Selection at one locus with many alleles, fertility selection, and sexual selection

Introduction

It's easy to extend the Hardy-Weinberg principle to multiple alleles at a single locus. In fact, we already did this when we were discussing the ABO blood group polymorphism. Just to get some notation out of the way, though, let's define x_{ij} as the frequency of genotype $A_i A_j$ and p_i as the frequency of allele A_i. Then

$$x_{ij} = \begin{cases} p_i^2 & \text{if } i = j \\ 2p_i p_j & \text{if } i \neq j \end{cases}$$

Unfortunately, the simple principles we've learned for understanding selection at one locus with two alleles don't generalize completely to selection at one locus with many alleles (or even three).

- For one locus with two alleles, heterozygote advantage guarantees maintenance of a polymorphism.

- For one locus with multiple alleles, there are many different heterozygote genotypes. As a result, there is not a unique pattern identifiable as "heterozygote advantage," and selection may eliminate one or more alleles at equilibrium even if all heterozygotes have a higher fitness than all homozygotes.

Selection at one locus with multiple alleles

When we discussed selection at one locus with two alleles, I used the following set of viabilities:

$$\begin{array}{ccc} A_1 A_1 & A_1 A_2 & A_2 A_2 \\ w_{11} & w_{12} & w_{22} \end{array}$$

You can probably guess where this is going. Namely, I'm going to use w_{ij} to denote the viability of genotype $A_i A_j$. What you probably wouldn't thought of doing is writing it as a matrix

$$
\begin{array}{ccc}
 & A_1 & A_2 \\
A_1 & w_{11} & w_{12} \\
A_2 & w_{12} & w_{22}
\end{array}
$$

Clearly we can extend an array like this to as many rows and columns as we have alleles so that we can summarize any pattern of viability selection with such a matrix. Notice that I didn't write both w_{12} and w_{21}, because (normally) an individual's fitness doesn't depend on whether it inherited a particular allele from its mom or its dad.[1]

Marginal fitnesses and equilbria

After a little algebra it's possible to write down how allele frequencies change in response to viability selection:[2]

$$
p_i' = \frac{p_i w_i}{\bar{w}} \quad ,
$$

where $p_i = \sum_j p_i w_{ij}$ is the marginal fitness of allele i and $\bar{w} = \sum_i p_i^2 w_{ii} + \sum_i \sum_{j>i} 2 p_i p_j w_{ij}$ is the mean fitness in the population.

It's easy to see[3] that if the marginal fitness of an allele is less than the mean fitness of the population it will decrease in frequency. If its marginal fitness is greater than the mean fitness, it will increase in frequency. If its marginal fitness is equal to the mean fitness it won't change in frequency. So if there's a stable polymorphism, all alleles present at that equilibrium will have marginal fitnesses equal to the population mean fitness. And, since they're all equal to the same thing, they're also all equal to one another.

That's the only thing easy to say about selection with multiple alleles. To say anything more complete would require a lot of linear algebra. The only general conclusion I can mention, and I'll have to leave it pretty vague, is that for a complete polymorphism[4] to be stable, none of the fitnesses can be too different from one another. Let's play with an example to illustrate what I mean.

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[1]If it's a locus that's subject to genomic imprinting, it may be necessary to distinguish $A_1 A_2$ from $A_2 A_1$. Isn't genetics fun?

[2]If you're ambitious (or a little weird), you might want to derive this yourself.

[3]At least it's easy to see if you've stared a lot at these things in the past.

[4]A complete polymorphism is one in which all alleles are present.

An example

The way we always teach about sickle-cell anemia isn't entirely accurate. We talk as if there is a wild-type allele and the sickle-cell allele. In fact, there are at least three alleles at this locus in many populations where there is a high frequency of sickle-cell anemia. In the wild-type, A, allele there is a glutamic acid at position six of the β chain of hemoglobin. In the most common sickle-cell allele, S, there is a valine in this position. In a rarer sickle-cell allele, C, there is a lysine in this position. The fitness matrix looks like this:

	A	S	C
A	0.976	1.138	1.103
S		0.192	0.407
C			0.550

There is a stable, complete polymorphism with these allele frequencies:[5]

$$p_A = 0.83$$
$$p_S = 0.07$$
$$p_C = 0.10 \quad .$$

If allele C were absent, A and S would remain in a stable polymorphism:

$$p_A = 0.85$$
$$p_S = 0.15$$

If allele A were absent, however, the population would fix on allele C.[6]

> **Weird property #1**: The existence of a stable, complete polymorphism does not imply that all subsets of alleles could exist in stable polymorphisms. Loss of one allele as a result of random chance could result in a cascading loss of diversity.[7]

If the fitness of AS were 1.6 rather than 1.138, C would be lost from the population, although the $A - S$ polymorphism would remain.

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[5]If you're wondering how I know that, feel free to ask. Otherwise, just take my word for it. Would I lie to you? (Don't answer that.)

[6]Can you explain why? Take a close look at the fitnesses, and it should be fairly obvious.

[7]The same thing can happen in ecological commmunities. Loss of a single species from a stable community may lead to a cascading loss of several more.

Weird property #2: Increasing the selection in favor of a heterozygous genotype may cause selection to eliminate one or more of the alleles not in that heterozygous genotype. This also means that if a genotype with a very high fitness in heterozygous form is introduced into a population, the resulting selection may eliminate one or more of the alleles already present.

Fertility selection

So far we've been talking about natural selection that occurs as a result of differences in the probability of survival, i.e., viability selection. There are, of course, other ways in which natural selection can occur:

- Heterozygotes may produce gametes in unequal frequencies, *segregation distortion*, or gametes may differ in their ability to participate in fertilization, *gametic selection*.[8]

- Some genotypes may be more successful in finding mates than others, *sexual selection.*

- The number of offspring produced by a mating may depend on maternal and paternal genotypes, *fertility selection.*

In fact, most studies that have measured components of selection have identified far larger differences due to fertility than to viability. Thus, fertility selection is a very important component of natural selection in most populations of plants and animals. As we'll see a little later, it turns out that sexual selection is mathematically equivalent to a particular type of fertility selection. But before we get to that, let's look carefully at the mechanics of fertility selection.

Formulation of fertility selection

I introduced the idea of a fitness matrix earlier when we were discussing selection at one locus with more than two alleles. Even if we have only two alleles, it becomes useful to describe patterns of fertility selection in terms of a fitness matrix. Describing the matrix is easy. Writing it down gets messy. Each element in the table is simply the average number of offspring produced by a given mated pair. We write down the table with paternal genotypes in columns and maternal genotypes in rows:

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[8]For the botanists in the room, I should point out that selection on the gametophyte stage of the life cycle (in plants with alternation of generations) is mathematically equivalent to gametic selection.

	Paternal genotype		
Maternal genotype	A_1A_1	A_1A_2	A_2A_2
A_1A_1	$F_{11,11}$	$F_{11,12}$	$F_{11,22}$
A_1A_2	$F_{12,11}$	$F_{12,12}$	$F_{12,22}$
A_2A_2	$F_{22,11}$	$F_{22,12}$	$F_{22,22}$

Then the frequency of genotype A_1A_1 after one generation of fertility selection is:[9]

$$x'_{11} = \frac{x_{11}^2 F_{11,11} + x_{11}x_{12}(F_{11,12} + F_{12,11})/2 + (x_{12}^2/4)F_{12,12}}{\bar{F}} \quad , \tag{1}$$

where $\bar{F}$ is the mean fecundity of all matings in the population.[10]

It probably won't surprise you to learn that it's very difficult to say anything very general about how genotype frequenices will change when there's fertility selection. Not only are there nine different fitness parameters to worry about, but since genotypes are never guaranteed to be in Hardy-Weinberg proportion, all of the algebra has to be done on a system of three simultaneous equations.[11] There are three weird properties that I'll mention:

1. $\bar{F}'$ may be smaller than $\bar{F}$. Unlike selection on viabilities in which fitness evolved to the maximum possible value, there are situations in which fitness will evolve to the *minimum* possible value when there's selection on fertilities.[12]

2. A high fertility of heterozygote $\times$ heterozygote matings is not sufficient to guarantee that the population will remain polymorphic.

3. Selection may prevent loss of either allele, but there may be no stable equilibria.

Conditions for protected polymorphism

There is one case in which it's fairly easy to understand the consequences of selection, and that's when one of the two alleles is very rare. Suppose, for example, that A_1 is very rare, then a little algebraic trickery[13] shows that

$$
\begin{aligned}
x'_{11} &\approx 0 \\
x'_{12} &\approx \frac{x_{12}(F_{12,22} + F_{22,12})/2}{F_{22,22}}
\end{aligned}
$$

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[9]I didn't say it, but you can probably guess that I'm assuming that all of the conditions for Hardy-Weinberg apply, except for the assumption that all matings leave the same number of offspring, on average.

[10]As an exercise you might want to see if you can derive the corresponding equations for x'_{12} and x'_{22}.

[11]And you thought that dealing with one was bad enough!

[12]Fortunately, it takes rather weird fertility schemes to produce such a result.

[13]The trickery isn't hard, just tedious. Justifying the trickery is a little more involved, but not too bad. If you're interested, drop by my office and I'll show you.

So A_1 will become more frequent if

$$(F_{12,22} + F_{22,12})/2 > F_{22,22} \tag{2}$$

Similarly, A_2 will become more frequent when it's very rare when

$$(F_{11,12} + F_{12,11})/2 > F_{11,11} \quad . \tag{3}$$

If both equation (2) and (3) are satisfied, natural selection will tend to prevent either allele from being eliminated. We have what's known as a *protected polymorphism.*

Conditions (2) and (3) are fairly easy to interpret intuitively: There is a protected polymorphism if the average fecundity of matings involving a heterozygote and the "resident" homozygote exceeds that of matings of the resident homozygote with itself.[14]

NOTE: It's entirely possible for neither inequality to be satisfied *and* for their to be a stable polymorphism. In other words, depending on where a population starts, selection may eliminate one allele or the other or keep both segregating in the population in a stable polymorphism.[15]

Sexual selection

A classic example of sexual selection is the peacock's "tail" feathers.[16] The long, elaborate feathers do nothing to promote survival of male peacocks, but they are very important in determining which males attract mates and which don't. If you'll recall, when we originally derived the Hardy-Weinberg principle we said that the matings occurred randomly. Sexual selection is clearly an instance of non-random mating. Let's go back to our original mating table and see how we need to modify it to accomodate sexual selection.

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[14]A "resident" homozygote is the one of which the populations is almost entirely composed when all but one allele is rare.

[15]Can you guess what pattern of fertilities is consistent with both a stable polymorphism and the *lack of* a protected polymorphism?

[16]The brightly colored "tail" is actually the upper tail covert.

| | | Offsrping genotype | | |
Mating	Frequency	A_1A_1	A_1A_2	A_2A_2
$A_1A_1 \times A_1A_1$	$x_{11}^f x_{11}^m$	1	0	0
A_1A_2	$x_{11}^f x_{12}^m$	$\frac{1}{2}$	$\frac{1}{2}$	0
A_2A_2	$x_{11}^f x_{22}^m$	0	1	0
$A_1A_2 \times A_1A_1$	$x_{12}^f x_{11}^m$	$\frac{1}{2}$	$\frac{1}{2}$	0
A_1A_2	$x_{12}^f x_{12}^m$	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{1}{4}$
A_1A_2	$x_{12}^f x_{22}^m$	0	$\frac{1}{2}$	$\frac{1}{2}$
$A_2A_2 \times A_1A_1$	$x_{22}^f x_{11}^m$	0	1	0
A_1A_2	$x_{22}^f x_{12}^m$	0	$\frac{1}{2}$	$\frac{1}{2}$
A_2A_2	$x_{22}^f x_{22}^m$	0	0	1

What I've done is to assume that there is random mating in the populations *among those individuals that are included in the mating pool.* We'll assume that all females are mated so that $x_{ij}^f = x_{ij}$.[17] We'll let the relative attractiveness of the male genotypes be a_{11}, a_{12}, and a_{22}. Then it's not too hard to convince yourself that

$$x_{11}^m = \frac{x_{11}a_{11}}{\bar{a}}$$
$$x_{12}^m = \frac{x_{12}a_{12}}{\bar{a}}$$
$$x_{22}^m = \frac{x_{22}a_{22}}{\bar{a}} \quad ,$$

where $\bar{a} = x_{11}a_{11} + x_{12}a_{12} + x_{22}a_{22}$. A little more algebra and you can see that

$$x_{11}' = \frac{x_{11}^2 a_{11} + x_{11}x_{12}(a_{12} + a_{11})/2 + x_{12}^2 a_{12}/4}{\bar{a}} \tag{4}$$

And we could derive similar equations for x_{12}' and x_{22}'. Now you're not likely to remember this, but equation (4) bears a striking resemblance to one you saw earlier, equation (1). In fact, sexual selection is equivalent to a particular type of fertility selection, in terms of how genotype frequencies will change from one generation to the next. Specifically, the fertility matrix corresponding to sexual selection on a male trait is:

	A_1A_1	A_1A_2	A_2A_2
A_1A_1	a_{11}	a_{12}	a_{22}
A_1A_2	a_{11}	a_{12}	a_{22}
A_2A_2	a_{11}	a_{12}	a_{22}

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[17]There's a reason for doing this called Bateman's principle that we can discuss, if you'd like.

There are, of course, a couple of other things that make sexual selection interesting. First, traits that are sexually selected in males often come at a cost in viability, so there's a tradeoff between survival and reproduction that can make the dynamics complicated and interesting. Second, the evolution of a sexually selected trait involves two traits: the male characteristic that is being selected and a female preference for that trait. In fact the two tend to become associated so that the female preference evokes a sexually selected response in males, which evokes a stronger preference in females, and so on and so on. This is a process Fisher referred to as "runaway sexual selection."

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