

BANGLADESH UNIVERSITY OF ENGINEERING AND TECHNOLOGY, DHAKA

L-4/T-1 B. Sc. Engineering Examinations 2020-2021

Sub : **BME 401** (Molecular Biology for Engineers)

Full Marks : 210

Time : 3 Hours

The figures in the margin indicate full marks.

The symbols have their usual meanings.

USE SEPARATE SCRIPTS FOR EACH SECTION

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**SECTION – A**There are **FOUR** questions in this section. Answer any **THREE**.

1. (a) Describe the effector functions of a special protein that is produced by the lymphocytes and plasma cells in the lymphoid organs and bone marrow, but performs its effector functions at sites distant from the production site. (20)
- (b) There are two pathways to present peptides by the major histocompatibility complex molecules to T cells. Compare and contrast these two pathways. (15)
  
2. (a) Cytolysis occurs when a cell bursts due to an osmotic imbalance that has caused excess water to diffuse into the cell. You have been asked to develop a drug to stop the cytolysis for a particular disease. What will be your approach from a molecular biology point of view? (15)
- (b) What is a cluster of differentiation? Why is it important? Discuss with appropriate examples. (10)
- (c) Pluripotent stem cells differentiate into several cells for the immune system. Briefly describe the stem cell hierarchy. (10)
  
3. (a) Naive CD4<sup>+</sup> T cells may differentiate into distinct subsets of cells in response to antigens, co-stimulators, and cytokines. Discuss the development and effector functions of one of these subsets where IL-4 is extensively used. (20)
- (b) Depending on the heavy chain molecule, there are 5 major antibodies in our immune system. Explain the functions of each antibody. (15)
  
4. (a) Explain the overall lymphocyte development process including the selection processes that shape the B and T lymphocyte repertoires. (20)
- (b) Write down the properties of cytokines. (15)

Contd ..... P/2

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**SECTION – B**

There are **FOUR** questions in this section. Answer any **THREE**.

5. (a) With suitable diagram, describe how proteins are imported into mitochondria and chloroplasts. (12)
- (b) Between sodium dodecyl sulfate and Triton X-100 which one is the stronger detergent? What happens to a membrane protein when it is mixed with a detergent? What would happen in the case when the phospholipids had only one hydrocarbon tail instead of two? (10)
- (c) In the events of fear or excitement, the adrenal medulla releases a hormone into the bloodstream. Name the hormone and describe how it stimulates glycogen breakdown in the skeletal muscle. (13)
6. (a) Assume you have constructed lipid vesicles that contain  $\text{Na}^+$  pumps as the sole membrane protein, and that each pump transports three  $\text{Na}^+$  one way and two  $\text{K}^+$  the other way in each pumping cycle. All the  $\text{Na}^+$  pumps have the portion of the molecule that normally faces the cytosol oriented toward the outside of the vesicles. Determine what would happen if: (20)
- (i) Your vesicles were suspended in a solution containing both  $\text{Na}^+$  and  $\text{K}^+$  ions and had a solution with the same ionic composition inside them.
- (ii) You add ATP to the suspension.
- (iii) You add ATP, but the solution-outside as well as inside the vesicles-contains only  $\text{Na}^+$  ions and no  $\text{K}^+$  ions.
- (iv) The concentrations of  $\text{Na}^+$  and  $\text{K}^+$  were as in (i), but half of the pump molecules embedded in the membrane of each vesicle were oriented the other way around so that the normally cytosolic portions of these molecules faced the inside of the vesicles. You then add ATP to the suspension.
- (v) You add ATP to the suspension described in (i), but in addition to  $\text{Na}^+$  pumps, the membrane of your vesicles also contains  $\text{K}^+$  leak channels
- (b) Gel electrophoresis can be used to isolate DNA fragments. Using this method, you have obtained a single-stranded DNA fragment (3' -GATCGATCC- 5') and you want to determine the complete sequence of that fragment. Discuss the steps with appropriate illustrations. (15)
7. (a) Sickle cell anemia is caused by mutated  $\beta$  globin gene. The mutation happens to destroy a sequence recognized by the restriction enzyme MstII. With necessary diagrams, discuss a laboratory technique that can detect sickle cell anemia in a patient. (20)
- (b) Describe the functions of: (i) Clathrin coating. (ii) SNARE proteins. (10)
- (c) Why did the cost of DNA sequencing drop over time? (5)

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8. (a) Describe with necessary diagram the different ways by which membrane proteins can associate with the lipid bilayer. (12)

(b) Suppose you are asked to isolate genes that codes for a particular mRNA. Which method will you use to accomplish this? Why will you choose this method over any other? (13)

(c) Discuss the following argument: "If transcription regulators control the expression of every gene, then the expression of these regulators must also be controlled by the expression of other regulators, and their expression must depend on the expression of still other regulators, and so on. There needs to be an infinite number of genes in the cells, most of which would code for transcription regulators." How does the cell function without achieving the impossible? (10)

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The symbols have their usual meanings.

USE SEPARATE SCRIPTS FOR EACH SECTION

**SECTION – A**

There are **FOUR** questions in this section. Answer any **THREE**.

1. (a) Although x-ray sources used in medical imaging are polyenergetic in nature, it is often desirable to model a polyenergetic x-ray beam as a monoenergetic source. What energy would a hypothetical monoenergetic source need to have in order to produce the same intensity as the true polyenergetic source using the same number of photons? (10)
- (b) Consider an object comprising three squares of the same size with width 20 cm, as shown in the following figure. The origin of the coordinate system is located at the center of the middle square. The linear attenuation coefficients in these three regions are  $\mu_1 = 0.1 \text{ cm}^{-1}$ ,  $\mu_2 = 0.2 \text{ cm}^{-1}$  and  $\mu_3 = 0.3 \text{ cm}^{-1}$ , respectively. (5+5+3)

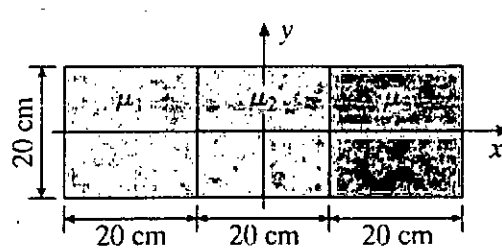


Figure for Question 1(b)

Assuming parallel ray geometry,

- (i) Find and sketch the 2D Radon transform of the object at  $\theta = 0^\circ$ .
- (ii) Find and sketch the 2D Radon transform of the object at  $\theta = 90^\circ$ .
- (iii) Find the backprojection,  $b_{45^\circ}(1, 1)$ .
- (c) Consider the following nine 1 cm X 1cm photomultiplier tubes (PMTs) used in a gamma imaging camera. (5+5+2)

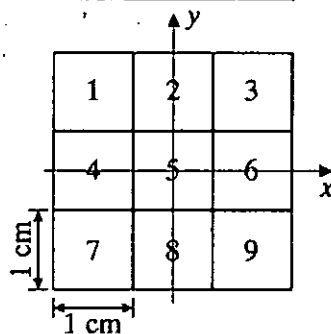


Figure for Question 1(c)

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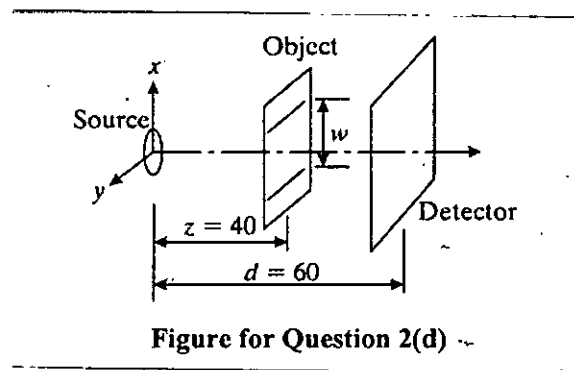
**Contd...Q.No. 1(c)**

The output of each PMT to a scintillation event is modelled as

$$a_i = 20 \exp\left(-\frac{(x - x_i)^2 + (y - y_i)^2}{5}\right)$$

where  $(x, y)$  is the location of the scintillation event, and  $(x_i, y_i)$  is the center of the  $i$ -th PMT.

- (i) Find the output of each PMT for a scintillation event that occurs at  $(-0.5, 0.5)$  cm.
  - (ii) What is the estimated position of the scintillation event?
  - (iii) Is the estimated position the same as its true position? If not, explain why.
2. (a) What are the main differences between x-ray projection radiograph and nuclear medicine imaging? (10)
- (b) With a diagram, show the components of an Anger scintillation camera. Mention the main functions of the components. (10)
- (c) Suppose photons from an x-ray source carrying energy of 100 keV are incident upon a subject and after interacting with the subject, some photons get scattered. The detector however decides that a photon has not been scattered if its energy is greater than 98 keV. (10)
- (i) What is the maximum scattering angle such that a photon will still be treated as traveling along a straight line?
  - (ii) If you are assigned the task of designing a detector system to eliminate all photons that have been scattered by more than  $30^\circ$ , what range of photon energies will you set the system to accept?
- (d) An x-ray imaging system is shown in Fig. 2(d). All the length units are in cm. (5)



Compute the following for the imaging system.

- (i) Object magnification
  - (ii) Source magnification
3. (a) Write short notes on any three of the followings: (15)
- (i) Slip ring
  - (ii) Intensifying screen
  - (iii) X-ray beam restrictors
  - (iv) Coincidence detection in positron emitting tomography (PET)

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**Contd...Q.No. 3**

(b) Mathematically show the effect of Compton scattering on radiographic image contrast and signal to noise ratio (SNR). (10)

(c) Roughly sketch the sinogram of the following image. The units are in cm. (10)

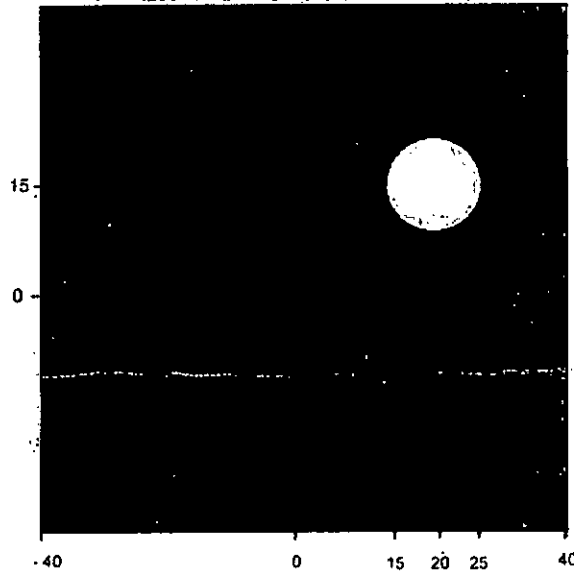


Figure for Question 3(c)

4. (a) Suppose you have designed an x-ray tube at your medical imaging research lab. An x-ray burst from this tube yields exactly  $10^4$  x-ray photons at energy  $E_1 = 60$  keV, and  $10^5$  x-ray photons at energy  $E_2 = 65$  keV. You are using this source to image a phantom which is shown in the figure below. (5+10+5)

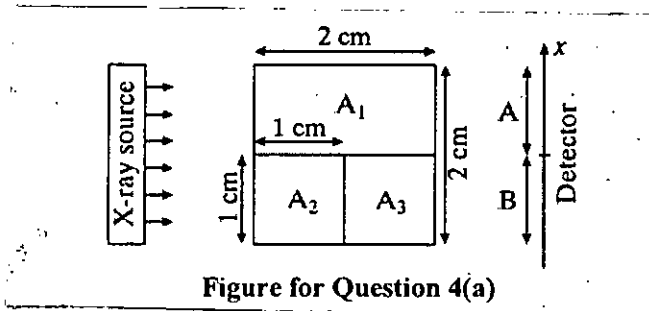


Figure for Question 4(a)

As can be seen, the phantom consists of three areas,  $A_1$ ,  $A_2$ , and  $A_3$ , as labeled. The linear attenuation coefficients  $\mu_1$ ,  $\mu_2$ ,  $\mu_3$  (units of  $\text{cm}^{-1}$ ) of these three areas at the two energy levels present in the x-ray beam are given in the following table.

Table for Question 4(a)

	$E_1$	$E_2$
$\mu_1$	0.2	0.4
$\mu_2$	0.3	0.1
$\mu_3$	0.5	0.4

Assuming a parallel beam of x-rays uniformly distributed over the extended source and neglecting the effect of Compton scattering.

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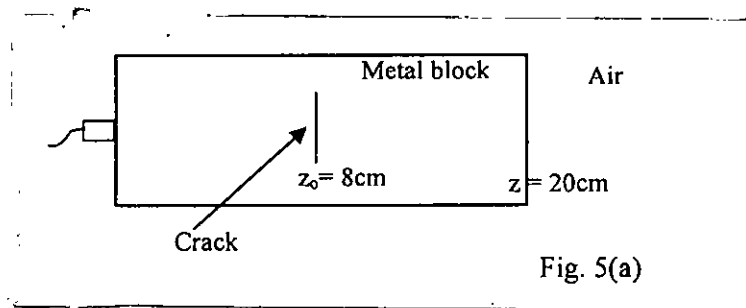
**Contd...Q.No. 4(a)**

- (i) Draw the energy spectrum associated with the x-ray pulse. Explain why the units associated with the numbers  $10^4$  and  $10^5$  in the spectrum must be photons-keV.
  - (ii) Determine the total number of x-ray photons per cm that hit the detector end.
  - (iii) Calculate the contrast of the image observed at the detector as a function of position  $x$  assuming that A is the target and B is the background. Also assume that x-ray intensity is proportional to the number of photons.
- (b) Show that the 1-D Fourier transform of a radiographic projection is a slice of the 2-D Fourier transform of the object being imaged. From this relation, derive the mathematical expression of the filtered backprojection technique. (10)
- (c) What is beam hardening? What are its causes? (5)

**SECTION – B**

There are **FOUR** questions in this section. Answer any **THREE**.

5. (a) A square ultrasound transducer is centered at the origin and pointed down the z-axis of a metal block of length  $z = 20$  cm (Fig. 5a). Suppose, there is a crack inside the block at  $z_0 = 8$  cm. Assume, the transducer fires a half-sine pulse at  $t=0$  and the amplitude of the generated pulse ( $A_0$ ) is  $50 \text{ N/cm}^2$ . The reflection coefficient of the crack is  $R_{\text{crack}}=0.1$  and the interface of the metal block and air is  $R_{\text{metal}} = 0.9$ . (15)



Sketch the A-mode signal (Amplitude vs  $z$ ). Label the axes and amplitude of the returning pulse properly up to 25 cm.

- (b) Consider an LSI medical imaging system with PSF given by: (20)

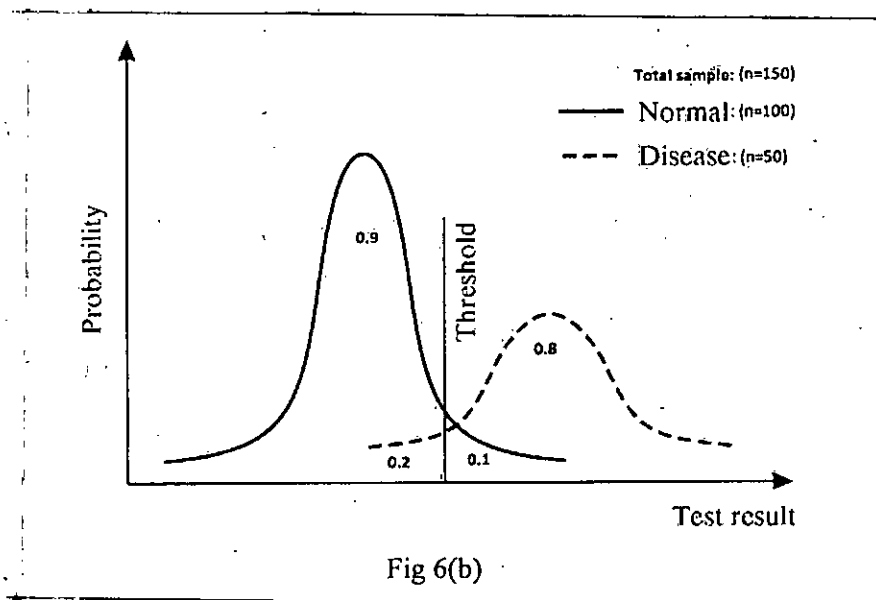
$$h(x, y) = \frac{1}{2\pi} e^{-(x^2+y^2)/2}$$

- (i) Calculate the MTF associated with this system.
- (ii) Plot the MTF as a function of frequency.
- (iii) If a sinusoidal object  $f(x, y) = 2 + \sin(\pi x)$  is imaged through the system, what is the percentage change in modulation caused by this system?

**BME 403**

6. (a) Briefly describe different components of MRI instrumentation with a neat diagram. **(15)**

(b)

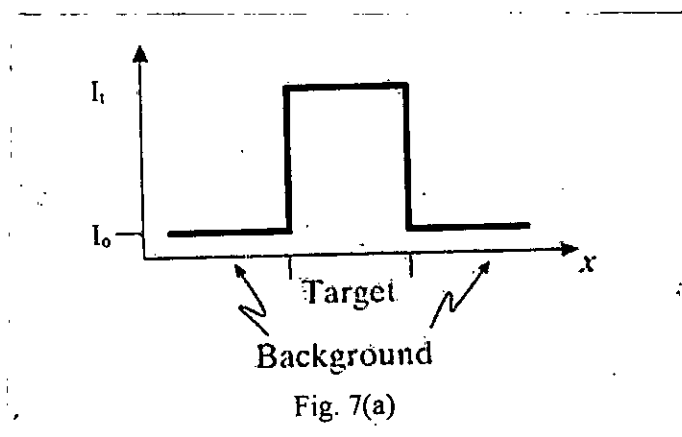


Based on the probability distribution shown in Fig. 6(b):

- (i) Determine the Sensitivity, Specificity, Diagnostic Accuracy, Prevalence, Positive Predictive Value (PPV), Negative Predictive Value (NPV).
- (ii) Explain the effect of shifting the threshold to the right.

(c) Consider a transducer made of a PZT crystal, which has a speed of sound  $c_T = 8,000$  m/s. If we want the transducer to work at a frequency of 8 MHz, what should be the thickness of the crystal? **(5)**

7. (a) Consider an image (Fig-7a) showing an organ with intensity  $I_o$  and a tumor with intensity  $I_t > I_o$ . What is the local contrast of the tumor? If we add a constant intensity  $I_c > 0$  to the entire image, what is the local contrast? Is the local contrast improved? **(15)**



- (b) Explain with proper illustrations, T1-weighted, T2-weighted and PD weighted image in MRI. **(15)**
- (c) Explain A-mode, M-Mode and B-Mode image in Ultrasound imaging. **(5)**



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8. (a) Consider a transducer placed at an angle ( $\theta$ ) with the blood stream. The transducer is operating in pulse echo mode and generating a plane wave of frequency ( $f_s$ ). Derive a relation between Doppler frequency ( $f_D$ ), velocity of sound ( $c$ ), transducer frequency ( $f_s$ ) and velocity of blood stream ( $v$ ). (10)

(b) What is Doppler effect? Suppose a 5 MHz transducer axis makes an angle  $30^\circ$  relative to the direction of motion of blood in a vessel. And the Doppler frequency you have measured is +100 Hz. What is the velocity of the bloods? Is it moving towards or away from the transducer? (Velocity of sound,  $c = 1540$  m/s). (10)

(c) Find the solution to the Bloch equation for,  $\vec{B} = B_0 \mathbf{k}$  and  $\vec{M}(0) = m_0 \mathbf{j}$

$$\frac{d\vec{M}}{dt} = \vec{M} \times \gamma \vec{B} \tag{15}$$

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**SECTION – A**

There are **FOUR** questions in this section. Answer any **THREE**.

1. (a) What are the comparative advantages and disadvantages of 2D monolayer and 3D biomaterials based cell culture? (10)
- (b) What are the risks of using allograft and xenograft? For a severely injured burn patient, which graft will you choose, autograft, allograft or xenograft? Why? (12)
- (c) 3D printed pill has already been approved by FDA in 2015. What could be the advantages of 3D printed pills? (7)
- (d) What is biocompatibility? (6)
  
2. (a) Name the compositions of extracellular matrix (ECM). Which component of ECM is responsible for the extensibility and elastic recoil properties of skin? How does that component vary between young and aged skin? (14)
- (b) You are designing a 3D scaffolds where you want to increase cell adhesion. Mention the possible ways you can consider to increase cell adhesion. Draw the schematic of cell attachment process with ECM. (13)
- (c) Why decellularization is important? Mention two clinical applications where decellularized matrixes have been using extensively. (8)
  
3. (a) With three circles Venn diagram show the application of biomaterials (polymers, metals and ceramics) in different devices. (10)
- (b) Name the tests to confirm the biocompatibility of a material according to ISO 10993. Describe the irritation reactivity and hemocompatibility studies in details? (14)
- (c) What is soft lithography? How can this technology be useful for localized cell growth? (11)
  
4. (a) Which characteristics define stem cells? Write down some clinical applications of iPSC. (9)
- (b) How are Yamanaka factors activated? (10)
- (c) Assume you are working on a bone degeneration research project for astronauts. If you need to choose a bioreactor for your research which one will you choose? Describe the working principle of this bioreactor. (16)

**BME 409**

**SECTION – B**

There are **FOUR** questions in this section. Answer any **THREE**.

5. (a) Explain how tissue engineered constructs made of electrically active biopolymers can help in drug delivery approaches. (10)
  - (b) What are the differences between a healthy cartilage and arthritic cartilage? How does cartilage on a chip mimic the compressive stress that the cartilage bear? (15)
  - (c) How can tissue engineering solve the future food scarcity problem? Write down the steps in brief. (10)
  
  6. (a) Explain distinct types of qualitative cytotoxicity assay for low-or high-density biomaterials. (10)
  - (b) Mention the ECM proteins that undergo cell-cell homophilic binding. Explain the mechanism of this process. (10)
  - (c) Explain the mechanism of the protection of bacteria against the attack of virus. How can we hijack this mechanism to use it in the genome editing? (15)
  
  7. (a) Using time plot, briefly explain the phases that occur during normal wound healing. (10)
  - (b) Describe the steps of the decellularization and recellularization of a rat liver and how they can be used as a bioreactor. (15)
  - (c) Explain the factors that dictate the host response in tissue engineering. (10)
  
  8. (a) Suppose you have made a tissue engineered product in the lab. What are the preclinical and clinical steps that are required before the marketing authorization? (12)
  - (b) Explain the in vitro culture parameters required for tissue engineering. (12)
  - (c) Write down the materials and methods required for the MTI assay of cytotoxicity test. (11)
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BANGLADESH UNIVERSITY OF ENGINEERING AND TECHNOLOGY, DHAKA

L-4/T-1 B. Sc. Engineering Examinations 2020-2021

Sub: **BME 441** (Neural Engineering)

Full Marks: 210

Time: 3 Hours

The figures in the margin indicate full marks

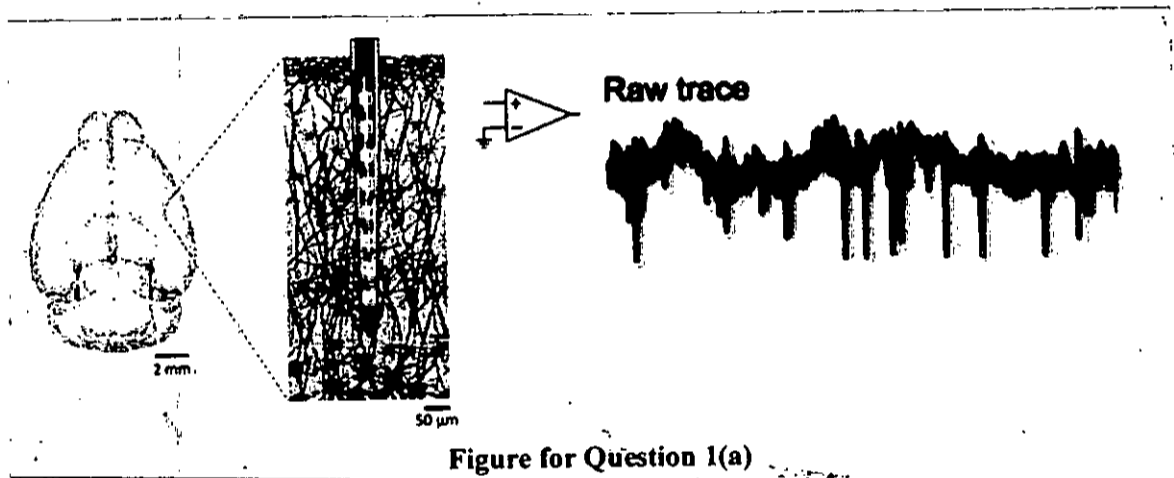
The symbols have their usual meanings.

USE SEPARATE SCRIPTS FOR EACH SECTION

**SECTION – A**

There are **FOUR** questions in this section. Answer any **THREE** questions.

1. (a) Suppose a 4-shank neural probe is implanted in a mouse brain. The raw trace of recorded broadband bioelectrical signal from the extracellular space is shown in Fig. 1(a). (10)



What are the two main types of signals that you can detect from the raw broadband signal after decomposing it into various frequency bands? Depict the basic physical principle schematically. Also mention their frequency bands and significance.

(b) Describe the fabrication process of Parylene-based neural electrodes. How do these neural probes differ from conventional neural microelectrodes in terms of efficiency, lifetime and biocompatibility? (15)

(c) What are the different types of glial cells? What are their functions? (10)

2. (a) Which mechanical properties must you take into consideration for choosing the material of a chronic brain implant? What unfavorable consequences may appear if there is mechanical mismatch between the neural probe and neural tissue? (10)

**BME 441**

**Contd... for Q. No. 2**

(b) Suppose you are recording electroencephalogram (EEG) signal from the F4 electrode and the C4 electrode of the 10-20 EEG acquisition system for a motor imagery (MI) brain computer interfacing (BCI) application as shown in Figure for Question 2(b). Both the F4 electrode and the C4 electrode of the 10-20 system use the mastoid A1 electrode as reference. Now for the MI task, you connect the F4 and C4 channels to two ends of an instrumentation amplifier with a goal of obtaining an output signal of 1V in amplitude. You also need to keep the frequency bandwidth of your output signal between 0.5-40 Hz.

(20)

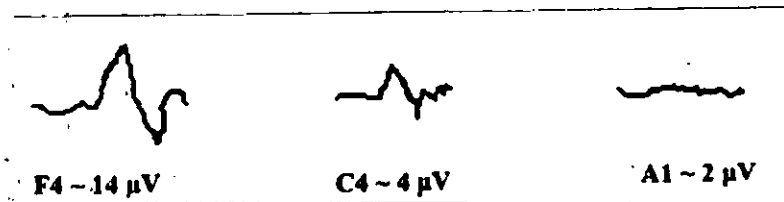


Figure for Question 2(b)

Design the instrumentation amplifier circuit that will yield the output signal of your desired amplitude and frequency component.

(c) Draw a signal flow diagram showing how signals move through the nervous system.

(5)

3. (a) Figure for Question 3(a) shows pattern reversal visually evoked potential (VEP) traces of right and left eye recorded from an adult female. Label the three basic components of VEP and comment on the normalcy for both eyes.

(10)

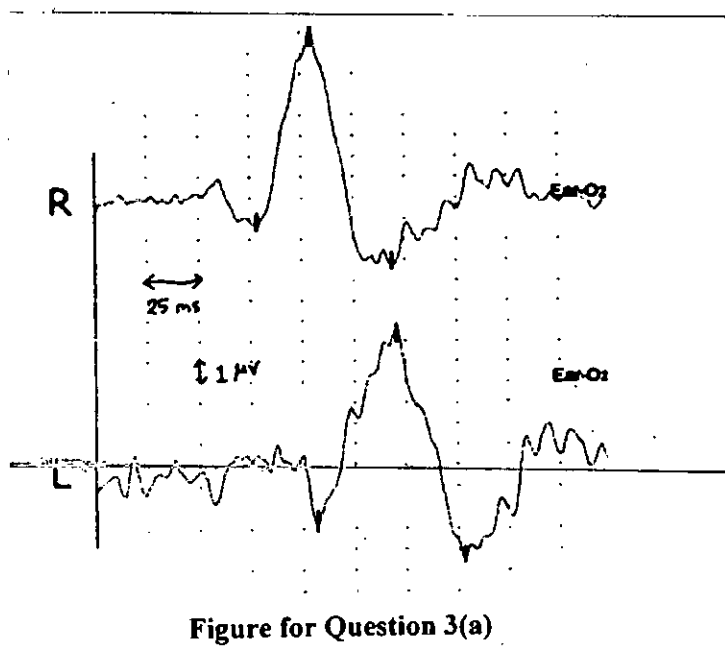


Figure for Question 3(a)

**BME 441**

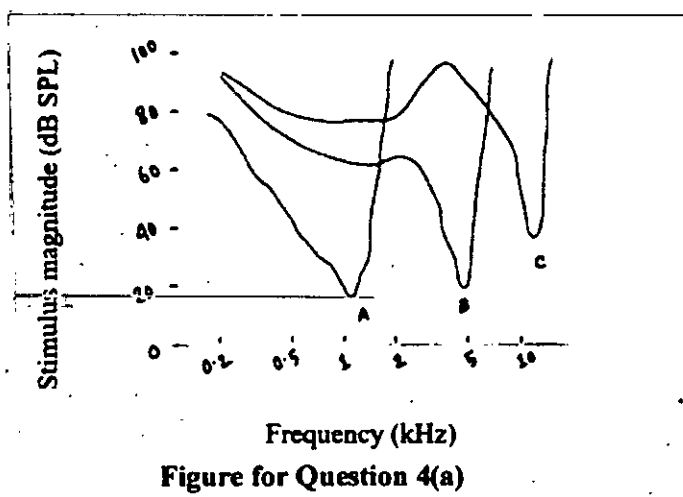
**Contd... for Q. No. 3**

(b) How do cochlear implants attempt to restore hearing? What are the basic components of a cochlear implant and what are their functions? (15)

(c) Write short notes on the following brain responses that are useful in building brain computer interfaces (BCIs). (10)

- (i) Population activity
- (ii) Imagined motor and cognitive activity

4. (a) Figure for Question 4(a) shows the tuning curves for three cochlear hair cells. Based on the curves, answer the following. (15)



- (i) What are the natural frequencies of the three hair cells?
- (ii) What are the stimulus sound pressure values in  $\mu\text{Pa}$  for the three hair cells at their corresponding natural frequencies? Note,  $P_{\text{ref}} = 20 \mu\text{Pa}$ .
- (iii) What is the significance of these curves?
- (iv) Draw the approximate positions of the hair cells in the basilar membrane of cochlea.
- (v) If a complex sound signal,  $x(t) = \sin(22,000\pi t) * \cos(9,000\pi t) * \sec(11,000\pi t) + \cos(5000\pi t)$ , is being played on the ear, which of the three hair cells will be stimulated?

(b) Describe different types of retinal implants. (10)

(c) Describe the frequency range and brain phenomena associated with the following EEG waves. (10)

- (i) Alpha
- (ii) Beta
- (iii) Gamma
- (iv) Mu
- (v) Theta

**BME 441**

**SECTION – B**

There are **FOUR** questions in this section. Answer any **THREE** questions.

5. (a) Describe a brain computer interface (BCI) application. Identify the current challenges in the application of BCI. (18)
- (b) Write down the differences between a stimulating and a recording neural electrode? (7)
- (c) Describe the mechanism of generation of BOLD signal in functional-MRI with schematic. (10)
6. (a) What is phantom limb? Describe the reorganization of sensory representation. (10)
- (b) Describe different types of charge-balanced, current waveforms used in neural stimulation with proper illustrations. (15)
- (c) Write the similarities and differences between functional-MRI (fMRI) and functional-NIRS (fNIRS) techniques. (10)
7. (a) As a Biomedical Engineer, suppose you are doing R&D to develop a Responsive Neurostimulator (RNS) for a company. What capabilities should the RNS have? Describe at least three of them. (25)
- (b) How can targeted muscle reinnervation (TMR) contribute to the development of an advanced prosthetic arm? (10)
8. (a) What is DBS? Briefly describe the components of NeuroPace RNS systems. (15)
- (b) Describe some of the common techniques (Cyclic Voltammtry, Impedance spectroscopy, and Voltage transient measurements) for electrochemical characterization of nerve electrode with necessary illustrations. (20)
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**SECTION – A**

There are **FOUR** questions in this section. Answer any **THREE**.

1. (a) What is meant by ethics? Define professional ethics and explain the core qualities of a professional. (15)  
(b) Critically explain the obstacles of professional responsibility. How do we overcome these obstacles? (20)
2. (a) Is there any difference between cost-benefit analysis theory and deontological theory? Which one is more acceptable and why? (15)  
(b) Discuss the case study of Merck & Co. Inc. dealt with the issue of river blindness. Why did the company invest so much money and effort to develop a drug that make no money? And what was the reply of the companies CEO Dr. Roy Vagelos regarding the question? Explain. (20)
3. (a) How do we define right? Explain with example the natural right, legal right and contractual right. (15)  
(b) Is there any right of an employee? Discuss the rights of an employee following Ronald Duska. (20)
4. (a) How is internal whistle blowing different from external whistle blowing? When is external whistle blowing morality justified? Explain. (15)  
(b) Discuss the nature of job discrimination. Compare and contrast the arguments against racial and sexual discrimination in job. (20)

**SECTION – B**

There are **FOUR** questions in this section. Answer any **THREE**.

5. (a) What type of obligations should the engineering profession and individual engineers assume with regard to the environment? (20)  
(b) Discuss the sub-minimal attitude, compliance attitude and progressive attitude of the industry toward the environment. (15)



**HUM 415**

6. (a) "Life is life, and equality valuable, whether it is a human life or an animal life".  
Discuss and offer comments. (15)
- (b) Discuss the use of animals as food. Is it morally acceptable? Justify your position. (20)
7. (a) What is euthanasia? Explain with example voluntary, involuntary and non-voluntary  
euthanasia. (20)
- (b) What are the arguments in favour of euthanasia? Explain and evaluate the guidelines  
introduced by the coreat of Netherlands in favour of euthanasia? (15)
8. (a) What are the rules of the Hippocratic oath? Explain the purpose of the Hippocratic  
oath. (15)
- (b) Explain and evaluate the feminist arguments related to abortion. (20)
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**SECTION – A**

There are **FOUR** questions in this section. Answer any **THREE** questions.

1. (a) Consider the following DNA sequence (of length 10) of an organism SP1. (5)

1	2	3	4	5	6	7	8	9	10
A	C	T	G	A	T	C	A	C	G

Assume that after 800 years, SP1 has evolved into SP1' through the following evolutionary events:

- (i) 'T' at position 3 is substituted by 'A'
- (ii) The substring "GAT" (starting from 4 to 6) is deleted
- (iii) "GT" is inserted after the 'C' at position 9.

Show the alignment of SP1 and SP1' and indicate the substitutions, insertions and deletions.

(b) Find the optimal global alignment of the following two sequences using  $-2$  as the gap penalty,  $-3$  as the mismatch penalty, and  $2$  as the score for a match. You have to use the Needleman-Wunsch algorithm, and show the corresponding dynamic programming (DP) table. In case there are multiple optimal alignments, find all of them. Please mark the paths, which correspond to the optimal alignments, in the DP table. (15)

ATCCTGT

TCTCT

(c) Consider the sequences and the scoring scheme mentioned in Q1(b). Find the optimal local alignment of these two sequences using Smith-Waterman algorithm. Show the DP table and mark the path that corresponds to the alignment. (15)

2. (a) For a given gene tree  $gt = (((((a,b),c),d),e),f)$ , and a species tree  $ST = (((((a,(b,c)),f),d),e)$ , explain the discordance between  $gt$  and  $ST$  using: (22)
- (i) Deep coalescence (DC),
  - (ii) Gene duplications and losses (GDL).

You have to find the optimal reconciliations, meaning that the number of extra lineages and duplications and losses should be minimized. Please show the reconciliations with appropriate figures (separate figures for DC and GDL) indicating the deep coalescence, duplication, and loss events. Report the numbers of extra lineages, duplications and losses.

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**Contd... for Q. No. 2**

(b) Suppose you are trying to construct a species tree on 20 different species. You have sampled 100 genes from each of these 20 species. Your supervisor has asked you to use a method called GT-est for constructing trees from sequence alignments, and SP-est (which is a summary method) for estimating species trees from gene trees. (8)

(i) How many times do you need to run GT-est and SP-est to estimate a species tree by summarizing gene trees?

(ii) How many times do you need to run GT-est and SP-est to estimate a species tree using "Combined Analyses"?

(c) Given a set  $G$  of  $k$  gene trees on  $n$  taxa, a species tree  $ST$  is consistent with  $k \times n_c$  triplets in  $G$ . How many quartets in  $G$  would be consistent with  $ST$ ? (5)

3. (a) What is meant by a *statistically consistent* species tree estimation method? Prove that triplets are statistically consistent estimators of species history. (10)

(b) (i) Consider the following set  $CS$  of clusters: {bc, ef, dh, abc, efg, defgh}. Trivial clusters (i.e., the clusters containing only one taxon and the cluster with all the taxa) are not included in  $CS$ . Is this a compatible set of clusters? If yes, show the corresponding tree. If not, explain why. (5+5=10)

(ii) How many quartets are there in a set of  $k$  gene trees on  $n$  taxa? How many of these quartets could be unique?

(c) Construct a tree on the leaf set {a,b,c,d,e} which is consistent with each of the following triplets. You have to show the intermediate steps of your algorithm. (15)

- |        |        |
|--------|--------|
| ac   b | ac   e |
| bd   a | bd   c |
| be   a | bd   e |
| de   a | be   c |
| ac   d | de   c |

4. (a) Consider the following five reads. Construct the overlap graph with minimum overlap 2 (meaning that there is an edge between two reads if the overlap between them is at least two). Find a shortest common superstring from that overlap graph. (18)

- TAGGCTA
- TAATACTTAGG
- AATTTGCTA
- GCTAGGAAT
- CTAGCTA

(b) Construct the De Bruijn graph from the following read using 3-mers. (10)

ATGCATTTGCATGCG

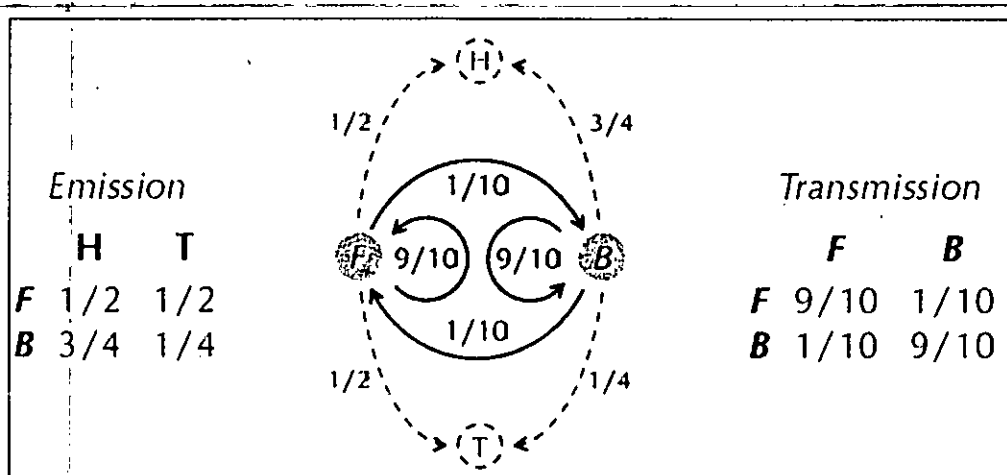
(c) Briefly discuss relative advantages and disadvantages of overlap graph and De Bruijn graph based genome assembly techniques. (7)

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**SECTION – B**

There are **FOUR** questions in this section. Answer any **THREE** questions.

5. (a) Write the pseudo code of a naive algorithm to find the number of occurrences of a pattern ( $P$ ) in a sequence ( $S$ ). For example, when  $S = "AGCGCGCACGCT"$  and  $P = "CGC"$ , your code should print 3. (10)  
 (b) What is a suffix array? Construct the suffix array for the string  $CGACTGTG\$.$  Write down the suffixes alongside the suffix array positions. (10)  
 (c) The Burrows-Wheeler transform (BWT) of a sequence is  $G\$\$CCAATCAG.$  Recover the original sequence through detailed steps. (15)
  
6. (a) What is a breakpoint graph? Explain with a suitable example. (10)  
 (b) State and prove the 2-Break distance theorem. (10)  
 (c) Consider a circular chromosome  $(+a+b-c-d+e+f)$ . Due to genome rearrangements, this chromosome splits into 2 circular chromosomes  $(+a+b)$  and  $(+c+d+e+f)$ . Represent each chromosome using a genome graph. Using separate pictures identify the 2-break(s) to represent this rearrangement. (15)
  
7. (a) For the crooked dealer HMM shown in the *Figure for Question 7(a)*, calculate the likelihood of the string "HTHT" being emitted. Show detailed calculation steps. (15)



*Figure for Question 7 (a): The crooked dealer HMM*

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**Contd... for Q. No. 7**

(b) Using the MSA of 5 proteins below, describe the steps to create a protein profile HMM. Show calculations for some (not all) of the transition and emission probabilities. Show the state diagram of the final HMM. (20)

A	C	D	E	F	A	C	A	D	F
A	F	D	A	-	-	-	C	C	F
A	-	-	E	F	D	-	F	D	C
A	C	A	E	F	-	-	A	-	C
A	D	D	E	F	A	A	A	D	F

- 8. (a) Briefly describe how a gene of interest can be replicated using a cloning vector. (10)
- (b) Explain with example how we can cut and paste DNA. (10)
- (c) What is a genome dot plot? Explain with an example. (10)
- (d) Briefly describe the SI and NSI isolates of HIV. (5)

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