BIOB480/BIOE548 notes 10/8/2024

Introduction

- Extension on Exam 2 and HW5: Get them in by EOD Friday.
- No change for HW6. It's posted—get me questions Thursday. Answers to 1-5 can be used more than once. Any other clarifying questions? (Feel free to reupload if you have already submitted.)
- Miller and Waits 2002 for Thursday.

Luikheart & Cornuet

See `12_slides.pdf` for discussion questions.

Clarifying the impact of bottleneckas on heterozygosity

Previously, we derived the expected loss of heteroygosity ($1 - \frac{1}{2N}$) using the binomial distribution and a special case of a bottleneck of $N = 2$ indviduals (see `12_class_notes.pdf`). I then tried to demonstrate an alternate a way to arrive at this result on the board and botched my explanation, so it feels worthwhile to revisit.

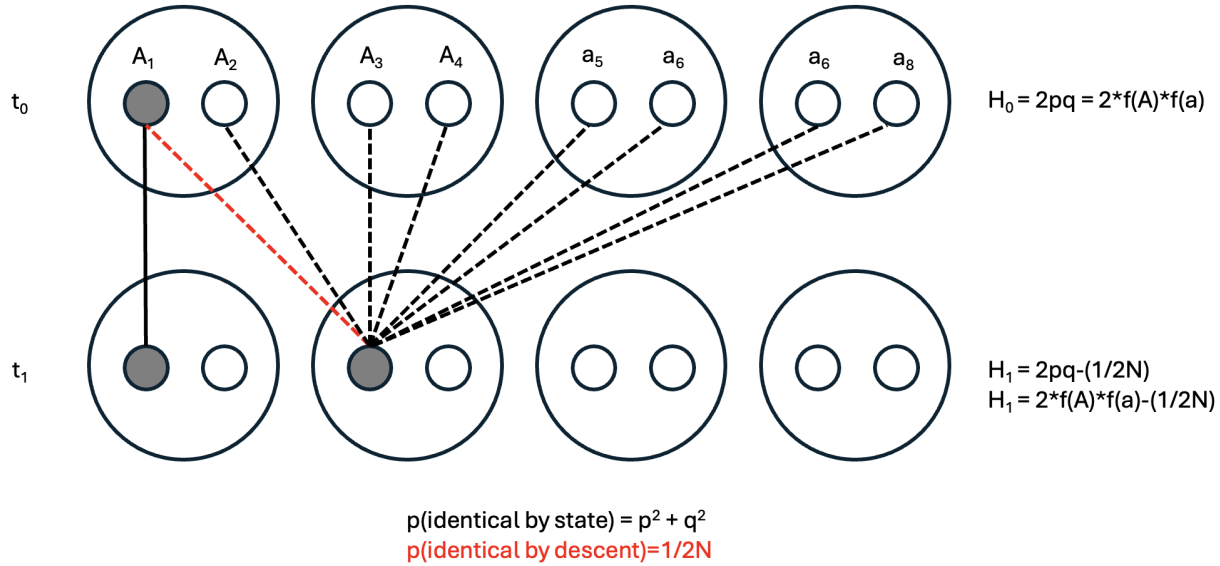
First, let's (re)define familiar terms. In a single individual, homozygosity and heterozygosity in an refer to the state of having identical or different alleles at a given locus (respectively). In a randomly mating population, however, homozygosity refers to the probability two alleles drawn at random are identical ($p^2 + q^2$) or different ($2pq$). As indicated in the parentheses, these probabilities are given by terms from Hardy-Weinberg proportions.

Given this reminder, consider a single-generation population bottleneck of size N, where a formerly large population is reduced to small numbers. The subsequent generation ($t+1$) will be formed from the $2N$ alleles present during the bottleneck. Selecting any two alleles in different individuals at random in generation $t+1$, the probability that they came from the same parental copy—in other words, are **identical by descent**—is simply 1 out of the total number of parental alleles, i.e. $\frac{1}{2N}$. (To make this more intuitive, select an allele in $t+1$ and its ancestor in t, then select a second allele in $t+1$. That second allele has $2N$ possible ancestors, with a $1/2N$ probability of the same ancestor as your first allele.)

Of course, other alleles may be **identical by state** (e.g., both be A_1s) but come from different parents. These will result in homozygotes, but not change their overall frequency.

Effective Population Size

One of the most important (and confusing) topics in population genetics, effective population size (denoted N_e) refers to the size of an ideal population that loses heterozygosity at the same rate as the observed population. Effective population size differs from census population size (N, i.e., the number of individuals you can count) due to fluctuations in population size, variation in family size, and overlapping generations. N_e/N ratios are typically very low, with 0.1 being a good estimate in the absence of any other information. (Up until this point, all our models have been implicitly using N_e! We'll be careful to clarify this in the future.)



Because in a randomly-mating population, heterozygosity (technically expected heterozygosity, or H_e) is the probability two alleles are different, this population-wide increase in identity-by-descent (i.e., homozygosity) of $1/2N$ each generation reduces H proportionally:

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

(Here, H_0 is the population's initial expected heterozygosity, while H_1 is the heterozygosity of the next generation.) Though we will not focus on it in this class, the loss of genetic diversity (as measure by $H - e$, or the probability two randomly drawn alleles are different) will vary across modes of inheritance: $\frac{1}{N_e}$ for haploid organisms, $\frac{1}{4N_e}$ $\frac{1}{1.5N_e}$ for sex chromosomes, $\frac{1}{N_{ef}}$ for mitochondrial DNA (which is maternally inherited—thus the subscript f). This tells us rates of genetic diversity loss will be greater in haploid than tetraploid organims, and in mtDNA than in sex chromosomes.

We can use the general relationship for diploid organisms above to predict the expected heterozygosity t generations in the future, which should take on a familiar form:

$$H_1 = (1 - \frac{1}{2N})H_0$$
$$H_2 = (1 - \frac{1}{2N})H_1 = (1 - \frac{1}{2N}) * (1 - \frac{1}{2N})H_0$$
$$H_2 = (1 - \frac{1}{2N})^t H_1$$
$$H_t \sim H_0 e^{\frac{-t}{2N}}$$

Heterozygosity thus decays exponentially at a rate determined by the effective population size.

We can apply this equation to determine the remaining heterozygosity at a particular time given initial heterozygosity and the (effective) number of individuals in the population. For example, if initial heterozygosity is 0.6, our population size is 50, and we are interested in the heterozgosity remaining at generation $t = 20$:

$$H_t = 0.6e^{\frac{-20}{2*50}} = 0.4912$$

To determine the effective population size required to maintain a particular level of heterozygosity in the population, we can isolate the variable N using the natural logarithm. Let's say we want to figure out the minimum population size required to maintain 40% of heterozygosity over 10 years:

$$0.40 = \frac{H_t}{H_0} = (1 - \frac{1}{2N_e})^{10} \sim e^{\frac{-10}{2N_e}}$$

$$ln(0.40) = \frac{-10}{2N_e}$$

$$ln(0.40) = \frac{-10}{2N_e}$$

$$ln(0.40) * 2N_e = -10$$

$$2N_e = \frac{-10}{ln(0.40)}; Ne = \frac{-5}{ln(0.30)} = 5.45$$

As mentioned above, effective population size will be impacted by factors like variation in the size of successive generations, fluctuating population size, and unequal sex ratios. The amount of heterozygosity retained over t generations will be the product of the effective population size in each:

$$\frac{H_t}{H_0} = \prod_i^t (1 - \frac{1}{2N_{ei}})$$

For three populations of size 10, 500, and 200, this would be:

$$\frac{H_t}{H_0} = \prod_i^t (1 - \frac{1}{2N_{ei}}) = (1 - \frac{1}{20})(1 - \frac{1}{1000})(1 - \frac{1}{400}) = 0.947$$

For fluctuating population sizes, N_e is calculated as a the harmonic mean of the population size at each of t timesteps:

$$N_e = \frac{1}{\frac{1}{t}\sum_i^t \frac{1}{N_i}}$$

Because the harmonic mean is more heavily impacted by small quantities than the arithmetic mean, Ne will be shaped by the minimum population sizes through time (which makes sense, given these miniature bottlenecks will lead to the biggest losses of heterozygosity).

It's worth looking at the derivation of effective population size under unequal sex ratios in detail. We'll start by considering the probability two alleles from different females are IBD from a female ancestor. This is equivalent to determining the loss of heterozygosity in females alone, and should be $\frac{1}{4}\frac{1}{2N_f}$. Here, $\frac{1}{4}$ refers to the probability (FF out of the possible combinations FF, FM, MF, and MM) both of selected individuals are females, while $\frac{1}{2N_f}$ refers to the probability the alleles are IBD in a female ancestor (this the numerator invoves the number of females—N_f—not overall population size). The loss of heterozygosity in males alone will have an identical form, giving us an overall expected loss of heterozygosity per generation given an unequal sex ratio:

$$\frac{1}{2N_e} = \frac{1}{4}\frac{1}{2N_f} + \frac{1}{4}\frac{1}{2N_e}$$

Isolating N_e is now just a matter of algebra:

$$\frac{1}{2N_e} = \frac{1}{8N_f} + \frac{1}{8N_m}$$

$$\frac{1}{2N_e} = (\frac{N_m}{N_m})\frac{1}{8N_f} + \frac{1}{8N_m}(\frac{N_f}{N_f}) = \frac{N_m}{8N_fN_m} + \frac{N_f}{8N_mN_f} = \frac{N_m + N_f}{8N_mN_f}$$

$$2N_e = \frac{8N_mN_f}{N_m + N_f}$$

$$N_e = \frac{4N_mN_f}{N_m + N_f}$$

For example, if we have 6 males and 2 females ($N = 8$ overall), Ne will be:

$$N_e = \frac{4 * 6 * 2}{6 + 2} = 6$$

i.e., 2 smaller than the census population size.