

7.03 Problem Set 6

Due before 5 PM on Monday, November 27

Hand in answers in recitation section or in the box outside of 68-120

1. a) Imagine a continent that has an indigenous population that has allelic variation of a gene that determines the ability of the body to store fat. Before modern times when food was scarce, a relatively rare allele (known as the “thrifty” allele) gives a heterozygous advantage of 2%. Individuals that are homozygous for the thrifty allele, because of health problems such as obesity and diabetes, have a fitness of 0.4. Calculate the expected frequency for the thrifty allele in this population.

<u>Genotype</u>	<u>Frequency</u>	<u>After selection</u>	<u>ΔFrequency</u>
A/A	p^2	p^2	0
A/a	$2pq = 2q$	$(1 + h) 2q$	$2hq$
a/a	q^2	$(1 - s) q^2$	$-Sq^2$

$$\Delta q = -Sq^2 + hq = 0 \text{ at steady state}$$

$$q = h/s = .02/.6 = .033$$

b) Explain why the rate of new mutations for the thrifty allele is not relevant for this calculation.

The rate of new mutations typically has an upper limit of 10^{-4} . This value is much smaller than the heterozygote advantage and may be regarded as negligible.

c) Now consider the same continent in modern times in which the population can be thought of having two parts: 10% of the population comes from the indigenous people described above, and 90% of the population has immigrated from Europe where the thrifty allele is so rare that its frequency is effectively 0. Modern high calorie, high fat diet individuals who are homozygous for the thrifty allele are considered to have an inherited obesity related disease. Assuming random mating of the two populations, calculate the frequency of inherited obesity on the continent.

Once the populations mix, there is a new allele frequency, q .

$$q = f(a) = .1 f(a_{\text{IND}}) + .9 f(a_{\text{EUR}}) = (.1 \times .03) + (.9 \times 0) = .0033$$

Since there is random mating, the new genotype frequency $f(a/a) = q^2$

$$f(a/a) = q^2 = (.0033)^2 = 1.1 \times 10^{-5}$$

d) What would the frequency of inherited obesity on the continent be if mating between individuals were completely assortative (i.e. no mixing between the immigrant and indigenous populations)?

There is no random mating, so we need to calculate genotype frequencies separately for each group.

$$f(a/a) \text{ in immigrant population} = 0$$

$$f(a/a) \text{ in indigenous population} = q^2 = (.033)^2 = 1 \times 10^{-3}$$

$f(a/a)$ in total population = $q^2 \times$ frequency of indigenous peoples in total population

$$f(a/a) = 1 \times 10^{-3} \times .1 = 1 \times 10^{-4}$$

2. In this problem we will derive general expressions for two of the more practical results from human population genetics – X-linked recessive traits occur more often in males than females and individuals with rare recessive traits often have parents who are related to one another.

a) Derive an expression, as a function of allele frequency (q), for the ratio of affected males to affected females for a X-linked recessive trait.

For an X-linked disorder, the frequency of affected males equals the frequency of the allele causing the disorder. Remember, males have one X-chromosome.

$$\text{Affected males} - f(X^a/Y) = q$$

$$\text{Affected females} - f(X^a/X^a) = q^2$$

$$\text{Affected males/Affected females} = q/q^2 = 1/q$$

b) Derive an expression, as a function of allele frequency (q), for the probability that an individual with a rare recessive trait will have parents who are first cousins relative to the probability of first cousin parents in the general population. Assume the *a priori* probability of parents who are first cousins is 0.005. You only need to derive a formula accurate for $q < 10^{-2}$ – make any reasonable simplifying approximations that you need.

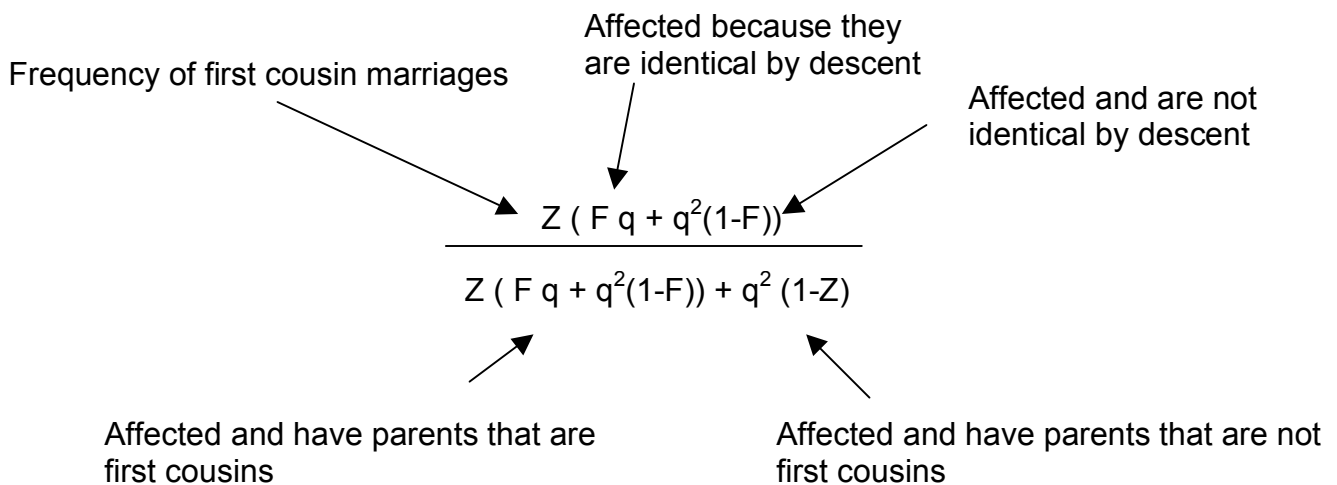
The term that we want is the following:

$$\frac{\text{Probability that an individual with a rare recessive trait will have parents who are first cousins}}{\text{Probability of first cousin parents in the general population}}$$

Let us first solve for the numerator of this term

$$\frac{\text{Percent of affected individuals with first cousin parents}}{\text{Total percent of affected individuals}}$$

This relationship can be described by the following:



Z= Frequency of first cousin marriages
 F= Inbreeding Coefficient
 q= allele frequency

$$\frac{Z (F q + q^2(1-F))}{Z (F q + q^2(1-F)) + q^2 (1-Z)}$$

This term is the numerator of our final answer. Remember that to get the final answer we must divide this term by the frequency of first cousin marriages in the population (Z). Doing this gives ...

$$\frac{F q + q^2(1-F)}{Z (F q + q^2(1-F)) + q^2 (1-Z)}$$

Simplifying ...

$$\frac{F + q (1-F)}{Z (F + q (1-F)) + q (1-Z)}$$

More simplifying ...

$$\frac{F + q (1-F)}{Z F + Z q - Z q F + q - Z q}$$

and finally

$$\frac{F + q (1-F)}{q + Z F (1 - q)}$$

This is the final simplified equation.

Notice as $q \rightarrow 0$ this term approaches $\frac{1}{Z}$

Therefore, as the allele frequency q decreases, the probability that an affected individual has parents that are first cousins increases

If we plug in the values for each of the components we arrive at the following solution:

$$\frac{1/16 + q (15/16)}{q + (1/200) (1/16)(1 - q)} = \frac{1/16 + q (15/16)}{q + ((1 - q) / 3200)}$$