ARSD College, University of Delhi

Model Course Handout/Lesson Plan

Course Name : B.Sc. (H) Chemistry						
Semester	**Course Code**	**Course Title**	**Lecture (L)**	**Tutorial (T)**	**Practical (P)**	**Credit (C)**
VI	32177905	DSE-4: Molecular Modelling and Drug Design	4	0	0	4
Teacher/Instructor(s)		Dr. Neeta Azad				
Session		2021-22				

Course Objective:

Objective of this course is to make students learn the theoretical background of principles of computational techniques in molecular modelling, evaluation and applications of different methods for various molecular systems, energy minimization techniques, analysis of Mulliken Charge & ESP Plots and elementary idea of drug design. **Course Learning Outcomes:**

Learning Outcomes: By the end of this course, students will be able to:
• Understand theoretical background of computational techniques and selective application to various molecular systems.
• Learn Energy minimization methods through use of different force fields.
• Learn ESP Plots by suitable soft wares, electron rich and electron deficient sites, • Compare computational and experimental results and explain deviations.
• Carry out Molecular dynamics (MD) and Monte Carlo (MC) simulations on several molecules and polymers.
• Learn QSAR properties and their role in molecular modelling, cheminformatics and drug discovery.
• Perform Optimization of geometry parameters of a molecule (such as shape, bond length and bond angle) through use of software like Chem Sketch and Argus Lab in interesting hands-on exercises.

Lesson Plan:

Unit No.	Learning Objective	Lecture No.	Topics to be covered
1.	Introduction of computational Chemistry and Molecular Modelling	1	Introduction of molecular modelling and drug design.
		2	Different MMDD methods and their use
		3	Difference between Molecular mechanics and quantum mechanical methods in MMDD
		4	Different types of MMDD methods their use, limitations etc.
		5	Molecular Dynamics, Monte Carlo
		6	Coordinate systems:

		7	Cartesian and Internal Coordinates,
		8	Bond lengths, bond angles and torsion angles,
		9	Writing Z -matrix
		10	Z- matrix for methane, ethane, ethene, ethyne, water, H2O2
		11	Z-Matrix for more new compounds
		12	Reading out the z-matrix from output of varius software
2.	Potential Energy Surfaces, Energy Minimization and Transition State Search	13	Potential energy surface
		14	Intrinsic Reaction Coordinates, Stationary points
		15-16	Photo transistors, quantum efficiency and responsivity
		17	Equilibrium points – Local and Global minima
		18-19	concept of transition state with examples: Ethane, propane, butane, cyclohexane
		20	Meaning of rigid and relaxed PES with examples
		21	Applications of computational chemistry to determine reaction mechanisms.
		22	Geometry optimization and energy minimization
		23	Methods of energy minimization: Multivariate Grid Search, Steepest Descent Method, Newton-Raphson method and Hessian matrix.
3.	Molecular Mechanics:	24	: Force Fields, Non-bonded interactions (van der Waals and electrostatic
		25-26	how to handle torsions of flexible molecules, van der Waals interactions using Lennard-Jones potential
		27-28	hydrogen bonding interactions, electrostatic term, Parameterization
		29-30	Applications of MM, disadvantages
		31-32	Software related to required calculations
		33-34	Different variants of MM: MM1, MM2, MM3, MM4
		35-36	More force fields like MM+, AMBER, BIO+, OPLS.GUI
4.	Molecular Dynamics	37	Radial distribution functions for solids, liquids and gases
		38	intermolecular Potentials (Hard sphere, finite square well and Lennard-Jones potential)
		39	concept of periodic box, ensembles (microcanonical, canonical, isothermal – isobaric)
		40-41	Ergodic hypothesis. Integration of Newton's equations (Leapfrog and Verlet Algorithms
		42	Rescaling, Simulation of Pure water – Radial distribution curves and interpretation
		43	TIP & TIP3P, Typical MD simulation
		44-45	Brief introduction to Langevin and Brownian dynamics
		46	Monte Carlo Method: Metropolis algorithm.
		47-48	Recap of all the topics covered
5.	Huckel MO and b-	49-50	Writing the Hamiltonian of a system, Brief recap

	initio methods		of H – atom solution, Units in quantum mechanical calculations
		51-52	Born-Oppenheimer approximation (recap), Antisymmetry principle, Slater determinants, Coulomb and Exchange integrals
		53-54	Examples of He atom and hydrogen molecule, Hartree-Fock method
		55-56	Basis sets, Basis functions, STOs and GTOs, diffuse and polarization functions. Minimal basis sets Advantages of ab initio calculations, Koopman's theorem, Brief idea of Density Functional Theory
		57-58	Semi-empirical methods: Brief idea of CNDO, INDO, MINDO/3, MNDO, AM1, PM3 methods. Other file formats – PDB. Visualization of orbitals – HOMO, LUMO, ESP maps.
		59-60	QSAR: Structure-activity relationships. Properties in QSAR (Partial atomic charges, polarizabilities, volume and surface area, log P, lipophilicity and Hammet equation and applications, hydration energies, refractivity). Biological activities (LD50, IC50, ED50.)

Evaluation Scheme:

No.	Component	Duration	Marks
1.	Internal Assessment • Quiz • Class Test • Attendance • Assignment		25
2.	End Semester Examination	3 hr	75

Details of the Course		
Unit	**Contents**	**Contact Hours**
I	Introduction: Overview of Classical and Quantum Mechanical Methods (Ab initio, Semi-empirical, Molecular Mechanics, Molecular Dynamics and Monte Carlo) General considerations. Coordinate systems: Cartesian and Internal Coordinates, Bond lengths, bond angles and torsion angles, Writing Z -matrix (ex: methane, ethane, ethene, ethyne, water, H2O2 .	12
II	Potential Energy Surfaces: Intrinsic Reaction Coordinates, Stationary points, Equilibrium points – Local and Global minima, concept of transition state with examples: Ethane, propane, butane, cyclohexane. Meaning of rigid and relaxed PES. Applications of computational chemistry to determine reaction mechanisms. Energy Minimization and Transition State Search: Geometry optimization, Methods of energy	11

	minimization: Multivariate Grid Search, Steepest Descent Method, Newton-Raphson method and Hessian matrix.	
III	Molecular Mechanics: Force Fields, Non-bonded interactions (van der Waals and electrostatic), how to handle torsions of flexible molecules, van der Waals interactions using Lennard-Jones potential, hydrogen bonding interactions, electrostatic term, Parameterization. Applications of MM, disadvantages, Software, Different variants of MM: MM1, MM2, MM3, MM4, MM+, AMBER, BIO+, OPLS.GUI.	13
IV	Molecular Dynamics: Radial distribution functions for solids, liquids and gases, intermolecular Potentials (Hard sphere, finite square well and Lennard-Jones potential), concept of periodic box, ensembles (microcanonical, canonical, isothermal – isobaric), Ergodic hypothesis. Integration of Newton's equations (Leapfrog and Verlet Algorithms), Rescaling, Simulation of Pure water – Radial distribution curves and interpretation, TIP & TIP3P, Typical MD simulation Brief introduction to Langevin and Brownian dynamics Monte Carlo Method: Metropolis algorithm.	12
V & VI	Huckel MO with examples: ethane, propenyl, cyclopropenyl systems, Properties calculated – energy, charges, dipole moments, bond order, electronic energies, resonance energies, Oxidation and reduction (cationic and anionic species of above systems) Extension to Extended Huckel theory and PPP methods Ab-initio methods: Writing the Hamiltonian of a system, Brief recap of H – atom solution, Units in quantum mechanical calculations, Born-Oppenheimer approximation (recap), Antisymmetry principle, Slater determinants, Coulomb and Exchange integrals, Examples of He atom and hydrogen molecule, Hartree-Fock method Basis sets, Basis functions, STOs and GTOs, diffuse and polarization functions. Minimal basis sets Advantages of ab initio calculations, Koopman's theorem, Brief idea of Density Functional Theory Semi-empirical methods: Brief idea of CNDO, INDO, MINDO/3, MNDO, AM1, PM3 methods. Other file formats – PDB. Visualization of orbitals – HOMO, LUMO, ESP maps. QSAR: Structure-activity relationships. Properties in QSAR (Partial atomic charges, polarizabilities, volume and surface area, log P, lipophilicity and Hammet equation and applications, hydration energies, refractivity). Biological activities (LD50, IC50, ED50.)	12
	Total	**60**

Suggested Books:

Sl. No.	**Name of Authors/Books/Publishers**	**Year of Publication/Reprint**
1.	Lewars, E. (2003), Computational Chemistry, Kluwer academic	2003

	Publisher	
2.	Cramer, C.J. (2004) Essentials of Computational Chemistry, John Wiley & Sons	2004
3.	Hinchcliffe, A. (1996) Modelling Molecular Structures, John Wiley & Sons.	1996
4.	Leach, A.R.(2001),Molecular Modelling, Prentice-Hall.	2001
Mode of Evaluation:	Internal Assessment / End Semester Exam	