BIOB480/BIOE548 notes 9/24/2024

Introduction

- Practice problems: another reason to read the book!
- Schedule change: out of town at a conference next week, so no class. Quiz 2 will be an open-book take home assignment due Thursday (but without the possibility of revisions). Thursday's coursework is TBD, but may involve a worksheet, or a video. Who knows! Will post updated syllabus and plan by EOD Thursday.
- Working on HW2, will have it and HW3 graded by end of week.

Review:

Last class we discussed the impact of mutation on allele frequencies. Key models included the time in t generations required for alelle frequencies to change from q_0 to q_t:

$$t = \frac{(q_0 - q_t)}{q_0 q_t} = \frac{1}{q_t} - \frac{1}{q_0}$$

...the expected number of mutations in n genes given mutation rate mu:

$$E(\text{no. mutations}) = \mu n$$

...the probability n genes *all* have mutations:

$$P(\text{all genes have mutations}) = \mu^n$$

...the probability there are *no* mutations in n genes:

$$P(\text{no genes have mutations}) = (1 - \mu)^n$$

...the frequency of allele A_1 in the next generation given unidirectional mutation to A_2 at rate μ:

$$p_1 = p_0(1 - \mu)$$

...the change in frequency of A_1 from generation p_0 to p_1 given unidrectional mutation rate μ:

$$\Delta p = -\mu p_0$$

...the number of generations required to go from A_1 allele frequency p_0 to p_t given mutation rate u:

$$t = \frac{-ln(p_0) - ln(p_t)}{u}$$

...and the equilibrium allele frequencies of A_1 and A_2 given mutation in two directions:

$$\hat{p} = \frac{v}{u+v};\ \hat{q} = \frac{u}{u+v}$$

Mutation-Selection Equilibrium

Next, we incorporate selection. Selection more or less inevitably act on the new mutations that are being continuously added to populations as the majority are deleterious (it's much easier to break something than improve it!). Intuitively, the overall change in the frequency of q will be equal to its change due to mutation and its change due to selection—a phenomenon known as **mutation-selection equilibrium**, or the balance between the addition of deleterious alleles by mutation and their removal by selection. For a deleterious recessive allele, this is: :

$$\Delta q = \Delta q_{mutation} + \Delta q_{selection}$$

Assuming a model of simple dominance, we know that deleterious mutations increase as a product of their forward mutation rate (u) and frequency (p), and decrease at rate determined by the one locus selection models we covered last week ($\frac{-spq^2}{1-spq^2}$). Therefore:

$$\Delta q = up - \frac{spq^2}{1 - sq^2}$$

Since sq^2 is an incredible small quantity for rare alleles, the denominator is essentially 1, so

$$\Delta q = up - spq^2$$

By definition, an equilibrium is when inputs (mutations) match outputs (alleles to selection) ($\Delta q = 0$). When this is true, $up \sim spq^2$. We can divide both sides of the similarity by sp to isolate q^2:

$$0 \sim up + spq^2;\ up \sim spq^2;\ \frac{up}{sp} = \frac{u}{s} \sim q^2$$

We then take the square root of the right side of the equation to derive the equilibrium frequency of A_2:

$$\hat{q} \sim \sqrt{\frac{u}{s}}$$

In plain English, the equilibrium frequency of q will be the square root of the ratio of mutation from A_1 to A_2 to mutation from A_2 to A_1. We further know that:

- The equilibrium only depends on the mutation rate and the selection coefficient
- Increased mutation rates will increase the frequency of A_2
- Increased strength of selection against it will decrease it.

Two simple examples:

Q: What is the mutation-selection equilibrium for a recessive lethal allele if the forward mutation rate is 3 x 10^{-5}?

A:

$$q \sim \sqrt{\frac{3x10^{-5}}{1}} \sim 0.0054$$

Q: What is the mutation-selection equilibrium for a recessive deleterious allele if the forward mutation rate is 1 x 10^{-5} and the selection coefficient is 0.1?

A:

$$q \sim \sqrt{\frac{3x10^{-5}}{0.1}} \sim 0.017$$

Migration-selection equilibrium

In the same vein, we can model the counteracting forces of migration and selection. (Because mutation is rare and only changes allele frequencies very slowly, this will be more important for most scenarios discussed in class). The change in the frequency of allele q is going to be determined by the proportion of alleles in a population of interest that are contributed by migrants, a variable we call m, multiplied by the difference in the frequency of q in the migrant population and the local population:

$$\Delta q = m(q_m - q_0)$$

For example, if migrants are fixed (homogenous) for an allele that is absent from the focal population, and contribute 20% of alleles to the focal population, we expect a change in q of +0.2 in a single generation:

$$\Delta q = 0.2(1 - 0) = 0.2$$

By similar logic, the frequency of q in the generation 1 (q_1) will be the sum of the product of m and q_m and the initial frequency of q and the proportion of alleles that are NOT migrants, which simplifies to the intial allele frequency plus the migration rate multiplied by the difference betwen the frequency of q in the migrant population and focal population:

$$q_1 = (1 - m)q_0 + mq_m = q_0 - mq_0 + mq_m = q_0 + m(q_m - q_0)$$

This gives us the basis for the derivation of Δq above:

$$\Delta q = q_1 - q_0 = (q_0 + m(q_m - q_0)) - q_0 = m(q_m - q_0)$$

As an example of its application, imagine a scenario in which we wish to estimate the migration rate of domestic dog alleles into a wild dog population. We will consider a locus that is *diagnostic* (fixed in one species or population and not the other), treat the new, hybrid population as q_0, q_1 as the initial allele frequency of "pure" wild dogs, and q_m as the allele frequency of domestic dogs:

wild dog	q_0	1
hybrid	q_1	0.78
dog	q_m	0

To do this need to isolate m from $q_1 = q_0 + m(q_m - q_0)$:

$$q_1 = q_0 + m(q_m - q_0)q_1 - q_0 = m(q_m - q_0)\frac{q_1 - q_0}{q_m - q_0} = mm = \frac{0.78 - 1}{0 - 1} = 0.22$$

If migration and selection form an equilibrium allele frequency, what is it? This question is relevant to the analysis of clines and hybrid zones. We again consider the overall change in q to be the sum of the change in q due to opposing forces:

$$\Delta q = \Delta q_{selection} + \Delta q_{migration}$$