PROBLEM SET 1 – KEY - EVOLUTIONARY BIOLOGY - FALL 2017

Hardy-Weinberg-Castle (20 pts total)

1. A population of Ladybird Beetles from North Carolina was genotyped at a single autosomal allozyme locus with two alleles (F and *S*) as follows:

Genotype	*FF*	*FS*	*SS*	Total
Number	375	140	18	533 (corrected 09/05/17)

   a. Characterize this population by its genotype frequencies. (1 pt)

      Observed Genotype Frequencies:

      Freq(FF) = 375/533 = 0.704
      Freq(FS) = 140/533 = 0.263
      Freq(SS) = 18/533 = 0.034

   b. Characterize the gene pool by the allele frequencies for *F* and *S*. (1 pt)

      Since we don't know if the population is in HWC equilibrium we can estimate the allele frequencies by:

      Freq(F) = p = Freq(FF) + ½(Freq(FS))

      Allele Frequencies:

      Freq(F) = p = 375/533 + ½(140/533) = 0.835
      Freq(S) = q = 18/533 + ½(140/533) = 0.165
      (Or use $q = 1 - p$ to solve for q)

   c. Using the Hardy-Weinberg-Castle Law, predict the genotype frequencies based on the allele frequencies. (1 pt)

      Expected HWC genotype frequencies

      $p^2 = (0.835)^2 = 0.697$
      $2pq = 2(0.835)(0.165) = 0.276$
      $q^2 = (0.165)^2 = 0.027$

2. The presence of spots in this Ladybird Beetle species is controlled by a single locus. The allele ***S*** confers spots while the allele ***s*** confers no spots. A breeding study shows that the ***S*** allele is completely dominant over the ***s*** allele. In a random sample of 758 individuals 28 completely lack spots.

   a. What are the expected frequencies of the three genotypes in this population? What assumption(s) did you make to solve this problem? (2 pts)

      If you assume the population is in HWC equilibrium then,

      $q^2 = 28/758 = 0.037$, $q = (0.037)^{1/2} = 0.192$, $p = 1 - q = 0.808$

      Expected HWC genotype frequencies

      $p^2 = (0.808)^2 = 0.653$
      $2pq = 2(0.808)(0.192) = 0.311$
      $q^2 = (0.192)^2 = 0.037$

3. Tay-Sachs disease is an autosomal-recessive degenerative disorder of the brain that usually leads to death in infancy or early childhood. Among Ashkenazi Jews the incidence of the condition is about 1 in 6000 births, but among non-Jews the incidence is about 1 in 500,000 births.

   a. What incidence of the disease would be expected among the offspring of matings between Ashkenazi Jews and non-Jews? (2 pts)

      If the allele frequencies of of the Tay-Sachs mutation among Ashkenazi Jews and non-Jews are denoted q_1 and q_2, respectively, then in the initial populations,

      $(q_1) = (1/6000)^{1/2} = 0.0129$ and $(q_2) = (1/500{,}000)^{1/2} = 0.0014$

      In offspring of matings between Jews and non-Jews, the expected frequency of homozygous recessives is $(q_1)(q_2) = (0.0129)(0.0014) = 1.806 \times 10^{-5}$, or about 1 in 55,000 births.

   b. If these offspring were to mate among themselves, what incidence of the disease would be expected among their offspring? (2 pts)

      Within the hybrid population, the allele frequency of the harmful recessive allele is,

      $q' = (q_1)(q_2) + \frac{1}{2}[(q_1)(1-q_2) + (q_2)(1-q_1)] = 0.0072$ (In principle this estimate should be adjusted to take into account the non-reproduction of the homozygous recessive genotype, but the correction is very small and can be neglected)

      With random mating in this set of individuals the frequency of homozygous recessives is,

      $(q')^2 = (0.0072)^2 = 5.184 \times 10^{-5}$, or about 1 in 19,000 births.

   c. Among the Ashkenazi Jews what is the expected HWC ratio of Tay-Sachs carriers (heterozygotes) to affected individuals (Tay-Sachs homozygotes)? (2 pts)

      $(q_1) = (1/6000)^{1/2} = 0.0129$ and $p_1 = (1 - q_1) = (1 - 0.0129) = 0.9871$

      The frequency of heterozygous carriers is $2p_1q_1 = 2(0.0129)(0.9871) = 0.0255$

      The frequency of homozygous recessives is $(q_1)^2 = (1/6000) = 1.667 \times 10^{-4}$

      The ratio of heterozygous carriers to homozygous recessives is,

      $(0.0255) / (1.667 \times 10^{-4}) = 152.8$

   d. Selection tends to reduce the frequency of deleterious alleles in a population. As the frequency of the Tay-Sachs allele goes down, what is the limit to the ratio of carriers to affected individuals? (1 pt)

      As q goes to 0, the ratio $2pq / q^2$ goes to ∞

   e. How can we explain the high incidence of Tay-sachs in the Ashkenazi Jews? (1 pt)

      The most likely explanation is that the Ashkenazi Jews are a relatively small closed population. Initial founder effects, and random genetic drift that can be very strong in small populations, can cause even highly deleterious alleles to increase to fairly high frequency. Since we had not talked about drift and founder effects prior to the problem set any reasonable answer was given credit. There are some other interesting ideas in the literature including heterozygote advantage in the presence of Tuberculosis and reproductive compensation that would generate excess heterozygotes.

4. One common feature of hybridization is that there is often an asymmetry such that females of one species will mate with males from another species but the opposite is not the case. Consider a hybrid population formed from females of Species 1 and males of Species 2.

   a. If the allele frequencies in the two species are not equal to begin with, after a single round of cross-species matings will the hybrid population be in HWC proportions? Support your conclusion with an algebraic solution. (2 pts)

   Since each individual has one parent from each of the two species, the genotype frequencies at any locus (for example, the A locus) in the next generation are:

   $$(p_1+q_1)(p_2+q_2) = \underset{AA}{(p_1p_2)} + \underset{Aa}{(p_1q_2 + p_2q_1)} + \underset{aa}{(q_1q_2)}$$

   where (p_1+q_1) are the allele frequencies in Species 1, and (p_2+q_2) are the allele frequencies in Species 2

   To determine if this hybrid population is in HWC proportions you have to work out the math for 2 generations (see below). It turns out that this populations is **NOT** in HWC. There is an excess of heterozygotes.

   b. If hybrid individuals can only mate amongst themselves, how long will it take for the hybrid population to achieve HWC proportions? (1 pt)

   Allele frequencies in the hybrid population in the 1st generation:

   $p = p_1p_2 + \frac{1}{2}(p_1q_2+p_2q_1) = p_1p_2 + \frac{1}{2}(p_1(1-p_2)+p_2(1-p_1)) = \frac{1}{2}(p_1+p_2) = \text{Freq (A)}$
   $q = q_1q_2 + \frac{1}{2}(p_1q_2+p_2q_1) = \frac{1}{2}(q_1+q_2) = \text{Freq (a)}$

   You can see that in the 1st generation the allele frequencies are now the average between the original male and female frequencies.

   Thus, with random mating all following generations will have genotype frequencies:

   AA $\quad \frac{1}{4}(p_m+p_f)^2$
   Aa $\quad \frac{1}{2}(p_m+p_f)(q_m+q_f)$
   Aa $\quad \frac{1}{4}(q_m+q_f)^2$

   So, it takes two generations to get into HWC proportions. The first round of matings equalizes the frequency differences between Species 1 and Species 2 and the second round puts it into HWC.

   If you compare the genotype frequencies in the 2nd generation to the 1st generation frequencies you can see they are different. For example, for the AA homozygotes (p_1p_2) vs. $\frac{1}{4}(p_1+p_2)^2$. An easy way to see if there is an excess of homozygotes or heterozygotes is to plug in some dummy allele frequencies.

   $P_1 = 0.3$, $p_2 = 0.7$
   $q_1 = 0.7$, $q_2 = 0.3$

   The frequency of the homozygous AA genotype in the first generation is $(p_1p_2) = (0.3*0.7) = 0.21$
   In the second generation the frequency is $\frac{1}{4}(p_1+p_2)^2 = \frac{1}{4}(0.3 + 0.7)^2 = \frac{1}{4}(1)^2 = 0.25$

   This result shows that there was a deficit of homozygotes in the first generation and an excess of heterozygotes.

5. In some species of Sheep the presence of horns is controlled by a single locus and determined by an allele that is dominant in males and recessive in females. If 96% of males have horns, what proportion of females have horns? (2 pts)

   Assume that there are two alleles, H (horns) and h (no horns), and three possible genotypes:

   Genotypes: **HH** **Hh** **hh**
   p^2 2pq q^2

   In males the **H** allele is dominant so that the frequency of horned individuals includes both homozygous **HH** and heterozygous **Hh** individuals; $p^2 + 2pq = 0.96$, and the frequency of unhorned homozygous **hh** individuals is $q^2 = 0.04$. Since this is likely an autosomal gene and not sex-linked, females will have the same allele and genotype frequencies as males. However, in females the **H** allele is recessive so that only the **HH** individuals will show horns.

   So,

   $q^2 = (1 - 0.96) = 0.04$
   $q = (0.04)^{1/2} = 0.2$
   $p = 1 - 0.2 = 0.8$
   $p^2 =$ **0.64 –** Frequency of HH homozygotes in this population

   64% of females will have horns.

6. Why is it difficult for selection to eliminate a completely recessive deleterious allele from a population? Why does it take so long for a new recessive beneficial allele to go to fixation in a population? (2 pts)

   It is very difficult for natural selection to eliminate a completely recessive allele because at low frequencies most of the alleles will be in the heterozygous state where they will have no phenotypic effect (see 3d above). As the allele gets increasingly rare the frequency of homozygous genotypes becomes even lower giving selection little opportunity for selection to act against the deleterious allele. Similarly, a new recessive beneficial mutation is initially found in the heterozygous state where the beneficial phenotype is not expressed. Only when the homozygous recessive genotype is formed can selection increase the frequency of this allele. Initially this takes some time, but once the frequency increases a bit it takes off.