Name : .....

Roll No. : .....

Invigilator's Signature : .....

CS/B. Tech (BT)/SEM-7/BT-703D/2011-12

2011
MOLECULAR MODELLING AND DRUG DESIGN

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 :

$10 \times 1 = 10$

i) Of the following which is NOT a minimization algorithm ?

a) Steepest descent

b) Conjugate gradient

c) Newton-Raphson

d) Modified Neglect of Diatomic Overlap.

ii) The Boltzmann factor is given by

a) $\exp(-E / RT)$

b) $\exp(-x^2)$

c) $\exp(-kT)$

d) none of these.

iii) Which of the following is NOT a force field ?

a) AMBER b) CHARMM

c) OPLS d) GEO.

iv) In Lipinski rule the molecular weight varies

a) 350 to 500 b) 100 to 150

c) 400 to 500 d) 230 to 250.

v) In drug design IND means

a) International New Drug

b) Investigation of New Disease

c) Investigational New Drug

d) Indian New Disease.

vi) In drug design MTD means

a) Maximum Treated Dose

b) Maximum Tolerated Dose

c) Maximum Time Does

d) Measurement to Treated Dose.

vii) 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.

viii) 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.

ix) A method for protein structure determination from which data is incorporated into the Brookhaven protein data bank is

a) Nuclear magnetic resonance spectroscopy

b) Fluorescence spectroscopy

c) Infrared spectroscopy

d) Atomic force microscopy.

x) Generally in Phase 1 the number of total human subjects is in the range of

a) 20 to 80 b) 50 to 100

c) 200 to 300 d) 500 to 1000.

xi) 'QSAR' stands for

a) Quantum Structure Action Relationship

b) Quantitative Structure Activity Relationship

c) Quantum Similarity Activity Relationship

d) None of these.

xii) Lead is a

a) Molecule with no property

b) Starting molecule of docking

c) Molecule with biological and pharmacological property

d) A software tool.

GROUP – B

(Short Answer Type Questions)

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

2. What is meant by 'ADME' of a drug ? How is it useful in drug-design ? 2 + 3

3. Define the following :

   a) ED_{50}

   b) LD_{50}

   c) Pharmacokinetics

   d) Pharmacodynamics

   e) QSPR.

4. Briefly describe the advantages and disadvantages of QSAR in drug-design. $2\frac{1}{2} + 2\frac{1}{2}$

5. What is a Lennard-Jones potential ? What are some of the microscopic parameters that are obtained from simulation results that are then compared to experimentally obtained results. 2 + 3

6. Briefly describe the 'Steepest descent' method used in energy minimization.

GROUP – C

(Long Answer Type Questions)

Answer any *three* of the following. $3 \times 15 = 45$

7. "Protein stability and folding plays an increasingly important role in the search of biopharmaceuticals (i.e. protein-based drugs)." Elaborate on the statement with the use of the following 3 informational categories :

   (i) Ramachandran-Sasisekharan plot

   (ii) The phenomenon of protein folding itself

   (iii) The hydrophobic effect. 5 + 5 + 5

8. a) Give a step-wise description of the Metropolis Monte Carlo algorithm. What makes this algorithm unique ?

   b) To what types of biological system processes have Monte Carlo simulations been successfully applied ?

   c) What is simulated annealing and what is it ideally suited for ?

   d) What are the factors that decide choice between Monte Carlo and molecular dynamics for carrying out a molecular simulation ? 5 + 2 + 4 + 4

9. a) What is one of the biggest advantages of combinatorial chemistry over classical synthetic chemistry ? Elucidate with an example from medicinal chemistry.

b) Briefly describe the three methods by which compounds in a combinatorial chemical library are identified. 6 + 9

10. Ludi is one of the approaches of De nuovo Drug designing.

a) Briefly describe what methodology it follows.

b) Briefly enumerate the functional steps of Ludi.

c) What are the major differences of Ludi and Ludi/CAP methods ? 4 + 8 + 3

11. a) Name four physico-chemical parameters and their mathematical representation that can be referred to as molecular descriptors specific to drug-design.

b) Use a flow-chart to depict the drug discovery process.

c) Briefly describe how clinical trial of a drug is conducted.

6 + 4 + 5