

5 SELECTION AND INTERACTIONS WITH OTHER EVOLUTIONARY PROCESSES.

5.1 VARIABLE SELECTION

Sometimes, the fitness of a genotype varies with time, place, or other circumstance. Frequency-dependent (f-d) selection is one example where the fitness of a genotype is not constant (it depends on the frequency of the genotype in the population.) There are several other kinds of variable selection. These forms of selection can, in principle, maintain genetic variation within populations. ***However, the extent to which they do so in real populations is controversial.*** We will deal with some of these topics in detail in the second half of the course.

5.1.a *Frequency-dependent selection*

Frequency dependent selection occurs with the average fitness of an allele depends upon its frequency in the population. Positive frequency dependence means the average fitness increases with allele frequency. Negative frequency dependence means the average fitness decreases with frequency. The two kinds of frequency dependence have opposite effects on the maintenance of genetic variation (see lecture slides and discussion in book).

5.1.b *Antagonistic Pleiotropy*

Some alleles have beneficial effects on one component of fitness, but deleterious effects on another component. For example, some alleles might contribute to high fertility, but might also cause increased mortality. Such alleles are said to experience antagonistic selection. Under some (relatively restrictive) circumstances, antagonistic selection can lead to maintenance of multiple alleles where some have beneficial effects on one fitness component, and others have beneficial effects on other components.

Antagonistic pleiotropy is one explanation for the evolution of senescence (aging). We will discuss evolutionary models of aging later in the course.

5.1.c *Sexual Antagonism*

If an allele that increases fitness in one sex causes a decrease in fitness in the other, then it is said to have **sexually-antagonistic** effects. Sexual antagonism can maintain genetic variation, and Haldane (1962) and Livingstone (1992) have described the conditions for the two-allele case. In general, sexual antagonism can lead to the maintenance of variance in two ways: by causing the fitness of the heterozygote to be higher than either homozygote when averaged over sexes, or by generating rather large fitness differences between the sexes. Although this phenomenon has received little attention compared to other mechanisms for maintaining variation, several recent *Drosophila* studies indicate that populations are polymorphic for sexually antagonistic alleles and that new mutations can have different effects in males and females (Mackay & Fry, 1996; Mackay, Fry, Lyman, & Nuzhdin, 1994; Mackay, Lyman, & Hill, 1995; Mackay, Lyman, Jackson, Terzian, & Hill, 1992; Rice, 1992; Rice, 1996).

Livingstone (1992) used the concept of sexual antagonism to model the maintenance of human hereditary hemochromatosis. The prevalence of hemochromatosis is over 10% in some human

populations and the disease affects men much more severely than women. The proposed advantageous effect of the allele is that women may gain protection from iron-deficiency anemia. Livingstone concluded that the level of polymorphism is consistent with a sexually antagonistic model. In order for the polymorphism to be maintained, however, the selective advantage accruing to females must be nearly exactly balanced by the disadvantage accruing to males. There is apparently no direct evidence that the selection coefficients meet these conditions.

The concept of sexual antagonism is important in some models of sexual selection, which we will discuss in the second half of the course.

5.1.d Variable Environments

It seems intuitively obvious that **spatial or temporal variation in environmental conditions** will maintain genetic variation. However, mathematical models show that variable environments will maintain genetic variation only under fairly restrictive conditions (Hedrick, 1986; Hoekstra, Bijlsma, & Dolman, 1985). Maintenance of polymorphism requires either strong selection on single loci, or a form of mean heterozygote advantage such that (averaged over all environments) heterozygotes have higher fitness than homozygotes (Hoekstra et al., 1985; Maynard Smith & Hoekstra, 1980). Hedrick (1986; 1976) considered both spatial and temporal variation in the environment, and concluded that although conditions for both cases are stringent, spatial variation is more likely to maintain polymorphism than is temporal variation. Habitat selection (Hedrick, 1990; Hoekstra et al., 1985), and limited gene flow among different environments (Christiansen, 1975) make the conditions somewhat less restrictive.

There has been continuing progress in theoretical treatment of this mechanism (Gillespie, 1991; Gillespie & Turelli, 1989). However, there have been only a few empirical tests relating quantitative variation to environmental variation. In *D. melanogaster*, Mackay (1980; 1981) observed increased V_A and h^2 for three morphological traits when she varied the concentration of alcohol spatially and temporally. Hedrick (1986) has criticized these results on methodological grounds, citing lack of appropriate controls, and pointing out several results of the experiment that are inconsistent with predictions of the model. In similar experiments, R.A. Riddle and co-workers also obtained equivocal results. They were unable to document a consistent association between genetic variation and variation in culture conditions in two species of flour beetles (Dawson & Riddle, 1983; Riddle, Dawson, & Zirkle, 1986; Zirkle & Riddle, 1983). So despite the intuitive appeal of this mechanism, its general importance in maintaining quantitative variation is uncertain.

5.2 INTERACTION OF SELECTION WITH OTHER EVOLUTIONARY PROCESSES

5.2.a Mutation-selection balance

Even though selection on rare recessives is inefficient, it will tend to decrease the frequency of rare deleterious recessives over a large number of generations. For example, **a recessive lethal at an initial frequency of 0.02 will be reduced in frequency to 0.01 in 50 generations**, if there is no recurrent mutation. However, if there is recurrent mutation to the deleterious recessive allele, there will be an equilibrium frequency of the allele, where the increase

in frequency due to recurrent mutation is exactly matched by the decrease in frequency due to selection.

Say the mutation rate from A1 → A2 (recessive deleterious allele) is equal to u , and the starting frequency of A1 is p and of A2 is q . The total number of new A2 mutations produced in a generation is then up . Selection is operating against these mutations, and the change in frequency caused by selection is $\frac{-spq^2}{W}$. If the mutation is rare, the mean fitness of the population is close to one, and the selection response can be approximated as $-spq^2$. At **equilibrium**, the mutation rate is balanced by selection, and $up = spq^2$

What is the frequency of the recessive deleterious mutation at the **mutation-selection equilibrium**?

$$up_e = sp_e q_e^2$$

$$u(1 - q_e) = s(1 - q_e)q_e^2$$

$$u - uq_e = sq_e^2 + sq_e^3$$

u is the mutation rate to recessive deleterious alleles. If q is small, then q^3 is really small, so we can set $q_e^3 = 0$. u is also small (on the order of 10^{-5} in eukaryotes), so we can also set $uq_e = 0$. Then, s

$$u = sq_e^2$$

$$q_e = \sqrt{(u/s)}$$

A recessive lethal mutation has a selection coefficient of 1. If the mutation rate is 10^{-5} , then $q_e = \sqrt{(u/s)} = \sqrt{(1/10^{-5})} = \sqrt{0.00001} = 0.003$. So, even very disadvantageous mutations like lethals can have a non-negligible frequency in populations due to recurrent mutation.

Q: What is the equilibrium frequency of a mildly deleterious recessive allele (one that reduces the fitness of a homozygote by 1%) if the mutation rate is 10^{-5} ?

Q: If you have 30,000 genes (60,000 alleles), how many mildly deleterious recessive alleles do you have?

Much of the genetic variation present in populations is thought to result from just such a balance between selection and mutation. But is most of the variation we see due to mutation-selection balance?

Q: What other forces can maintain variation?

A:

5.3 SELECTION AND GENE FLOW (COVERED IN LECTURE 3B)

Q: What if gene flow is opposed by natural selection? Could this maintain variation?

A: If the migration rate is low, relative to the strength of selection, migration-selection balance can maintain genetic variation. The equilibrium frequency of a recessive allele that is introduced into a population by migration and is opposed by selection is approximately $m q^* / s$

If the A allele reduces the fitness of heterozygotes by 10% on the island, what is the equilibrium frequency of A?

5.4 SELECTION AND GENETIC DRIFT

See Text, pp. 81-83.

Remember that the magnitude of genetic drift depends on effective population size, so the rate at which populations differentiate due to drift also depends on population size. The differences between populations (F_{ST}) will increase every generation as:

$$\Delta F_{ST} = \frac{1}{2N_e}$$

So the smaller the effective population size, the faster differences accumulate due to drift. Selection can oppose drift, but stronger selection is needed to oppose drift in smaller populations. In fact, selection will primarily determine allele frequencies, only if

$$s > \frac{1}{2N_e}$$

Otherwise, allelic frequencies are determined primarily by drift, and allelic variants are effectively neutral. This concept is the basis for the Neutral Theory of Molecular evolution, Developed by Moto Kimura in the mid-20th century. The idea is that most molecular variants are subject to such weak selection that they evolve essentially neutrally (by drift). So the rate of molecular evolution depends mostly on N_e , and very little on selection. This theory is a very useful null model in evolution, since it can be used to construct tests of evolution by selection vs. evolution by drift (neutral evolution).