SCHOOL OF PHYSICAL SCIENCES

Centre of Advanced Study in Crystallography and Biophysics

Crystallography and Biophysics

P. Karthe, Ph.D. - Professor & Head
K. Gunasekaran, Ph.D. - Assistant Professor
V. Rajakannan, Ph.D. - Assistant Professor
D. Gayathri, Ph.D. - Assistant Professor
Preethi Ragunathan, Ph.D. - Assistant Professor
Gugan. K, Ph.D. - Assistant Professor

M.Sc. BIOPHYSICS: Eligibility for Admission

"A Candidate who has qualified with B.Sc Degree or equivalent accepted by the Syndicate of this University in Physical, Chemical and Life Sciences provided they have studied Mathematics at their Higher Secondary School level"

PK : Dr. P.Karthe, KG: Dr. K. Gunasekaran, RK: Dr. V. Rajakannan, DG: Dr. D. Gayathri, PR: Dr. Preethi Ragunathan, GK: Dr. Gugan K

FIRST SEMESTER

PHY C001	Elementary Crystallography	C	3	1	0	4	DG
PHY C002	Principles of Macromolecular Structure & Function	C	4	0	0	4	PK
PHY C003	Mathematics for Biophysics	C	4	0	0	4	RK/GK
PHY C004	Molecular Cell Biology	C	3	1	0	4	PR
PHY C005	Macromolecular Structure & Function (Theory & Practice)	C	3	1	0	4	GK/RK
PHY E001	Computational Biology	E	2	1	0	3	GK
PHYE002	Molecules and Medicine	E	2	1	0	3	PR

SECOND SEMESTER

PHY C006	Principles and Applications of Spectroscopy to Biomolecules	C	3	1	0	4	KG
PHY C007	Physical Studies of Macromolecules in Solution	C	3	1	0	4	DG
PHY C008	Molecular Biology of the Gene	C	3	1	0	4	PR
PHYE003	Basic Structural Biology (for Other Dept. students)	E	2	1	0	3	PK
PHYE004	Basics of Molecular Virology	E	2	1	0	3	RK
PHYE005	Introduction to Chemoinformatics and Computer aided Drug Design	E	2	1	0	3	GK
PHYE006	Proteins and Proteomics	E	2	1	0	3	DG

THIRD SEMESTER

PHY C009	Three Dimensional Structure Determination of Drug Molecules	C	3	1	0	4	DG
PHY C010	Seminars in Biophysics	C	0	4	0	4	KG/DG/PR/GK
PHY C011	Macromolecular Crystallography	C	3	1	0	4	PR
PHY C012	Crystallography Laboratory	C	0	0	4	4	KG/RK
PHY E006	Membrane Biophysics & Neuro Biophysics	E	2	1	0	3	RK
PHY E007	Fundamentals of Molecular Spectroscopy (for other Dept. students)	E	2	1	0	3	KG

FOURTH SEMESTER

PHY C013	Biophysics of the Immune System	C	3	1	0	4	RK
PHY C014	Project Work	C	0	0	4	4	All Faculty
PHY C015	Biophysics Laboratory	C	0	0	4	4	PR/DG
PHY E008	Protein Purification & Characterization	E	2	1	0	3	KG

COURSE ABSTRACT: M. Sc. BIO PHYSICS

FIRST SEMESTER

PHY C001	Elementary Crystallography	C	3	1	0	4	PK

Crystal systems and space groups, X-ray scattering, techniques of X-ray generation, recording of diffraction patterns, Symmetry deduction, absolute configuration.

PHY C002	Principles of Macromolecular Structure & Function	C	4	0	0	4	PK

Stereochemistry, conformational analysis, proteins structure, protein folding, nucleic acid structure, polysaccharide structure, macromolecular assembly.

PHY C003	Mathematics for Biophysics	C	4	0	0	4	RK/GK

Basic statistics, vector algebra, Differential & Integral Calculus, Differential equations, Fourier Transformations, convolution theorem.

PHY C004	Molecular Cell Biology	C	3	1	0	4	PR

ECM, Cell architechture, Protein modifications, signaling, cell cycle

PHY C005	Macromolecular Structure & Function (Theory & Practice)	C	3	1	0	4	RK/GK

Structure visualization softwares, Sequence alignment softwares/web sources will be introduced to have hands on training.

PHY E001	Computational Biology	E	2	1	0	3	GK

Strings, Graphs and Algorithms ; Probability Theory - Molecular Simulation and Dynamics - interaction and metabolic networks in cells Strings, graphs and algorithms

PHYE002	Molecules and Medicine	E	2	1	0	3	PR

Protein structure- inflammatory and cardiovascular diseases, infectious diseases, drugs acting on nervous system

SECOND SEMESTER

PHY C006	Principles and Applications of Spectroscopy to Biomolecules	C	3	1	0	4	KG

Infrared, Raman, UV spectroscopy, ORD & CD, NMR spectroscopy, fluorescence spectroscopy, simple applications.

PHY C007	Physical Studies of Macromolecules in Solution	C	3	1	0	4	DG

Chemical Thermodynamics, statistics of linear polymers, osmotic pressure, diffusion, light scattering, viscosity, electrophoresis, chromatography.

PHY C008	Molecular Biology of the Gene	C	3	1	0	4	PR

Replication, gene expression, regulation of gene expression, recombination, cell cycle and growth regulation

PHY E003	Elementary Structural Biology	E	2	1	0	3	PK

Elementary Crystallography - X-ray scattering -Experimental methods - Structure Determination – Protein Crystallography.

PHY E004	Basics of Molecular virology	E	2	1	0	3	RK

PHY E005	Introduction to Chemoinformatics and Computer aided Drug Design	**E**	2	1	0	3	GK

Chemical structure, QSAR, Virtual Screening, Force Field, CADD, Protein Folds

PHY E006	Proteins and Proteomics	E	3	1	0	3	DG

Classification of protein structure, protein separation / characterization methods and protein-protein interaction techniques

THIRD SEMESTER

PHY C009	Three Dimensional Structure Determination of Drug Molecules	C	3	1	0	4	DV

Crystallographic statistics - Direct Methods - Tangent formula - use of quartets - Structural Data Base

PHY C010	Seminars in Biophysics	C	0	4	0	4	KG/DG/PR/GK

Students are required to give seminars on advanced topics in Biophysics and related topics. Students will be Evaluated by a faculty committee in a manner similar to Theory papers.

PHY C011	Macromolecular Crystallography	C	3	1	0	4	PR

Macromolecular crystallization techniques, Mounting the crystals, structure solution and refinement, interpretation of results.

PHY C012	Crystallography Laboratory	C	0	0	4	4	KG

Students have to perform the prescribed experiments in crystallography.

PHY E007	Membrane Biophysics & Neuro Biophysics	E	2	1	0	3	RK

Membrane constituents and structure, membrane potentials, Ion transport, nerve cells, sensory systems, and mechanism of action.

PHY E007	Fundamentals of Molecular Spectroscopy (for other Dept. students)	E	2	1	0	3	KG

Electromagnetic Spectrum - Microwave, IR and Raman Spectroscopy - Structure determination of simple molecules

FOURTH SEMESTER

PHY C013	Biophysics of the Immune System	C	3	1	0	4	RK

Cellular basis of Immune response - T and B Lymphocytes - antibodies - antigens - T cell receptors.

PHY C014	Project Work	C	0	0	4	4	All Faculty

Each student will submit a Project Report on a chosen topic under the guidance of a Supervisor.

One semester project work under the guidance of a faculty member. The student is required to carry out individual experimental / computational work and submit a dissertation. The work carried out is to be presented before a committee of faculty members for evaluation followed by Viva – Voce Examination

PHY C015	Biophysics Laboratory	C	0	0	4	4	PR/DG

Students have to perform the prescribed experiments in Biophysics

PHY E008	Protein Purification & Characterization	E	2	1	0	3	KG

Isolation, Extraction of biomolecules from various sources, Precipitation and fractionation, Column Chromatography -Different Gel matrices, Affinity & Pseudo Affinity and classical techniques.

PHY C001	Elementary Crystallography	C	3	1	0	4	DG

Elementary Crystallography: External features and symmetry - unit cell and Miller indices -crystal systems - Bravais lattices - point groups and space groups - X-ray diffraction - Laue equations - Bragg's law - reciprocal lattice and its application to geometrical Crystallography.

X-ray scattering: Atomic scattering factor - diffraction by a space lattice - structure factor equation - electron density and Fourier series - Fourier Transform and crystal diffraction - diffraction by real crystals - Lorentz and polarization factor - primary and secondary extinctions.

Experimental methods: Generation, detection and properties of X-rays - filters monochromators - absorption coefficients - choice of radiation, synchrotron radiation.
Outlines of Powder, Laue, Weissenberg and precession photography.
Intensity estimation and deduction of structure factor amplitudes - Wilson plot - scale and temperature factors - symmetry deduction and determination of space groups - test for centro symmetry - use of intensity statistics in space group determination.
Anomalous scattering and violation of Friedel's law - absolute configuration.

Powder Diffraction: Powder photographs - interpretation of powder photograph ASTM index.

Fiber Diffraction: Theory of diffraction by helical structures and application to alpha helix and DNA.

Elements of electron and neutron diffraction: principles of neutron scattering neutron scattering lengths - applications of neutron scattering techniques in crystal structure analysis - comparison of X - ray and neutron scattering.

References

1. Structure determination by X-ray Crystallography. M.F.C Ladd & R.A. Palmer. Springer Publications.
2. Fundamentals of Crystallography. C. Giacavazzo et al. International Union of Crystallography. Oxford Science Publications.
3. X-ray Structure determination: A Practical Guide. Geroge H. Stout & Lyle H. Jensen. Wiley-Blackwell Publications.
4. Elements of X-ray diffraction. B.D. Cullity.Addison-Wesley Publishing Company Inc.
5. The basics of crystallography and diffraction. C. Hammond. Oxford Science Publications.
6. Introduction to crystallography. Donald E Sands. Dover Publications.
7. An Introduction to Crystallography. M.M. Woolfson. Cambridge University Press.

PHY C002	Principles of Macromolecular Structure & Function	C	4	0	0	4	PK

Stereochemistry and concept of conformation: Asymmetric carbon atom - optical, geometric stereoisomerism - chirality - Fischer convention - L and D residues - torsion angle - hindered rotation.

Conformational analysis: van der Waal's radii or effective no bonded radii of atoms contact distancecriteria - Noncovalent forces determining biopolymer structure dispersion forces - electrostatic interactions - van der Waal' s interactions - hydrogen bonds - hydrophobic interactions - distortional energies - description of various interactions by potential functions - elementary ideas of minimization of conformational energy and molecular dynamics.

Principles of protein structure : Structural implications - Concept of rigid planar peptide unit - *cis* and *trans* configuration - structural implication conformations of a pair of linked peptide units - torsion angles phi and psi - Steric hindrance - hard sphere approximation - allowed and disallowed conformations Ramachandran Diagram - specific effects of proline and glyline - conformationally constrained amino acids and their importance.

Levels of organization of polypeptide chains: primary, secondary, tertiary and quaternary structures - types of secondary structures - alpha helix, beta sheet, reverse turns - Super secondary structures - alpha, beta and alpha / beta classification of proteins.

Structure of fibrous proteins: Structure of collagen - structure of silk and wool, structure muscle protein and mechanism of muscle contraction.

Structure and function of globular proteins: Structure and action of myoglobin, hemoglobin, lysozyme, chymotrypsin, pepsin, dehydrogenases - enzyme - substrate interactions.

Protein folding: Anfinsen's principle - Levinthal paradox - Semi empirical Methods of protein structure prediction - Molten globular states - conformational intermediates chaperones and their function.

Principles of nucleic acid structure: Conformations of nucleosides and nucleotides- Watson and Crick's base-pairings and their implications. Non Watson and Crick pairing schemes - base stacking interactions - DNA polymorphism - structure of ADNA, BDNA and ZDNA - helical transitions. Non-uniform helical DNA Structure. Unusual DNA structures - hairpins, bulges, cruciform, triplexes, tetraplexes.

Structure of RNA and RNA - DNA hybrid duplexes - Structure of tRNA - Structure of Hammer head ribozymes. Elementary ideas of secondary and tertiary structures of large RNA's.

Principles of polysaccharide structure: Stereoisomerism of hexapyranose sugars conformation of mono and disaccharides - structures of maltose, cellobiose and laminaribiose and their polymers - bacterial cell wall polysaccharides.

The structure of macromolecular assembly: Principles of packing of protein subunits in rod and spherical viruses - structure of chromatin - Elementary ideas of the Structure of 50s and 30s ribosomal particles.

References:

1. Principles of Protein Structure, by Georg E. Schulz and R. Heiner Schirmer
2. Biochemistry, 4th Edition, 2011, by Donald Voet, Judith G. Voet
3. Introduction to Protein Structure, by Carl-Ivar Brändén and John Tooze
4. Principles of Nucleic Acid Structure, by Wolfram Saenger.
5. Virus Structure, by Robert W. Horne.

PHY C003	Mathematics for Biophysics	C	4	0	0	4	RK/GK

This paper is designed to educate students to learn crystallography concepts with ease.

Basic Statistics - applications
Vector Algebra - applications
Differential & Integral Calculus – applications
Differential equations – Applications
Laplace & Fourier Transformations – applications
Convolution Theorem

Reference:

Statistical Methods by S.P.GUPTA, Sultan Chand & Sons Publishers, New Delhi
Structure Determination by X-ray Crystallography, Mark Ladd & Rex Palmer, Springer, Newyork

PHY C004	Molecular Cell Biology	C	3	1	0	4	PR

Unit I
Extracellular matrix (ECM), components of ECM, Fibronectin, laminin, collagen. Heparin sulphate, proteoglycans, role of ECM in cell growth and survival. Cell to cell adhesion; cell junctions, Tight junctions. Desmosomes, connexins, selectins, integrins. Ig superfamily and cell cell adhesion in contact inhibition.

Unit II
Microfilaments, actin, cytoskeleton, G and F actin, Dynamics of actin assembly and polymerization and myosin and molecular motors. Microtubule structure and dynamics, microtubular organizing centres. Dynamic instability, microtubule associated protein (MAPs), kinesin, dynein and intracellular transport. Kinetochore architecture and spindle assembly. Focal adhesion points. Microvilli and pseudocodial extensions. Intermediate filaments; types and functions.

Unit III
Protein targeting to endoplasmic reticulum, golgi and lysosome complex in protein targeting, chaperones and protein folding. GPI anchoring targeting of proteins to mitochondria. Glycosylation post translational modification. Basis of lysosome storage disease.

Unit IV
Autocrine, paracrine, endocrine, cell signalling, steroids and Juxtracrine, communication. Nitric oxide carbon monoxide. Paracrine factores involved in communication- FGF's Hedgehog family, Wnt family, IGF-Beta super family, BMP family, G-protein cyclic AMP pathway, IP3 pathway, RTK pathway, RTK dimerization and autophosphorylation, SH2 domains, MAP kinase pathway, smad pathway, JAK signalling pathway, WNT pathway.

Unit V
Eukaryotic cell cycle; cell growth and extracellular signals, molecular basis of cell cycle regulation, cell cycle checkpoints, cyclin and dependent kinases, Rb regulation exit from cell cycle. Mis-mpf and m-phase events. Oncogenes, proto-oncogenes and viral oncogenes. Oncogene activation; tumor suppressor genes, apoptosis; survival and death factors, cell death receptors, cell to cell interaction.

References:

1. Molecular Cell Biology 6th Edition by Harvey lodish, Arnold Beck and Chris A. keiser
2. Essential Cell Biology, Fourth Edition By Bruce Alberts, Dennis Bray, Karen Hopkin, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts, Peter Walter

PHY C005	Macromolecular Structure & Function (Theory & Practice)	C	3	1	0	4	GK/RK

Theory & Hands on Training on (laboratory Paper) -
Expasy Web server and its utility in Primary, Secondary and Tertiary structures of proteins.
Web based sequence alignment protocols for amino acid and nucleotide sequences
Protein Data Bank and corresponding utility tools
Homology Modeling of proteins
EMBL web server and utilities
Applications of Molecular visualization softwares – Rasmol, PyMol, Swiss PDB Viewer

PHY E001	Computational Biology	E	2	1	0	3	GK

Strings, Graphs and Algorithms ; Probability Theory -Molecular Simulation and Dynamics -interaction and metabolic networks in cells Strings, graphs and algorithms

General concept of a string – DNA and protein sequences as strings – string operations – prefixes and suffixes – definition of graphs – classification of graphs – algorithms – definitions – P, NP, NP-hard and NP-complete algorithms Probability theory

Introduction – simple ideas about distributions – discrete distributions (Bernoulli, Binomial, Uniform, Geometric, and Poisson) – continuous distributions (Uniform, Normal, Exponential, Gamma and Beta) – Statistical inference – Introduction to classical and Bayesian inference Algorithms on strings

Sequence comparison and database searching – global, local and semi global comparison – DNA fragment assembly – the ideal case and complications – phylogenetic tree construction – parsimony – RNA secondary structure prediction Molecular simulation and dynamics

Basic molecular dynamics – equations of motion – potential functions – integration computations – Initial state – boundary conditions – equilibration – dynamics protocols – trajectories – analyses of results – AMBER, CHARMm, -simple applications to proteins and nucleic acids Miscellaneous topics

Micro arrays and analyses – DNA computing – Hamiltonian path problem – systems biology – interaction and metabolic networks in cells – wholcell simulations – E-cell and V-cell.

Reference Books:

1. Molecular Modeling Principles and Applications (2nd Ed.) by Andrew R. Leach, Prentice Hall, USA. 2001
2. Bioinformatics by David W. Mount, Cold Spring Harbor Laboratory Press. 2001
3. Bioinformatics Methods And Applications: Genomics Proteomics And Drug Discovery", S. C. Rastogi, Parag Rastogi, Namita Mendiratta, PHI Learning Pvt. Ltd., 3rdedition, 2008.
4. Bioinformatics: Databases and Algorithms, N. Gautham, Narosa Publications, 2006.

PHYE002	Molecules and Medicine	E	2	1	0	3	PR

Proteins and three dimensional structure- common chemical diagrams-some common molecules

Inflammatory and cardiovascular diseases: How do anti-inflammatory drugs work? - Overview of inflammation- Aspirin-Naproxen

Eicosanoids-Anti-diabetic and cholesterol lowering agents

Infectious diseases- Antibioitics- drug resistance- antiviral agents- antifungal agents- anti-malarial and anti-parasitic agents

Drugs acting on nervous system- Pain and analgesia- hypnotics and anti-smoking- neurodegenerative and psychiatric diseases

References:

1. Molecules and Medicine by E.J. Corey, Barbara Czako and Laszlo Kurti.
2. Finkel, Richard; Cubeddu, Luigi; Clark, Michelle (2009). *Lippencott's Illustrated Reviews: Pharmacology 4th Edition*. Lippencott Williams & Wilkins. pp. 1–4.
3. Miller, AA; Miller, PF (editor) (2011). *Emerging Trends in Antibacterial Discovery: Answering the Call to Arms*. Caister Academic Press.

SECOND SEMESTER

PHY C006	Principles and Applications of Spectroscopy to Biomolecules	C	3	1	0	4	KG

Infrared spectroscopy: General principles of spectroscopy - origins of rotational and vibration spectra - anharmonic oscillator - molecular symmetry - overtone and combination bands - experimental aspects and methods - optical density investigation of molecular structure with special reference to deuterium exchange, hydrogen bonding - applications to polypeptides and proteins, principles of FTIR spectroscopy-advantages.

Raman spectroscopy: Principles - experimental aspects - advantages of Raman spectroscopy - Laser as Raman source - advantages - Raman spectra of amino acids - application to proteins and nucleic acids - Laser Raman spectroscopy.

Absorption spectroscopy: Principles - experimental aspects of visible and UV spectroscopy - absorption of chromophores - chemical analysis by visible and UV light - applications to protein and nucleic acid structures with respect to denaturation. **ORD and CD** : Principles of optical activity - Cotton effect - relation between ORD and CD - physical origins - application to estimation of secondary structures in proteins structural characterization of nucleic acids.

NMR spectroscopy: General principles - classical picture - resonance condition Bloch equations - relaxation phenomena and measurements - effect of relaxation times on line-width - Fourier transform technique - chemical shifts - coupling constants Karplus equation - NOE effects - Proton magnetic resonance (PMR), spectra of amino acids and peptides - conformation of amino acids and peptides - application to proteins with reference to helix coil transition and denaturation - PMR applications to characterization of base pairs and nucleotide conformation.

Fluorescence spectroscopy : Basic principles - experimental set up - chromophores in biological systems - applications. **Some Modern Techniques:** Elementary aspects of atomic force microscopy, confocal microscopy and optical tweezers. Simple applications to biopolymers.

References:

Fundamentals of Quantum Chenistry, James E. House, 2005
Fundamentals of Molecular Spectroscopy, Banwell C,N., 1994
Molecular Symmetry and spectroscopy, Bunker, P.R. and Jensen, P., 1998
Group theory and its applications in chemistry, Raman, K.V., 1994
Molecular Structure and Spectroscopy, Aruldhas, G., 2008
Spectroscopic identification of organic compounds, Silverstein, R.M, 1998
Pharmaceutical applications of Raman spectroscopy, Edited by Slobodan Sasic., 2007
NMR in biology, Dwek., 1977
Methods in ENzymology Vol 402, Burlingame, A. 2005
Spectra of atoms and molecules, Bernath, P.F., 2005
Biophysical Chemistry, Cantoer and SHimmel, Part II, 2004
Organic spectroscopic structure determination, Taber, D. F., 1948, 2007
Basic one and two dimensional NMR spectroscopy, Friebolin, H., 1998
Laser spectroscopy and other topics, Series, G.W., 1985

PHY C007	Physical Studies of Macro – - molecules in Solution	C	3	1	0	4	DG

Thermodynamics: Fundamental principles of the thermodynamics of solutions partial molal and partial specific volumes - chemical potential in ideal and real solution - colligative properties and molecular weight - the total free energy of a solution - excluded volume for dilute solutions & flexible polymers.

Statistics of linear polymers: Molecular weight averages and distributions - average dimensions - end-to-end distance - radius of gyration - interaction between polymer segments and solvent molecules and its effect on the end-to-end distance.

Osmotic pressure: Principles of osmotic pressure - van't Hofrs law - concentration dependence of osmotic pressure - effect of electrostatic charge on the thermodynamic behavior in solution - equilibrium across a semi-permeable membrane - Donnan effect - osmotic pressure of solutions containing macro ions - osmotic pressure of protein solutions - membrane potentials - phase equilibria - solubility and freezing point melting points of crystalline polymers - solubility of crystalline proteins.

Diffusion: Macromolecular diffusion - Fick's law of diffusion - experimental determination of diffusion coefficients - Einstein and Sutherland equation. Ultracentrifugation: General principles - Lamm's equation - Svedberg equation sedimentation velocity - sedimentation equilibrium - determination of molecular weight from sedimentation data - shape information from sedimentation data - density gradient methods - molecular weight averages - applications of the analytical ultracentrifuge.

Light Scattering: Elastic and inelastic scattering - light scattering by macromolecules Zimm plot - estimation of chain dimensions - experimental results on some proteins and nucleic acids. Low angle X-ray scattering: General principles - determination of radius of gyration and end to end distance.

Viscosity: General principles - frictional coefficient - Newtonian flow Poiseuille's law for capillary flow - experimental measurement of the viscosity of liquids - specific and intrinsic viscosities - Einstein-Simha equation for the viscosity of suspensions - applications of viscosity measurements.

Electrophoresis: Principles of electrophoresis - factors affecting electrophoresis micro electrophoresis - its applications - moving boundary electrophoresis course electrophoresis - slab gel electrophoresis and tube gel electrophoresis separation of macromolecules and other applications - isoelectric focusing and isotachophoresis - preparative electrophoresis.

Chromatography: General principles - paper chromatography - TLC - column chromatography - gas, liquid chromatography - ion exchange chromatography - exclusion chromatography - affinity chromatography - high performance liquid chromatography - applications to macromolecules.

References

Physical Biochemistry. D. Freifelder. W.H. Freeman & Company.

Biophysical Chemistry, Charles R. Cantor & Paul R. Schimmel, W.H. Freemann & Company.

Physical Principles and Techniques of Protein chemistry - Part A & B. S.J. Leach. Academic Press New York.

A Biologist Guide to Principles and Techniques of Practical Biochemistry.K. Wilson & K.H. Goulding. Edward Arnold Publishers.

Physical Chemistry of Macromolecules. C. Tanford. John Wiley & Sons.

Physical Biochemistry. K.F. von Holde. Prentice-Hall Inc.

Physical Chemistry with applications to the Life Sciences - Part I & II. D. Eisenberg & D. Crothers. The Benjamin Cummings Publishing Company.

Physical Chemistry for the Biosciences. Raymmond Chang. University Science Books.

PHY C008	Molecular Biology of the Gene	C	3	1	0	4	PR

Unit I:
DNA replication and repair **:**Enzymes of replication, prokaryotic replication mechanisms, the cellular replisome, eukaryotic DNA replication, the role of topoisomerases and telomerase, regulation of replication. DNA repair mechanisms – Direct repair, excision repair, mismatch repair, recombination repair, SOS response, eukaryotic repair systems.

Unit II :
Prokaryotic gene expression**:** Transcription – subunits of RNA polymerase, σ factor and promoter recognition, alternative σ factors, *E. coli* promoters, Rho-dependent and independent termination of transcription. Translation – organization of the ribosome, the genetic code, its universality, deciphering the genetic code, wobble hypothesis, activation, initiation, elongation and termination of translation in *E. coli.* The role of tRNA and rRNA, suppressor tRNAs and inhibitors of protein synthesis.

Unit III:
Regulation of prokaryotic gene expression**:** The *lac* operon, identification of operator and regulator sequences by mutations, induction and repression, Foot-printing and gel-shift assays for identification of protein-DNA interactions. Catabolite repression. Trp operon – Attenuation,alternative secondary structures of trp mRNA. Regulation of translation by small RNA molecules, Control of lytic development in λ phage.

Unit IV:
Recombination and mobile genetic elements**:** The Holliday model, general recombination in *E. coli*, site-specific recombination, transposons, transposition, phase variation in *Salmonella*, Retroviruses and retroposons.

Unit V:
Cell cycle and growth regulation**:** Cyclins, cyclin – dependent kinases, molecular basis of cell cycle regulation, role of p53 and Rb proteins, checkpoints in cell cycle regulation, Apoptosis – various stimuli and pathways.
Oncogenes and cancer **:** Molecular Mechanisms**-**Proto-oncogenes, activation of proto-oncogenes, regulation of gene expression by oncoproteins, viral oncogene products, growth factor receptor kinases, components of signal transduction cascade.

References:

- **Lewin B:**Genes 8**;** Prentice Hall; International Ed edition (2004)
- **Watson JD , Baker TA, Bell S, Gann A, Levine M, Losick R** Molecular Biology of the Gene; Addison Wesley; (2004)
- **Alberts B, Bray D, Hopkin K, Johnson A, Lewis J, Raff M, Roberts K, Walter P :** Essential Cell Biology; Garland Science (2003)**Lodish H, Darnell JE:**Molecular Cell Biology; W.H.Freeman & Co Ltd

PHY E003	Basic Structural Biology	E	2	1	0	3	PK

Unit I

X-rays - Crystals - unit cell and Miller indices - crystal systems - Bravais lattices - point groups and space groups - Waves - Complex numbers - X-ray diffraction - Bragg's law

Unit II

X-ray generation - X-ray detectors - Data collection strategies - Measures of quality of intensity Data - Resolution limit - Completeness and multiplicity of data

Unit III

Protein isolation - Gene Cloning Vectors – PCR - cloning in *E. coli* – Protein expression - Separation Techniques of biomolecules – Purification of proteins - Protein crystallization: Crystallization methods, handling protein samples, precipitants, buffers and pH, temperature, Flexible Sparse Matrix Screen, Interpretation of crystallization drop, seeding, crystallization using oil, crystallization for cryo-data collection

Unit IV

Structure determination techniques - Phase problem - Molecular replacement method - Isomorphous replacement method - preparing heavy atom derivatives - Anomalous scattering - Multiwave length anomalous dispersion technique

Unit V

Electron density maps - Viewing electron density maps - electron density of different resolutions - interpretation of electron density maps

Unit VI

Structure refinement - quality indicator: the R_{factor} - rigid body refinement with restraints - minimizing bias from the model - rebuilding poor parts of a model - producing the final map and the model

Unit VII

Accuracy of the final model - Ramachandran map - tools for structure analysis

References:

1. Outline of Crystallography for Biologists, By David Blow, Oxford Univ. Press, 2012.
2. Crystallography made crystal clear, By Gale Rhodes, Academic Press, 2000.
3. A basic course in Crystallography, By JAK Tareen and TRN Kutty, Universities Press, 2001.
4. Crystal Structure Analysis-A Primer, By JP Glusker & KN Trueblood, Oxford University Press, 2010.

PHY E004	Basics of Molecular virology	E	2	1	0	3	RK

Introduction and history of virology, living host systems, cell culture and serological/immunological Methods, Ultrastructural Studies, *in vitro* experimental technics

The function and formation of virus particles, capsid symmetry and virus architecture, helical and icosahedral capsids, enveloped viruses and complex virus structures, protein-nucleic acid interactions and genome packaging, virus receptors - recognition and binding

The structure and complexity of virus genomes, molecular and virus genetics, virus mutants, genetic and non-genetic interactions between viruses, DNA genomes, segmented and multipartite virus genomes, reverse transcription and transposition, evolution and epidemiology

Overview of virus replication, the replication cycle, expression of genetic information, control of prokaryote and eukaryote gene expression, genome coding strategies, transcriptional and post-transcriptional control of expression

Virus infections of plants, immune responses to virus infections in animals, virus-host interactions, prevention and therapy of virus infection, virus vectors and gene therapies, mechanisms of cellular injury, viruses and immunodeficiency, virus related diseases

References:

Principles of Molecular Virology, Fifth Edition -Alan J. Cann
Fundamentals of Molecular Virology, 2nd Edition-Nicholas H. Acheson
Principles of Virology -S. Jane Flint, Lynn W. Enquist, Vincent R. Racaniello, Anna Marie Skalka

PHY E005	Introduction to Chemoinformatics and Computer aided Drug Design	**E**	2	1	0	3	GK

Representation and Manipulation of 2D Molecular Structures, Representation and Manipulation of 3D Molecular Structures, Databases and data sources in chemistry.

Deriving a QSAR Equation: Simple and Multiple Linear Regression, Designing a QSAR "Experiment", Analysis of High-Throughput Screening Data, Virtual Screening.

Predictions of properties of compounds, structure- spectra correlations, chemical reactions and synthesis design, Drug designing: molecular docking, De-novo ligand designing- and structure-based methods.

Scoring functions: forcefields, surface area based functions, knowledge based potentials, searching procedures: grid based, stochastic methods, building complete protein structures using homology modeling, fold recognition, Ab-initio methods, Analysis of Folds.

Protein Function Prediction, Metabolic Pathway analysis, Computer aided drug designing, Pharmacogenomics and Pharmacogenetics.

Reference Books:

1. Molecular Modeling Principles and Applications (2nd Ed.) by Andrew R. Leach, Prentice Hall, USA. 2001
2. Bioinformatics Methods And Applications: Genomics Proteomics And Drug Discovery", S. C. Rastogi, Parag Rastogi, Namita Mendiratta, PHI Learning Pvt. Ltd., 3rdedition, 2008.

PHY E006	Proteins and Proteomics	E	3	1	0	3	DG

Protein structure and classification: Amino acids structure and general properties, primary, secondary, tertiary and quaternary structure of proteins, conformation, Ramachandran plot, protein folding patterns, protein stability and denaturation.

Protein separation techniques: Ion-exchange, size-exclusion and affinity chromatography techniques, Polyacrylamide gel electrophoresis, isoelectric *focusing*, 1D and 2D SDS PAGE for proteome analysis, tryptic gel digestion.

Protein characterization methods - I: Based on mass & size – Mass spectrometry (MALDI ion source, ToF/quadrupole analyzer), Sedimentation, Light Scattering, Surface Plasmon Resonance.

Protein characterization methods - II: Based on electromagnetic property – Absorption spectroscopy, Fluorescence Spectroscopy, Circular Dichroism; Based on thermodynamic property – Isothermal Titration Calorimetry, Differential Scanning Calorimetry.

Protein-Protein interaction: Pull-down assay using Glutathione S-transferase (GST) tagged protein, Yeast two hybrid system, Phage display.

References:

Introduction to Protein Structure, Carl Branden & John Tooze, Garland Science.
Proteomics: From protein sequences to function, S.R. Pennington & M.J. Dunn, Bios Scientific Publishers.
Biophysical Chemistry, Charles R. Cantor & Paul R. Schimmel, Freemann & Company.
Physical Chemistry for the Biosciences. Raymmond Chang. University Science Books.

THIRD SEMESTER

PHY C009	Three Dimensional Structure Determination of Drug Molecules	C	3	1	0	4	DG

Crystallographic statistics: Direct Methods -Tangent formula -use of quartets -Structural Data Base

Basic Concepts in Crystallography: Crystallographic statistics – Phase problem – Direct Methods – Origin definition – Structure invariants and semi-invariants – Sayre's equation – Tangent formula – Hand propagation – Use of quartets.

Difference stages of Structure Determination: Various stages in the structure determination of small molecules using Direct Methods – Limitations of Direct Methods.

Use of SHELXS Package: Demonstration of the program package SHELXS for solving a small molecule – Refinement of structures – Analysis of structural features.

Computer Programmes for Analysis of results: Usage of computer programs to actually determine the three-dimensional structure of a small molecule and to analysis the results.

Interpretation of results: Structure – Function relationship of some small molecules – Cambridge Structural Database.

References:

Solution of the Phase Problem: The Centrosymmetric Crystal. H. Hauptam & J. Karle. American Crystallographic Association.
Direct Methods in Crystallography. C. Giacavazzo. London and New York Academic Press.
Theory and Practice of Direct Methods in Crystallography. M.F.C. Ladd & R.A. Palmer. Springer.
Direct Methods in Crystallography. M.M. Woolfson. Oxford Clarendon Press.

PHY C010	Seminars in Biophysics	C	0	4	0	4	KG/DG/PR/GK

Each student will submit a Project Report on a chosen topic under the guidance of a Supervisor. One semester project work under the guidance of a faculty member. The student is required to carry out individual experimental / computational work and submit a dissertation. The work carried out is to be presented before a committee of faculty members for evaluation followed by Viva – Voce Examination.

PHY C011	Macromolecular Crystallography	C	3	1	0	4	PR

Crystallization : Protein crystallization techniques - preparation of heavy atom derivatives

Mounting the crystals - Data Collection - MAD measurements, synchrotron radiation, Area detectors and Image Plates.

Structure solution methods : Determination of heavy atom positions - correlation of origins - phase calculations using isomorphous replacement and anomalous dispersion methods - multiple wave length anomalous dispersion methods - Molecular replacement.

Structure refinement: Difference Fourier methods -low, medium and high resolution electron density maps - density modification - refinement of models - least squares technique - weighting schemes - R-indices - rigid body refinement - restrained and constrained refinement -solvent flattening and omit maps - molecular dynamics refinement.

Interpretative of results: PROCHECK, - Ramachandran plot - rms deviations.

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REFERENCES

1. Crystallography made crystal clear by Gale Rhodes
2. Biomolecular crystallography: Principles, Practice and applications to Structural Biology
3. Phasing in crystallography: A modern perspective by Carmelo Giacovazzo
4. Protein crystallography (Molecular Biology Series) by T.L. Blundell and Lewis Johnson.

PHY C012	Crystallography Laboratory	C	0	0	4	4	KG

Test for CentroSymmetry
Structure factor calculation
Wilson plot
Bond Length and Bond Angle calculation
Conformation of a ring system
Least square plane calculation
Structure determination using SHELXS86
Structure refinement using SHELXL 97
Wingx package for structure solution, refinement and structural analysis
Crystallization of small molecules
Crystallization of proteins
X-ray diffraction Data collection and Data reduction for protein crystal
Structure determination by molecular replacement method

PHY E007	Membrane Biophysics & Neuro Biophysics	E	2	1	0	3	RK

Membrane Constituents : Review of chemistry and biochemistry of constituents of membranes - lipids, phospholipids, lipoproteins, models of membrane structure.

Nervous System: Organization of the nervous system - Membrane potentials - origins of membrane potential - electrochemical potentials - Donnan equilibrium - Nernst equation - Goldman equation.

Ion Transport : Membrane transport - diffusion-facilitated diffusion - membrane transport proteins - carrier mediated transport - channel mediated transport.

Nerve Cells : Excitable tissues - nerve and muscle cells - nerve conduction - the generation and transmission of the Action Potential - The Hodgkin-Huxley model Voltage-gated channels – patch clamp technique.

The synapse - transmission of impulses across synaptic junctions - neurotransmitters and their mechanism of action.

Volume conduction - electrical activity of the heart - electrocardiography - Other body potentials used in medical diagnosis - EEG, EMG.

References:

Biophysics, W. Hoppe, W. Lohmann, H. Markl and H. Ziegler. Springer Verlag, Berlin (1983)
Bioelectric Phenomena, R. Plonsey & D.J. Fleming. McGraw-Hill Book Company, New York(1969)
An Inroduction to Molecular Neurobiology. Z.W. Hall, Sinauer Associates Inc. Publishers Sunderland, Massachusetts USA (1996)

PHY E007	Fundamentals of Molecular Spectroscopy (for other Dept. students)	E	2	1	0	3	KG

Spectrum - Basic elements of practical spectroscopy.

Microwave Spectroscopy: The pure rotation of molecules - classification of rotors rotational spectra of diatomic and simple polyatomic molecules as rigid and non- rigid rotors- Techniques and instrumentation.

Infrared Spectroscopy: The vibrating diatomic molecule - Diatomic vibrating - rotator - Rotation - vibration spectrum of diatomic molecules - Breakdown of Born Oppenheimer approximation - Interaction of rotation and vibration - vibrations of polyatomic molecules - Influence of rotation on the spectra of polyatomic molecules Techniques and Instrumentation. Principles of Fourier Transform Infrared Spectroscopy.

Raman Spectroscopy: Introduction - Polarization of light and Raman effect- pure rotational Raman spectrum - vibrational Raman spectrum - Techniques and Instrumentation. Principles of Laser Raman Spectroscopy.

Other related topics: Optical activity & application of CD Spectroscopy in analyzing the structure of biomolecules- Principles of UV & NMR spectroscopy - applications in structure analysis of bio-molecules - Introduction to Mass spectrometry and applications. **Microscopy:** SEM & STM, Atomic Force microscopy, confocal microscopy, single molecule spectroscopy.

References:

Fundamentals of Quantum Chemistry, James E. House, 2005
Fundamentals of Molecular Spectroscopy, Banwell C,N., 1994
Molecular Symmetry and spectroscopy, Bunker, P.R. and Jensen, P., 1998
Group theory and its applications in chemistry, Raman, K.V., 1994
Molecular Structure and Spectroscopy, Aruldhas, G., 2008
Spectroscopic identification of organic compounds, Silverstein, R.M, 1998
Pharmaceutical applications of Raman spectroscopy, Edited by Slobodan Sasic., 2007
Spectra of atoms and molecules, Bernath, P.F., 2005
Organic spectroscopic structure determination, Taber, D. F., 1948, 2007
Basic one and two dimensional NMR spectroscopy, Friebolin, H., 1998
Laser spectroscopy and other topics, Series, G.W., 1985

PHY C013	Biophysics of the Immune System	C	3	1	0	4	RK

Cellular basis of immune response - general properties of the immune system - humoral and cell-mediated immunity – T and B lymphocytes – immunoglobulins (antibodies) – antigens – haptens and epitopes – immunological memory.

Antibodies – structural classes – light and heavy chains – variable and hypervariable regions – antigen binding site – three dimensional structure of antibodies – structural basis of antigen binding to antibody – monoclonal antibodies.

Generation of antibody specificity – instructive and selective theories – clonal selection theory – organization and expression of the antibody genes – Mechanism of generation of antibody diversity – germline, somatic recombination and somatic mutation hypothesis.

T cell receptors – Major histocompatibility complex proteins – the complement system – pathways – regulation of immune responses – hypersensitivity – autoimmunity.

Reference

Kuby IMMUNOLOGY by Thomas J. Kindt, Barbara A. Osborne, Richard Goldsby. W.H.Freeman Publisher, New York.

PHY C014	Project Work	C	0	0	4	4	All Faculty

Each student will submit a Project Report on a chosen topic under the guidance of a Supervisor. One semester project work under the guidance of a faculty member. The student is required to carry out individual experimental / computational work and submit a dissertation. The work carried out is to be presented before a committee of faculty members for evaluation followed by Viva – Voce Examination.

PHY C015	Biophysics Laboratory	C	0	0	4	4	PR/DG

1. Crystallization, preparation and mounting of crystals.
2. Size Exclusion chromatography.
3. Thin Layer Chromatography
4. Critical solution temperature.
5. Agarose Electrophoresis.
6. SDS-PAGE
7. Immuno Blotting (Western Blot)
8. Plasmid DNA isolation
9. Transformation of Plasmid into Bacteria.
10. Restriction Digestion Analysis
11. Ion Exchange Chromatography
12. Concentration measurements of macromolecules

PHY E008	Protein Purification & Characterization	E	2	1	0	3	KG

Extraction procedures: Protein extraction from plants, bacteria, animal cells and tissues – Precipitation methods & Fractionation by precipitation methods

Chromatography: General principles - paper chromatography - TLC - column chromatography - Introduction to various column materials and different coupling chemistries.

Classical methods: ion exchange chromatography, size exclusion chromatography, hydrophobic chromatography, Hydroxy apatite chromatography. Affinity & pseudo affinity chromatography- FPLC - applications to macromolecules.

Electrophoresis – SDS and Native PAGE – Zymogram – Tripsinolysis for sequencing – Proteases - Inhibition kinetics – Protein concentration determination – protein crystallization.

IgG, IgM – sub classes - Antibody purification methods – Protein-G – Protein-A – Pull down assays – Immuno technology

References:

Protein Purification, Principles and Practice., Scopes, Robert K., 1994.
Principles of Biochemistry., Albert L. Lehninger, David L. Nelson, Michael Cox., 2004.
Molecular Cloning: A Laboratory Manual, Vols 1,2 and 3
J.F. Sambrook and D.W. Russell, 2001.
Crystallization of Biological Macromolecules., Alexander McPherson – 1999
Protein Crystallization: Techniques, Strategies, and Tips : a Laboratory Maual., Terese M. Bergfors., 1999.
Laboratory Methods in Enzymology: Protein, Part 2

PHY C005	Macromolecular Structure & Function (Theory & Practice)	C	3	1	0	4	GK/RK

Theory & Hands on Training on (laboratory Paper) -

Expasy Web server and its utility in Primary, Secondary and Tertiary structures of proteins.

Web based sequence alignment protocols for amino acid and nucleotide sequences

Protein Data Bank and corresponding utility tools

Homology Modeling of proteins

EMBL web server and utilities

Applications of Molecular visualization softwares – Rasmol, PyMol, Swiss PDB Viewer

PHY E005	Introduction to Chemoinformatics and Computer aided drug design	E	2	1	0	3	GK

Representation and Manipulation of 2D Molecular Structures, Representation and Manipulation of 3D Molecular Structures, Databases and data sources in chemistry.

Deriving a QSAR Equation: Simple and Multiple Linear Regression, Designing a QSAR "Experiment", Analysis of High-Throughput Screening Data, Virtual Screening.

Predictions of properties of compounds, structure- spectra correlations, chemical reactions and synthesis design, Drug designing: molecular docking, De-novo ligand designing- and structure-based methods.

Scoring functions: forcefields, surface area based functions, knowledge based potentials, searching procedures: grid based, stochastic methods, building complete protein structures using homology modeling, fold recognition, Ab-initio methods, Analysis of Folds.

Protein Function Prediction, Metabolic Pathway analysis, Computer aided drug designing, Pharmacogenomics and Pharmacogenetics.

Reference Books:

3. Molecular Modeling Principles and Applications (2nd Ed.) by Andrew R. Leach, Prentice Hall, USA. 2001
4. Bioinformatics Methods And Applications: Genomics Proteomics And Drug Discovery", S. C. Rastogi, Parag Rastogi, Namita Mendiratta, PHI Learning Pvt. Ltd., 3rdedition, 2008.