COLUMBIA UNIVERSITY

DEPARTMENT OF BIOSTATISTICS

P8149 – HUMAN POPULATION GENETICS

Exercise Sheet 2 (Model Answers)

Question 1

Assuming linkage equilibrium, the frequencies of the gametes are:

$$
\begin{aligned}
freq(A_1B_1) &= p_1p_2 = (.3)(.2) = .06,\\
freq(A_1B_2) &= p_1q_2 = (.3)(.3) = .09,\\
freq(A_1B_3) &= p_1r_2 = (.3)(1-.2-.3) = .15\\
freq(A_2B_1) &= q_1p_2 = (1-.3)(.2) = .14\\
freq(A_2B_2) &= q_1q_2 = (1-.3)(.3) = .21\\
freq(A_2B_3) &= q_1r_2 = (1-.3)(1-.2-.3) = .35
\end{aligned}
$$

[3 marks]

Question 2

We have $p_A + p_a = 1$ and $p_B + p_b = 1$ so that

$$
\begin{aligned}
&(p_A + p_a)(p_B + p_b) = 1\\
\therefore \quad & p_Ap_B + p_Ap_a + p_ap_B + p_ap_b = 1
\end{aligned}
$$

[3 marks]

Question 3

(a) We have

$$p_A = g_{AB} + g_{Ab}$$
$$\frac{1}{2} = \frac{1}{3} + g_{Ab}$$
$$\therefore \quad g_{Ab} = \frac{1}{6}$$

Similarly,

$$p_b = g_{Ab} + g_{ab}$$
$$\frac{1}{2} = \frac{1}{6} + g_{ab}$$
$$\therefore \quad g_{ab} = \frac{2}{6} = \frac{1}{3}$$

Finally,

$$\begin{aligned} g_{aB} &= 1 - g_{Ab} - g_{AB} - g_{ab} \\ &= 1 - \frac{1}{6} - \frac{1}{3} - \frac{1}{3} \\ &= \frac{1}{6} \end{aligned}$$

(b) Since the loci are on different chromosomes, the recombination fraction is $\theta = 1/2$. Further the disequilibrium parameter D can be calculated as

$$D = g_{AB} - p_A p_B = \frac{1}{3} - \frac{1}{2}\left(\frac{1}{2}\right) = \frac{1}{12}.$$

Therefore, the frequency of the gamete AB in the next generation is

$$g_{AB}^{*} = g_{AB} - \theta D = \frac{1}{3} - \left(\frac{1}{2}\right)\left(\frac{1}{12}\right) = \frac{7}{24}.$$

Therefore, the frequency of the game Ab in the next generation is

$$g_{Ab}^{*} = p_A - g_{AB}^{*} = \frac{1}{2} - \frac{7}{24} = \frac{5}{24}.$$

Similarly,

$$g_{aB}^{*} = p_B - g_{AB}^{*} = \frac{1}{2} - \frac{7}{24} = \frac{5}{24}$$

and

$$g_{ab}^{*} = 1 - g_{AB}^{*} - g_{Ab}^{*} - g_{aB}^{*} = 1 - \frac{7}{24} - \frac{5}{24} - \frac{5}{24} = \frac{7}{24}.$$

(c) This time $\theta = 3/10$. Using the same formulas as in (b) above,

$$g_{AB}^{*} = g_{AB} - \theta D = \frac{1}{3} - \left(\frac{3}{10}\right)\left(\frac{1}{12}\right) = \frac{37}{120},$$

$$g_{Ab}^{*} = p_A - g_{AB}^{*} = \frac{1}{2} - \frac{37}{120} = \frac{23}{120}$$

$$g_{aB}^{*} = p_B - g_{AB}^{*} = \frac{1}{2} - \frac{37}{120} = \frac{23}{120}$$

$$g_{ab}^{*} = 1 - g_{AB}^{*} - g_{Ab}^{*} - g_{aB}^{*} = 1 - \frac{37}{120} - \frac{23}{120} - \frac{23}{120} = \frac{37}{120}.$$

(d) Allowing random mating for a long time, eventually $D = 0$, so that

$$g_{AB}^{(\infty)} = p_A p_B = \frac{1}{2}.\frac{1}{2} = \frac{1}{4}.$$

Similarly,

$$g_{Ab}^{(\infty)} = g_{aB}^{(\infty)} = g_{ab}^{(\infty)} = \frac{1}{2}.\frac{1}{2} = \frac{1}{4}.$$

[1+1+1+1=4 marks]

Question 4

genotype	Mean weight (g)	Scaled weights
A_1A_1	14	4
A_1A_2	12	2
A_2A_2	6	-4

Therefore, $a = 4$ and $d = 2$.

(a) (i) Average effect of A_1 is

$$\alpha_1 = q\left\{a + d\left(q - p\right)\right\} = .1\left\{4 + 2\left(.1 - .9\right)\right\} = .24.$$

Average effect of A_2 is

$$\alpha_2 = -p\left\{a + d\left(q - p\right)\right\} = -.9\left\{4 + 2\left(.1 - .9\right)\right\} = -2.16\,.$$

(ii) Average effect of A_1 is

$$\alpha_1 = q\left\{a + d\left(q - p\right)\right\} = .4\left\{4 + 2\left(.4 - .6\right)\right\} = 1.44\,.$$

Average effect of A_2 is

$$\alpha_2 = -p\left\{a + d\left(q - p\right)\right\} = -.6\left\{4 + 2\left(.4 - .6\right)\right\} = -2.16\,.$$

(b)(i) When q = .1, the breeding values for q are

$$A_{11} = \alpha_1 + \alpha_2 = .24 + .24 = .48$$
$$A_{12} = \alpha_1 + \alpha_2 = .24 - 2.16 = 1.92$$
$$A_{22} = \alpha_2 + \alpha_2 = -2.16 - 2.16 = -4.32$$

(ii) When q = .4, the breeding values for q are

$$A_{11} = \alpha_1 + \alpha_2 = 1.44 + 1.44 = 2.88$$
$$A_{12} = \alpha_1 + \alpha_2 = 1.44 - 2.16 = -.72$$
$$A_{22} = \alpha_2 + \alpha_2 = -2.16 - 2.16 = -4.32$$

(c) (i) When q = .1, the dominance deviations are

$$D_{11} = -2q^2 d = -2\left(.1\right)^2\left(2\right) = -.04$$
$$D_{12} = 2pqd = 2\left(.9\right)\left(.1\right)\left(2\right) = .36$$
$$D_{22} = -2p^2 d = -2\left(.9\right)^2\left(2\right) = -3.24$$

When q = .4, the dominance deviations are

$$D_{11} = -2q^2 d = -2\left(.4\right)^2\left(2\right) = -.64$$
$$D_{12} = 2pqd = 2\left(.6\right)\left(.4\right)\left(2\right) = .96$$
$$D_{22} = -2p^2 d = -2\left(.5\right)^2\left(2\right) = -1.44$$

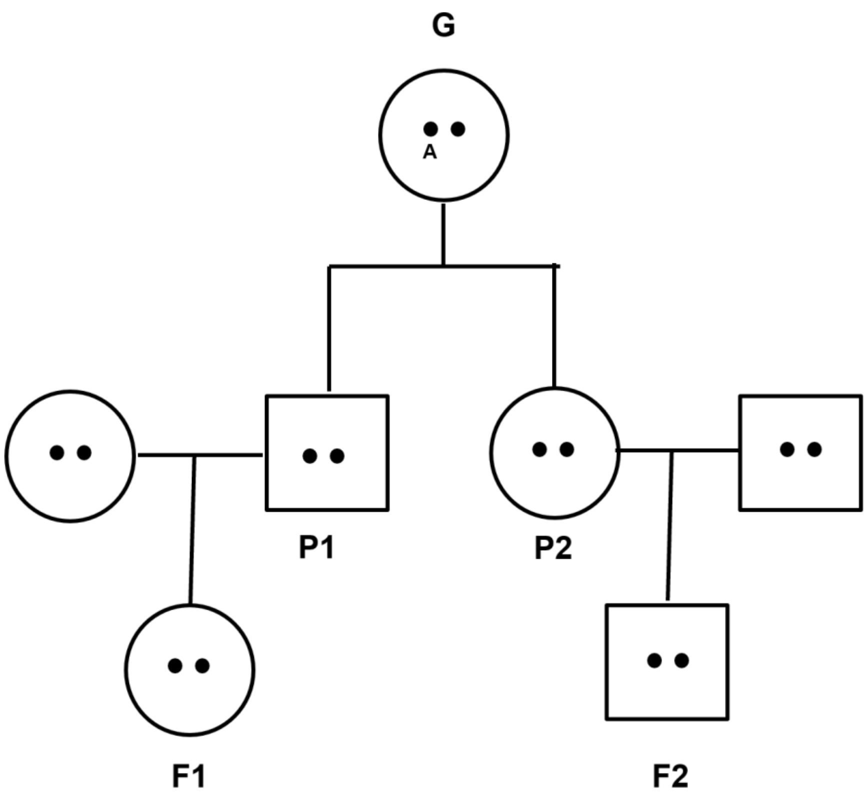
[1+1+2=4 marks]

Question 5

We have

$$\operatorname{cov}\left(X_p, Y_p\right) = r_0\left(0\right) + r_1\left(\frac{V_A}{2}\right) + r_2\left(V_A + V_D\right),$$

where r_0, r_1, r_2 are the probabilities that the two relatives share 0, 1, and 2 alleles that are ibd, respectively. Consider the two first cousins F1 and F2 emanating from parents such that one of each pair are full siblings (P1 and P2), as shown below:



It is impossible for F1 and F2 to share 2 alleles which are ibd, so $r_2 = 0$. However, sharing one allele which is ibd is possible. Suppose F1 has inherited one particular allele A from her grandparent G. The probability that F2 also inherits A is the probability that his mother inherited A (=1/2) multiplied by the probability that F2 also inherits A (=1/2). Hence $r_1 = 1/2 \times 1/2 = 1/4$ and

$$\operatorname{cov}\left(X_p, Y_p\right) = \frac{V_A}{8}$$

Now a regression of Y_p on X_p will have slope

$$b = \frac{\operatorname{cov}\left(Y_p, X_p\right)}{\operatorname{var} X_p} = \frac{V_A / 8}{V_p} = \frac{1}{8} h^2$$

Hence

$$h^2 = 8b,$$

as required.

[3+3=6 marks]