Subject Code : P8BTE5

ELECTIVE COURSE III-2: MOLECULAR MODELING AND DRUG DESIGNING

UNIT- I

Introduction to the concept of molecular modeling, molecular structure and internal energy, applications of molecular graphics, coordinate systems, potential energy surfaces,
-local and global energy minima.
Molecular mechanics: general features of molecular mechanics- force field, bond stretching, angle bending, torsional terms, non-bonded interactions; force field parametrisation and transferability; energy minimization: derivative and non-derivative methods, applications of energy minimization.

UNIT -II

Molecular dynamics simulation methods: molecular dynamics using simple models, molecular dynamics with continuous potential-setting up and running a molecular dynamic simulation, constraint dynamics; Monte Carlo simulation of molecules.-Simulation for conformational analysis. *Ab initio*, dft and semi empirical methods.

UNIT- III

Recent advances in drug design methodologies- Biomolecular structure, Structure activity relationship, Pharmacokinetics, Pharmacophoric pattern, ADME Properties, quantitative structure activity relationship, Use of genetic algorithms and principle component analysis in the QSAR equations.

UNIT -IV

Macromolecular modeling- Software tools for modeling bio-molecules. Molecular electrostatic potentials, charge analyses. Protein conformations, folding and mutation through modeling-design of ligands for known macro molecular target sites.
Drug-receptor interaction, classical SAR/QSAR studies and their implications to the 3-D
modeler, 2-D and 3-D database searching, pharmacophore identification and novel drug
design.

UNIT -V

Molecular docking: Docking-Rigid and Flexible Structure-based drug design for all classes of targets- Theories of enzyme inhibition - Enzyme Inhibition strategies.- Enzyme inhibition as a tool for drug development –Examples.
Finding new drug targets to treat disease- strategies for target identification and lead design- Use of Genomics and Proteomics for understanding diseases at molecular level- -new targets for anti-cancer drugs, Drugs that rescue mutant p53's.

REFERENCES

1. Andrew Leach. 1996. Molecular Modelling: Principles and Applications (2nd Edition), Addison Wesley Longman, Essex, England.
2. Alan Hinchliffe. 2003. Molecular Modelling for Beginners, John-Wiley and Sons New York.
3. Cohen, N. (Ed.).1996. Guide Book on Molecular Modeling in Drug Design, Academic Press, San Diego.
4. Frenkel, D. and B. Smit. 1996. Understanding Molecular Simulations. From Algorithms to Applications. Academic Press, San Diego, California.
5. Rauter, C. and K. Horn. 1984. X-ray crystallography and drug design, Elsevier.
6. Kalos, M. and P. A. Whitlock. 1986. Monte Carlo Methods. John Wiley & Sons, New York,.
7. McCammon, J.A. and S.C. Harvey. 1987. Dynamics of Proteins and Nucleic Acids. Cambridge University Press, Cambridge.
8. Rapaport, . D.C. 2004. The Art of Molecular Dynamics Simulation. Cambridge University Press, Cambridge, England.
9. Shanmughavel, P. 2006. Trends in Bioinformatics**,** Pointer Publishers, Jaipur, India.
10. Hansch, Corwin, Leo, Albert, Hockma, D.H. 1995. Exploring QSAR. American Chemical Society, Washington D.C.