Genetics 320, Problem Set Nine (15 points)

1 (2 points): Consider a locus with four alleles (A_1 to A_4) at the following frequencies: $p_1 = 0.1$, $p_2 = 0.2$, $p_3 = 0.3$, $p_4 = 0.4$. Assume random mating and all other Hardy-Weinberg conditions. What is the frequency of

(a) A_2A_3? $2\,p_2\,p_3 = 0.12$

(b) A_4A_4? $p_4^2 = 0.16$

(c) All heterozygotes involving allele A_2? $2\,p_2\,(1 - p_2) = 0.32$

(d) All heteroyzgotes? $1 - (p_1^2 + p_2^2 + p_3^2 + p_4^2) = 0.70$

(e) Of a mating between A_1A_2 and A_3A_3 parents.

> ***Prob(A_1A_2) =$2\,p_1\,p_2 = 0.04$, Prob(A_3A_3) = $p_3^2 = 0.09$, Hence, Prob($A_1A_2 \times A_3A_3$ mating) = Prob(father = A_1A_2, mother = A_3A_3) + Prob(father = A_3A_3, mother = A_1A_2) $= 2\,(0.04 \cdot 0.09) = 0.0072$.***

2 (2 points): Let $p(0) = \text{freq}(A)$ in the initial generation (which we call generation 0). Assuming Hardy-Weinberg conditions:

(a) What is the frequency of AA homozygotes in the next generation (generation 1)? $p(0)^2$

(b) What is the frequency of heterozygotes involving A in generation 1? $2\,p(0)\,[\,1 - p(0)\,]$

(b) Given these genotype frequencies, show that $p(1) = \text{freq}(A \text{ in generation } 1) = p(0)$.

> $p(1)$ = ***freq(AA in gen 1) + (1/2)freq(Aa in gen 1) =*** $p(0)^2 + (1/2)2\,p(0)\,[\,1 - p(0)\,] = p(0)^2 + p(0) - p(0)^2 = p(0)$

3 (2 points): This problem examines what happens when there are different allele frequencies in the two sexes (as would occur if one mates males from one population with females from a second). Assume an autosomal locus, where the frequency of allele A in the male and female founding populations is p and r, respectively. Assuming all other Hardy-Weinberg conditions hold,

(a) What is the frequency of AA homozygotes in their offspring? $p \cdot r$

(b) What is the frequency of $A-$ heterozygotes? $p \cdot (1 - r) + (1 - p) \cdot r$

(c) What is the frequency of allele A in their male offspring? In their female offspring?

> ***The frequency of A in the next generation is freq(AA) + (1/2)freq($A-$). Since we are dealing with an autosomal locus, these frequencies are the same in both sexes. Hence, freq(A in males) = freq(A in females) =*** $p \cdot r + (1/2)[p \cdot (1-r) + (1-p) \cdot r] = p \cdot r + (p+r)/2 - p \cdot r = (p + r)/2$.

(a) What happens to the allele and genotype frequencies in subsequent generations?

> ***In the next generation, both sexes have the same allele frequencies, so the genotypes follow Hardy-Weinberg frequencies with freq(A) =*** $(p + r)/2$.

4 (2 points): Now consider when happens with the two sexes show different frequencies for an X-linked gene. Let the frequency of allele A (on an X-linked locus) be 0.25 in males and 0.8 in females in the founding population (generation 0). Assuming all other Hardy-Weinberg conditions hold,

(a) What is the frequency of AA homozygotes in their female offspring in generation 1?

freq(AA) = freq(A from father)*freq(A from mother) = $0.25 \cdot 0.8 = 0.2$

(b) What is the frequency of $A-$ heterozygotes in their female offspring in generation 1?

freq($A-$) = freq(A from father)*freq(not-A from mother) + freq(not-A from father)*freq(A from mother) = $0.25 \cdot 0.2 + 0.75 \cdot 0.8 = 0.65$

(c) What is the frequency of AY hemizygotes in their male offspring in generation 1?

freq(AY) = freq(A from mother) = 0.8.

(d) What are the frequencies of AA homozygotes, $A-$ heterozygotes (in females), and AY hemizygotes in generation 2?

Using the results from (a) - (c), freq(A in fathers in generation 1) = 0.8 [from (c)], while freq(A in mothers in gen 1) = freq(AA in mothers in gen 1) +(1/2)freq($A-$ in mothers in gen 1) = 0.2 + (1/2)0.65 = 0.525
freq(AA) = freq(A from father)*freq(A from mother) = $0.8 \cdot 0.525 = 0.42$
freq($A-$) = freq(A from father)*freq(not-A from mother) + freq(not-A from father)*freq(A from mother) = $0.8 \cdot 0.475 + 0.2 \cdot 0.525 = 0.485$
freq(AY) = freq(A from mother) = 0.525.

5 (2 points): Consider the $M/N, S/s$ blood group data from the Ugandan population in Table 26.2. Suppose the recombination frequency between these two loci is $c = 0.05$.

(a) If these gametes combine at random, what is the frequency of MM individuals? Of Ss individuals? Of $MMSs$ individuals?

freq(M) = freq(MS) + freq(Ms) = 0.134 + 0.357 = 0.491, freq(N) = 1-freq(M) = 0.509
freq(S) = freq(MS) + freq(NS) = 0.134 + 0.071 = 0.205, freq(s) = 1-freq(S) = 0.795
freq(MM) = freq(M)· freq(M) = $0.491^2 = 0.241$
freq(Ss) = 2 freq(S)· freq(s) = $2 \cdot 0.205 \cdot 0.795 = 0.326$
freq($MMSs$) = freq(MS from father) · freq(Ms from mother) + freq(Ms from father)· freq(MS from mother) $= 2 \cdot 0.134 \cdot 0.357 = 0.097$

(b) For these gamete frequencies, what is the disequilibrium (if any) for MS gametes? For Ms gametes?

$D_{MS} =$ ***freq(MS) - freq(M)· freq(S) =*** $0.134 - 0.491 \cdot 0.205 = 0.033$
$D_{Ms} =$ ***freq(Ms) - freq(M)· freq(s) =*** $0.357 - 0.491 \cdot 0.795 = -0.033$

(c) After ten generations of random mating, what is the expected disequilibrium for MS gametes? For Ms gametes?

$D_{MS}(10) = (1-c)^{10} D_{MS}(0) = 0.95^{10} \cdot 0.033 = 0.0198$
$D_{Ms}(10) = (1-c)^{10} D_{Ms}(0) = 0.95^{10} \cdot (-0.033) = -0.0198$

(c) After ten generations of random mating, what is the expected frequency of $MMSs$ individuals?

freq(MS gamete in gen 10) = freq(M) · freq(S) + $D_{MS}(10) = 0.491 \cdot 0.205 + 0.0198 = 0.1205$
freq(Ms gamete in gen 10) = freq(M) · freq(s) + $D_{Ms}(10) = 0.491 \cdot 0.795 + (-0.0198) = 0.3705$
freq($MMSs$) = 2· freq(MS) · freq(Ms) = $2 \cdot 0.1205 \cdot 0.3705 = 0.0893$

6 (2.5 points): Geneticists in Finland have isolated a genetic locus which gives the dreaded *dential* phenotype, in which individuals enjoy drilling in other people's mouths. Two linked marker loci have been isolated, and the following haplotype frequencies are seen for normal and *dential* chromosomes:

	Chromosome type	
Marker haplotype	*Dential*	Normal
M_1N_1	0.860	0.120
M_1N_2	0.044	0.280
M_2N_1	0.091	0.180
M_2N_2	0.005	0.420

(a) What was the haplotype on which the original *dential* mutant arose? M_1N_1

(b) Assuming 100 generations, what is the *dential* - M recombination frequency? The *dential* - N recombination frequency?

The frequency of allele M_1 on* dential *chromosomes is $q_{M_1} = 0.860 + 0.044 = 0.904$. ***Hence,*** $c_{M_1} = 1 - q^{1/100} = 1 - (0.904)^{1/100} = 0.001$

The frequency of allele N_1 on* dential *chromosomes is $q_{N_1} = 0.860 + 0.091 = 0.951$. ***Hence,*** $c_{N_1} = 1 - q^{1/100} = 1 - (0.951)^{1/100} = 0.0005$

(c) What does the resulting genetic map look like?

The only remaining issue is which locus (the* dential *gene, M or N is in the middle. The key here is that ths double recombinant should be the rarest type. Here, this is the M_2N_2 class. Since this contains the* dential *gene, this implies* dential *is in the middle, giving

M — (c = 0.001) —* dential *— (c = 0.0005) — N

7 (1.25 point): Suppose a population shows inbreeding, with inbreeding coefficient $F = 3/4$. In this population, the frequency of a recessive disease allele d is 10^{-3}.

(a) What is the expected frequency of diseased individuals (dd) in this population?

Under inbreeding, freq(dd) = $F \cdot$ freq(d) + (1-F)$\cdot$ [freq(d)]^2 $= (3/4) \cdot 10^{-3} + (1/4) \cdot 10^{-6} = 0.00075$

(b) What would the frequency of dd individuals be if this population was undergoing random mating?

Under random mating, freq(dd) = [freq(d)]^2 $= 10^{-6}$

(c) What is the increased disease risk due to inbreeding?

$0.00075/10^{-6} = 750$

8 (1.25 point): Recall under genetic drift that the time back to common ancestry for two random sequences follows a geometric distribution (relevant formulae can be found either in your probability notes or on the probability handout from the first part of the course).

(a) For a population of size $N = 100$, what is the probability that two random sequences will have a common ancestor no older than 100 generations ago? 1000 generations?

Recall for the geometric that the probability of (at least) one success in the first t trails is $1 - (1 - p)^t$

Here, $p = 1/(2N) = 1/200 = 0.005$. ***Hence, Prob(no ancestor older than 100 generations)***

= $1-(0.995)^{100}=0.394$

Likewise, Prob(no ancestor older than 1000 generations) **=** $1-(0.995)^{1000}=0.9933$

(b) For a population of size $N=1000$, what are probabilities for 100 and 1000 generations?

Here, $p=1/(2N)=1/2000=0.0005$. ***Hence, Prob(no ancestor older than 100 generations)*** **=** $1-(0.9995)^{100}=0.0488$

Likewise, Prob(no ancestor older than 1000 generations) **=** $1-(0.9995)^{1000}=0.394$