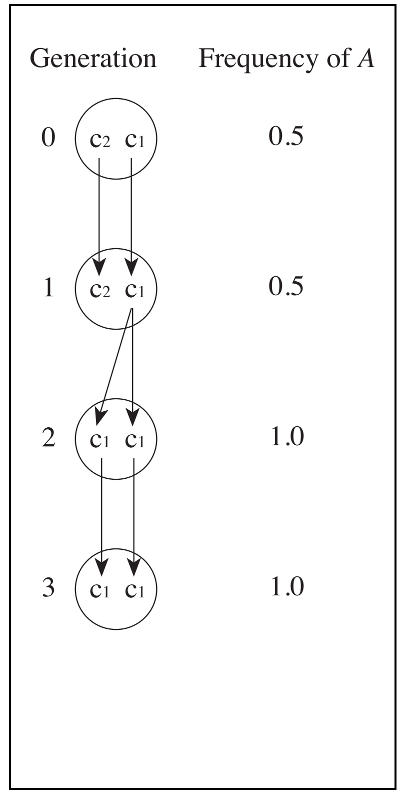
FINITE POPULATION SIZE: GENETIC DRIFT

READING: Nielsen & Slatkin pp. 21-27

– Will now consider in detail the effects of relaxing the assumption of infinite-population size.

– Start with an extreme case: a population of size $N = 1$ (an annual, self-fertilizing diploid plant).



- The sequence of events shown at right *could* occur at a particular locus:

- Notice:

  (1) Allele copies in individuals from generation 2 on are both descended from the same ancestral allele, c_1 (i.e., they are IBD)

  (2) If c_1 were an *A* allele, and c_2 an *a* allele, then the frequency of *A* changes from 1/2 to 1.

- Will see that these features are true of *any* finite sized population:

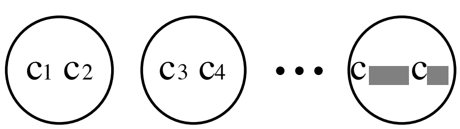
  (1) The level of inbreeding (homozygosity) increases.
  – eventually, all alleles will have descended from a single copy in an ancestor.

  (2) Allele frequencies will change due to randomness of meiosis.
  – eventually, the entire population will be homozygous.
  – This process of evolutionary change is called "**random genetic drift**."

- Inbreeding and random genetic drift are two important consequences of finite population size.
  – We already discussed another when considering mutation.

– To study consequences in more detail, it will help to study the following thought experiment:

- Consider a hermaphroditic population of size *N* with 2*N* gene copies at a locus:



- Each individual contributes a large (but equal) number of eggs and sperm to a gamete pool.

- N offspring are formed by drawing 1 egg and 1 sperm from pool at random.

- NOTE: Since $2N$ different allele copies can contribute to the gamete pool, the probability that a particular gene copy is drawn is $1/2N$.
  - – Given that, the probability that the *same* allele copy is chosen again is <u>*still*</u> $1/2N$ due to the large & equal number of gametes shed by each individual.

- **Inbreeding Due to Finite Population Size**

  – Consider how the inbreeding coefficient, f_t, changes in the population from generation $t-1$ to generation t.

  – *Fact*: Because each generation is formed by random mating between all N *individuals* (including selfing), the inbreeding and kinship coefficients are the identical.

  – Each offspring is formed by randomly choosing 2 alleles from the parent population, so:

  (a) with probability $1/2N$, the same allele copy is chosen twice
  - since the same allele is being copied, the inbreeding coefficient = 1.

  (b) with probability, $1-1/2N$, two different parental genes are chosen
  - these genes are IBD with probability = f_{t-1}.

  – Putting these together: $f_t = (1/2N)\cdot 1 + (1-1/2N)f_{t-1}$

  – If $f_0 = 0$, what is f_t?

  - Consider $h_t \equiv 1 - f_t$ = Prob. of <u>*non*</u>-identity of alleles
  - Then $h_t = (1/2N)\cdot 0 + (1-1/2N)h_{t-1} = (1-1/2N)h_{t-1}$.
  - If $h_0 = 1$, then $h_1 = (1-1/2N)$, $h_2 = (1-1/2N)^2$,...,$h_t = (1-1/2N)^t$ or

  $$f_t = 1 - h_t = 1 - \left(1 - \frac{1}{2N}\right)^t \rightarrow 1 \text{ as } t \rightarrow \infty.$$

  – i.e., Alleles at each locus will eventually be IBD with probability 1.

  - The rate of approach to complete inbreeding ($f = 1$) is roughly inversely proportional to population size.

    – E.g., for 50% of the population to become inbred, it takes ≈ 14,400 generations for populations of size N = 10,000, and ≈ 138 generations for a population of size N = 100.

- **Genetic Drift Due to Finite Population Size**

  – Two views of genetic drift:

    (a) Within a single population.
    - random changes in allele frequencies occur until $p = 0$ or 1 is reached; no further change occurs after that.

    (b) Across replicate populations.
    - Replicate population allele frequencies diverge through time.

  – Relation between the two views:

    - overall statistical properties across replicate populations are interpreted as probabilities of particular outcomes within a single population, and vice versa.

- The above idealized model was used by Wright and Fisher to study drift.

  –Will refer to it as the "Wright-Fisher model."

  – Specifically assume
    - Population of size N with $2N$ gene copies per locus
    - Suppose i of these are A alleles ($p = i/2N$)

  – Q: How many copies of A will there be in the next generation?
  A: It depends, unless $i = 0$ or $2N$

  – Better Question: What is $P_{ij} \equiv \Pr\left(N_A^{(t+1)} = j \,\middle|\, N_A^{(t)} = i\right)$?

    - Since each gene copy is drawn independently, this question is mathematically equivalent to the probability of getting j heads in $2N$ tosses of a coin whose probability of heads in any single toss is $i/2N$.

    - These probabilities are given by the **binomial distribution**:

$$P_{ij} = \binom{2N}{j} p^j (1-p)^{2N-j} \qquad \text{where} \qquad p = i/2N \quad \text{and} \quad \binom{2N}{j} = \frac{2N!}{j!(2N-j)!}$$

      – From an "across populations" view, imagine replicate populations each of size N and with i copies of the A allele, then P_{ij} = fraction of all populations with j copies of the A allele in the next generation.

  – Now let's use the Wright-Fisher model with these probabilities to study some properties of genetic drift in finite populations.

– *Q*: What is the average frequency of *A* over all replicate populations?
A: Binomial expectation: $E[j] = 2Np = 2N(i/2N) = i$ or, in terms of frequencies, $\bar{p}_1 = p_0 = i/2N$.

• Punch Line: No Change is *expected*. In fact, $\bar{p}_t = p_0$.

– *Q*: How much do allele frequencies vary across the (initially identical) replicate pops?
A: Binomial variance: $\mathrm{Var}(j) = 2Np_0(1 - p_0)$ so that $\mathrm{Var}(p_1) = p_0(1 - p_0)/2N$.

• Can show that $\mathrm{Var}(p_t) = \left[1 - (1 - 1/2N)^t\right] p_0(1 - p_0) \rightarrow p_0(1 - p_0)$ as $t \rightarrow \infty$.

• Term in brackets should remind you of f_t: $f_t = 1 - (1 - 1/2N)^t$

• In fact: $f_t = \dfrac{\mathrm{Var}(p_t)}{p_0(1 - p_0)} = \dfrac{\mathrm{Var}(p_t)}{\bar{p}_t(1 - \bar{p}_t)}$

– This suggests way to estimate *f* in an extent population.
– Remark: f_t above is exactly what we found for the Wahlund Effect!?!

– **Three Quantitative Conclusions:**

(1) PROBABILITY OF FIXATION:

Q: If Freq(*A*) = *p* initially, what is the probability *A* will become fixed or lost?

– Answer 1 (replicate populations) Know:
  • All populations will eventually become fixed (i.e., $p_\infty = 0$ or $p_\infty = 1$).
  • Since the *average* frequency of *A* never changes, *p* populations must be fixed for *A* and (1 – *p*) will have lost *A*.
  ∴ Probability *A* is fixed = *p*, lost = 1 – *p*.

– Answer 2
  • In any one population, all alleles will eventually be descended from a single gene copy.
  • The chance that the lucky gene copy is an *A* allele is just the frequency of *A* in the original population
  ∴ Probability *A* is fixed = *p*, lost = 1 – *p*

• Note: This conclusion is *independent of the population size*!

(2) DECLINE IN HETEROZYGOSITY

Q: What happens to the average frequency of heterozygotes?

– Let $H_t = 2p_t(1-p_t)$
– Can show $E(H_{t+1}) = (1-1/2N)H_t$

• Variation is lost, but very slowly if *N* is large.

– e.g., if $N = 10^6$, 0.00005% of current heterozygosity is lost per generation.

– Mendelian inheritance is thus a very powerful force for maintaining genetic variation in "large" populations (Flip side: drift is weak force in depleting genetic variation in large populations).

• Decline in expected heterozygosity does <u>not</u> imply heterozygote deficiencies within replicate subpopulations (as with the Wahlund effect).

– Randomly mating subpopulations are in approximate H-W proportions.

– The overall decline in heterozygosity is due to those subpopulations that are becoming fixed for different alleles.

(3) <u>TIME TO FIXATION</u>

Q: How many generations will it take for drift to cause fixation of either *A* or *a*?

– On average, it takes $\bar{t}(p) = -4[(1-p)\ln(1-p) + p\ln p]N$ generations.

– Note that $\bar{t}(p)$ depends on *p* and *N*
  • $\bar{t}(p) \propto N$
  • e.g., if $p = 0.5$ initially, $\bar{t}(0.5) \approx 2.7N$ generations.
  • This may be a long time for large populations.

• Population Bottlenecks

– During population crashes or colonization events, a population may experience short periods with low numbers.

• Numerous biologists have emphasized the importance of such "founder-flush" events in evolution.

– From a population genetics standpoint want to ask: What are the effects of drift during "population bottlenecks".

- *A*: Depends on
  - (a) how *small* a population becomes.
  - (b) how *long* it remains small.

– Will examine the issue from two perspectives.

(1) Effect of bottlenecks on heterozygosity

- Consider a population bottleneck of 1 generation to $N = 2$.
  - – Assume the population recovers to large size in generation 2.
- Know that $E(H_{t+1}) = (1 - 1/2N)H_t$ or $\frac{E(H_{t+1} - H_t | H_t)}{H_t} = -1/2N$

  – In this case, only 25% of the heterozygosity is expected to be lost

- Conclude: Appreciable amounts of heterozygosity will be lost due to drift only if population is small for an appreciable amount of time.

(2) Effect of bottleneck on the number of alleles

- Expect common alleles to persist, rare ones to be lost

- Probability that an allele of frequency p is lost during a 1-generation bottleneck $= P_{t0} = (1-p)^{2N}$.

- Consider the following probabilities that an allele with frequency p will be lost during a 1-generation bottleneck of size N:

	N			
	2	10	100	10,000
p				
0.5	0.06	9.5×10^{-7}	6.2×10^{-61}	$< 10^{-999}$
0.1	0.66	0.12	7.1×10^{-10}	7.1×10^{-916}
0.01	0.96	0.82	0.13	5.1×10^{-88}
0.0001	0.9996	0.998	0.98	0.14

- Notice that rare alleles are likely to be lost, however, their loss has little effect on heterozygosity.

- The time needed to recover previous heterozygosity and # of alleles depends on what mechanism restores variation.

  – E.g., with mutation this would take a long time to accomplish.

- Conclude

1) Common alleles are unlikely to be lost during a bottleneck

2) Rare alleles are highly prone to being lost.

– Implications:

- If evolution relies mainly on common alleles, a few generations of small population size won't have much effect one population's long-term adaptive potential.

- If, in contrast, evolution relies on rare alleles, then bottlenecks erode the ability of populations to adapt.