INDIAN STATISTICAL INSTITUTE

B.STAT. (HONS.) 3rd Year

Statistical Methods in Genetics

End Semester Examination 2024-2025

Date: May 2, 2025 Maximum marks=100 Time: 3 hours

Answer all the questions.

1. For an autosomal biallelic locus, will the Hardy-Weinberg law hold if in the initial generation the relative frequencies of the three genotypes are different for males and females? Justify your answer with appropriate derivations. (10)

2. Show that the proportion of heterozygotes at an autosomal biallelic locus is halved in each generation of self-mating (i.e., selfing), but the frequencies of the alleles remain the same over generations. (7)

3. Suppose that an autosomal locus is in Hardy-Weinberg equilibrium and the proportion of heterozygotes at that locus is 0.825. What can you infer about the number of alleles at this locus? Justify your answer. (6)

4. Consider a disorder controlled by two unlinked autosomal biallelic loci with alleles (A,a) and (B,b), respectively. Suppose an individual is affected if and only if he/she has genotype aabb. If p_1 is the conditional probability of an offspring being affected given that exactly one of the parents is affected and p_2 is the conditional probability that an offspring is affected given both parents are unaffected, show that $p_2 = p_1^2$. (9)

5. (a) Suppose the ABO blood group locus is in Hardy-Weinberg equilibrium in a population. What is the probability that an individual with AB blood group will have an AB mother in this population?

   (b) If in a random sample of n individuals from this population, n_O, n_A, n_B and n_{AB} denote, respectively, the frequencies of individuals with O, A, B and AB blood groups, describe the EM algorithm to obtain the maximum likelihood estimators of the frequencies of the alleles A,B and O. (4+13=17)

6. Consider two autosomal biallelic loci with alleles (A,a) and (B,b), respectively. If δ denotes the coefficient of linkage disequilibrium between two loci, i.e., $\delta = P(AB) - P(A)P(B)$, then show that $-1/4 \leq \delta \leq 1/4$. (8)

7. Consider a phenotype determined by an autosomal biallelic locus, with alleles A and a. Suppose the disorder is recessive, that is, individuals only with aa genotype are affected; otherwise, they are unaffected. If in a random sample of n individuals from a population which is in Hardy-Weinberg equilibrium at this locus, n_1 individuals are affected and n_2 individuals are unaffected, obtain the maximum likelihood estimator of the population frequency, q, of allele a. Show that the estimator is negatively biased. Also, find the asymptotic variance of the estimator. (8)

8. An outrageously careless hospital, located in a population which is in Hardy-Weinberg equilibrium at the ABO blood group locus, gives transfusions at random. What is the probability of a person getting a mismatched blood transfusion in this population? (To refresh your memory, group [O] can give to anyone, [A] to [A] or [AB], [B] to [B] or [AB], and [AB] only to [AB].) (5)

9. Consider the following model: $Y_i = \mu_i + e_i$, for $i = 1, 2$. μ_i is the conditional mean of Y_i given the quantitative trait locus (QTL) genotype and is equal to α_i, β_i, or $-\alpha_i$, respectively, according as the genotype is AA, Aa or aa; while e_i is the random error component with mean 0, variance σ_i^2 and the correlation between e_1 and e_2 is ρ, irrespective of the QTL genotype. Let the covariance between μ_i and e_i is 0 for $i = 1, 2$. Assuming that the QTL is in Hardy-Weinberg equilibrium, find the correlation between Y_1 and Y_2. (14)

10. A normal woman with a colour-blind father married a normal man, and their first child, a boy, had hemophilia. Both colour blindness and hemophilia are due to X-linked recessive mutations, and the probability of recombination between the two genes is 0.1. This couple plans to have a second child. What is the probability that the child will have (a) hemophilia? (b) colour blindness? (c) both hemophilia and colour blindness? (d) neither hemophilia nor color blindness? (4x4=16)