BIOB480/BIOE548 notes 9/17/2024

Introduction

- HW1 and quizzes graded.
- Quiz: Median 68, Mean 64, high 96. Revisions due in one week (9/23)—get up to half credit back! Come to office hours if you need help.
- HW2 due tomorrow: any questions?

Natural selection

As mentioned above, Hardy-Weinberg Proportions assume random mating, infinite population sizes, no mutation, no migration, and no natural selection. We will now develop a single locus model for allele frequency changes that relaxes the last of these constraits. Let's begin with an extreme example—a lethal recessive disease. The following table lays out phenotypes, genotypes, and frequencies under HWP. It also details relative fitness (in which the most-fit genotype is 1, and others are scaled proportionally.)

phenotype	normal	normal	dead	total
genotype	AA	Aa	aa	1
relative fitness	1	1	0	1
freqs	p^2	$2pq$	q^2	1
freqs after selection	$p^2 * 1$	$2pq * 1$	$q^2 * 0$	$1 - q^2$
adjusted freqs	$\frac{p^2}{1-q^2}$	$\frac{2pq}{1-q^2}$	0	1

The frequency of the recessive allele (q) in the next generation is therefore the number recessive homozygotes (now 0) + 1/2 the number of heterozygotes divided by the total number of individuals minus the recessive homozgygotes that perished:

$$\frac{0 + pq}{1 - q^2} = \frac{q(1-q)}{(1-q)(1+q)} = \frac{q}{1+q}$$

(Note that since $p + q = 1$, $p = 1 - q$).

The change in the frequency of q (Δq) will be the difference between the new frequency of q (q_1) and and its initial frequency (q):

$$\Delta q = q_1 - q = \frac{q}{1+q} - q = \frac{q}{1+q} - \frac{q(1+q)}{1+q} = \frac{q - q(1+q)}{1+q} = \frac{q - q + q^2}{1+q} = \frac{-q^2}{1+q}$$

We can expand this model for nonlethal cases where homozygous recessive genotypes have lower relative fitness by a quantity s, which w will refer to as the *selection coefficient*:

phenotype	normal	normal	sickly	total
genotype	AA	Aa	aa	1
relative fitness	1	1	1 - s	1
freqs	p^2	$2pq$	q^2	1

freqs after selection	$p^2 * 1$	$2pq * 1$	$q^2 * (1 - s) = q^2 - sq^2$	$1 - sq^2$
adjusted freqs	$\frac{p^2}{1-sq^2}$	$\frac{2pq}{1-sq^2}$	$\frac{q^2-sq^2}{1-sq^2}$	1

What, then, will happen to the frequency of allele p given a q has a fitness of $1-s$? We know that its frequency in the next generation will be the adjusted frequency of homozygotes plus 1/2 the adjusted frequency of heterozygotes:

$$p_1 = \frac{p^2}{1-sq^2} + \frac{1}{2}(\frac{2pq}{1-sq^2}) = \frac{p^2+pq}{1-sq^2} = \frac{p(p+q)}{1-sq^2} = \frac{p}{1-sq^2}$$

This gives us p_1, or the frequency of p in the next generation. (Note again that one step above involves substituting $p+q$ for 1.) The change (Δ) in p between generations is simply $\Delta p = p_1 - p$:

$$\Delta p = \frac{p}{1-sq^2} - p = \frac{p}{1-sq^2} - \frac{p(1-sq^2)}{1-sq^2} = \frac{p-p(1-sq^2)}{1-sq^2} = \frac{p-p+spq^2}{1-sq^2} = \frac{spq^2}{1-sq^2}$$

This tells us three things: that p will increase in frequency, and that its degree of increase depends on the initial frequency of q and the value of the selection coefficient, s.

The last case we will address is partial dominance, which we will model with the addition of a dominance coefficient, h. (Under complete dominance, $h = 0$; under additive inheritence, $h = 0.5$.)

phenotype	normal	normal	sickly	total
genotype	AA	Aa	aa	1
relative fitness	1	1 - hs	1 - s	1
freqs	p^2	$2pq$	q^2	1
freqs after selection	p^2	$2pq(1-hs) = 2pq - 2hspq$	$q^2(1 - s) = q^2 - sq^2$	$1 - 2hspq - sq^2$
adjusted freqs	$\frac{p^2}{1-2hspq-sq^2}$	$\frac{2pq}{1-2hspq-sq^2}$	$\frac{q^2-sq^2}{1-2hspq-sq^2}$	1

Turning this into an expression for Δp is a little gnarly:

$$\Delta p = p_1 - p = \frac{p^2}{1-2hspq-sq^2} + \frac{1}{2}\frac{2pq-2hspq}{1-2hspq-sq^2} - p = \frac{p^2+pq-hspq}{1-2hspq-sq^2} - p$$

$$\Delta p = \frac{p^2+pq-hspq}{1-2hspq-sq^2} - \frac{p(1-2hspq-sq^2)}{1-2hspq-sq^2} = \frac{(p^2+pq-hspq)-p(1-2hspq-sq^2)}{1-2hspq-sq^2}$$

$$\Delta p = \frac{p((p+q-hsq)-(1-2hspq-sq^2))}{1-2hspq-sq^2}$$

Once again substituting 1 for $p+q$:

$$\Delta p = \frac{p(1-hsq-1-2hspq-sq^2)}{1-2hspq-sq^2} = \frac{p(-hsq+2hspq-sq^2)}{1-2hspq-sq^2} = \frac{p((2pq-q)hs+sq^2)}{1-2hspq-sq^2} = \frac{spq((2p-1)h+q)}{1-2hspq-sq^2}$$

Because $2p-1 = p+p-1$ and $p = 1-q$, $2p-1 = p+1-q-1 = p-q$:

$$\Delta p = \frac{spq((p-q)h+q)}{1-2hspq-sq^2}$$

That's about as good as we can get it! Liam Revell has an app to analytically solve this equation (see `08_slides.pdf` for questions): https://phytools.shinyapps.io/selection/