Balancing selection

Natural selection will usually reduce genetic diversity, either by selecting against deleterious alleles, or by selecting for beneficial alleles. Selection against deleterious alleles causes them to be removed from the population (or at least reduced to low levels), and selection for beneficial alleles can cause them to become fixed, which means that only the beneficial allele remains.

Selecting for beneficial alleles seems like a good thing, but the fitness of a phenotype depends on the environment. For example, a rattlesnake's rattle may be a good way to warn predators to stay away before people arrived in North America, but now that people tend to kill rattlesnakes when they find them it may become a liability in densely populated areas.

Under certain circumstances, though, natural selection can maintain genetic diversity. Examples of this include:

- Heterozygote advantage
- Frequency-dependent selection
- Antagonistic pleitropy
- Environmental heterogeneity/fluctuating conditions

We can explore the first two using the apps I've written for you, on the course web site.

**Heterozygote advantage**.

Remember the example of heterozygote advantage for carriers of sickle-cell anemia in Africa. Heterozygotes with one copy of the sickle-cell anemia gene do not get sickle-cell anemia, so their fitness is higher than homozygotes, who tend to die before reaching reproductive age. Homozygotes for the normal allele do not get sickle cell either, but they are more susceptible to malaria, which is a disease caused by a microorganism that lives in the blood of infected people, and is transmitted by biting insects. The sickle-cell allele confers protection against malaria, so heterozygotes have higher fitness than people who are homozygous for the normal allele as well.

Open the natural selection app we used before. Start with the number of generations set to 1000.

Set the relative fitnesses to 0.8 for RR, 1 for RS, and 0.2 for SS – heterozygotes have the highest relative fitness. We will treat R as the normal allele, and S as the sickle-cell allele.

Set the frequency of R (p) to 0.5 (which will set q to 0.5).

Look at the graphs, and answer the following questions:

A. How does the selective advantage for heterozygotes affect the frequencies of:

i. SS?

ii. S (q)?

iii. RR?

iv. RS?

v. R (p)?

B. Does changing the frequncy of R change the ultimate outcome? That is, do you still end up with both R and S maintained in the population if you make R either rare or common in the first generation?

C. If we find a cure for malaria, and make it available to everyone, what do you think would happen to the sickle-cell allele? Why?

**Frequency-dependent selection**

Now open the frequency-dependent selection app. In this app the fitness of the phenotypes depends on how common or rare the phenotype is. Each phenotype has the greatest fitness when it is rare, but as selection begins to increase the frequency of the phenotype its fitness decreases. When both of the phenotypes have the same fitness we expect selection to stop, so the frequencies of the alleles that we see should be the ones that produce phenotype frequencies with equal fitness. You can see this illustrated in the first graph in the app – the dominant and recessive phenotypes have equal fitness at a frequency of 0.5 for the dominant (and thus 1-0.5 = 0.5 for the recessive), so we expect the phenotypes to be equally common in the popuation at equilibrium.

The only thing you can change in the frequency-dependent selection app is the allele frequency for R. For simplicity, the app only models complete dominance – RR and RS have the same phenotype, so the frequency of the phenotype is the sum of the RR and RS genotype frequencies.

1. Initially p is set to 0.5 – start with that, and answer the following questions.

A. Do the **fitnesses** start out the same for both phenotypes? Do they become the same after a few generations?

B. Do the **genotype frequencies** end up at values that give equal numbers of the R and S phenotypes? That is, do you get 50% SS, and 50% combined RR and RS?

C. Do the **genotype** and **allele frequencies** stop changing once the fitnesses are equal for the two phenotypes?

2. Now change the frequency of R to 0.01.

A. The fitnesses start much further from equal than before, but do they still converge on equal values? At what generation?

B. Are there any changes in the final frequencies for the genotypes or alleles?

3. Now change the frequency of R to 0.99.

A. Does everything reach equilibrium in just 10 generations? If not, increase the number of generations until they do equilibrate – how many generations did it take for the fitnesses to become the same?

B. Once the fitnesses were the same, were the frequencies of the alleles and genotypes the same as before?

C. Explain how this shows you that frequency-dependent selection maintains alleles in the population.