Selection and genetic drift

Introduction

There are three basic facts about genetic drift that I really want you to remember, even if you forget everything else I’ve told you about it:

1. Allele frequencies tend to change from one generation to the next purely as a result of random sampling error. We can specify a probability distribution for the allele frequency in the next generation, but we cannot specify the numerical value exactly.

2. There is no systematic bias to the change in allele frequency, i.e., allele frequencies are as likely to increase from one generation to the next as to decrease.

3. Populations will eventually fix for one of the alleles that is initially present unless mutation or migration introduces new alleles.

Natural selection introduces a systematic bias in allele frequency changes. Alleles favored by natural selection tend to increase in frequency. Notice that word “tend.” It’s critical. Because there is a random component to allele frequency change when genetic drift is involved, we can’t say for sure that a selectively favored allele will increase in frequency. In fact, we can say that there’s a chance that a selectively favored allele won’t increase in frequency. There’s also a chance that a selectively disfavored allele will increase in frequency in spite of natural selection.

Loss of beneficial alleles

We’re going to confine our studies to our usual simple case: one locus, two alleles. We’re also going to consider a very simple form of directional viability selection in which the heterozygous genotype is exactly intermediate in fitness.

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\begin{array}{ccc}
A_1A_1 & A_1A_2 & A_2A_2 \\
1 + s & 1 + \frac{1}{2}s & 1
\end{array}
\]

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After solving a reasonably complex partial differential equation, it can be shown that the probability that allele $A_1$ is fixed, given that its current frequency is $p$ is

$$P_1(p) = \frac{1 - e^{-2Ne^sp}}{1 - e^{-2Ne^s}}.$$  \hspace{1cm} (1)

Now it won’t be immediately evident to you, but this equation actually confirms our intuition that even selectively favored alleles may sometimes be lost as a result of genetic drift. How does it do that? Well, it’s not too hard to verify that $P_1(p) < 1$. The probability that the beneficial allele is fixed is less than one meaning that the probability it is lost is greater than zero, i.e., there’s some chance it will be lost.

How big is the chance that a favorable allele will be lost? Well, consider the case of a newly arisen allele with a beneficial effect. If it’s newly arisen, there is only one copy by definition. In a diploid population of $N$ individuals that means that the frequency of this allele is $1/2N$. Plugging this into equation (1) above we find

$$P_1(p) = \frac{1 - e^{-2Ne^s(1/2N)}}{1 - e^{-2Ne^s}}$$

$$\approx 1 - e^{-Ne^s(1/N)} \text{ if } 2Ne^s \text{ is “large”}$$

$$\approx s \left(\frac{Ne}{N}\right) \text{ if } s \text{ is “small.”}$$

In other words, most beneficial mutations are lost from populations unless they are very beneficial. If $s = 0.2$ in an ideal population, for example, a beneficial mutation will be lost about 80% of the time.\(^4\) Remember that in a strict harem breeding system with a single male $Ne \approx 4$ if the number of females with which the male breeds is large enough. Suppose that there are 99 females in the population. Then $Ne/N = 0.04$ and the probability that this beneficial mutation will be fixed is only 0.8%.

Notice that unlike what we saw with natural selection when we were ignoring genetic drift, the strength of selection\(^5\) affects the outcome of the interaction. The stronger selection is the more likely it is that the favored allele will be fixed. But it’s also the case that the larger the population is, the more likely the favored allele will be fixed.\(^6\) Size does matter.

\(^1\)Remember, I told you that “it can be shown that” hides a lot of work.

\(^2\)The beneficial allele.

\(^3\)Unless $p = 1$.

\(^4\)The exact calculation from equation (1) gives 82% for this probability.

\(^5\)i.e., the magnitude of differences in relative viabilities

\(^6\)Because the larger the population, the smaller the effect of drift.
Table 1: Fixation probabilities for a deleterious mutation as a function of effective population size and selection coefficient for a newly arisen mutant ($p = 0.01$).

### Fixation of detrimental alleles

If drift can lead to the loss of beneficial alleles, it should come as no surprise that it can also lead to fixation of deleterious ones. In fact, we can use the same formula we’ve been using (equation (1)) if we simply remember that for an allele to be deleterious $s$ will be negative. So we end up with

$$P_1(p) = 1 - e^{2N_esp}.$$  \hspace{1cm} (2)

One implication of equation (2) that should not be surprising by now is that even a deleterious allele can become fixed. Consider our two example populations again, an ideal population of size 100 ($N_e = 100$) and a population with 1 male and 99 females ($N_e = 4$). Remember, the probability of fixation for a newly arisen allele allele with no effect on fitness is $1/2N = 5 \times 10^{-3}$ (Table 1).

### Conclusions

I’m not going to try to show you the formulas, but it shouldn’t surprise you to learn that heterozygote advantage won’t maintain a polymorphism indefinitely in a finite population. At best what it will do is to retard its loss. There are four properties of the interaction of drift and selection that I think you should take away from this brief discussion:

1. Most mutations, whether beneficial, deleterious, or neutral, are lost from the population in which they occurred.

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7Because its probability of fixation is equal to its current frequency, i.e., $1/2N$. We’ll return to this observation in a few weeks when we talk about the neutral theory of molecular evolution.

8In some cases it can actually accelerate its loss, but we won’t discuss that unless you are really interested.
2. If selection against a deleterious mutation is weak or $N_e$ is small, a deleterious mutation is almost as likely to be fixed as neutral mutants. They are “effectively neutral.”

3. If $N_e$ is large, deleterious mutations are much less likely to be fixed than neutral mutations.

4. Even if $N_e$ is large, most favorable mutations are lost.

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As with mutation and migration, what counts as large or small is determined by the product of $N_e$ and $s$. If it’s bigger than one the population is regarded as large, because selective forces predominate. If it’s smaller than one, it’s regarded as small, because drift predominates.