Lectures 3  Population Genetics. Previously, we derived

\[ p_{t+1} = \frac{p(pW_{11} + qW_{12})}{\bar{W}} \]

Note that \( pW_{11} + qW_{12} \) = mean fitness of allele 1

How to estimate mean fitness of allele 1??

Now, we want to solve for the change in \( p \), delta \( p \) (note: we dropped the subscripts for \( p_t \) to give just \( p \))

\[ \Delta p = p_{t+1} - p_t = \frac{p(pW_{11} + qW_{12})}{\bar{W}} - p \]

\[ \Delta p = p \left[ \frac{(pW_{11} + qW_{12})}{\bar{W}} - 1 \right] \]

With some algebra, you can show that (see also box 6.3 in Freeman&Heron 3rd ed)

\[ \Delta p = \frac{p[pW_{11} + qW_{12} - \bar{W}]}{\bar{W}} \]

, where the part in brackets is the “average excess”

\[ \Delta p = \frac{pq[p(W_{11} - W_{12}) + q(W_{12} - W_{22})]}{\bar{W}} \]
\[ \Delta p = \frac{pq[p(W_{11} - W_{12}) + q(W_{12} - W_{22})]}{\bar{W}} \]

There is an equilibrium when \( \Delta p = 0 \).
Where are the equilibria in terms of \( p \) and \( q \)?
What happens when \( W_{11} = W_{12} = W_{22} \)? Is that an equilibrium? If so, what kind?

Solving for the case where \( \Delta p = 0 \) and solving for \( p \), we get \( \hat{p} \) (called "\( p \) hat," where the "hat" is the indication of an equilibrium point)

\[ \hat{p} = \frac{W_{12} - W_{22}}{2W_{12} - W_{11} - W_{22}} \]

When will \( \hat{p} \) be on the interval between zero and one? In other words, when will there be a genetic polymorphism? (Show on the board.)
\[ \hat{p} = \frac{W_{12} - W_{22}}{2W_{12} - W_{11} - W_{22}} \]

When will \( \hat{p} \) be on the interval between zero and one? In other words, when will there be a genetic polymorphism? (Show on the board.)

step 1. Q: when is \( \hat{p} < 1 \)? A: when \( W_{12} > W_{11} \)

step 2. Q: when is \( \hat{p} > 0 \)? A: when \( W_{12} > W_{22} \) What does that all mean?

Now let 
\[
\begin{align*}
W_{11} &= 1 - s \\
W_{12} &= 1 \\
W_{22} &= 1 - t
\end{align*}
\]

Show that \( \hat{p} = t/(t+s) \)? What kind of equilibrium is it, assuming \( s>0, \ t>0 \)?
Question: Will natural selection always lead to an increase in population mean fitness?

Alternative stable states. Importance of starting conditions.

Is NS an optimizing force?
Remember that

\[ \Delta p = \frac{pq[p(W_{11} - W_{12}) + q(W_{12} - W_{22})]}{\bar{W}} = \frac{p[pW_{11} + qW_{12} - \bar{W}]}{\bar{W}} \]

Now let,

\[ W_{11} = 1 \]
\[ W_{12} = 1 - hs \]
\[ W_{22} = 1 - s \]

Note: the expected fitnesses are not “frequency dependent”

where \( h \) is the dominance coefficient, and \( s \) (little \( s \)) is the selection coefficient.

If \( h=1 \), which allele is dominant? If \( h=0 \), which allele is dominant? What happens when \( h=0.5 \) (we call this co-dominance)?
If we assume that \( s \) is small, then \( W_{\text{bar}} \) is approximately equal to one.

Under this assumption, we get

\[
\Delta p \approx \frac{pq[p(1-(1-hs))+q((1-hs)-(1-s))]}{1}
\]

\[
\Delta p \approx pqs[ph+q(1-h)]
\]

So, very clearly, \( \Delta p \) depends on allele frequencies, the strength of selection, and dominance.

If allele 1 is a favored dominant \((h=0)\), what is \( \Delta p \)?

If allele 1 is a favored recessive \((h=1)\), what is \( \Delta p \)?

If allele 1 is “co-dominant” \((h=1/2)\), what is \( \Delta p \)?

Assuming allele 1 is rare \((p \text{ close to zero})\), what difference does it make to the initial rate of change, \( \Delta p \)?
If we assume that $s$ is small, then $W_{\text{bar}}$ is approximately equal to one.

Under this assumption, we get

$$\Delta p \approx \frac{pq[p(1-(1-hs))+q((1-hs)-(1-s))]}{1}$$

$$\Delta p \approx pqs[ph+q(1-h)]$$

So, very clearly, $\Delta p$ depends on allele frequencies, the strength of selection, and dominance.

If allele 1 is a favored dominant ($h=0$), what is $\Delta p$? $\Delta p \approx pqs[q] \approx pq^2 s$

If allele 1 is a favored recessive ($h=1$), what is $\Delta p$? $\Delta p \approx pqs[p] \approx p^2 qs$

If allele 1 is “co-dominant” ($h=1/2$), what is $\Delta p$? $\Delta p \approx pqs / 2$

Assuming allele 1 is rare ($p$ close to zero), what difference does it make to the initial rate of change, $\Delta p$?
Now, modify your excel file to iterate

\[ p_{t+1} = \frac{p(pW_{11} + qW_{12})}{W} \]

for

\[ W_{11} = 1 \]
\[ W_{12} = 1 - hs \]
\[ W_{22} = 1 - s \]

**Assignment:** Excel Population-Genetic exercise #1 due 08 Sept 2015. There will be "individual differences" in formatting, but hand in 3 pages that have the info contained in the example given for lecture 3 on the course web site:
http://www.indiana.edu/~curtweb/Teaching/L567.html.
Graph the results for \( s=0.1 \), and \( h = 0, 0.5 \) and 1. You will need to extend the number of generations to about 1200.
Frequency of allele 1

(see popgen assign#1.xlsx)
Mutation-Selection Balance

You can also get a stable polymorphism when there is a balance between natural selection and mutation.

Let $u$ be the mutation rate from allele 1 to allele 2. Assume that that mutation rate from allele 2 to allele 1 is zero.

With this new tweak, we have

$$p_{t+1} = \frac{p(pW_{11} + qW_{12})(1-u)}{\bar{W}}$$

Let’s assume that allele 1 is dominant ($h=0$) and favored by selection. Hence it should go virtually to fixation (in an infinite population) in the absence of any opposing force, like mutation. Specifically, let’s assume that:
\[ W_{11} = 1 \]
\[ W_{12} = 1 \]
\[ W_{22} = 1 - s \]

At equilibrium, \( p_{t+1} - p = 0 \). Solving for this equilibrium, you can show that (see website lecture 3 for derivation (http://www.indiana.edu/~curtweb/Teching/L567.html)).

\[ 1 - \hat{p} = \hat{q} = \frac{\sqrt{u}}{\sqrt{s}}. \]

Hence for \( u > 0 \), allele 2 is maintained by a balance between natural selection and mutation. (see also Box 6.10 in Freeman and Heron 3rd edition). Verify this using your excel simulation.

Do you think the results are reasonably robust to the assumption of no mutation for allele 2 to 1 (at least for the present scenario)?
Optional (but highly recommended. I will assume you know the material in the exercises): conduct the two computer exercises in the “Population Genetic Exercises” Folder on Oncourse (L567). I also sent these to you by email.

Time permitting... Chalk talk: mean, variance, and covariance.

For solution for phat. See “phat solution.nb”