Genetics 320, Problem Set 12

Due Wednesay 8 December 2004 at 11 am

1 (1 point): Consider a population of size $N = 10^5$ and a mutation rate of $u = 10^{-6}$,

(a) Assuming the Infinite alleles model, what is the probability that a random individual is a heterozygote?

Here $4Nu = 4 \cdot 10^5 \cdot 10^{-6} = 0.4$***, hence***

$$H = \frac{4Nu}{1+4Nu} = \frac{0.4}{1.4} = 0.286$$

(b) Recall that the number of mutations follows a Poisson distribution (See Problem 7 of PS 1). Assuming that the common ancestor to two random sequences occurs $2N$ generations ago, what is the probability that two randomly-chosen sequences differ by one mutation? By two mutations? By five mutations?

If the time back to the common ancestor is $2N$ ***generations, then the expected number of new mutations is*** $2 \cdot (2N) \cdot u = 0.4$***, and the probability of*** k ***mutations follows a Poisson distribution with parameter 0.4. Hence,***

Prob$(1$ ***mutation***$) = (0.4)^1 e^{-0.4}/1! = 0.268$.

Prob$(2$ ***mutations***$) = (0.4)^2 e^{-0.4}/2! = 0.054$.

Prob$(5$ ***mutations***$) = (0.4)^5 e^{-0.4}/5! = 0.000057$

(c) What is the probability for this population size that two randomly-chosen alleles have there most recent common ancestor in the last 10,000 generations? 25,000 generations? 50,000 generations?

Recall that the per-generation probabilty of a common ancestor in the last generation is $p = 1/(2N)$***. Hence, Prob(NO common ancestor) =*** $(1-p)$***, and thus Prob(No common ancestor in the last*** t ***generations) =*** $(1-p)^t$***. Thus, Prob(common ancestor within the last*** t ***generations) = 1- Prob(No common ancestor in the last*** t ***generations) =*** $1-(1-p)^t$.

Here $p = (1/2 \cdot 10^5)$***, so that*** $(1-p) = 0.999995$.

For t = 10,000, $1 - 0.999995^{10,000} = 0.049$

For t = 25,000, $1 - 0.999995^{25,000} = 0.118$

For t = 50,000, $1 - 0.999995^{50,000} = 0.221$

2 (2 points): In an infinite population, what happens for each of the following fitnesses

(a) $W_{AA} = 1$, $W_{Aa} = 1.001$, $W_{aa} = 1.002$ ***a fixed***

(b) $W_{AA} = 0.95$, $W_{Aa} = 0.94$, $W_{aa} = 0.85$ ***A fixed***

(c) $W_{AA} = 1$, $W_{Aa} = 1$, $W_{aa} = 0.75$ ***A fixed***

(d) $W_{AA} = 1$, $W_{Aa} = 0.75$, $W_{aa} = 0.75$ ***A fixed***

(e) $W_{AA} = W_{Aa} = W_{aa}$ ***Hardy-Weinberg. Alleles frequencies unchanged.***

3 (2 points): Suppose we sample 1000 individuals and the number of offspring they leave. Focusing on a specific diallelic locus, we find the following:

Genotypes:	AA	Aa	aa
Numbers observed	160	480	360
Average number of offspring:	10.5	12.0	12.5

(a) Setting $W_{aa} = 1$, what are the relative fitnesses of the three genotypes?

$W_{AA} = 10.5/12.5 = 0.84$, $W_{Aa} = 12.0/12.5 = 0.96$, ***and*** $W_{aa} = 1$.

(b) What is the change in the frequency of allele A after one generation of selection?

Freq(A after selection) = Freq(AA after selection) + (1/2) Freq(Aa after selection). Here, initial freq(AA) = 0.16, freq(Aa) = 0.48, freq(aa) = 0.36, giving the initial frequency of A as 0.16 + (1/2) 0.48 = 0.4.

$\overline{W} = W_{AA} \cdot 0.16 + W_{Aa} \cdot 0.48 + W_{aa} \cdot 0.36 = 0.84 \cdot 0.16 + 0.96 \cdot 0.48 + 1 \cdot 0.36 = 0.9552$

Freq(AA after selection) = $0.16 \cdot (W_{AA}/\overline{W}) = 0.16 \cdot (0.84/0.9552) = 0.14$

Freq(Aa after selection) = $0.48 \cdot (W_{Aa}/\overline{W}) = 0.48 \cdot (0.96/0.9552) = 0.482$

Hence, Freq(A after selection) $= 0.14 + (1/2) \cdot 0.482 = 0.381$. ***Thus the change in allele frequnecy is 0.381 - 0.4 = -0.019***

4 (2 points): Suppose the fitnesses at a locus are $W_{AA} = 1 - s$, $W_{Aa} = 1$, and $W_{aa} = 1 - t$. For freq(A) $= t/(s + t)$, show that

(a) $W_A = W_a = \overline{W}$.

$$W_A = pW_{AA} + (1-p)W_{Aa} = \left(\frac{t}{s+t}\right) \cdot (1-s) + \left(\frac{s}{s+t}\right) \cdot 1 = \frac{t - ts + s}{s+t}$$

$$W_a = pW_{Aa} + (1-p)W_{aa} = \left(\frac{t}{s+t}\right) \cdot 1 + \left(\frac{s}{s+t}\right) \cdot (1-t) = \frac{t - ts + s}{s+t}$$

Hence, $W_A = W_a$. ***Since*** $\overline{W} = pW_A + (1-p)W_a$, ***it follows that*** $\overline{W} = W_A = W_a$.

(b) Showing that the change in freq(A) = the change in freq(a) = 0.

Recalling that $\Delta p_A = p_A(W_A - \overline{W})/\overline{W}$, ***since*** $W_A - \overline{W}$, ***it immediately follows that*** $\Delta p_A = 0$. ***The same argument holds for*** Δp_a.

5 (2 points): Consider a locus with five alleles. Two populations are considered, with the following allele frequencies and marginal fitnesses:

Population one

Allele:	A_1	A_2	A_3	A_4	A_5
Frequency:	0.1	0.2	0.5	0.1	0.1
Marginal fitness:	3.5	1.2	4.0	3.3	6.2

Population Two

Allele:	A_1	A_2	A_3	A_4	A_5
Frequency:	0.2	0.1	0.1	0.3	0.3
Marginal fitness:	1.5	2.5	2.0	4.5	2.4

Compute the change in the frequency of allele A_3 in both populations.

$\overline{W} = \sum_{i=1}^{5} W_{A_i}$ ***Freq(A_i). Hence, for populations one and two,***

$\overline{W}$(***pop 1***) $= 0.1 \cdot 3.5 + 0.2 \cdot 1.2 + 0.5 \cdot 4.0 + 0.1 \cdot 3.3 + 0.1 \cdot 6.2 = 3.54$

$\overline{W}$(***pop 1***) $= 0.2 \cdot 1.5 + 0.1 \cdot 2.5 + 0.1 \cdot 2.0 + 0.3 \cdot 4.5 + 0.3 \cdot 2.4 = 2.82$

Hence, in population one, $\Delta p_3 = p_3(W_3 - \overline{W})/\overline{W} = 0.5 \cdot (4.0 - 3.54)/3.54 = 0.065$

In population two, $\Delta p_3 = p_3(W_3 - \overline{W})/\overline{W} = 0.1 \cdot (2.0 - 2.82)/2.82 = -0.029$

6 (1 point): Individuals homozygous for the sickle-cell allele (ss) die before reproducing. However, normal/sickle heterozygotes (Ss) have greater fitness that normal homozygotes (SS) due to increased resistance to marlia. If the frequency of s in equilibrium populations is 0.2, what is the fitness advantage of Ss relative to SS individuals?

Under balancing selection, if the fitnesses of $W_{ss} : W_{sS} : W_{SS}$ ***are*** $0 : 1 : 1 - t$***, then the frequency of allele*** s ***at equilibrium is*** $t/(t+1)$***. Thus,*** $0.2 = t/(t+1)$ ***or*** $0.2 \cdot (t+1) = t$ ***or*** $0.2 = 0.8t$ ***or*** $t = 0.2/0.8 = 0.25$***. Hence,*** $W_{Ss}/W_{SS} = 1/(1-t) = 1/0.75 = 1.33$***.***