Name : .....

Roll No. : .....

Invigilator's Signature : .....

CS/B.Tech/(BT-NEW)/SEM-6/BT-604B/2013

2013

MOLECULAR MODELING AND DRUG DESIGNING

Time Allotted : 3 Hours *Full Marks :* 70

The figures in the margin indicate full marks.

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

GROUP – A

(Multiple Choice Type Questions)

1. Choose the correct alternatives for any *ten* of the following : 10 × 1 = 10

i) Which one of the following is a first order minimization method ?

a) Steepest descent

b) Newton-Raphson

c) Genetic

d) Evolutionary.

ii) ADME means

a) Addition Division Multiplication and Energy

b) Administration Distribution Metabolism and Excretion

c) About Drug Metabolism Effect

d) Additional Drug Mechanism Essential.

iii) The term $\sum_{bonds} K_r \ (r - r_o)^2$ in an energy expression is indicative of

a) torsion angle interactions

b) van der Waals interactions

c) Hydrogen bond

d) Bond stretching.

iv) IC_{50} means

a) Concentration of a drug that is required for 50 per cent inhibition in an assay

b) Concentration of a drug that is required for 50 per cent activation in an assay

c) 50 mg of a drug that is required for 50 per cent inhibition in an assay

d) 50 μg of a drug that is required for 50 per cent activation in an assay.

v) Which of the following software programmes is used for automated *de novo* drug design ?

a) LUDI

b) DOCK

c) CoMFA

d) CHEM3D.

vi) Which of the following calculations would generally be carried out using molecular mechanics ?

a) Energy minimization

b) Molecular orbital energies

c) Transition-state geometries

d) Electrostatic potentials.

vii) Which of the following statements is not true of cyclic structures ?

a) They are normally more rigid than acyclic structures

b) They are locked into the active conformation

c) They are useful in determining the active conformation of a series of related compounds

d) They are normally more difficult to synthesize than acyclic molecules.

viii) Which of the following groups is least susceptible to cytochrome P450 enzymes ?

a) Terminal methyl groups

b) Allylic carbons

c) Benzylic carbon atoms

d) Quaternary carbon atoms.

ix) Conjugate Gradient method is

a) first order minimization technique

b) second order minimization technique

c) a docking program

d) none of these.

x) Factor that effect rates of drug distribution in our body is

a) Blood perfusion

b) Membrane permeability

c) Both (a) & (b)

d) pH.

xi) Potential energy function is a sum of

a) Energy of all atoms

b) Expression of forces acting on electron

c) the bonded and non-bonded force fields

d) total energy of the system.

xii) In MD force acting on each atom can be calculated using

a) Newton's equation

b) Taylor's series

c) Born-open heimer approximation

d) Gibbs function.

GROUP – B

(Short Answer Type Questions)

Answer any *three* of the following. $3 \times 5 = 15$

2. Define the following :

a) Prodrug

b) Pharmacokinatics

c) ED_{50}

d) Pharmacodynamics

e) LD_{50}

3. Briefly give an itemwise definition of the following :

a) bioactive conformation of a molecule

b) computer a ided drug design. $2 \times 2\frac{1}{2}$

4. Write short notes on any *one* of the following based on drug designing :

a) Target Discovery

b) Target Validation

c) Assay Development.

5. What is Prodrug ? Define Apparent Volume distribution of Drug. Calculate Apparent Volume distribution of Drug when amount of drug injected is 100 mg & plasma drug concentration at $t = 0$ is 10 mg/l. 1 + 1 + 3

6. What do you mean by docking ? What are different types of docking ? Give example. 2 + 3

GROUP – C

(Long Answer Type Questions)

Answer any *three* of the following. 3 × 15 = 45

7. a) How chemicals are selected for making drugs ?

   b) Explain steps of SBDD using a flow chart.

   c) Give three examples of drug designed using SBDD.

   5 + 6 + 4

8. a) Define a force field in the context of molecular modeling. What are its key contributors ? Write out the full form of a functional force field defining all the terms and symbols. 1 + 2 + 5

   b) Use either of the force fields CHARMM or AMBER and briefly describe its unique features and applicability in molecular modeling calculations of force field. 7

9. a) What are the different methods adopted in drug design to discover a lead molecule ?

   b) Explain them with examples. Explain briefly about electronic parameters used in QSAR.

   c) Describe the importance of chelates in medicine.

   8 + 4 + 3

10. Define drug as a pharmacological point of view. Describe briefly different types of dug dose. Explain the characteristic curve of drug Concentration with time after administration of single oral dose. Morphine has an apparent volume distribution of 220L and a half-life of elimination of 3 hrs. In a 70 kg man, what is its approximate rate of clerance ? What are the two parameters commonly utilized to describe lipophilicity of drug candidates ? Briefly describe the effect of P450 enzymes on drug metabolism. 1 + 3 + 3 + 3 + 2 + 3

11. a) What is the difference between a local energy minimum and a global energy minimum ?

    b) The harmonic potential function of bond stretching is expressed as

    $V_{bonds} = 0.5\ K_b\ (r_{AB} - r_{AB}^{\circ})^2$. The Stretching force constant for the bond $A - B$ is 200 kcal/mol/A^2 and the equilibrium bond length r_{AB}° is 1.5 $\mathring{A}$.

    i) Sketch the potential as a function of $A - B$ separation.

    ii) What is the energy if the bond is compressed by 0.5 $\mathring{A}$?

    iii) What is the energy if the bond is stretched by 50 $\mathring{A}$?

    c) State the name of optimization method used in the molecular modeling. 3 + 6 + 2 + 2 + 2