B.TECH/BT/6TH SEM/BIOT 3241(BACKLOG)/2021

MOLECULAR MODELING & DRUG DESIGNING
(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) The term $\sum_{bonds} K_r (r - r_o)^2$ in an energy expression is indicative of
(a) torsion angle interaction., (b) van dar Waals interactions.
(c) hydrogen bonds, (d) bond stretching.

(ii) Potential energy function of diatomic molecule 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.

(iii) Glomerular filtration depend on the
(a) plasma protein binding (b) renal blood flow
(c) both (a) and (b) (d) none of the above.

(iv) Which of the following enzymes is a microsomal enzyme
(a) Cytochrome P_{450} (b) Trypsine
(c) Lipase (d) none of the above

(v) Factor that effects rates of drug distribution in our body is
(a) blood perfusion (b) membrane permeability
(c) both (a) and (b) (d) pH.

(vi) Following is a ligand-based drug design approach
(a) Docking (b) QSAR
(c) Dynamics (d) Monte Carlo.

(vii) One of the following is not molecular descriptor
(a) Molecular weight (b) Log P
(c) Molecular absorption (d) Refractive index,

(viii) The specificity of a ligand binding site on a protein is based on
(a) the absence of competing ligands
(b) the amino acid residues lining the binding sit
(c) the presence of hydrating water molecules
(d) the opposite chirality of the binding ligand.

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

(x) Pharmacophore is a
(a) Receptor (b) Molecular structure feature
(c) Drug effect (d) Substrate effect

Group – B

2. (a) How are finite difference techniques used to generate molecular dynamics trajectories?

(b) Write out the steps of the Velocity Verlet algorithm. Explain precisely what are the differences between the velocity Verlet and the standard Verlet algorithms.

(c) How is molecular dynamics integrated into the process of experimental structure determination of a protein?

3 + 5 + 4 = 12

3. (a) What are the specific application domains of Configurational Bias Monte Carlo (CBMC)?

(b) Use a diagram to explain the insertion of a 3-unit molecule into a lattice. How does the CBMC method deal with the insertion problem? (Hint: Rosenbluth weight).

(c) Explain the term and significance of the probability expression rand (0,1) <= $W_{l, trial}$ /$W_{l, old}$ in the context of the CBMC algorithm.

(d) For a branched macromolecule, what is the probability expression for generation of a particular configuration in the CBMC method? Assume Lennard-Jones, torsional and bond angle terms to be decoupled. Define all the terms in the expression.

3 + 3 + 2 + 4 = 12

Group – C

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

(b) What are principle based on which molecular mechanics (MM) methods are developed? What are the applications of MM?

(c) 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.

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

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

(b) Describe kinetics of drug elimination.

(c) Describe the mechanism of drug metabolism.

(3 + 3) + 3 + 3 = 12

Group – D

6. (a) Write the names of different roots of drug delivery. What you understand by pharmacodynamics of a drug? Describe graphical nature dose-response and dose-binding graphs of a drug showing EC_{50}, Emax.

(b) What are spare receptors for a drug? Describe it's nature with graph.

(c) Explain prodrug with an example? Define apparent volume distribution of drug. Calculate apparent volume distribution of drug when amount of a drug injected is 100 mg and plasma drug concentration at t=0 is 10 mg/L.

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

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

(b) What is bioavailability of a drug. It depends on which factors? Describe with experimentally how we can calculate this, with graph.

(c) Describe the mechanism of drug interaction with different types of receptor present in a human cell with a diagram**.**

(d) A new drug is under study in phase 1 trials. It is found that this molecule is avidly taken up by extravascular tissues so that the final total amount in the extravascular compartment at steady state is 100 times the amount remaining in the blood plasma. What is the probable volume of distribution in a hypothetical person with 8 L of blood and 4 L of plasma?

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

Group – E

8. (a) Explain the steps of the DOCK algorithm using a schematic diagram. How are distance geometry constraints accounted for in DOCK? What is the approach for incremental construction of a ligand in first generation docking algorithms like DOCK?

(b) How is ligand and receptor flexibility ideally accounted for in a docking method? Explain with reference to constraints of rigid body docking and availability of

appropriate fragment databases. In a tabular fashion, compare the characteristics of GRAMM with that of LUDI.

(2 + 2 + 2) + (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;

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

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

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

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

6 + 2 + (2 × 2) = 12

Department & Section	Submission Link
BT	https://classroom.google.com/c/MzY1MjcyNzY2ODEx/a/MzY1Mjc4NDUzMDA3/details