Multidrug resistance mechanisms

E. Mendelian laws & concepts, Sex-linked inheritance, Sex influenced traits, linkage, crossing over

F. Chromosomes & genes, types, gene families, genome mapping, mutations – types, mutagens, studies on mutants, molecular mechanisms, forward and reverse genetics.

G. Techniques in genetics – FISH, Chromosomal painting, comparative genome hybridization, Linkage mapping, molecular markers.

H. Chromosomal disorders – types, structural and numerical, Prenatal diagnosis, Cancer gene panels.

I. Genome organization of viruses, bacteria, recombination, methods of gene transfer etc.,

J. Gene pools, allele frequencies, Hardy Weinberg equation, non-random breeding, genetic drift, gene flow, selection, speciation.

K. Genome wide analysis (GWAS) – variants, Model organisms – Bacteria, Yeast, C.elegans, Mamalian cell lines, mice.

Unit- 4: Advanced Molecular and Cell Biology

A. Membrane structure and function- (Structure of model membrane, lipid bilayer and membrane protein diffusion, osmosis, ion channels, active transport, membrane pumps, mechanism of sorting and regulation of intracellular transport, electrical properties of membranes).

B. Structural organization and function of intracellular organelles (Cell wall, nucleus, mitochondria, Golgi bodies, lysosomes, endoplasmic reticulum, peroxisomes, plastids, vacuoles, chloroplast, structure & function of cytoskeleton and its role in motility).

C. Organization of genes and chromosomes (Operon, unique and repetitive DNA, interrupted genes, gene families, structure of chromatin and chromosomes, heterochromatin, euchromatin, transposons).

D. Cell division and cell cycle (Mitosis and meiosis, their regulation, steps in cell cycle, regulation and control of cell cycle).

E) DNA replication, repair and recombination , RNA synthesis and processing - transcription factors and machinery, Transcription in Prokaryotes and Eukaryotes, Protein synthesis and processing, translational proof-reading, translational inhibitors, Post- translational modification of proteins.

F) Control of gene expression at transcription and translation level (regulating the expression of phage, viruses, prokaryotic and eukaryotic genes, role of chromatin in gene expression and gene silencing). Gene regulation at transcription initiation: Constitutive and Regulatory control, Regulation of bacterial mRNA elongation by attenuation, CRISPR.

G) Transcription factors and combinatorial control of eukaryotic gene regulation, Epigenetic regulation of eukaryotic gene expression, Role of RNAs in eukaryotic gene expression regulation, Gene expression regulation in developmental stages

H) Cell communication and cell signalling: Host parasite interaction Recognition and entry processes of different pathogens like bacteria, viruses into animal and plant host cells, alteration of host cell behaviour by pathogens, virus-induced cell transformation, pathogen-induced diseases in animals and plants, cell-cell fusion in both normal and abnormal cells.

I) Cancer: Genetic rearrangements in progenitor cells, oncogenes, tumor suppressor genes, cancer and the cell cycle, virus-induced cancer, metastasis, interaction of cancer cells with normal cells, apoptosis, therapeutic interventions of uncontrolled cell growth.

Unit 5: Applied Biology and Methods in Biology

A. Microbial fermentation and production of small and macro molecules, vaccines, diagnostics, Tissue and cell culture methods for plants and animals, Transgenic animals and plants, molecular approaches to diagnosis and strain identification. Genomics and its application to health and agriculture, including gene therapy.

B. Bioresource and uses of biodiversity, Concepts of Ecology and Ecosystems, Threats etc., Breeding in plants and animals, including marker – assisted selection Bioremediation and phytoremediation. Biosensors and Applications.

C. Isolation and purification of RNA , DNA (genomic and plasmid) and proteins, different separation methods.

D. Molecular cloning of DNA or RNA fragments in bacterial and eukaryotic systems. Expression of recombinant proteins using bacterial, animal and plant vectors. Isolation of specific nucleic acid sequences Generation of genomic and cDNA libraries in plasmid, phage, Cosmid, BAC and YAC vectors.

In vitro mutagenesis and deletion techniques, gene knock out in bacterial and eukaryotic organisms. Nucleic acid blotting and hybridization - Preparation of DNA and RNA probes, Applications of hybridization-based tests, Labelling methods (Radioactive and Non-radioactive).

E. DNA sequencing methods, strategies for genome sequencing. Methods for analysis of gene expression at RNA and protein level, large scale expression, such as micro array based techniques Isolation, separation and analysis of carbohydrate and lipid molecules RFLP, RAPD and AFLP techniques.

F. Antibody generation, Detection of molecules using ELISA, RIA, western blot, immunoprecipitation, flowcytometry and immunofluorescence microscopy, detection of molecules in living cells, in situ localization by techniques such as FISH and GISH.

G. Direct, Indirect methods of gene transfer, Agrobacterium mediated gene transfer, Electroporation, Lipofection, Microinjection and Biolistics.

H. Gene silencing strategies - Antisense RNA technology, RNAi technology, microRNA technology, CRISPR-Cas9 for genome editing and CRISPR – Cas 13 technologies.

I. Introduction to NGS Sequencing – Illumina Technology, Denovo sequencing or Resequencing; Exome sequencing; RNA sequencing; Small RNA sequencing; Metagenomics; NGS workflow: DNA/RNA isolation and quantitation; Fragmentation (different methods – Physical / Enzymatic/ Chemical); Library preparation, ATAC-Sequencing, Bisulfite sequencing, Chip-Sequencing, Bisulfite sequencing, MIRA, BisChip Sequencing, Applications of transcriptomics - case studies.

J. Differential proteomics and Cell Map Proteomics. iTRAQ, Metabolomics-an overview, basic sample preparation strategies- extraction, derivatization. Targeted Vs Untargeted metabolomics.

K. Single Cell Omics: Methods of Single Cell Isolation – Micromanipulation, Immunopanning, FACS, Magnet activated cell sorting, Laser Microdissection, Method of single-cell type nuclei, Isolation of cell specific molecules.

M. Statistical Methods: Measures of central tendency and dispersal; probability distributions (Binomial, Poisson and normal); Sampling distribution; Difference between parametric and non-parametric statistics; Confidence Interval; Errors; Levels of significance; Regression and Correlation; t-test; Analysis of variance; X^2 test;; Basic introduction to Multivariate statistics, etc.

<u>Unit 6:</u> Computational Biology:

A. Nucleotide sequence databases, Primary nucleotide sequence databases - ENA, Genbank, DDBJ; Specialized genome databases – GOLD, TAIR, SGD. Literature Databases – PUBMED. Protein structure and function, Protein Primary structure, Amino acid residues, Secondary, Tertiary, Quaternary Structure of Protein, Protein sequence databases - UniprotKB (SwissProt/ TrEMBL), Sequence motif databases/Secondary Protein sequence databases -Pfam, PROSITE, Interpro. Protein structure databases, Protein Data Bank - SCOP, CATH, KEGG, PubChem databases, Interactome databases.

B. Concept of Sequence alignment, Phylogenetics - Rooted and unrooted trees, Molecular Clock Hypothesis, Distance based data - UPGMA and Neighbor Joining Methods. Character based data: Maximum Parsimony and Maximum likelihood method. Methods of tree evaluation – Bootstrapping.

C. Concept of Protein modeling, Ab-initio based protein modeling, Protein homology modeling, Energy minimization. Basics of Molecular dynamics. Concept of Docking. Protein-protein docking algorithms and programs, Ligand Protein docking. QSAR. Identification of Drug targets, Active site prediction, Molecular modeling, ADMET studies.

Unit-7: Immunology, Animal and Medical Biotechnology:

A. Innate and Adaptive Immune Responses, Hematopoiesis, Cells of the immune system, Primary and Secondary Lymphoid Organs. Innate immune recognition, Pattern Recognition Receptors, Toll-like receptor signaling, Barriers of innate immunity, The complement system - concept, characteristics and components, Complement Activation - Classical, Alternative and Lectin pathways, Results of complement activation, Complement deficiencies, Mechanism of Phagocytosis.

B. Features and Phases of adaptive response, Antigen Presenting Cells, Concept of Antigens, Pathways of antigen processing and presentation - Endogenous and Exogenous Antigen Pathways, Cell Mediated Response - types, Development and Function of Effector T cells, Migration of Effector T cells, Role of T and NK cells in cell mediated immunity - Function of regulatory T cells, T cell mediated cytotoxicity.

C. B-cell receptor, Maturation of B cells, Selection, Activation and Proliferation of B cells, Thymus-dependent and independent antigens, Differentiation of B cells - Affinity maturation, Class Switching, Generation of plasma and memory cells, Humoral Response, Structure of Antibodies, Classes and function of Antibodies, Organization of Immunogenes, Rearrangement of variable regions in immunoglobulin, Somatic Recombination and genetic diversity in Ig genes, Allelic Exclusion, Clonal Selection Theory.

D. Different types of transplants, Allorecognition, Mechanism and stages of allograft rejection, Overview of organ transplantation, Skin transplantation and artificial skin, Concept of xenotransplantation.

E. Host-symbiont interaction, Mucosal immunity and role of gut microbiota, Viral immunity, Bacterial Immunity, Fundal immunity, Parasite immunity, Evasion strategies of microbes and parasites.

F. History, Scope and applications of animal cell culture- Advantages and limitations. Laboratory setup and equipment. Types of cell culture media. Preparation and sterilization of media and supplements. Balanced salt solution, complete media and its biochemical ingredients. Serum and- serum free media, artificial media. Isolation of tissue. Disaggregation of tissue – Mechanical and Enzymatic methods. Different culture techniques, Secondary culture. Passaging number; characteristics of animal cells in cultures; Suspension culture, Embryonic and Adult stem cell culture. Continuous cell lines, Maintenance of cell Lines- Cryopreservation and Germplasm storage. Cell counting and viability assay- MTT, LDH and Alamar assay. Growth phases of cells in culture. Assisted reproductive Technology (ART) and In vitro fertilization.

Unit 8: Industrial, Plant and Environmental Biotechnology

A. Historical overview of industrial fermentation process microorganisms, mode of operation, General requirements of fermentation processes, Basic concepts of Upstream and Downstream processing in Bioprocess. Target for improvement, Optimization, methods of strain improvement, screening and detection, preservation. Media used in fermentation a overview, media sterilization and approach to scale up in industry

B. Design and operation of bioreactors, Types: airlift, bubble column, packed bed and fluidized bed reactors, Stability analysis of bioreactors. Scale up criteria for bioreactors based on oxygen transfer, power consumption and impeller tip speed and agitation; agitation of liquids; gas-liquid systems; gas-solid suspensions; agitator scale up.

C. Introduction to downstream processing principles, characteristics of biomolecules and bioprocesses. Cell disruption strategies. Separation : Unit operations for solid-liquid separation, filtration and centrifugation, flocculation, precipitation and settling of particles Isolation : Adsorption, liquid-liquid extraction, aqueous two-phase extraction, membrane separation: ultrafiltration and reverse osmosis, dialysis, precipitation of proteins by different method. Product finishing:

Crystallization principles Equipment used, Drying principles-Equipment for drying and Lyophilization Use of chromatography in purification at the industrial level.

D. Enzyme immobilization : Physical and chemical techniques for enzyme immobilization –adsorption, matrix entrapment, encapsulation, cross-linking, covalent binding. Detailed production steps for Beer and alcohol, Antibiotics Mycoprotein production, Amino acids, Polyhydroxyalkanoates, Anthracyclines, Botox.

E. Entrepreneurship in Biotechnology: Identifying Startup capital Resource requirements; estimating Startup cash requirements; Develop financial assumptions; Constructing a Process Map; Positioning the venture in the value chain; Launch strategy to reduce risks; Startup financing metrics; The Legal Environment; Approval for New Ventures; Taxes or duties payable for new ventures.

F. Bioethics and Safety: Introduction to Bioethics and Biosafety: definition and needs of Bioethics, Social and Ethical issues in biotechnology. Biosafety: definition and needs of biosafety, levels of biosafety, applications of biosafety at workplace, Biosafety during development of biotech products. Examples and case studies. Ethical issues regarding genetically modified organisms (foods and crops); bioethics in biodiversity and resource management. Animal cloning and human cloning and their ethical aspects.

G. The transgenic crop landscape, Plant transformation techniques, strategies for engineering stress tolerance, GMOs for pest and disease resistance, abiotic stress tolerance, herbicide tolerance, biofortification. Regulatory Frameworks. Molecular markers, Marker assisted selection, Genomics and Proteomics in crop improvement, RNAi, CRISPR/Cas9 gene editing tools.

H. Bioremediation: Introduction, Types (In situ, Ex situ), Techniques - Bioaugmentation, Biofilters, Bioreactors, Biostimulation, Bioventing, Composting. Examples of organisms used in Bioremediation. Organisms for bioremediation applications: Bacillus spp., Pseudomonas spp., Aspergillus spp., Algae spp. Biocontrol: NPV, Bacillus thuringiensis, B. sphaericus, Baculovirus. Biofuels: Bioethanol, Biogas.

Unit: 9 Research Methodology concepts:

A. Natural science vs social science research, qualitative vs quantitative research, overview of the research process, criteria of good research. Identifying and critiquing elements of research, including the hypothesis and methodology.

B. Identifying a research area of interest, importance of originality and impact, exploratory versus incremental research, why do a literature survey, Systematic Vs Scoping reviews, identifying research gaps, information literacy, methods and techniques of literature survey, scientific search engines, reference management systems, narrowing and defining the research problem, finding research protocols, establishing a framework for scientific research.

C. Overview of research design, hypothesis and overview of hypothesis testing, types of errors and their control. Framework of individual experiments, The need for experimental controls: Negative and positive controls, Reagent and Method controls, The need for replicates: Biological Replicates, Technical Replicates, Experimental Repeats, Randomization of samples, Time Courses, and Dose Responses. Repeatability, Reproducibility, Reliability, Specificity and sensitivity of instruments and techniques.

D. Overview of the types of data, primary and secondary data collection methods, Managing big data, data curation, physical and e-lab notebooks, an overview of statistical tests for data analysis, numerical and graphical data, types of graphs.

E. Data fabrication, plagiarism, authorship issues, Image manipulation, duplicate publications, investigation and consequences of scientific misconduct.

F. Types of Scientific communication: Research papers, Research proposals, Posters, Project report; Publishing, H-index, Impact factors in publishing. Elements of effective scientific communication, scientific illustrations.