CS/M.Tech (BT)/SEM-2/MBT-203/09
BIOINFORMATICS & DRUG DESIGN (SEMESTER - 2)

1. ....
   Signature of Invigilator

2. ....   **Reg. No.**
   Signature of the Officer-in-Charge

Roll No. of the Candidate

CS/M.Tech (BT)/SEM-2/MBT-203/09
ENGINEERING & MANAGEMENT EXAMINATIONS, JULY – 2009
BIOINFORMATICS & DRUG DESIGN (SEMESTER - 2)

Time : 3 Hours]   [Full Marks : 70

INSTRUCTIONS TO THE CANDIDATES :

1. This Booklet is a Question-cum-Answer Booklet. The Booklet consists of **36 pages**. The questions of this concerned subject commence from Page No. 3.

2. a) In **Group – A**, Questions are of Multiple Choice type. You have to write the correct choice in the box provided **against each question**.

    b) For **Groups – B** & **C** you have to answer the questions in the space provided marked 'Answer Sheet'. Questions of **Group – B** are Short answer type. Questions of **Group – C** are Long answer type. Write on both sides of the paper.

3. **Fill in your Roll No. in the box** provided as in your Admit Card before answering the questions.

4. Read the instructions given inside carefully before answering.

5. You should not forget to write the corresponding question numbers while answering.

6. Do not write your name or put any special mark in the booklet that may disclose your identity, which will render you liable to disqualification. Any candidate found copying will be subject to Disciplinary Action under the relevant rules.

7. **Use of Mobile Phone and Programmable Calculator is totally prohibited in the examination hall.**

8. You should return the booklet to the invigilator at the end of the examination and should not take any page of this booklet with you outside the examination hall, **which will lead to disqualification**.

9. Rough work, if necessary is to be done in this booklet only and cross it through.

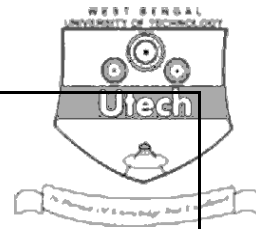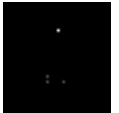**No additional sheets are to be used and no loose paper will be provided**

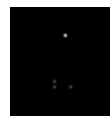----

FOR OFFICE USE / EVALUATION ONLY
Marks Obtained

					Group – A					Group – B		Group – C			Total Marks	Examiner's Signature
Question Number																
Marks Obtained																

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Head-Examiner/Co-Ordinator/Scrutineer
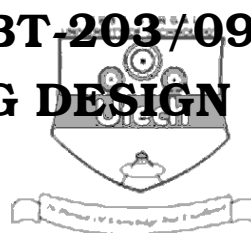
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SEMESTER - 2

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GROUP – A
(Multiple Choice Type Questions)

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

i) A lead compund is

   a) a clinically used drug

   b) a prototype with the desired biological/pharmacological activity

   c) a polymer

   d) all of these.

ii) Pick the odd one out

   a) Bootstrapping   b) Jukes Cantor

   c) Caveats   d) Jacknifing.

iii) Monophyletic group is

   a) a group of taxa descended from a single common ancestor

   b) a pair of taxa descended from a single common ancestor

   c) five taxa descended from a single common ancestor

   d) a group of species descended from a single common ancestor.

iv) In the anti-inflammatory drug sulindac the active pharmaceutical agent is

     a) the metabolic reaction product of sulindac

     b) sulindac itself

     c) dimenhydrinate

     d) prontosil.

v) An optimal Q_3 protein secondary structure prediction score (cf. with some low-resolution experimental techniques) is

     a) 60%   b) 75%

     c) 80%   d) 50%.

vi) Phylogeny with multifurcating branches is called

     a) paraphyletic   b) lineage

     c) polytomy   d) evolutionary tree.

vii) The correct full form of UPGMA is

     a) unweighted pair group method using arithmetic average

     b) unweighted pair group method using arithmetic addition

     c) unweighted pair group mean using arithmetic average

     d) unweighted pair group method using algorithmic average.

viii) Structure prediction of α-helical transmembrane segment includes use of

     a) hydrophobicity   b) neural networks

     c) evolutionary information   d) all of these.
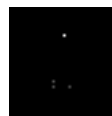
ix) Solvent interactions are simulated in molecular dynamics by

    a) simulating motion of proteins in a box of water molecules

    b) simulating protein motion *in-vivo*

    c) simulating protein motion in a solvent as a continuous medium

    d) all of these.
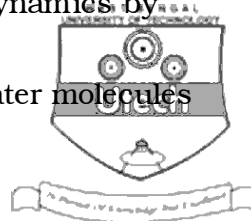
x) PSSM stands for

    a) position specific scoring models

    b) positional specific scoring models

    c) position specific scoring matrix

    d) position specific scoring match.

xi) The Free-Wilson method for occurrence of additive substituent effects is given by

    a) $BA = \Sigma a_i \, x_i + \mu$

    b) $\text{Log } l/C = -a \, \Pi^2 + b \, \Pi$

    c) $\text{Log } A = x_1 a + x_2 b + x_3 c + \ldots\ldots + \text{constant}$

    d) $\text{Log } x = ax + bx^2 + c.$

xii) For *in-vivo* systems, the therapeutic index is given by

    a) LD_{50}/ED_{50} b) $1 - ED_{50}/LD_{50}$

    c) $\left(1 + LD_{50} \right)$ d) $\left(1 - LD_{50}/ED_{50} \right).$
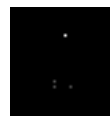
GROUP – B

(Short Answer Type Questions)

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

2.   a)   Define structurally specific and non-specific drugs ; what are the differences between the two type of drugs; what is the Ferguson principle parameter range for these two types of drugs ?

     b)   Draw a line diagram of a beta-barrel protein. Where are they located ? $3 + 2$

3.   State the difference between any *two* of following : $2 \propto 2\frac{1}{2}$

     a)   Maximum parsimony and maximum likelihood method

     b)   Distance based methods and character based methods

     c)   PAM and BLOSSUM matrix

     d)   Global alignment and local alignment.

4.   Explain how molecular dynamics techniques are integrated into the process of protein structure determination by NMR and *X*-ray crystallography ; your answer should be specific.   5

5.   Many proteins from pathogens have human homologues. Assume you had a methods for comparing the determinants of specificity in the binding sites of two homologous proteins. How could you use such a method to select novel target for drug design ?   5

6.   Describe the basics of the statistical models developed from multiple sequence alignment.   5

7. Explain how receptor fitting methodologies are still relevant to molecular graphics based drug design inspite of the absence of definitive 3D structural information for most receptors. Illustrate with 2 examples.   3 + 2

8. Sequence alignment and evolutionary distance can be estimated by Bayesian statistical methods. Justify the statement.   5

9. Write short notes on any *two* of the following : $2 \propto 2\frac{1}{2}$

   a) T-coffee

   b) Homologation and drug potency

   c) Profile

   d) ClustalW.

GROUP – C
(Long Answer Type Questions)
Answer any *three* of the following. $3 \propto 15 = 45$

10. a) Write down the basic steps followed in UPGMA method to draw a phylogenetic tree.   5

   b) Sometimes the tree generated by the UPGMA method does not represent the real tree. State the approach by which this problem can be solved.   2

   c) Some specific statistical methods play a major role in verification of phylogenetic tree analysis. Justify the statement.   2
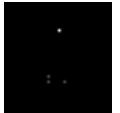
d)   Find out the informative and non-informative site between the following

sequences with suitable reasons :   6

   i)   A A G A G T G C A

   ii)   A G C C G T G C G

   iii)   A G A T A T C C A

   iv)   A G A G A T C C G.

11.   What structural features in integral membrane proteins make structure prediction of

such proteins relatively easier ? What is the positive inside rule and what is it used

for ? Draw a schematic of the rule. Why are dedicated algorithms necessary for

transmembrane protein/span prediction ? Cite an example of one such algorithm.

3 + 4 + 2 + 4 + 2

12.   a)   What do you mean by a molecular clock ?   1

   b)   Discuss the various categories of tree building methods citing their main

characteristics.   4

   c)   Use UPGMA to reconstruct a phylogenetic tree using the following distance

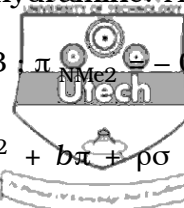matrix :   7

	A	B	C	D
B	3	–	–	–
C	5	4	–	–
D	8	8	9	–
E	11	10	12	8

   d)   Explain the role of parametric and non-parametric bootstrapping in phylogenetic

tree evaluation.   3
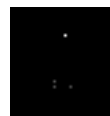
13. a) Caculate log P for the antihistaminic drug, diphenylhydramine. Assume
($\pi_{CH2} = 0\cdot50$; $\pi_{Ph} = 2\cdot13$ $\pi_{CH} = 0\cdot3$; $\pi_{OCH2} = -0\cdot73$; $\pi_{NMe2} = -0\cdot95$)

b) The potency of a drug defined by $\log 1/C = -a\pi^2 + b\pi + p\sigma + cE_s + dS + E$ represents a linear free energy approach towards drug design. Define all the terms in the equation and the inherent assumptions involved.

c) Explain the statistical basis of the above equation for QSAR studies.   5 + 5 + 5

14. a) Discuss the basic approaches in pair-wise and multiple sequences alignment and cite their importance.   3 + 3

b) Explain breifly the Heuristic method.   3

c) Calculate the score for the following alignments :   6

GATGGTGTCACGTCTG

GCTAGTCACATCCTG

Assume that purine-purine or perimidine-pyrimidine match = 1; purine-pyrimidine or pyrimidine-purine match = – 5; opening gap penalty = – 2, length penalty = – 1.

15. a) What are the specific effects on lead modification produced by bioisosteric replacements ? Give two examples of non-classical bioisosteres.

b) The lgo ($1/K_i$) of two substituted phenyl based inhibitors was determined and expected to be a simple linear function of hydrophobicity : $\log (1/K_i) = a\Pi + c$. Use the data below to develop the QSAR equation :

Substituent	log (l/K_i)	II	
n-butyl	7·75	2·13	
F	6·57	0·14	8 + 7
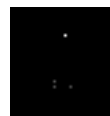
16. a) Outline stepwise with a diagram how 3D-QSAR is carried out using comparative molecular field analysis.

    b) Explain from an algorithmic viewpoint why a size/torsional energy grid is needed and the impact grid size has on the results of such a computation.

    c) In physico-chemical terms, explain how docking predicts ligand geometry and affinity for a target.   5 + 5 + 5

17. a) In molecular modeling and drug design, what is the role of the distance matrix ?

    b) Construct a distance matrix for a simple polypeptide of your choice.

    c) How do molecular descriptors like topological torsion and atom pair assist in drug design computations ?   4 + 6 + 5

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END