

Selection (continued)

Recall Wright's equation for change in allele frequency under selection:

$$\Delta p = \frac{p(1-p)}{2\bar{w}} \frac{d\bar{w}}{dp}$$

What about the $p(1-p)/2$ term?

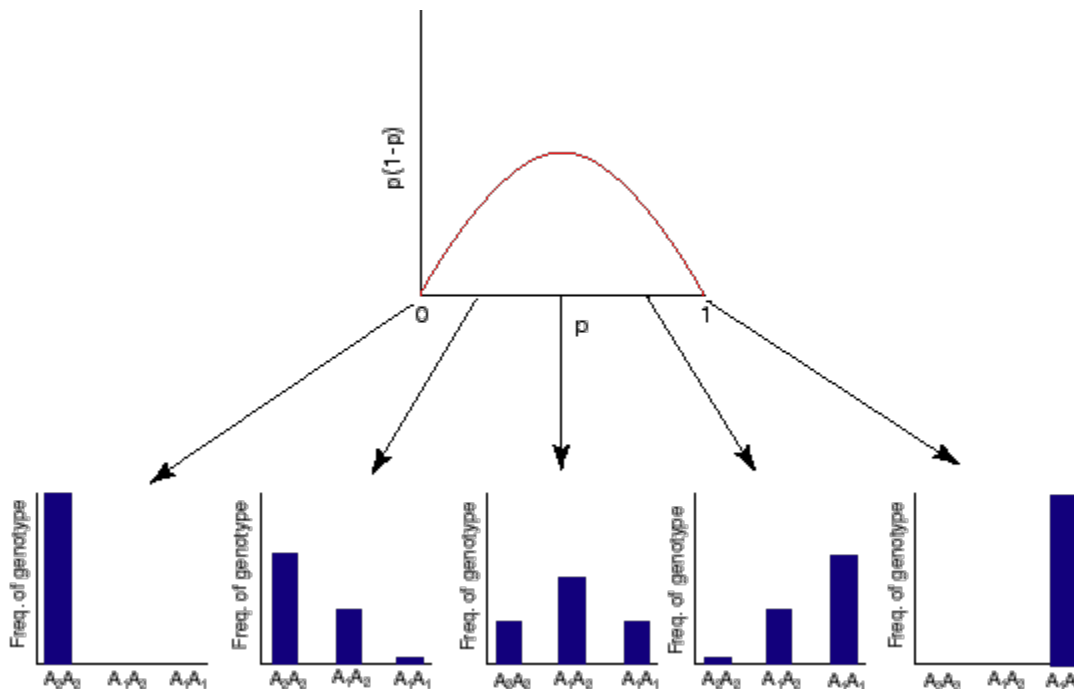
Define the value of a genotype as the frequency of A_1 within it:

$$A_1A_1 = 1$$

$$A_1A_2 = 1/2$$

$$A_2A_2 = 0$$

Then $p(1-p)/2$ is the variance in genotypes. This is zero at $p=0$ and $p=1$ and is maximized at $p=0.5$.



This just represents the fact that there is maximum variation in genotypes at intermediate allele frequencies.

The rate of evolution is thus determined by the variance in genotypes multiplied by the slope of a fitness function.

An important consequence of this is that **selection becomes relatively weak near the boundaries ($p = 0$ and $p = 1$), since the variance in genotypes is low there.**

By contrast, Mutation is strongest as an evolutionary force at the boundaries.

Maintenance of variation by mutation-selection balance

Consider the case in which allele A_2 mutates to allele A_1 at a rate μ_1 , while A_1 mutates to A_2 at rate μ_2 .



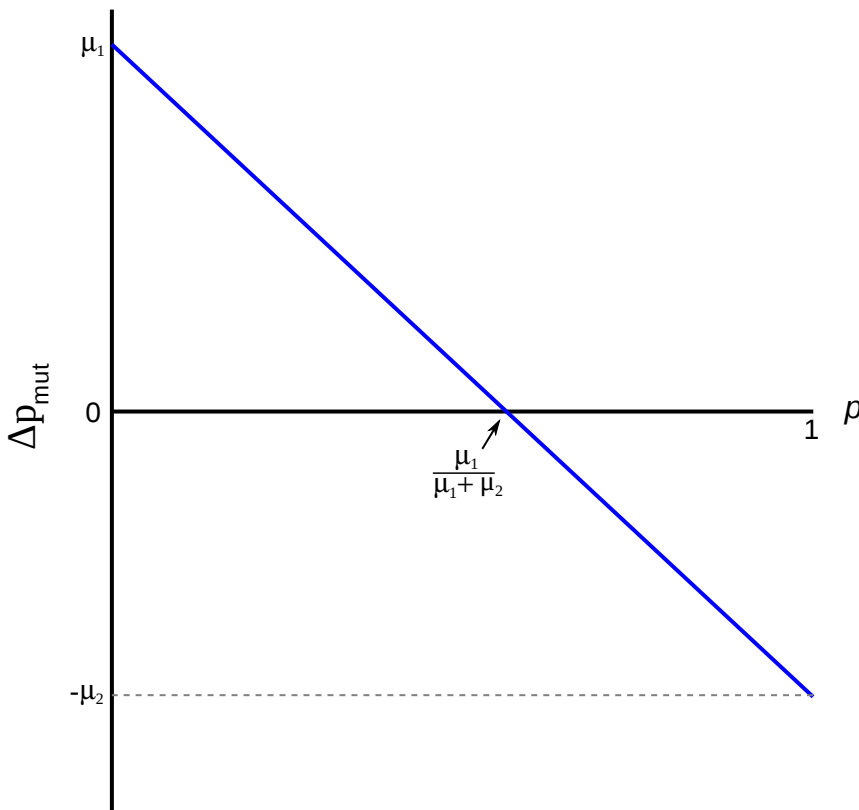
The change in allele frequency *just due to mutation* is now:

$$\Delta p_{mut} = \mu_1(1 - p) - \mu_2 p$$

We can rewrite this to see that it is a straight line with intercept μ_1 and slope $-(\mu_1 + \mu_2)$:

$$\Delta p_{mut} = \mu_1 - (\mu_1 + \mu_2)p$$

A plot of the change due to mutation as a function of p looks like this:



The important point here is that, **as an evolutionary force, mutation is**

strongest at the boundaries ($p = 0$ and $p = 1$), and weaker at intermediate allele frequencies.

Combined with the fact that selection is weak near the boundaries, this means that mutation can overpower selection near $p = 0$ and $p = 1$.

Now consider the case of selection against a recessive allele with these genotypic fitness values:

$$w_{11} = 1-s, w_{12} = 1, w_{22} = 1.$$

We wish to find the equilibrium allele frequency resulting from the combined effects of selection (reducing the frequency of A_1) and mutation (causing A_1 to reappear). This is the **mutation-selection equilibrium**.

$$\text{Here, } \bar{w} = 1 - sp^2, \text{ so } d\bar{w}/dp = -2sp.$$

At mutation-selection equilibrium, the value of p will be very small, so p^2 will be extremely small and we can assume that $\bar{w} = 1$. Also, the mutation rates will be quite small (on order 10^{-5} or smaller), so we can ignore the $\mu_2 p$ term in the change due to mutation.

Making these simplifications, denoting μ_1 as simply μ , and combining the change due to selection and mutation, we get:

$$\Delta p = -sp^2(1-p) + \mu(1-p).$$

At equilibrium, $\Delta p = 0$, so we have:

$$sp^2(1-p) = \mu(1-p)$$

So, the equilibrium frequency of a deleterious recessive allele under mutation and selection is:

$$\hat{p} = \sqrt{\frac{\mu}{s}}.$$

For example, if $\mu = 10^{-5}$ and $s = .1$ (fairly strong selection), then:

$$\hat{p} = 0.01.$$

Note that this would mean that a fair number of copies of the allele would be present in a population of a few thousand individuals.

The population of Lubbock is around 250,000 diploid people, so 500,000 haplotypes for each locus.

For our example, that means that Lubbock would have around 5,000 copies of a fairly deleterious recessive allele.

This process of mutation to slightly deleterious alleles balanced by selection,

iterated over many different loci, can maintain a substantial amount of genetic variation in a population.

The evolutionary significance of this is that natural populations harbor many rare, slightly deleterious, alleles.

This means that, if the environment changes, most populations evolve quickly in response, since there are alleles already present that are better adapted to the new environment.