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Make sure that you are given 11 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 from the following word list and describe the definition and characteristics of each.

- (1) Continuity of functions
- (2) Improper integral
- (3) Leibniz's rule for the  $n$ th derivative
- (4) Coefficient of correlation
- (5) Probabilistic distribution
- (6) Independent and dependent variables
- (7) Recursive function
- (8) Euler graph
- (9) breadth-first search
- (10) Jacobi matrix
- (11) Phase portrait
- (12) Linear stability analysis
- (13) Semi-conservative replication
- (14) Nucleotide
- (15) Transcriptional regulator
- (16) Cell membrane
- (17) Cell cycle
- (18) Genetic code

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[2] Calculus

Question 1

The hyperbolic function  $\sinh x, \cosh x$  is defined as following:

$$\sinh x = \frac{e^x - e^{-x}}{2}, \cosh x = \frac{e^x + e^{-x}}{2}$$

$k$  is a positive constant. Answer the following questions.

- (1) Find the value of  $\cosh^2 kx - \sinh^2 kx$ .
- (2) Express the derivative of  $\sinh kx, \cosh kx$  using in terms of  $\sinh kx$  and  $\cosh kx$ , respectively.
- (3) Express  $\sinh 2x$  and  $\cosh 2x$  in terms of  $\sinh kx$  and  $\cosh kx$ , respectively.
- (4) Calculate the indefinite integral  $\int \frac{1}{\sqrt{x^2 + 1}} dx$ .

Question 2

Assume the value of the function  $f(x_1, x_2, \dots, x_n)$  is a extremum at  $(x_1, x_2, \dots, x_n) = (x_1^*, x_2^*, \dots, x_n^*)$  subject to  $g(x_1, x_2, \dots, x_n) = 0$ . Then, the equation of  $F(x, y, \lambda) \equiv f - \lambda g$ ,

$$\frac{\partial F}{\partial x_i} = \frac{\partial F}{\partial \lambda} = 0, (i = 1, 2, \dots, n).$$

has the solution of  $(x_1, x_2, \dots, x_n, \lambda) = (x_1^*, x_2^*, \dots, x_n^*, \lambda^*)$ . This strategy is called the method of Lagrange multipliers.

- (1) Find the value of  $(x, y)$  on a unit circle that maximize  $x + 2y$ .
- (2) Among the rectangular parallelepipeds with a surface area of  $6\sqrt{6}$ , find the three-dimensional figure with the largest volume.

Question 3

Given  $D = \{(x, y) | 0 \leq x + y \leq 1, 0 \leq x - y \leq 1\}$ , let  $I = \iint_D \frac{x - y}{1 + x + y} dx dy$ . Answer the following questions:

- (1) Draw the region  $D$ .
- (2) Compute  $I$ .

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[3] Statistics

Question 1

The blood types of 100 university class members were investigated. The results are as follows: Suppose that you are planning to perform

A	O	B	AB
36	33	22	9

a chi-square goodness-of-fit test to determine whether the blood type ratio of this class is different from the approximate blood type ratio of Japanese residents, i.e.,  $A:O:B:AB=4:3:2:1$ .

- (1) Calculate the value of the chi-square statistic.
- (2) Specify the value of the degree of freedom of the chi-square distribution to be used in this statistical test.

Question 2

A regression analysis was performed using the data of body fat ratio and weight obtained from a student group.

ANOVA table for body fat ratio					Coefficient table					
Source of variation	DF	SS	MS	F	P Term	Coef	SECoef	T	P	
Regression	1	1.33	1.33	0.10	0.75	Constant	26.89	4.67	5.76	0.000
Residual	17	217.09	12.77			Weight	0.0207	0.0641	0.32	0.751
Total	18	218.42								

- (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 95 percent confidence interval for the slope of the fitted line? Choose a number.  
① (0.0102, 0.0312)    ② (−0.115, 0.156)    ③ (0.0104, 0.0414)

Question 3

Consider a mountain village often hit by landslides caused by heavy rainfall. Researchers separated a  $2,000 \times 2,000$  meter area in this village, which included mountains forests and rivers, into  $10 \times 10$  meter meshes (40,000 meshes in total), and collected the primary data below from every mesh. Suppose that there are no differences in geological features among meshes.

- ① Land use as of July 2023 (used as residential land, commercial land, farmland, fruit forest, forestry land, wilderness, non-agricultural forests, and rivers)
- ② Whether or not there has been any change in the land use since 1965.
- ③ The altitude at the center of the mesh
- ④ Whether there are roads or not.
- ⑤ Point precipitation during the July 2023 heavy rainfall
- ⑥ Whether there was a landslide caused by the July 2023 heavy rainfall or not

Using the above primary data, as well as secondary data and indicators that can be calculated from the primary data, we will consider **three** different "matters of concern" and conduct statistical analysis (including hypothesis testing). For each analysis, describe the following item.

1. Matters of concern
2. Working hypothesis (either one null or alternative hypotheses)
3. Primary data to be used (Choose multiple numbers from above)
4. Statistical method ("XYZ analysis")

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- .....
5. How you can calculate the secondary data or indices that will be used in the "Statistical method" from the "Primary data to be used"

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

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[4] Information science

Question 1

Answer each of the following questions.

- (1) Using the multiplication theorem, prove Bayes' theorem.
- (2) The proportions of individuals with and without disease A are 0.0002 and 0.9998, respectively. Assume that a test for A is conducted. The table below shows the positive and negative rates for individuals with and without disease A. Given a positive test result, find the probability that the person is unaffected by the disease.

	Positive rate	Negative rate
With A	0.860	0.140
Without A	0.070	0.930

Question 2

Assume that  $N$  data points  $\{-2, -1, 0, 1, 2\}$  are obtained from a one-dimensional normal distribution  $N(\mu, \sigma^2)$ . Find the maximum likelihood estimates of  $\mu$  and  $\sigma^2$ .

Question 3

Consider a one-dimensional normal distribution  $N(\mu, \sigma^2)$  with a known variance parameter  $\sigma^2$ . Assume that  $N$  data points  $\{x_i\}$  are obtained from this distribution. Answer the following questions.

- (1) Find the likelihood function  $L(\mu; \{x_i\})$  for the mean parameter  $\mu$  given the data points  $\{x_i\}$ .
- (2) Assuming a prior probability distribution of  $N(\mu_0, \sigma_0^2)$ , find the posterior probability  $p(\mu | \{x_i\}, \mu_0, \sigma_0^2)$  for  $\mu$ .

Question 4

Consider the recurrence relation  $a_n = 2a_{n-1} - 3a_{n-2}$  with initial conditions  $a_0 = 1, a_1 = 2$ . Answer the following questions.

- (1) Find  $a_2, a_3$ , and  $a_4$ .
- (2) Create a program using a recursive function that takes any  $n \geq 0$  as input and outputs  $a_n$ . Use a clear expression method such as natural language, mathematical expressions, or pseudo-programming languages.

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[5] Nonlinear dynamics

Question 1

Biological populations cannot grow infinitely due to resource and habitat constraints. Express this effect using the carrying capacity  $K$  ( $K > 0$ ) and answer the following questions about the logistic equation below, which captures the fluctuations in the size of population (or biomass)  $x$ .

$$\dot{x} = rx \left(1 - \frac{x}{K}\right)$$

- (1) Let  $r \neq 0$ . Find all fixed points to the system.
- (2) Let  $r \neq 0$ . For each of cases where  $r > 0$  and  $r < 0$  respectively, perform local stability analyses for the all fixed points.
- (3) Explain how the system behaves when  $r = 0$ .

Question 2

The equation of motion for the mass-spring-damper system is described as

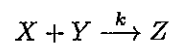
$$m\ddot{x} + b\dot{x} + kx = 0,$$

where  $m, b, k > 0$ . Answer the following questions regarding this model.

- (1) Let  $y = \dot{x}$ . Find the equation that  $\dot{y}$  satisfies using  $x$  and  $y$ .
- (2) Let  $x = \begin{pmatrix} x \\ y \end{pmatrix}$ . If you express the model with a linear differential equation,  $\dot{x} = Ax$ , show a matrix  $A$ .
- (3) Show the condition of the parameters where damped oscillations occurs.

Question 3

Chemicals X, Y, and Z react with a reaction rate constant  $k$ .



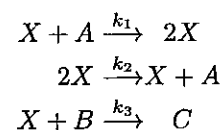
In this case, if the concentrations of X, Y, and Z are  $x$ ,  $y$ , and  $z$ , then

$$\dot{x} = -kxy, \quad \dot{z} = kxy$$

holds, which is called the law of mass action. hold where the concentrations of  $X, Y, Z$  are  $x, y, z$ , respectively. Hereafter, we assume  $x(0) = x_0, z(0) = 0$  and the concentration of Y is kept at  $y_c$ . Answer the following questions.

- (1) Find  $x(t)$ .
- (2) Find  $z(t)$ .

Next, we consider the chemical reaction as follows:



where the concentration of  $A, B$  is kept at  $a, b$  respectively.

- (3) Find the equation  $\dot{x}$  satisfies.
- (4) Express the condition where  $x = 0$  is stable fixed point using  $a, b, k_1, k_3$ .
- (5) Which bifurcation occurs when the stability of the fixed point at  $x = 0$  changes from stable to unstable?

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[6] Molecular biology

Question 1

Fill in the blanks in the following sentences. DNA is composed of bases, (a), and phosphoric acid. There are four types of bases, which are adenine, (b), cytosine, and (c). Chromosomes are present in the cell nucleus, and within the chromosomes, DNA wraps around proteins called (d), forming units known as nucleosomes. Furthermore, these nucleosomes fold into structures called (e). Within these chromosomes, the entire genetic information of an organism (f) is recorded as DNA base sequence information. In humans, somatic cells contain (g) chromosomes, which consist of (h) pairs of homologous chromosomes.

Gene expression is the process by which the information in DNA is transcribed into mRNA and subsequently translated by (i) to synthesize proteins. During transcription, a specific region of DNA called the (j) binds to (k), and mRNA is synthesized by (l). Translation is the process of translating the information from mRNA into proteins, where mRNA binds to (i), and (m) brings the corresponding amino acids to the mRNA codons using their anticodons. (i) links these amino acids together by bonds called (n), forming a polypeptide chain. Finally, this polypeptide chain folds (the (o) of the protein) and a functional protein is synthesized.

Question 2

Answer the following questions about the basic principles of PCR (Polymerase Chain Reaction).

- (1) PCR consists of the following three steps per cycle. In Step 1, what experimental procedure is carried out and what happens to the DNA as a result? Explain considering that the DNA bases are connected by hydrogen bonds.

Step 1: DNA denaturation

Step 2: Annealing

Step 3: Extension

- (2) In Step 2, short DNA strands called primers are attached to the target DNA sequence. The underlined section of the DNA base sequence below is the coding region for the genetic information of a protein. Design the necessary primers to include the entire length of this protein. The primer length should be 20 bases.

CGGAATTCGCGTTTTTATTTTAATTTTCTTTCAAATACTTCTAGCTAGAGTATTTTACAACAATTACCAACAACAACAACAACAA  
CAACAACATTACATTTTACATTCTACAACCTACAGCCatggcggacctggccgagtgcaacatcaaagtgatgtgtcgttcagacctc  
tcaacgagtcctgaagtgaaccgcgacagaagtagacatcgccaagtttcagggagaagacacggtcgtgatcggtccaagccttatgc  
atttgatcgggtgttcagtcacgacatc . . . . . agaaaaaacgagcagctgagatgatggcatctt  
tactaaaaggtaccTAGAGTAGCCAAACGAATTCGAGCTCGGTACCGGGGATCCTCTAGAGTCGACCTGCAGGCATGCAAGCTGAT  
CCGGCTGCTAACAAAGCCGAAAGGAAGCTGAGTTGGCTGCTGCCACCGCTGAGCAATAACTAGCAAACTAGTTTACGGCTAGCGCGG  
GATGCGACGCGCGGTGCGCTCTTATCCGGCTTCCTATATCAGGCTGTGTTAAGACGCGCGCGCTTCGCCAAATCCCTATGCCGGTT  
CGACGGCTGGACAAAATACTGTTTATCTTCCAGCGCAGGCAGGTTAATGTACCACCCAGCAGCAGCGGTATCCAGCGCGTATATA  
CCTTCGGCGGTACCT

- (3) In Step 3, starting from the primer, the DNA strand is replicated according to the base sequence of the template DNA. Name the enzyme that works to extend the primer during this process.

Question 3

Fill in the blanks in the following passage: DNA has the property of binding two DNA strands together in a base sequence-specific manner. This property can also be applied in engineering, making it possible to create nanometer-sized structures using DNA. For example, DNA origami can be created by binding a long circular single-stranded DNA called (a) to a specific position of a



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short single-stranded DNA called (b) , folding it into a desired shape. Additionally, small DNA nanostructures called DNA tiles self-assemble into larger DNA nanostructures by interconnecting with single-stranded DNA sequences called (c) .

#### Question 4

Even a single-stranded DNA can form various secondary structures. Design the underlined sequence of the following single-stranded DNA base sequence to create a single-stranded DNA that forms a hairpin loop structure. Also, design the DNA that signals the opening of the loop structure. The notation of the DNA should be represented with the 5' end on the left.

5'-TACGAGCCAGGGGAAXXXXXX-3'

#### Question 5

When designing DNA structures, it is also important to adjust the concentration of each DNA strand. Answer the following questions about DNA concentration adjustment.

- (1) The absorbance of a 10-base DNA with a molar extinction coefficient of  $\epsilon = 100000 \text{ L}/(\text{mol} \cdot \text{cm})$  was measured and found to be 0.10. Calculate the molar concentration (mol/L) of this DNA. Also, convert it to mass concentration (ng/ $\mu\text{L}$ ). Assume the path length of the light is 1 cm and the average molecular weight of DNA is 330.
- (2) There is a DNA solution with a concentration of  $2.0 \times 10^{-5} \text{ mol/L}$ . Using ultrapure water, you want to dilute this solution to a DNA concentration of  $5.0 \times 10^{-6} \text{ mol/L}$ . If the total volume of the DNA solution after dilution is to be 100  $\mu\text{L}$ , determine the required amount of the original DNA solution and the amount of ultrapure water to be used for dilution.

[7] Cell biology

Question 1

Answer the following questions about cells.

(1) Explain the functions of the following cell organelles:

- (a) Nucleus
- (b) Mitochondria
- (c) Golgi apparatus
- (d) Lysosomes

(2) Regarding microtubules and actin filaments, which are the main components of the cell, and the cytoskeleton, answer the following questions:

- (a) Structural characteristics
- (b) Nucleotide used for polymerization
- (c) Name of the building block of protein
- (d) Two main functions within the cell
- (e) General names of complementary motor proteins (provide two for microtubules to complete the answer)

(3) What are the flat membrane structures and protruding structures formed at the leading edge of cell migration called?

(4) Explain nucleation and critical concentration in the context of the polymerization process of the cytoskeleton.

Question 2

Select the microscope that is considered appropriate from the list below for observing each of the following samples:

- (1) 3D fluorescence imaging of cells
- (2) Fluorescently labeled cytoskeleton on the cover glass surface in a system with a large amount of fluorescent dye
- (3) Inner molecular structure of viruses
- (4) Observing the surface structure of live cells at nanometer-scale resolution
- (5) Observing the surface structure of bacteria at nanometer-scale resolution

<Microscope List> (abbreviations are acceptable)

- Scanning electron microscope (SEM)
- Transmission electron microscope (TEM)
- Confocal laser scanning microscope (CLSM)
- Total internal reflection fluorescence microscope (TIRFM)
- High-speed atomic force microscope (HS-AFM)

Question 3

Select the appropriate combination of protein purification and analysis methods from the list below for the following tasks:

- a. Purification of His-tagged fusion proteins
- b. Separation and analysis of proteins with different molecular sizes (with denaturation)
- c. Fractionation of proteins with different molecular sizes
- d. Purification of GST-tagged proteins
- e. Separation of polymerized microtubules from cell extracts

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.....  
<Protein Purification and Analysis Methods List>Each item can be selected only once. Answer with the capital letters assigned to each term.

- A. Glutathione affinity column chromatography
- B. SDS polyacrylamide gel electrophoresis
- C. Ni-NTA affinity column chromatography
- D. Ultracentrifugation
- E. Gel filtration chromatography (size exclusion chromatography)

#### Question 4

Given the following information about the binding of streptavidin and biotin, the association rate constant ( $k_{\text{on}}$ ) for streptavidin is approximately  $1.0 \times 10^8 \text{ M}^{-1}\text{s}^{-1}$ , and the dissociation rate constant ( $k_{\text{off}}$ ) is approximately  $1.0 \times 10^{-6} \text{ s}^{-1}$ . Calculate the dissociation constant ( $K_d$ ) for this binding reaction. (Note:  $\text{M} = \text{mol/L}$ )

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Answer to Question [1]

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