

1. Strength of selection for Adh^F on ethanol-soaked fly food. Cavener and Clegg (*Evolution* 35, 1-10, 1981) used wild-caught *Drosophila melanogaster* to establish experimental populations of flies that were grown either on standard fly food (cornmeal-molasses-agar) or on the same food supplemented with 10% ethanol. For 50 generations they tracked allele frequencies at 10 different enzyme loci that were polymorphic for alleles that could be assayed by starch-gel electrophoresis of the proteins. Adh (alcohol dehydrogenase) showed by far the strongest and most consistent pattern, which is summarized in the original figure from the paper (left) and in the figure from your textbook (right) (Freeman and Herron, *Evolutionary Analysis*, 4th edn, page 185).

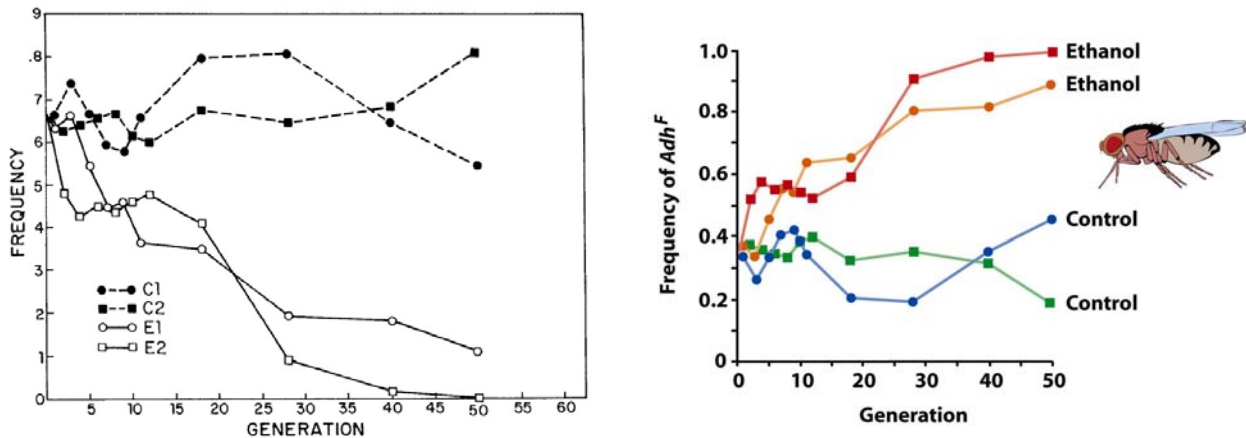


FIG. 1. Adh^S -frequencies for two control replicate populations (C_1 and C_2) and two ethanol selected replicate populations (E_1 and E_2).

The original figure plots the frequency of the *Slow* allele on the vertical axis, but the textbook figure plots the frequency of *Fast* (*i.e.*, it inverts the figure). Cavener and Clegg initiated all four experimental populations with flies taken from the same laboratory stock population, so they did not directly control the initial allele frequencies at any locus. Instead, the initial frequencies were those that occurred in the laboratory stock that was used to initiate the experiment. The initial frequency of Adh^F was $p \approx 0.35$, so the frequency of Adh^S was $q \approx 0.65$. (Note that the decimal points are missing from all but one of the numbers on the vertical axis of Cavener and Clegg’s original figure.) The paper’s main conclusion is that *Fast* was strongly favored in the ethanol-soaked experimental populations: by generation 50 it had fixed in one and reached a frequency of almost 0.9 in the other. This was not particularly surprising, because FF homozygotes were already known to show twice as much Adh enzyme activity as SS homozygotes.

From the data as displayed in the graphs you can estimate the relative fitnesses of the two alleles (*Fast* and *Slow*) in the high-ethanol environments by fitting a simple model of selection to the observed (average) change in allele frequencies over a given number of generations. To make things simple, let the fitness of the SS homozygotes be $1-s$ relative to a fitness of 1 for the FF homozygotes, and assume that the fitness of FS heterozygotes is *intermediate* ($W_{FS} = 1 - \frac{1}{2}s$, which is to say that the *Fast* and *Slow* alleles interact *additively*, or are *codominant*, with respect to fitness). Your job is to estimate s , which is the relative fitness *difference* between FF and SS homozygotes.

The expected change in allele frequency (from one generation to the next) is a function of the marginal allelic fitnesses, the mean fitness, and the allele frequency itself. Since these quantities all change with the allele frequency, we can’t easily calculate Δp exactly for more than one generation at a time. But we can *approximate* the multi-generational allele-frequency change under certain circumstances. For

$$\Delta p = pq(\bar{W}_1 - \bar{W}_2)/\bar{W}$$

example, with additive allelic interactions (heterozygote fitness intermediate between the homozygotes), the *difference* between the two homozygote *marginal fitnesses* depends on s but not p , so it does not change with the allele frequencies. And when the allele frequencies are not too far from 0.5, the product pq remains close to 0.25. In addition, the mean fitness will always be fairly close to 1 unless s is very large, so the denominator can simply be ignored. Thus, if we consider just the first few generations of the experiment, when both alleles have frequencies near 0.5, we can approximate the one-generation change in allele frequency as $0.25 \times (\text{difference between the marginal fitnesses})$.

So, here's a way to estimate s approximately. First, derive an algebraic expression for the difference between the marginal fitnesses of the two alleles when the heterozygote fitness is intermediate. (It's a simple function of s only.) Second, from the graphs above, estimate the allele-frequency change in the first few generations of the high-ethanol treatments, when both alleles have frequencies near 0.5. (Obviously, you should average over the two replicates of this treatment. For example, after 5 generations I would say that the average frequency of *Fast* has risen to around 0.5. You may think the best estimate is a bit higher or lower than this, or you may prefer to use a different number of generations, like 10 or 15 or 20. That's fine.) Third, turn your estimate of the *total* allele-frequency change into a *per-generation* change (*i.e.*, divide it by the number of generations from the beginning of the experiment). Finally, set your expression for the one-generation change in allele frequency equal to your estimate of the average allele-frequency change in the early generations of the experiment, and solve for s . $W_{SS} = 1-s$.

2. Flower color, pollinators and dominance. White flowers (genotype rr) are recessive to red (RR and Rr) in an outbreeding plant species. In a large random sample, you count 200 white-flowered plants and 800 red-flowered plants. What's the frequency of the red allele (R)? One generation later, you count 250 white and 750 red plants. What was the change in allele frequency (of r and/or R)? If this change was caused by a preference of the local pollinators (night-flying moths) for white flowers, and not by drift, or selection at some linked locus, or magic or whatever, then what were the relative fitnesses of white-flowered and red-flowered plants in the first (parental) generation?

Hint: There are harder and easier ways to frame this problem. It will make your life easier if you set the fitness of red-flowered plants to 1.0, and focus on the frequency of the dominant R allele, which will then have a marginal fitness of 1.0 regardless of its frequency.

3. Heterozygote advantage and homozygote lethality. Freeman and Herron use a computer simulation to estimate the relative fitnesses of the three genotypes in the Mukai and Burdick experiment (VV, VL and LL) as $\{0.74 : 1 : 0\}$. Derive this result "by hand", using a simple extension of our general algebraic model of selection (as explained in the lecture slides for February 4th, and on the natural selection handout). Hint: At the interior allele-frequency equilibrium, $p' = p$. This implies that $[W_V/W] = 1$.

4. Harmful alleles at mutation-selection balance. Work out the expected *allele* and *genotype frequencies* for deleterious recessive alleles with selection coefficients against the recessive homozygotes of $s = 0.01, 0.1$ and 1 , and with mutation rates (from the dominant "wild-type" allele to recessive deleterious alleles) of $10^{-5}, 10^{-6}$ and 10^{-7} per gene per generation (*i.e.*, nine cases in all). What are the implications for outbreeding species, on the assumption that many genetic loci have only minor "fine tuning" functions, as suggested by the experiment of Thatcher, Shaw and Dickinson?