Sr. No. of Question Paper   :

Unique Paper Code   :   32177905

Name of the Paper   :   DSE: Molecular Modelling and Drug Design

Name of the Course   :   **B. Sc (Hons.) Chemistry**

Semester   :   VI

Duration   :   2 hours

Maximum Marks   :   75

Instructions for Candidates

1. All questions carry equal marks.
2. Answer **four questions** in all.
3. First part of each question carries 6.75 marks.
4. Remaining parts of each question carry 6 marks.
5. Attempt all parts of a question together.

1)   a. State the approximation which forms the basis of a potential energy surface (PES). From the perspective of a chemist, what types of points on a potential energy surface are significant and why? Also differentiate between a relaxed and rigid PES.

      b. What do you understand by energy minimization of a molecule? Give brief explanation of a second order derivative method of energy minimization.

      c. How does the Verlet algorithm used in molecular dynamics simulation works? Give its advantages and drawbacks. How is Verlet algorithm different from Leap Frog algorithm?

2)   a. What information is provided by RDF plots? Give a comparative overview of radial distribution function (RDF) plots for a substance in solid, liquid and gaseous state.

      b. Differentiate between (any two)

      i.   Monte Carlo Simulation and Molecular Dynamics Simulation.

      ii.   Simple Huckel method and Extended Huckel method

     iii.   Spin orbital and spatial orbital

c. What is Ergodic Hypothesis? 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?

3)

a. Molecular mechanics is essentially empirical, while methods like PPP, CNDO, and AM1 are semiempirical. Give reason. Briefly mention the key features of the PPP, CNDO and AM1 semi-empirical methods.

b. i) How do you account for non-bonded interactions in Molecular mechanics? Explain

ii) What do you mean by parametrization of a force field? How many parameters do you think a reasonable forcefield would need to minimize the geometry of CCl_3-CH_2OH?

c. Which of the following is more stable? Explain using Hückel Molecular Orbital theory

      i.   allyl radical

      ii.   allyl cation

     iii.   allyl anion

4)

a. Using the Hückel Molecular Orbital theory calculate the molecular orbitals and their energies for ethylene molecule. According to HMO theory, the β value for ethylene is -30 KJ/mol. Find the energy of photon that will excite from HOMO to LUMO.

b. Enlist the key features of commonly used forcefields OLPS, CHARMM and MM3 methods? Which of the above is more suited for carrying out the following calculations

      i.   Simulation of nitrobenzene deoxygenase

      ii.   Energy difference between different conformers of a medium-size organic molecule

     iii.   Heat of vaporization of ionic liquids

c. Write down the number of basis functions for methane (CH_4) using the following basis sets:

    i.   3-21G*

    ii.   6-31G(d,p)

    iii. STO-3G

5)   a. i) The Lennard-Jones potential is represented by

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

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

ii) The value of the Hammett constant for -CF_3 and -Cl when placed at meta position in benzoic acid are 0.46 and 0.37 respectively. Similarly, the value of σ for -CH_3 and -OCH_3 when placed at para position in benzoic acid are -0.14 and -0.28, respectively. Discuss the significance of the values of the Hammett constant provided.

b. Classify the following as aromatic, nonaromatic or antiaromatic on the basis of HMO

    i.   Cyclopentadienyl anion

    ii.   Cyclobutadiene

    iii. Cyclohepatrienyl cation

c. i) DFT calculation should be characterized as semi-empirical rather than ab-initio. Explain.

ii) What are electrostatic potential maps? Give their significance.

6)   a. Define Partition coefficient. Calculate the partition coefficient of a drug if its concentration in octanol is 0.02 M and the concentration of drug in water is 0.0021 M. What happens to the lipophilicity of the compound if the partition coefficient increases? What is the value of partition coefficient if the drug distributes itself equally between octanol and water?

b. i) Why is Hartree procedure called self-consistent field procedure.

ii) How does the inclusion of polarization and diffuse function improve the basis set?

c. Give the expression for coulomb and exchange integrals. Also give their physical significance.