

Assignment (MMDD)2020

1. Answer all 6:
- (a) Explain the following terms with suitable diagram:
 - (i) Global Minima
 - (ii) Local Minima
 - (iii) Saddle Point
 - (b) Explain Markov chain of states.
 - (c) What is Ergodic Hypothesis? Explain.
 - (d) Give strengths and limitations of DFT.
 - (e) Construct a Z-matrix for acetone using appropriate labels.
 - (f) Differentiate between canonical and microcanonical ensemble. (12)
2. (a) Calculate the pK_a for *para*-chlorophenol using Hammett equation if the dissociation constant for phenol is 1068×10^{-10} , provided $\sigma_p = 0.68$, $\rho = 2.25$, under identical conditions of solvent, temperature and pressure.
- (b) Formulate Schrödinger wave equation for a system having two protons and one electron. Is it possible to solve this equation? Why or why not?
- (c) Expand and explain (**Any five**)
- (i) MNDO
 - (ii) OPLS
 - (iii) QSAR
 - (iv) TIPs
 - (v) PM3
 - (vi) SCF (3,4,5)
3. (a) Calculate the bond order of ethene radical anion and charges on both carbon atoms when the occupied orbitals are represented by:
- $$\Psi_1 = 0.707\phi_1 + 0.707\phi_2$$
- $$\Psi_2 = 0.707\phi_1 - 0.707\phi_2$$
- (b) How does the conjugate gradient method differ from the steepest descent method?
- (c) Define the term “force field”. Describe the terms of a typical molecular mechanics force field. You should write down the equation, explain the variables, and explain briefly what they represent. (4×3=12)
4. (a) Classify the following molecules as aromatic or non-aromatic on the basis of Hückel's rule for aromaticity. (**Any three**)
- (i) Pyrrole
 - (ii) Pyridine

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(iii) Thiophene

(iv) Naphthalene

(b) Explain briefly the approximations used in SHM. Write down simple Hartree-Fock matrices for butadiene and cyclobutadiene. (6,6)

5. (a) Draw well-labelled radial distribution plots for different states of matter and explain each one in brief.

(b) Two methods that are generally used for the optimization of molecular geometries are the 'Steepest Descent' and 'Newton-Raphson' method. Briefly outline the advantages and disadvantages of these two techniques.

(c) The horse power generated by a wheel is proportional to $u(v-u)$ where u is the velocity of the wheel, which is variable and v is the velocity of jet which is fixed. Show that efficiency of the wheel will be maximum at $u = v/2$. (6,4,2)

6. (a) The force field term describing bond stretching is given by

$$U(r) = c(r - r_{eq})^2 - d(r - r_{eq})^3,$$

For a A-B single bond, the parameters are $c = 300 \text{ kcal mol}^{-1} \text{ \AA}^{-2}$, $d = 10 \text{ kcal mol}^{-1} \text{ \AA}^{-3}$, and $r_{eq} = 1.500 \text{ \AA}$. Suppose the initial structure built for a molecule containing an A-B bond has a A-B bond length of 2.000 \AA . Show how the energy minimization progresses for the Steepest Descent method taking the value of time step as 0.001. Show the calculations for first two iterations only.

(b) Sketch a potential energy diagram that shows a conformational analysis of *n*-butane and also explain the stability of various conformers of *n*-butane.

(c) Explain briefly various models to simulate water in Molecular Dynamics simulation. (4,4,4)

7. (a) Define Molecular descriptor. How are they related to biological descriptors? Explain any two biological descriptors.

(b) What is the basic difference in underlying principle of CNDO and PPP methods? Outline the similarities and differences between *ab initio* and semi-empirical methods.

(c) How can one mathematically define atomic orbital? Explain any two such mathematical functions. (4,4,4)

8. Write short notes on any **three** of the following:

(a) Leapfrog Algorithm

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- (b) Steepest Descent method
- (c) STOs and GTOs
- (d) EHM

9. Answer all 6:

- (a) Define Z-matrix. Draw a Z-matrix for acetaldehyde.
- (b) What is the energy gradient? How is the gradient used in energy minimization?
- (c) Distinguish between (Any **two**):
 - (i) Spin orbital and spatial orbital
 - (ii) SHM and EHM
 - (iii) First-order and second-order saddle point
- (d) Describe two techniques used to reduce computational time for molecular dynamics simulations.
- (e) How can one mathematically define atomic orbital? Explain any two such mathematical functions.
- (f) What are the strengths and limitations of DFT (12)

10. (a) Describe all steps involved in setting up a molecular dynamics simulation of a membrane protein with a ligand. You can assume that there is a crystal structure of the protein with the ligand. Why do you always minimize the structures before running MD?

(b) Formulate Schrödinger wave equation for a system having one proton and two electrons. Is it possible to solve this equation? Why or why not?

(c) Define the term “force field”. Describe the terms of a typical molecular mechanics force field. You should write down the equation, explain the variables, and explain briefly what they represent.

(4x3 = 12)

11. (a) Graphically express three ways describing the stationary point for a continuous and differentiate function.

(b) Explain time-average and ensemble-average with the help of appropriate expressions. How are they related to each other? What is their significance in simulation studies?

(c) Calculate the pK_a for para-nitrobenzoic acid using Hammett equation if the dissociation constant for phenol is 6.3×10^{-5} , provided $\sigma_p = 0.78$, $\rho = 1.00$, under identical conditions of solvent, temperature and pressure.

(d) What do you mean by the term “canonical orbital”? How do they differ from spatial orbitals?

(4x3 = 12)

12. (a) How is hydrophobicity and hydrophilicity of a molecule accounted for in QSAR analysis? Explain with the help of at least one descriptor of each.

(b) Calculate the π electron energy and delocalization energy of the cyclopropenyl radical, anion and cation using simple Hückel theory.

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- (c) What are the problems faced in dealing with minimizing a transition state? How can one prove that the resultant structure is a transition state and not a stable intermediate?
(d) Explain the physical significance of σ and ρ in a Hammett equation with an example.
(4×3=12)

13. (a) Write the extended form of the following (Any **four**):

- (i) GUI
- (ii) OPLS
- (iii) TIPs
- (iv) CHARMM
- (v) PM3

(b) What is the basic difference in underlying principle of INDO and MNDO methods? Outline the similarities and differences between *ab initio* and semi-empirical methods.

(c) Explain in brief the strengths and weaknesses of semi-empirical methods. Explain by taking specific and suitable examples. (4,4,4)

14. (a) The occupied Hückel π molecular orbitals for C_2 and C_3 of 1,3-butadiene can be written as:

$$\Psi_2 = 0.371\phi_1 + 0.602\phi_2 + 0.602\phi_3 + 0.371\phi_4$$

$$\Psi_3 = 0.602\phi_1 + 0.371\phi_2 - 0.371\phi_3 - 0.602\phi_4$$

Calculate the bond orders between C_2 and C_3 carbon atoms and atomic charges on these two carbon atoms.

(b) Allinger and co-workers developed a series of force fields to deal with molecular geometries and energies. Explain any one such force field. Also, explain one force field used in MM to simulate liquids.

(c) What is the common basic principle of *ab initio*, semi-empirical and DFT methods?

(d) What do you mean by the term quadrupole and octapole? Explain with suitable examples.

(4,4,2,2)

15. (a) Explain all the steps of energy minimization using Newton-Raphson method with the help of a suitable example. Explain any one variant of Newton-Raphson method.

(b) Draw and discuss the potential energy diagrams of cyclohexane as a function of C-C-C-C torsion angle.

(c) The force field term describing bond stretching is given by

$$U(r) = c(r - r_{eq})^2 - d(r - r_{eq})^3,$$

For a A-B single bond, the parameters are $c = 280 \text{ kcal mol}^{-1} \text{ \AA}^{-2}$, $d = 08 \text{ kcal mol}^{-1} \text{ \AA}^{-3}$, and $r_{eq} = 1.400 \text{ \AA}$. Suppose the initial structure built for a molecule containing an A-B bond has a A-B bond length of 1.950 \AA . Show how the energy minimization progresses for the Steepest Descent method taking the value of time step as 0.001. Show the calculations for first two iterations only.

(4,4,4)

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16. Explain briefly **any three** of the following:
- Verlet Algorithm
 - Hartree-Fock Method
 - Hammett Equation
 - PPP
17. a. What is partition coefficient (P) in QSAR studies?
- Write a Hammett equation and explain its application.
 - Write a short note on SCF method.
18. a. List the differences between SHM and EHM.
- What are the strengths and weaknesses of SHM?
 - Classify the following as aromatic, nonaromatic or antiaromatic on the basis of HMO
- Cyclopentadienyl anion
 - Cyclobutadiene
 - Cyclopropenyl cation
 - Cyclopentadienyl cation
 - Cycloheptatrienyl cation
19. A. For what type of molecules is simple Huckel method applicable?
- What are the most important results that can be obtained from Huckel calculations?
 - Write down the simple Huckel Fock matrices for ethane, allyl radical and cyclopropenyl radical.
20. A. The SHM (simple Huckel method) predicts the resonance energy of cyclopropenyl cation, anion and radical to be the same. Actually we expect the resonance energy to decrease as we add π electrons. Why should this be the case?
- What molecular feature cannot be obtained at all from simple Huckel method? Why?.
 - How many carbons would a fully conjugated polyene have if its Fock matrix is 400×400 ?
21. 1). Which would require more empirical parameters, extended Huckel method or a molecular mechanics force field?
- 2) Which one among each of the following groups, is more stable? Explain using Huckel molecular orbital theory:
- Cyclopropenyl radical, cyclopropenyl cation, cyclopropenyl anion.
 - propenyl radical, propenyl anion, propenyl cation
 - $(\text{CH})_5^-$, $(\text{CH})_5$, $(\text{CH})_5^+$ (CYCLIC)
22. A. Show that maximum stabilization is observed in a molecule if the number of π electrons is equal to N and N can be written as $4n+2$ as per Huckel's rule.

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- b. Show that if one electron is added or removed from benzene, the resulting structures are less stable than benzene using Huckel method.
- c. Calculate the pi electron energy and delocalization energy of the following molecules:
 - a. propenyl radical, anion, cation
 - b. cyclopropenyl radical, anion, cation
 - c. cyclobutadiene
 - d. butadiene
 - e. benzene

Note: you may refer to the Energy levels of these molecules as given by Huckel method.

23. Calculate the π bond order of the C=C bond in (use their wave functions from textbook)

- a. cyclopropenyl radical, anion, cation
 - b. propenyl radical, anion, cation
24. a. In the extended Huckel method, how many atomic orbital wavefunctions will the basis set of ethylene consist of? What will be the order of the Fock matrix in this case? What will be the order of Fock matrix if simple Huckel method is used?
- b. What do you understand by the term “minimal valence basis set”?
 - c. Write the secular determinant for 1,4-butadiene on the basis of Huckel MO theory.
25. A. What do you mean by virtual orbitals?
- b. Enlist the various steps required in deriving the Roothan-Hall equations $\mathbf{FC}=\mathbf{SC}\epsilon$
 - c. State the molecular features that can be calculated using ab initio calculations.
26. A. List the strengths and weaknesses of ab initio calculations over molecular mechanics and EHM.
- b. What do you mean by polarization functions and diffuse functions?
 - c. Explain each term in 6-31++G** basis set.
 - d. Why is Hartree procedure called self consistent field procedure?
27. A. What is the main advantage of an all-valence electron method like, say CNDO over a purely π electron method like PPP?
- b. Although both AM1 and PM3 normally give good molecular geometries, they are not too successful in dealing with geometries involving H bond. Suggest reasons for this deficiency.
 - c. Write a short note on SCF method.
28. A. How are semi-empirical methods different from Molecular Mechanics methods?
- b. How are semi-empirical methods different from Ab-initio methods?
 - c. Write a short note on Koopman's theorem.

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29. A. Can the Schrodinger equation be solved exactly for a species with two protons and one electron? Why or why not?
- State the Antisymmetry principle.
 - Why is there a need to convert the SWE in terms of Cartesian coordinates to SWE in terms of polar coordinates?
30. A. Write SWE for H atom in terms of polar coordinates.
- Why is there a need for Approximate methods? Explain any one briefly.
 - Write the SWE for:
 - He atom
 - H₂ molecule.
- Can it be solved exactly? Suggest any one method to solve.
31. A) Why do internal coordinates or z-matrix have six coordinates less than the Cartesian system or crystallographic system?
- B) Construct the z-matrix for a simple ethanol molecule by using appropriate labels. (Other simple examples of small molecules may also be tried).
32. A. What is QSAR?
- What is the difference between 2D- QSAR and 3D-QSAR?
 - How the biological parameter are different from the structural parameter in QSAR studies?
33. A. What is Ki or IC50 (molar concentration of compound leading to 50% inhibition of enzyme) constant and how it is related to K_d.
- List types of structural parameters used in QSAR? (like electronic parameter, hammett, hydrophobicity etc. has to be described)
 - What is polarizability. Arrange the following in increasing order of polarizability
He, Ne, Ar
Methane, ethane, propane, butane
34. A. What is partition coefficient (P) in QSAR studies?
- Write a Hammett equation and explain its application.
 - Explain Steric factor as one of Physicochemical parameter in QSAR ?
35. A. How QSAR equation relates biological activity to molecular electronic characteristic and hydrophobicity.
- Give an expression for a 'molecular mechanics' potential energy function of the type used for standard macromolecular simulations. Include intra- and intermolecular terms. State clearly what each energy term represents, and its physical origin.
 - What does the term force field represent in Molecular mechanics?

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36. A. What is the relationship between the term force field and potential energy?
- What is parametrizing the force field in molecular mechanics?
 - A typical force field model for propane contains 10 bond-stretching terms, 18 angle-bending terms, 18 torsional terms and 27 non-bonded interactions.
 - Explain the origin of these terms.
 - A sizeable number of terms are thus included in the force field model, even for a molecule as simple as propane. Even so, the number of terms is many fewer than the number of integrals that would be involved in an equivalent ab initio quantum mechanical calculation. Explain.

37. A. What does the concept of 'transferability' and 'atom type' mean in a force field?
- One of the functional forms to represent torsional angles in MM force field is the following.

$$v(\omega) = \sum_{n=0}^N \frac{V_n}{2} [1 + \cos(n\omega - \gamma)]$$

What does various symbols represent in this equation?

- Write a short note on Lennard-Jones 12-6 potential.
38. A. The Lennard-Jones potential is represented by

$$v(r) = 4\epsilon \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^6 \right]$$

Where,

ϵ is the depth of the potential well,

r is the distance between the particles,

σ is the finite distance at which the inter-particle potential is zero,

and r_m is the distance at which the potential reaches its minimum.

Prove that

$$r_m = 2^{1/6} \sigma \approx 1.122 \sigma$$

- How is the electrostatic contribution modeled in a force field of molecular mechanics?
Give the simplest expression for the same.
 - What are the applications of Molecular mechanics?
39. A. Out of the following force fields, which one is the most accurate way of modelling hydrocarbons?

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- a) AMBER
 - b) CHARMM
 - c) MM3
 - d) OPLS
- b. Out of the following force fields, which one is the most accurate way of modelling bulk liquids?
- a) AMBER
 - b) CHARMM
- c. Which is the fastest computational chemistry method and which is the slowest? Explain giving reasons.
40. A. What advantages does computational chemistry have over wet chemistry?
- b. Should calculations from first principles (ab initio) necessarily be preferred to those which make some use of experimental data (semiempirical)?
 - c. What is geometry optimization? Why is this process for transition states more challenging than for minima?
41. a. Deabbreviate the following terms and briefly describe them in not more than two lines:
- a) CNDO
 - b) AM1
 - c) PM3
- 42.a. What is parametrizing the force field in molecular mechanics?
- b. How with the help of a diagram why it is not correct to say that a transition state is a maximum on a PES.
 - c. Explain for a reaction $A - B$, how the potential energy change on a PES is related to the enthalpy change of the reaction. What would be the problem with calculating a free energy/geometry surface?
43. A. What is geometry optimization? Why is this process for transition states (often called transition state optimization) more challenging than for minima?
- b. What is Hessian? What uses does it have in computational chemistry?
 - c. Why is it usually good practice to calculate vibrational frequencies where practical, although this often takes considerably longer than geometry optimization.
44. A. What are higher order saddle points?
- b. If gravity plays role in chemistry, then why are vibrational frequencies different for C – D and C – H bonds?
 - c. Why are chemists rarely interested in finding and characterizing second order and higher order saddle points?
45. A. If a species has one calculated frequency very close to 0 cm^{-1} , what does that tell you about the calculated potential energy surface in that region?

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- b. The ZPE of many molecules is greater than the energy needed to break a bond; for example, the ZPE of hexane is about 530 kJ mol⁻¹ while the strength of a C – C or a C – H bond is only about 400 kJ mol⁻¹. Why then do such molecules not spontaneously decompose?
 - c. Only certain parts of a potential energy surface are chemically interesting, some regions are flat and featureless while yet other parts rise steeply and are thus energetically inaccessible. Explain.
46. A. How will you differentiate between a minimum and a saddle point?
- b. What does a saddle point in a potential energy surface indicate?
 - c. What do you understand by “hilltop”? Explain using a suitable example.
47. A. What do you understand by energy minimization of a molecule?
- b. Discuss a first order derivative method to attain the energy minimization in molecules.
 - c. Give brief explanation of a second order derivative method of energy minimization.
48. A. Out of Newton Raphson method and Steepest Descent method, which one is preferable and why?
- b. Write a short note on the followings
 - a) Multivariate grid search
 - b) Langevin & Brownian dynamics
 - c. Give any two applications of Metropolis Algorithm.
49. A. Describe the principle behind Monte Carlo Simulations.
- b. Draw and compare radial distribution function (RDF) plots for solid, liquid and gas.
 - c. What information is provided by RDF plots?
 - d. Explain any one Intermolecular potential used for describing interactions between molecules in molecular dynamics.
50. A. Define Ensemble.
- b. Explain why having vacuum outside a simulation box is not a good idea and how using periodic boundary conditions overcome this problem?
 - c. What is Ergodic Hypothesis?
51. a. What is the purpose of Rescaling? How is it done?
- b. Name the model used for simulation of pure water.
 - c. Draw pair distribution function plot for O-O, H-H, O-H for water.
52. A. Draw Radial Distribution plot for liquid Argon at temperature of 100 K.
- b. Explain how the time step should be selected in a Molecular Dynamics simulation. What problems arise from too large or too small value of time step?
 - c. Differentiate between canonical and microcanonical ensemble

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53. A. How Verlet Algorithm used in molecular dynamics simulation different from Leap Frog Algorithm?
- b. What is the underlying principle of DFT?
- c. Why should standard DFT methods be characterized as semiempirical and not as ab initio calculation procedures?
54. A. What are the approximations used in HMO?
- b. Write down the simple Huckel Fock matrices for (i) propenyl radical; (ii) propenyl anion system.
- c. What are the most important results that can be obtained from Huckel calculations?
55. A. Enlist the various steps required in deriving the Roothan-Hall equations $\mathbf{FC}=\mathbf{SC}\epsilon$
- b. What is a basis set? What is the difference between the basis set of extended Huckel method and ab initio STO-3G basis set?
- c. List the strengths and weaknesses of ab initio calculations over molecular mechanics and EHM.
56. a. What do you mean by polarization functions and diffuse functions?
- b. Explain each term in 6-31++G** basis set.
- c. Why is Hartree procedure called self consistent field procedure?
57. A. What is the main advantage of an all-valence electron method like, say CNDO over a purely π electron method like PPP?
- b. Although both AM1 and PM3 normally give good molecular geometries, they are not too successful in dealing with geometries involving H bond. Suggest reasons for this deficiency.
- c. How are semi-empirical methods different from Molecular Mechanics methods?
58. A. State the Antisymmetry principle.
- b. Why is there a need to convert the SWE in terms of Cartesian coordinates to SWE in terms of polar coordinates?
- c. Distinguish between
- (i) Spin orbital and spatial orbital
 - (ii) Molecular Dynamics and Monte-carlo simulation
 - (iii) Ab-initio method and DFT
59. A. What is Ergodic Hypothesis?
- b. How Verlet Algorithm works. Give its advantages and drawbacks.
- c. What is the purpose of Rescaling? How is it done?
60. A. What do you understand by a potential energy hypersurface? Explain using a suitable example.

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- b. Explain the terms: local minimum, global minimum, saddle point? Using suitable diagrams.
- c. Draw and discuss the potential energy diagrams of the following molecules as a function of torsion angle:
Butane.