Syllabus IT451 Computational Structural Biology M.Sc Third Semester

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Basics of Protein Structure: Physical and Chemical Properties of aminoacids and Polypeptides. Theoretical and experimental methods for determination of sizes of proteins. Physical nature of noncovalent interactions. Motifs of protein structure: Hydrophobic and hydrophilic regions, Alpha-helix, Beta sheets, Loops, Topology diagrams & various structural motifs Conformational properties of proteins, Ramachandran Plot, Secondary, Super Secondary, Tertiary and Quaternary structure of Proteins. Protein folding & Levinthal Paradox, Post translation modification of proteins, Protein sequence, structure and function relationships

Protein Structure Determination by X-ray diffraction: Isolation and Purification of Proteins, Basic principles of X-ray diffraction studies, phase determination, calaculation of Electron Density Map, Interpretation of the electron density map. Refinement of the Structures.. NMR, Electron microscopy Techniques for structure determination, Structure evaluation methods.

Structural Databases: PDB, NDB,, MMDB, CATH, SCOP, FSSP, DALI, protein structural alignment databases, protein-protein interaction database, protein-ligand databases,PubChem, ChEMBL and ZINC databases

Basics of Nucleic Acid Structure, Carbohydrates and Lipids

Protein Structure prediction methods/Molecular Modeling

Domain Assignment methods: Identifying structural domains in protein: first and second generation algorithms for domain assignments, domain assignment based on graph theoretical methods.

Secondary Structure Prediction methods: Secondary structure assignment methods:DSSP/STRIDE for known structures. Statistical methods of Chou and Fasman, Garnier-Osguthorpe-Robson, Stereochemical method of Lim and nearest neighbour, Neural network method etc, Fold Recognition and threading
methods

Classification of three dimensional structures of proteins, structural alignment methods:

Prediction of structural classes, motifs, folds and domains, classification of three dimensional structures in Brook haven Protein Data Bank (HSSP, SCOP, FSSP, CATH). pairwise/multiple structural alignment methods CE, Dali, SSAP, VAST, concept of rigid body translation and rotation, RMSD, Z score for structural comparison and classification.

Comparative modeling of proteins

Muliple structural alignment of proteins, Template Selection, Backbone modeling , loop building (search / generation), sidechain generation and model evaluation and validation (Ramachandran plot analysis, Procheck, Whatcheck,ERRAT score,Prove, VERIFY3D and PROSA), Energy minimization, Model databases and software for molecular modeling.Molecular visualization and graphics. Solvent accessible surfaces, Identification of Binding site(s) and validation and comparision of binding site(s). protein function assignment at molecular level, protein-protein interaction

Overview of Protein folding process and abnitio Structure prediction methods

Advanced Molecular simulation Techniques:

Empirical force field for biomolecular simulations, Potential Energy Function (bond length potential, aond angle potential, torsional potential, van der wals potential and coulomb potential), classical representations of electrostatics (Poisson-Boltzmann, Generalized Born) Energy minimization – minimization algorithms, simplex method, steepest descent
method, Newton-Raphson, Conjugate gradient, Variable metrics methods. Geometry optimization and energy minimization. Conformational analysis and optimization methods – using systematic searching, simulated annealing, Monte Carlo search, genetic algorithms, and distance geometry methods. Molecular Dynamics simulations, Monte Carlo Simulations, Calculation of Free energy using simulation techniques. Free energy estimations, thermodynamic cycle, incorporation of solvation effects (implicit and explicit)

Reading :

Introduction to Protein Structure, Branden & Tooze, Garland Publishing, Inc, New York

Structural Bioinformatics, Phil Bourne

Molecular Moelling : Principles & Applications, Andrew R. Leach, Prentice Hall

The art of Molecular Dynamics Simulations. Rapport, Cambridge University Press