STRUCTURAL BIOLOGY

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PRE-REQUISITES : This is an introductory course so anyone should follow it, basic knowledge of biology might be helpful

INTENDED AUDIENCE : Biotechnology/Pharmaceuticals/Bioinformatics /Chemistry and related programs Also it would be a nice introductory course to, research scientists in biotechnology, pharma industry, veterinarians and clinicians/medical people involved in basic research.

INDUSTRIES APPLICABLE TO : Pharmaceutical, Biotechnology, Biochemical Engineering

COURSE OUTLINE :

Post NGS (Next Generation Sequencing) era has completely changed the way of understanding research, especially in the field of biomedical science. Today the complete genome sequencing of an organism is done in a few days providing the researchers with thousands of genes hence thousands of protein sequences. But to proceed further we need to understand the three-dimensional architecture of the protein molecules. The current course would take an initiative to educate the students in gathering knowledge about the structural units forming biological macromolecules, their architectural hierarchies, the basics of the structural biology techniques, their pros and cons, how to read and visualize 3D structure files, etc. The course also include introduction to molecular dynamics and case studies explaining the probable application of the acquired knowledge. But most importantly this course is an attempt to help linking the biological events to understand how biological macromolecules are generated, folded and get functional. Understanding those fundamentals would help students towards studying follow up advanced courses like Advanced structural biology, Macromolecular crystallography, Cryo-Electron Microscopy, Nuclear Magnetic Resonance, Structure-based drug designing, protein engineering, etc. In summary, this course would open up the gate of modern research-related courses in the field of Drug Designing and macromolecule based engineering.

ABOUT INSTRUCTOR :

Prof. Saugata Hazra is a Associate Professor in the Department of Biotechnology at the Indian Institute of Technology, Roorkee. An alumnus of IIT Kharagpur, Prof. Hazra has obtained his Ph.D. degree from the University of Illinois; Chicago (2004- 2010) in Structural Biology and Structure based Drug Designing and post-doc from St. Jude Children Research Center, Memphis, USA (2010-2011) and Albert Einstein College of Medicine, NY, USA, in the major area of Structural Biology. He joined IIT Roorkee in 2014. Current research in his group centers on catalytic divergence of enzymes involved in antimicrobial drug resistance and structure based enzyme engineering towards waste valorization. Prof. Hazra is teaching UG/PG courses like Macromolecular Crystallography, Bioinformatics, Computational Biology, and Biochemistry since his joining in IITR. He has published in several peer reviewed journals and recipient of awards like James graduate fellowship, DST-Young Scientist Award and Frontiers of Engineering from Royal Academy of Engineering etc.throughout his career. View Faculty Profile: https://www.saugatahazralab.com/

COURSE PLAN :

Week 1: Introduction: Flow of the history of biological inventions, basic Biological Macromolecules of life, i.e., Protein, Nucleic Acid, Carbohydrates & Lipid/Fat, and a comparison between polymers and "3C"ecrets of covalent bond, nucleic acid, DNA sequencing, PCR innovation, gene sequencing to genome sequencing, introduction to NGS and its different platforms, arrival of Post Genomic Era, the effect of HGP, and experimental three-dimensional structure determination techniques.

Week 2: Protein: Amino acids and their properties, Protein Chemistry, Chirality, Peptide bond, and Levels of protein structures, Dihedral angles, Peptide bond, and Ramachandran Plot, Super Secondary Structures, Motif, Domains, Non-covalent interactions, Folding of Protein, Thermodynamics, and Kinetics of protein folding, Characterization of Proteins.

Week 3: Introduction to Structural Biology Techniques: cellular organization, resolution structure determining technique with their ranges of the resolution, the success of X-ray crystallography from single molecule to a crystal, X-ray Crystallography, Crystallization in X-ray Crystallography, Crystal mounting in X-ray Crystallography.

Week 4: X-ray Crystallography: Production of X-ray and its properties, unit cell, symmetry, and lattice, the geometry of the crystal system, Crystal Symmetry, Instrumentation in X-ray Crystallography, Data collection, and processing

Week 5: X-ray Crystallography: Data Analysis of X-ray Crystallography - Diffraction Patterns, Indexing, Bragg's Law, Laue equation, Relation between "Laue equation and Bragg's Law", Lattice Transformation, Ewald Sphere, Laue Condition for Diffraction and Ewald Sphere, Structure Factors and Diffraction Pattern, Atomic Scattering Factor, Anomalous Dispersion, Analytical expression of the phase, Fourier Transformation, introduction to Phase Problem. Phase problem - Phase Problem, Patterson Function, How to solve phase problem, Heavy atom replacement methods, Isomorphous replacement, Anomalous dispersion, phase problem associated with crystal diffraction and common techniques to recover phase resolving different phase improvement methods. Refinement and Structure deposition to PDB - aspects of structure refinement, motivation, application, the procedure of simulated annealing, PDB repository, atomic model deposition as well as different PDB validation suites.

Week 6: NMR: Introduction to NMR, basic Principles of NMR and Instrumentation, NMR Sample Preparation and Chemical Shift related concepts, Factors effecting NMR Spectra (1D & 2D), 2D & 3D NMR Spectroscopy focusing on protein structure.

Week 7: Spectroscopy: Introduction to Spectroscopy, UV-Vis and CD spectroscopy, Fluorescence Spectroscopy and Green Fluorescence Protein (GFP), Infrared & Raman Spectroscopy for protein, Raman Spectroscopy, Raman Microscopy and Raman Crystallography for studying protein.

Week 8: Microscopy: Introduction to Microscopy, Functioning details of Cryo-Electron Microscopy (Cryo-EM), Cryo-Electron Microscopy: Data Collection and Analysis, A concise story of advancement Cryo-EM, Protein Data Bank.

Week 9: Molecular Visualizations: History of Molecular Visualizations of Biological Macromolecules, Description of structure-related files (.pdb, .mmcif, .mtz, etc.), Demonstration of COOT, 3D visualization using Pymol, Demonstration of Pymol.

Week 10: Molecular Dynamic Simulation: Why we need MD Simulation, Molecular Dynamic Simulation Process, Build a realistic atomistic model of the system, the algorithm behind simulation process, Concept of Topology and Parameter files, Major components in a force field, the concept of solvation, solvent models, Periodic Boundary Condition, Concept of Central Simulation Box, Phase Space, Concept of Ensembles, Energy Minimization (EM), potential energy surface (PES), Determination of EM, types of EM methods and their algorithms, Steps in MD Simulation, Application of Molecular Dynamic Simulation.

Week 11: Protein Engineering: What, How & Which of Protein Engineering, How to make logical Protein Engineering: Process of Rational design, a success story of Rational Protein designing: Focusing on De Novo Process, Designing Protein by mimicking nature: Process of Directed Evolution, Achievement, Challenges, and Future direction in the field of Protein Engineering.

Week 12: Structure-Based Drug Discovery: Introduction to Structure-Based Drug Discovery (SBDD), Rational Drug Discovery, Docking Based Virtual Screening: Progress, Challenges and Future perspective, What makes a small molecule an ideal drug: Developing in silico ADMETox Model, Structure-Based Drug Discovery: Case study and Conclusion