

Genetics...

We keep hearing how the loss of genetic diversity is an important problem, so let's delve into this issue a little further.

Let's assume we remember the basics about chromosomes, loci, alleles, genes, etc. You might want to review some of this if you don't (or come by and ask me).

I. Hardy Weinberg

Most of you should remember this from Animal Biology (or possibly genetics). But let's review the basic principles:

Suppose we have two alleles for a particular locus (or a little less accurately we could say a gene with two alleles), and following the notation from the text:

A_1 and A_2

Then an individual can be either:

A_1, A_1

A_1, A_2

A_2, A_2

If we let the proportion of $A_1 = p$, then $A_1, A_1 = p \times p = p^2$.

If we let $q = 1-p$, then we also have $A_2, A_2 = q \times q = q^2$.

And finally, A_1, A_2 would be $2pq$ (binomial expansion).

Thus we have $p^2 + q^2 + 2pq = 1$ (or 100%).

(Also, $p + q = 1$)

Essentially, if we know either p or q (or p^2 or q^2) we can figure out the proportions for everyone in the population.

In the days before DNA fingerprinting and such, this was a big deal since there was no other way of estimating the number of heterozygotes vs. the number of homozygotes (if we're talking a dominant-recessive relationship).

Even today, these techniques are not cheap, so depending on what we're trying to find out, these Hardy-Weinberg laws are quite

useful.

Incidentally, we can easily extend the Hardy Weinberg equations to three (or more) alleles:

$$p + q + r = 1, \text{ and } p^2 + 2pq + q^2 + 2qr + r^2 + 2pr = 1, \text{ etc.}$$

- fortunately, since there are only two alleles, we don't have to worry about terms involving pqr (or pqrs, etc.)

- it obviously does get more complicated, and the solution may not always be quite as easy as in the two allele case.

Now we're ready to come up with an estimate of heterozygosity (how heterogeneous is the population)

$$h_j = 1 - p_{ij}^2$$

Here j = locus j , and i = frequency of allele i . So, lets use this to estimate the heterozygosity for the example on p. 173.

$$A_1 = p = 0.6$$

Thus we have $p^2 = 0.36$, and if the 1 subscript in our A_1 is i , then we would get:

$$h_j = 1 - .36 = .64 \text{ XXX WRONG XXX.}$$

What mistake was made? Well, it's the equation above. It should read:

$$h_j = 1 - \sum p_{ij}^2, \text{ where the sum is across the } i.$$

So to fix things, we have $p^2 = p_1^2 = 0.36$, and $q^2 = p_2^2 = 0.16$ and from this we get:

$$h_j = 1 - (.36 + .16) = .48 \quad (\text{which should be obvious from the example})$$

Two comments:

- Always be a little careful - as I've mentioned a couple of times, there are mistakes in many texts.

- I am not a geneticist, and it is possible that geneticists may define things a little differently, but the math just doesn't make sense

unless it's fixed up like this.

Now the mean heterozygosity can be estimated as follows:

$$H = \frac{\sum h_j}{L}$$

where L is the number of loci examined (perhaps H-bar would be a better symbol, but I'm willing to believe this has been redefined).

So where does that leave us?

First, if we do calculate heterozygosity, what does it mean? We need to compare this to some standard.

- For example, a small isolated population of the eastern barred bandicoot (another Australian marsupial) was found to have a heterozygosity of zero.
- Before ascribing problems to this population due to zero heterozygosity, it pays to compare it to a larger population.
- As it turns out a larger population of the same species was available in Tasmania, and this, too, had a heterozygosity of zero.

Something else that's important:

- Does this mean the eastern barred bandicoot really has a heterozygosity of zero?
 - probably not. It's only for those loci that were tested that we have a heterozygosity of zero. See the discussion in the text about the problems that can arise from electrophoresis.

(only about 5 - 10% of DNA coding for proteins is sampled by electrophoresis, and as the ability to sample more DNA goes up it appears we are better able to distinguish populations and individuals).

- Don't mistake this for genetic diversity!

Some comments:

- In mammals, H varies from 0.00 to about 0.26, and averages an absurdly low 0.04. In about 11% of mammals it's zero.
- In birds, H varies from 0.00 to 0.13 and averages 0.06.
- Invertebrates are roughly three times as heterozygous as vertebrates.
- Remember this text is about eight years old - the field of genetics is changing very rapidly!
- This is based on electrophoresis. There are other methods:

“DNA fingerprinting”

- allows us to more directly sample the variability and genetic makeup of organisms.
- there are several methods of doing this, and they're getting better all the time.

An example comparing the two techniques:

Northern elephant seals had been reduced to about 100 individuals at the turn of the century (19th/20th).

Electrophoresis showed essentially no heterozygosity.

DNA fingerprinting indicated high levels of similarity, thus confirming the results of electrophoresis.

However, by 1989, the populations of northern elephant seal had recovered to about 125,000 individuals, and they were doing reasonably well.

What, exactly, is the impact of low genetic diversity?
(E.g., what is the impact in cheetahs?)

II. Genetic drift

Remember the assumptions of Hardy-Weinberg? Here they are, literally pasted in from the Animal Biology lecture notes:

- 1) Large population size (no random effects from really small populations) [OVERHEAD, fig. 23.4, p. 451].

- 2) No movement of genes in or out of population.
- 3) No net mutations (we haven't really talked about mutations).
- 4) Random mating.
- 5) No natural selection.
- (6) We could add random assortment of chromosomes)

Some of these are kind of obvious, and don't really concern us at the moment. But item 1 needs some discussion.

The problem is essentially the same as that caused by small populations and survivorship (i.e., what's the probability of surviving, as discussed last time).

Without going into the details too much, let's look at that overhead to see what's going on.

The three "rules" given on page 177 are merely the application of probability to this problem.

But, this can be quantified further. We can actually determine what we expect to happen to heterozygosity from one generation to the next.

If we ignore (as we so often do) annoying secondary influences (i.e., the other assumptions in Hardy-Weinberg), we can come up with the following relationship, that compares heterozygosity between the offspring and the parent generation:

$$H_1 = H_0 \left(1 - \frac{1}{2N} \right)$$

Notice that if N is small, the second term in the parenthesis will be larger, and more heterozygosity will be lost. If N is large, there's very little difference between H_1 and H_0 (e.g., plug in 100,000, and you get $1 - 0.00005$).

The text also present a formula for determining this over multiple generations.

III. Effective genetic population size

When populations are small, the effective size of the population may be smaller than it appears. Logically, if the sex ratio is 1:1, then it should be obvious that more alleles have a chance of making it into the next generation than if we had, for example, just one male and 9 females.

There's less of a likelihood of losing alleles if the numbers were 5 and 5 (obviously 5 males will have a better chance of transmitting all the alleles in the parent generation than 1 male).

Note that for genetic factors, a skewed sex ratio is bad, but when simply population factors are considered, a sex ratio favoring females is better. This is given by:

$$N_{eg} = \frac{4N_m N_f}{N_m + N_f}$$

- N_{eg} equals the actual population size only if $N_m = N_f = N_m^2$. Otherwise this is less than the actual population size.

- The example in the text (1 male, 9 females) is wrong (again!). The answer here should be 3.6 (which is still a lot less than 10). The second example is correct, however.

The important point to realize here is that the effective population size can be influenced by sex ratios, or other factors:

family size - it makes sense that if some individuals contribute more progeny than others, genetic diversity can be affected

fluctuating numbers - if the population is going up and down, it should also be apparent that this will be affected (the text does not provide enough details here to really figure things out unless one plugs in a lot of numbers)

For both these issues we'll dispense with the math.

IV. Estimating inbreeding

Inbreeding - mating between close relatives. Obviously, as populations decrease, the probability of this happening goes up.

In zoos, this can be estimated fairly well by looking at pedigree tables.

In the wild, one would have to keep careful track of marked individuals, but even then one can't follow a wild animal 24 hours a day.

Direct measures such as DNA fingerprinting can help determine this (it's used all the time in paternity cases or criminal investigation, and for the same reason).

If we define F as the probability that two alleles at any particular locus will be the same (due to descent), then $F = 0.25$ for a mating between full siblings (and unrelated parents), or for matings between an offspring and one of its parents.

- Incidentally, notice that if we're looking at genetic defects, the probability of a genetic defect goes way up if siblings mate. There's a reason why there are so many prohibitions against marrying within one's close family! More on this soon.

Note that since F is the probability that two alleles will be the same (by descent), it's also the amount of heterozygosity lost by this mating. If we want to preserve heterozygosity, this is not the way to do it).

An illustration of this is in the next little section, where the authors use the same example as before under Hardy-Weinberg, but add in an F value of 0.1

So instead of 0.48 for heterozygosity, we have to subtract of an additional $0.1(.6)(.4)(2) = .048$, so we get $.48 - .048 = .432$

Since the parents are related at a level of .1, a pure application of Hardy-Weinberg is invalid.

V. Inbreeding depression.

This is not necessarily the same as inbreeding

- Many species cope quite well with inbreeding (for example, species that self-fertilize).
- The main cause for concern here is the accumulation of deleterious traits (or genetic diseases).

As mentioned above, if there's a high degree of inbreeding, the amount of heterozygosity goes down. As this goes down, homozygosity increases (this had better be obvious by now!).

As homozygosity increases, the probability of getting two “bad” alleles increases. Thus the concern about inbreeding depression.

The problem, though, is that it’s not clear just what the effect of all this has on wild populations, or even if it’s possible to get accurate estimates in wild populations. Two examples:

- Superb wrens in Australia were followed for a number of years, and by observing marked individuals, it appeared that inbreeding was exceptionally high, reaching up to 21%.

- A subsequent analysis using genetic techniques showed that 65% of nestlings were actually fathered by wrens other than those attending the nest.

- Points out the difficulty of doing this in wild populations.

- Great tits in an isolated island population showed a 7.5% decrease in hatching for each 10% increase in estimated inbreeding (this was a very long term study, starting in 1912!).

- But, fledglings that survived had a higher reproductive output!

- Aargh! So what does it all mean?

- That last line is the point - we’re not at all sure what it means (a point made again by the cheetah).

It is obvious, however, that in zoos and elsewhere problems have cropped up repeatedly due to inbreeding depression. And the fact that alleles are lost is indisputable.

- A study of mice (*Peromyscus leucopus*) which were raised under highly inbred conditions showed much lower survival once released.

- Zoos take great pains to try to preserve as much diversity as possible by arranging matings etc. etc.

VI. Genetic variation and fitness

(We skipped over a little section about genetic drift and inbreeding, but it seems to state the obvious).

We’ll only summarize the main points here.

Fitness is directly related to the rate of increase or reproductive rate. Simply, if an animal is reproducing more, it's more fit (right from the definition of Natural Selection).

Inbreeding can adversely affect fitness, generally depressing it. A nice theoretical graph is shown on page 185. Note that this is THEORETICAL (better would be "hypothetical"; it's far from fact).

It does show, however, that if we can ignore everything else, fitness declines as the inbreeding coefficient (F) increases. Interestingly enough, as the level of inbreeding declines to extreme values, fitness declines again.

- Termed "outbreeding" depression.

- The authors make a big deal of this, but it seems that all this means is that as you cross different "species" you start getting into trouble (e.g., tigers & lions).

- This has been known for centuries.

Let's not worry about outbreeding, but stay focused on inbreeding depression.

- This is a case where a lot of theory would indicate that inbreeding reduces fitness, but we have no hard evidence of what's going on.

- Caution: There is very good reason to be concerned, but we just don't know enough about the interactions going on here to know what the long term consequences are.

Incidentally, the point should be made that it seems fairly obvious that inbreeding would leave a population more susceptible to pathogens. Genetic similarity has been blamed for several instances of disease outbreaks in agriculture and zoos, but we don't have a really good example from wild populations.

As the text point out: "ascribing an outbreak of disease in a species that has low heterozygosity is coincidence, not causality".

As an aside, be very careful when putting cause and effect together (mention storks and babies).

So what are we left with?

Should we try to manage wild populations for genetic diversity?

By using corridors?

By isolating different populations so that they become different from one another (thus increasing overall heterozygosity)?

There are no clear answers here.

In zoos, the answer is pretty obvious, however, and they seem to be doing the right thing. We'll talk more about zoos in a later lecture.