VI Semester

Paper No- 18: Computational Biology and Drug Design Marks: 150

This course will introduce the discipline of computational biology and drug design. It has been designed to explain the different aspects of nucleotide and protein sequence analyses, sequence alignments and their applications in understanding biology. The course will also emphasize on the strategic issues in drug discovery and development, principles of computational methods involved in lead generation virtual screening, quantitative structure-activity relationship and molecular docking.

THEORY **Total Lectures: 48**

Unit I: Introduction to computational biology (2 Lectures)
(Chapter 1: Mount)
What is computational biology and bioinformatics, internet and bioinformatics, chemoinformatics. Introduction to linux and common terminal commands.

Unit II: Biological databases and genome browsers (10 Lectures)
(Chapter 2 and 6: Mount)
Introduction to various databases and their classification (primary and secondary databases) e.g. NCBI, DDBJ, EMBL, ENSEMBL, UCSC and their use in laboratories: literature, sequence, structure, medical, enzymes and metabolic pathways databases.

Unit III: Sequence alignment and visualization (8 Lectures)
(Chapters 3, 4 and 5: Mount)
Local and global sequence alignments (Needleman-Wunsch and Smith-Waterman algorithms), pair-wise (BLAST and FASTA algorithms) and multiple sequence alignment (Clustal W) and its importance. Theory behind BLAST- how Hidden Markov Model (HMM) can be used to model a family of unaligned sequences or a common motif within a set of unaligned sequences and further be used for discrimination and multiple alignment, BLAST score, aminoacid substitution matrices, s-value and e-value, calculating the alignment score and significance of e and p value.

Unit IV: Phylogenetic analysis (4 Lectures)
(Chapter 14: Baxevanis and Ouellette)
Basics and tools for phylogenetic analysis, cladistics, tree-building methods (character and distance based methods), construction of phylogenetic trees (PHYLIP) and identifying homologs.

Unit V:Microarray analysis (3 Lectures)
(Chapter 13: Mount; Chapter 9 and 16: Baxevanis and Ouellette)
Introduction and use of DNA microarray to assay gene expression, designing of the experiment, analysis and biological interpretation, principle and applications of protein microarray.

Unit VI: Drug discovery pipeline (3 Lectures)
(Chapter 1, 2: Smith and O'Donnell)
Drug life cycle, stages of drug discovery and strategic issues in drug discovery.

Unit VII: Lead generation (6 Lectures)
(Chapter 12, 18: Patrick)
2D and 3D molecular structures, molecular descriptors and fingerprints, molecular similarity and diversity, topological descriptors, quantitative structure-property relationships.

Unit VIII: Overview of drug development (12 Lectures)
(Chapter 15, 17, 18: Patrick)
HTS, clinical trials, applications of chemo informatics in drug research (chemical libraries, protein 3D modeling, characterization of binding site, virtual screening, protein-ligand interactions, prediction of pharmacological properties, Introduction to drug databases, PubChem and their use in drug development, Lipinski's rule of five, concept of energy minimization and force fields, introduction to rational drug design using example.

PRACTICALS

1. Retrieval of information from databases.
2. Sequence alignment using BLAST and Clustal W.
3. Phylogenetic analysis using PHYLIP.
4. Microarray analysis using Bioconductor.
5. Molecular format conversion and hands-on molecular visualization program for displaying, animating and analyzing large bio-molecular systems using 3-D graphics.
6. Homology Modeling using SPDBV, model structure refinement using SPDBV and model validation using What Check and Pro Check.
7. Comparing structures, mutations, studying interactions creating electrostatic potential diagrams.
8. Virtual screening and molecular docking using AUTODOCK.

ESSENTIAL BOOKS

1. Bioinformatics: Sequence and Genome analysis, 2nd edition (2004), David W. Mount, Cold Spring Harbour Laboratory Press.
2. Bioinformatics: A practical guide to the analysis of genes and proteins, 3rd edition (2004), Andreas D. Baxevanis and B.F. Francis Ouellette, John Wiley and Sons.
3. Introduction to Medicinal Chemistry, 4th edition (2009), Graham l. Patrick, Oxford University Press.
4. The Process of New Drug Discovery and Development, 2nd edition (2006), C.G. Smith and J.T. O'Donnell, Informa Healthcare.

SUGGESTED READINGS

1. Cheminformatics (2003), J. Gasteiger, Thomas Engel; Wiley-VCH .
2. Molecular modeling - Principles and Applications, 2nd edition (2003), A. R. Leach, Pearson Education Limited, UK.
3. Cheminformatics in Drug Discovery(2006), edited by. T.I. Opera; Wiley Publishers.
4. Molecular dynamics simulation: elementary methods (1992), J. M. Haile, Wiley-Interscience, New York.