(d) Morphine has an apparent volume distribution of 220 L, and half life of elimination of 3 hours. In a 70 Kg man, what is its approximate rate of clearance?

**(1 + 3) + 4 + 2 + 2 = 12**

## Group – E

8. (a) How is force field parameterization done in the OPLS force field? How are principles of structure based drug design (SBDD) used to design and develop HIV-I protease inhibitors? (*Your answer should highlight design constraints and be in a flowchart format)*.

(b) What are the primary purposes of scoring functions for molecular docking? What would be the complete expression for binding free energy (for ligand binding to a receptor) using such a scoring function? Draw a diagram to represent the 'piecewise linear potential' scoring function.

**(2 + 4) + (2 + 2 + 2) = 12**

9. Hantsczh developed QSAR equations that were first used to rationalize biological activity by relating the latter to a molecule's electronic characteristics and hydrophobicity.

(a) Define the parameters of the following QSAR equation and explain their significance with respect to the above statement:

$$\log (1/C) = k_1 \log P - k_2 (\log P)^2 + k_3\sigma + k_4$$

(b) What properties of a potential drug does the hydrophobic component represent?

(c) How can the above equation be re-parameterized with the term π? What are the physicochemical implications of this newly parameterized equation?

**6 + 2 + ( 2 + 2) = 12**



# B.TECH/BT/6TH SEM/BIOT 3241/2017
# MOLECULAR MODELLING AND DRUG
# (BIOT 3241)

**Time Allotted : 3 hrs** **Full Marks : 70**

***Figures out of the right margin indicate full marks.***

***Candidates are required to answer Group A and any 5 (five) from Group B to E, taking at least one from each group.***

***Candidates are required to give answer in their own words as far as practicable.***

## Group – A
## (Multiple Choice Type Questions)

1. Choose the correct alternative for the following: **10 × 1 = 10**

(i) In either molecular dynamics or Monte Carlo simulations, configuration storage capacity ranges from
(a) 50 - 100 steps (b) 5 - 25 steps
(c) 500 - 1000 steps (d) 200 - 300 steps.

(ii) ADME means
(a) Addition Division Multiplication and Energy
(b) Absorption Distribution Metabolism and Excretion
(c) About Drug Metabolism Effect
(d) Additional Drug Mechanism Essential.

(iii) Which of the following choices can be a docking calculation?
(a) 1 ligand-1 protein (b) Many ligands-1 protein
(c) 1 ligand-many protein (d) all of the above.

(iv) $IC_{50}$ means
(a) Concentration of a drug that is required for 50 percent inhibition in an assay
(b) Concentration of a drug that is required for 50 percent activation in an assay
(c) 50 mg of a drug that is required for 50 percent inhibition in an assay
(d) 50 μg of a drug that is required for 50 percent activation in an assay.

(v) Simulated Annealing can be related to
(a) Molecular dynamics simulation (b) Monte Carlo simulation
(c) LINUX based computation (d) Newton-Raphson algorithm.

(vi) Which of the following is NOT a derivative minimization method?
(a) Steepest descent (b) Conjugate gradient
(c) Simplex (d) Quasi Newton.

(vii) Which of the following are classical isosteres?
(a) $CH_3$,$NH_2$,OH,F (b) $CH_3$, $C_2H_5$, $C_3H_7$
(c) S - S (d) none of the above.

(viii) Which one of the following is not molecular descriptor?
(a) Molecular weight (b) Log P
(c) Molecular absorption (d) Refractive index.

(ix) Different poses of a target receptor and ligand are simulated in
(a) Rigid docking (b) QSAR (c) CoMFA (d) Flexible docking.

(x) A pharmacophore is defined as
(a) a molecule that carries essential features responsible for a drug's biological activity
(b) a molecule without biological activity
(c) a molecule that carries non-essential biological information
(d) a kinetically fast reacting molecule.

## Group – B

2. (a) Briefly enumerate two applications of the Configurational Bias Monte Carlo (CBMC) method.

(b) How does the behaviour of Monte Carlo simulation (MCS) and Molecular Dynamics Simulation (MDS) *complement and differ* in their ability to *explore phase space*?

(c) Give two examples of techniques that have combined MCS and MDS.

(d) How have hybrid MCS-MDS methods been used to perform long-time simulations of DNA molecules? Name two distinct properties of such hybrid simulations.

**2 + 3 + 2 + ( 3 + 2) = 12**

3. (a) How does the Boltzmann factor figure in the steps of Monte Carlo method?

(b) List the common derivative and non-derivative minimization methods.

(c) Outline the steps of the steepest descents method using diagram(s).

(d) The antibiotic netropsin (a DNA inhibitor) was modeled using an automated docking program. Explain the minimization procedures adopted to obtain the structure *closest* to the *global minimum*.

**2 + 3 + 3 + 4 = 12**





## Group – C

4. (a) Describe the role of following physicochemical parameters in drug design:
(i) Ionization constants (ii) chelation
(iii) solubility (iv) partition co- efficient.

(b) Write the mathematical equation for the calculation of total molecular mechanics potential energy of a molecule in the context of molecular modelling, explaining all the terms.

(c) The harmonic potential function of a bond stretching is expressed as

$$V_{bonds} = 0.8\, K_b\, (r_{AB} - r_{AB}^{o})^2$$

The stretching force constant for the bond A – B is 200 kcal/mol/$A^2$ and the equilibrium bond length $rAB^o$ is 1.5 $A^o$.
i) Sketch the potential as a function of A – B separation.
ii) What is the energy if the bond is stretched by 60 $A^o$?
iii) What is the energy if the bond is compressed by 0.6 $A^o$?

**( 1 + 1 + 1 +1 ) + 4 + ( 1 + 1 + 2) = 12**

5. (a) Describe molecular descriptor with a example. Give the Structure Activity Relationship of Morphine.

(b) What are the differences between a local energy minimum and global energy minimum?

(c) Describe the "Lipnski's rule of five".

**(3 + 3) + 3 + 3 = 12**

## Group – D

6. Describe the following based on drug designing with example :
(a) Target Discovery
(b) Assay Development
(c) Clinical trials for drug discovery.

**(3 × 4) = 12**

7. (a) What is combinatorial chemistry? Describe any one approach of combinatorial chemistry with example.

(b) Explain the steps of SBDD using a flow chart and give example of a successful drug developed by SBDD.

(c) Define characteristics curve of drug concentration with time after administration of single dose.