

# COLUMBIA UNIVERSITY

## DEPARTMENT OF BIOSTATISTICS

### P 8149 - HUMAN POPULATION GENETICS

exercise sheet 3 (covers chapter 5 and 6)

Date Date: Mon NOV 10, 2025

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#### Question 1 (3 marks)

Show that  $\bar{w} \leq 1$  (see Eq. 5.1 in your Lecture Notes). Assume the fitnesses are standardized relative to the maximum fitness.

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#### Question 2 (1+2 = 3 marks)

The zygote-to-adult relative viabilities are 1, .5 and .25 for the  $AA$ ,  $Aa$ , and  $aa$  genotypes, respectively. Assume random mating.

(a) Starting with the zygotic frequency of  $A$  being .2, what are the genotype frequencies in the adult population?

(b) Suppose you do not know the fitnesses and you can only observe the adult population. A naive method to estimate viabilities is to use the ratios of observed genotypic frequencies to expected frequencies under Hardy-Weinberg equilibrium. Given that the observed genotype counts for  $AA$ ,  $Aa$ , and  $aa$  are 165, 562 and 339, respectively, what are the relative estimates of relative viabilities using the Hardy-Weinberg deviation technique?

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#### Question 3 (2+1 = 3 marks)

The following fitnesses were estimated for humans living in a malarial environment in West Africa as a function of their genotype at the hemoglobin  $\beta$ -chain locus:

genotype	$AA$	$AS$	$SS$	$AC$	$SC$	$CC$
fitness	.9	1.0	.2	.9	.71	1.31

(a) Given these fitnesses and the assumption of random mating in an infinitely large population, calculate each population's average fitness and the average excess and rate of change of allele frequency for all three alleles for populations with the following gene pools:

	freq( $A$ )	freq( $S$ )	freq( $C$ )
pop. 1	.9	.05	.05
pop. 2	.85	.05	.10
pop. 3	.75	.05	.20

(b) Do the initial allele frequencies affect the course of adaptive evolution in the above cases (i.e., are the signs in the changes of allele frequencies the same)?

#### Question 4 (2 marks)

Assume that a typical gene in the human genome has a mutation rate of  $2 \times 10^{-6}$  per gene per cell division. If one generation involves an average of 36 cell divisions, what is the mutation rate per gene per generation?

#### Question 5 (2 marks)

For the two-way neutral mutation model, show that  $\tilde{q} \approx .91$  for any values of  $u$  and  $v$  as long as  $u = 10v$ . What is the equilibrium value if  $u = 100v$ ?

#### Question 6 (1+2 = 3 marks)

A population of 20 individuals were genotyped at a particular locus. Calculate the observed and expected heterozygosities in each of the following situations:

- (a) The locus had only two alleles,  $A_1$  and  $A_2$ ; 10 individuals were  $A_1A_1$  and 10 were  $A_1A_2$ .
- (b) All 20 individuals were heterozygous at the locus and each allele in the heterozygotes was present only once.

#### Question 7 (1+1+2 = 4marks)

The following 5 DNA sequences were sequenced at 15 nucleotide sites.

A	A	T	C	G	A	G	A	C	T	T	T	A	G	C
A	T	T	C	C	A	G	A	T	T	T	A	A	G	C
A	T	T	C	C	A	G	A	T	T	T	A	A	G	C
A	A	T	C	G	A	G	A	C	T	T	T	A	G	C
T	A	T	C	G	A	G	A	C	T	A	T	C	C	C

- (a) What are the number of segregating sites in the sample?
- (b) Estimate the nucleotide polymorphism in the sample.
- (c) Estimate the nucleotide diversity in the sample.

## ANSWERS:

Q2: (b) Relative fitnesses of AA, Aa, and aa are .816, 1, and .865, Q3: (a) Average fitnesses are 0.907325 for pop.1, 0.90895 for pop. 2, 0.91835 for pop. 3; averages excesses of (A, S, C) are (-0.002325 0.038175 0.003675) for pop.1, (-0.00395 0.02205 0.02255) for pop. 2, (-0.01335 -0.01635 0.05415) for pop., Q4:  $7.2 \times 10^5$ , Q5: If  $u = 100v$ , then  $\tilde{q} = .99$  approx., Q6 (a) expected het.= .375, (b) expected het.=.975; Q7 (b) .53, (c) 4.0

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Dr P Gorroochurn: 10/28/2025