

Mathematics, Biology, and Computer Science

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Make sure that you are given 10 Question Sheets and 3 Answer Sheets.

One answer sheet should be used per question.

Question [1] is compulsory. You **must** answer this question. (60 points).

Questions [2] - [7] are elective. **Select** and answer **two questions** from [2] through [7] (70 points each).

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**[1] (Compulsory question)**

Select four words from the list below, and describe the meaning and characteristics of each in approximately 100 words.

- (1) Taylor expansion
- (2) Leibniz formula (for nth derivatives)
- (3) Intermediate value theorem
- (4) Cross-validation
- (5) p-value
- (6) Correlation coefficient
- (7) Machine learning
- (8) Diffusion model
- (9) Markov chain
- (10) Jacobian
- (11) Pitchfork bifurcation
- (12) Hysteresis
- (13) Exons and introns
- (14) Gene expression
- (15) DNA sequencing
- (16) Cell motility
- (17) Protein folding
- (18) Cytoskeleton

[2] Calculus

**Problem 1**

For the function  $f(x) = -\log(\cos x)$  defined on  $-\frac{\pi}{2} < x < \frac{\pi}{2}$ , answer the following questions.

- (1) Find the derivatives  $f'(x)$  and  $f''(x)$ .
- (2) Draw the sign chart for  $f'(x)$  and describe the general shape of  $f(x)$ .
- (3) Write the equation of the osculating circle of  $f(x)$  at  $x = 0$ . Here, for a function  $y = f(x)$ , the osculating circle  $y = R(x)$  at a point of tangency  $x = a$  is defined as the curve satisfying  $f(a) = R(a)$ ,  $f'(a) = R'(a)$ , and  $f''(a) = R''(a)$ .

**Problem 2**

For a real number  $x$  and a non-negative integer  $n$ , the Legendre polynomial  $P_n(x)$  is defined by

$$P_n(x) = \frac{1}{2^n n!} \frac{d^n}{dx^n} (x^2 - 1)^n$$

where  $0! = 1$  and  $\frac{d^0}{dx^0} = 1$ .

Answer the following questions.

- (1) Find  $P_0(x)$ ,  $P_1(x)$ ,  $P_2(x)$ , and  $P_3(x)$ .
- (2) For  $n, m \in \{0, 1, 2, 3\}$  with  $n \neq m$ , show by calculation that

$$\int_{-1}^1 P_n(x) P_m(x) dx = 0.$$

- (3) Let  $f(x) = x^3 + x^2 + x + 1$ . When expanding  $f(x)$  as  $f(x) = a_0 P_0(x) + a_1 P_1(x) + a_2 P_2(x) + a_3 P_3(x)$ , find the value of the coefficient  $a_0$ .

**Problem 3**

Answer the following questions.

- (1) Let  $x = \tan \frac{\theta}{2}$ . Express  $\sin \theta$  and  $\cos \theta$  in terms of  $x$ .
- (2) Find the value of the following definite integral:

$$\int_0^{\frac{\pi}{2}} \frac{\cos \theta}{1 + \sin \theta + \cos \theta} d\theta$$

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[3] Statistics

Question 1

The gender ratio of master's and doctoral students enrolled this academic year at a certain graduate school is as follows.

|                  | Female | Male |
|------------------|--------|------|
| Master's program | 125    | 196  |
| Doctoral program | 50     | 57   |

Suppose that you want to test whether the gender ratio differs between the master's and doctoral programs using the chi-square test of independence.

- (1) Write the expected frequency table under the null hypothesis. Show the values either as decimals rounded to two decimal places or as reduced fractions.
- (2) Specify the value of the degree of freedom of the chi-square distribution to be used in this statistical test.

Question 2

Using data on seed weight and plant density measured across multiple field communities for a single plant species, a regression analysis was performed with seed weight as the dependent variable and density as the independent variable. The following is the output from the statistical software used.

| ANOVA table for seed weight |    |       |       |        |       | Coefficient table |          |         |        |       |
|-----------------------------|----|-------|-------|--------|-------|-------------------|----------|---------|--------|-------|
| Source of variation         | DF | SS    | MS    | F      | P     | Term              | Coef     | SECoef  | T      | P     |
| Regression                  | 1  | 10554 | 10554 | 111.45 | 0.000 | Constant          | 311.898  | 8.574   | 36.38  | 0.000 |
| Residual                    | 18 | 1705  | 95    |        |       | Density           | -0.68773 | 0.06515 | -10.56 | 0.000 |
| Total                       | 19 | 12259 |       |        |       |                   |          |         |        |       |

DF: degree of freedom, SS: squared sum, MS: mean square, F:  $F$  value, P:  $p$  value, Coef: coefficient, SECoef: standard error of coefficient, T:  $t$  value

- (1) Summarize the conclusions of the regression analysis in one sentence.
- (2) What proportion of variance is explained by the fitted line?
- (3) Which one is the value for correlation coefficient between seed weight and plant density? Choose a number and describe the reason for your choice.  
(i) 302.910    (ii) 0.62431    (iii) -0.89944

Question 3

A graduate student conducted a questionnaire survey on people's sense of fairness, inspired by the study by Micheli & Gagnon (2020 *Scientific Reports*). The survey included 84 Japanese university students. Each participant was individually asked the following five questions:

1. A set of 10 lottery tickets (one of which is a winning ticket worth 1,000 JPY) must be distributed between two students in a 9-to-1 ratio. Before the distribution, the pair witnessed a minor helping opportunity, and one of them helped. Do you think it is fair or unfair to give 9 tickets to the student who helped?
2. Another pair was given a quiz with 100 knowledge questions before the distribution. Do you think it is fair or unfair to give 9 tickets to the student who scored higher?
3. For a pair of students in the same academic year, do you think it is fair or unfair to give 9 tickets to the student with the higher student ID number?
4. For a same-gender pair, do you think it is fair or unfair to give 9 tickets to the taller student?

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5. For a mixed-gender pair, do you think it is fair or unfair to give 9 tickets to the male student?

All participants responded to all questions. Based on the collected response data, what kinds of statistical analyses could be considered? Describe **three** different analyses. For each analysis, describe the following item.

(i) Matters of concern (ii) Null hypotheses (iii) Statistical method (e.g., "Conduct multiple regression analysis with XXX as the response variable and XXX and XXX as independent variables.")

When marking, consideration is given to whether each "(i) matter of concern" is sufficiently different to each other.

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[4] Computer science

Question 1

Describe the hidden Markov model (HMM) in about 500 characters.

Question 2

Elementary school student A is thinking about the combination of snacks to bring for the school trip next week. The types of snacks are freely chosen, but the total cost must be less than or equal to  $U$  yen. A is considering  $n$  types of snacks,  $x_1, x_2, \dots, x_n$ , and for each snack, the price  $p_i$  in yen and A's satisfaction  $s_i$  are given. Here, the subset of snacks  $x_1, \dots, x_i$  whose total cost is less than or equal to  $100j$  yen, and for which the sum of the satisfaction is maximized, is represented by the array  $D[i][j]$ . Note that the prices of all snacks are in multiples of 100 yen. Answer the following questions:

(1) Find  $D[3][3]$  for the table below, given that  $U = 300$  yen.

| Snack Type   | $x_1$ | $x_2$ | $x_3$ | $x_4$ | $x_5$ |
|--------------|-------|-------|-------|-------|-------|
| Price        | 100   | 200   | 100   | 300   | 100   |
| Satisfaction | 60    | 50    | 70    | 30    | 50    |

(2) Derive the recurrence relation for  $D[i][j]$ .

(3) Write a calculation program to compute  $D[n][U]$  using the recurrence relation from (2). You can use natural language, mathematical expressions, or pseudocode for the program.

(4) Explain how to find the combination of snacks that gives the value of  $D[n][U]$ .

Question 3

Consider rolling a die  $D$   $n$  times. Let  $c_i$  be the number of occurrences of face  $i$  ( $i = 1, \dots, 6$ ). Answer the following questions:

(1) Let  $p_i$  denote the probability parameter for face  $i$  of the die  $D$ . Show the likelihood function for the observed results  $c_1, \dots, c_6$ .

(2) Find the value of  $p_i$  that maximizes the likelihood function shown in (1).

(3) Provide the confidence interval for  $p_i$  as calculated in (2).

[5] Nonlinear dynamics

Question 1

Answer the following questions regarding fixed points and bifurcations.

- (1) The system  $\dot{x} = x$  has one fixed point. Give an example of a system that has three fixed points.
- (2) Give an example of a system that has exactly one semi-stable fixed point.
- (3) Give an example of a system that has infinitely many fixed points.
- (4) Give an example of a system exhibiting a bifurcation where the number of fixed points increases from 0 to 2, and specify its bifurcation parameter.
- (5) Give an example of a system exhibiting a bifurcation where the number of fixed points increases from 2 to 4, and specify its bifurcation parameter.

Question 2

Consider the system

$$\begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix} = \begin{pmatrix} a & -b \\ -b & a \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix}$$

where  $0 < a < b$ .

- (1) Find the eigenvalues of the matrix  $\begin{pmatrix} a & -b \\ -b & a \end{pmatrix}$  and also give the eigenvectors corresponding to each eigenvalue.
- (2) Give the set of initial conditions  $(x(0), y(0))$  for which  $(x, y)$  converges to  $(0, 0)$  as  $t \rightarrow \infty$ .
- (3) Give the set of initial conditions  $(x(0), y(0))$  for which  $(x, y)$  diverges to  $(-\infty, \infty)$  as  $t \rightarrow \infty$ .

Question 3

The following system represents a mathematical model of fishing activity:

$$\frac{dN}{dt} = rN \left(1 - \frac{N}{K}\right) - H \frac{N}{A + N}$$

Here,  $t$  is time,  $N$  is the biomass of a certain fish species in a given water area, the parameters  $r, K, A$  are positive real numbers, and  $H$  is a non-negative real number. The parameter  $H$  is called the fishing effort; when no fishing is conducted,  $H = 0$ . This system can be nondimensionalized using  $x = \frac{N}{K}$  and  $\tau = rt$  as follows:

$$\frac{dx}{d\tau} = x(1-x) - h \frac{x}{a+x}$$

- (1) Express the parameters  $h$  and  $a$  of the nondimensionalized system in terms of  $r, K, H$ , and  $A$ .
- (2) When  $h = 0$ , there are two fixed points  $x^*$ . Find the values of  $x^*$ .
- (3) Obtain the condition for  $h$  and  $a$  with which there is a stable fixed point within the range  $x > 0$ .

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[6] Molecular biology

Humans are symbiotic with thousands of species of gut bacteria, i.e., the gut microbiota. The influence of the microbiota's metabolome on mental and physical health is increasingly being revealed, and the gut microbiome is called "The second genome." The following experimental procedures are planned to investigate the diversity—what kinds of bacteria exist and their ratios—of gut microbiota.

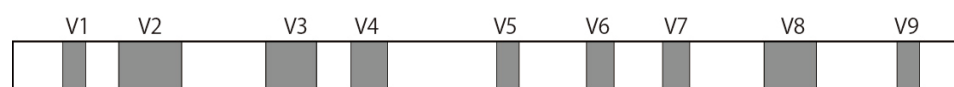
1. Extract metagenomes of the gut microbiota from fecal samples.
2. PCR amplification of 16S ribosomal RNA (16S rRNA) gene.
3. DNA sequencing of PCR-amplified samples.
4. Matches with the reference sequences in the database.

Question 1

Explain how ribosomes function in the cell using approximately 30 words.

Question 2

The following figure shows a schematic of the 16S rRNA gene. The gray areas, V1–V9, represent hypervariable regions, while the white areas represent conserved regions. Based on the figure, explain why the 16S rRNA gene is used to analyze microbiome diversity in approximately 100 words.



Question 3

List all the essential materials needed for PCR amplification in a laboratory tube. Then, describe the function of each material.

Question 4

The experimental procedures described in the question have limitations as a method for investigating the diversity of the gut microbiota. Explain the reasons for these limitations in approximately 50 words.

Question 5

Analyzing the microbial species present in a specific environment by extracting metagenomes from that environment and then performing DNA sequencing is known as metagenome analysis. Suggest a research plan involving metagenomes from environments other than the human gut, and explain the purpose and methods in detail.

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[7] Cell biology

Question 1

Answer each of the following questions.

- (1) Select all correct statements regarding the differences between eukaryotic and prokaryotic cells.  
A. Prokaryotic cells lack DNA. B. Eukaryotic cells have a nucleus enclosed by a nuclear membrane. C. Prokaryotic cells contain mitochondria. D. Eukaryotic cells always possess a cell wall.
- (2) Which of the following correctly describes the primary function of the Golgi apparatus?  
A. ATP synthesis B. Protein translation C. Protein modification and secretion D. DNA replication
- (3) The endoplasmic reticulum includes the rough ER and smooth ER. Explain the functional differences between them.
- (4) From the following organelles, select all that possess a double-membrane structure.  
A. Mitochondria B. Lysosome C. Nucleus D. Endoplasmic reticulum E. Chloroplast F. Vacuole

Question 2

Lamellipodia are flat structures formed at the leading edge of moving cells, driven by the actin cytoskeleton. The actin cytoskeleton consists of filamentous structures formed by the continuous association of monomeric G-actin. Given that the free G-actin concentration is  $5 \mu\text{M}$ , the barbed-end on-rate is  $11 \mu\text{M}^{-1}\text{s}^{-1}$ , the off-rate is  $1.4 \text{s}^{-1}$ , and the critical concentration is  $0.13 \mu\text{M}$ , answer the following (M=mol/L).

- (1) Calculate the elongation rate (subunits  $\text{s}^{-1}$ ).
- (2) If the length increment per actin subunit is  $2.7 \text{ nm}$ , calculate the membrane protrusion rate ( $\text{nm s}^{-1}$ ).

Question 3

Cellular waste and unwanted structures are degraded within lysosomes, vesicle-like organelles. Lysosomes maintain an acidic internal environment (low pH) where specialized enzymes operate. A research team investigated the properties of "lysosomal enzyme X." Answer the following questions based on their findings.

- (1) Researchers reported, "enzyme X has minimal activity in the cytoplasm but high activity within lysosomes." Why is it beneficial for cells that this enzyme remains inactive in the cytoplasm? Provide the most appropriate explanation.
- (2) Researchers observed that cells with damaged lysosomal membranes did not immediately die. Considering this observation, describe the "safety mechanism" enzyme X likely possesses, based on the provided information.
- (3) Suggest a method for detecting the localization of lysosomal enzyme X in living cells.
- (4) Under certain conditions, enzyme X's reaction rate was  $v = 4 \mu\text{mol}/\text{min}$  at a substrate concentration  $[\text{S}] = 1.0 \text{ mM}$ . If the maximum reaction rate is  $V_{\text{max}} = 10 \mu\text{mol}/\text{min}$ , calculate the Michaelis constant  $K_{\text{m}}$ .

Question 4

During a research practical at a university, students observe cultured human cells to study the structure and dynamics of various organelles. They need to choose among optical microscopes, fluorescence microscopes, phase-contrast microscopes, and electron microscopes. Based on the following interactions, answer the questions.

- (1) Student A said, "I want to observe particles moving within the cytoplasm of living cells." Identify the most suitable microscope for this purpose and explain your choice.

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- (2) Student B aims to observe mitochondria in extremely high detail. Select the most suitable microscope from the provided options and explain your choice.
  - (3) Student C used a fluorescence microscope to observe intracellular proteins but found the fluorescent signal weakened gradually and eventually became undetectable. Explain why this phenomenon occurs.

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Answer to Question [1]

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