

Lecture Handout 17: Mutation in a finite population

Mutation combined with genetic drift (with little or no selection) forms the basis of neutral theories of evolution (chapter 8).

Model: mutation produces mutant allele called A_1 (not A_2 as before), which is due to a mutation in a population where only allele A_2 existed.

Initial frequency of A_1 is $p_0 = 1/(2N)$
Probability of fixation of A_1 is also $1/(2N)$
Probability of loss of A_1 is $1 - 1/(2N)$ (same
as probability of fixation of original allele A_2)

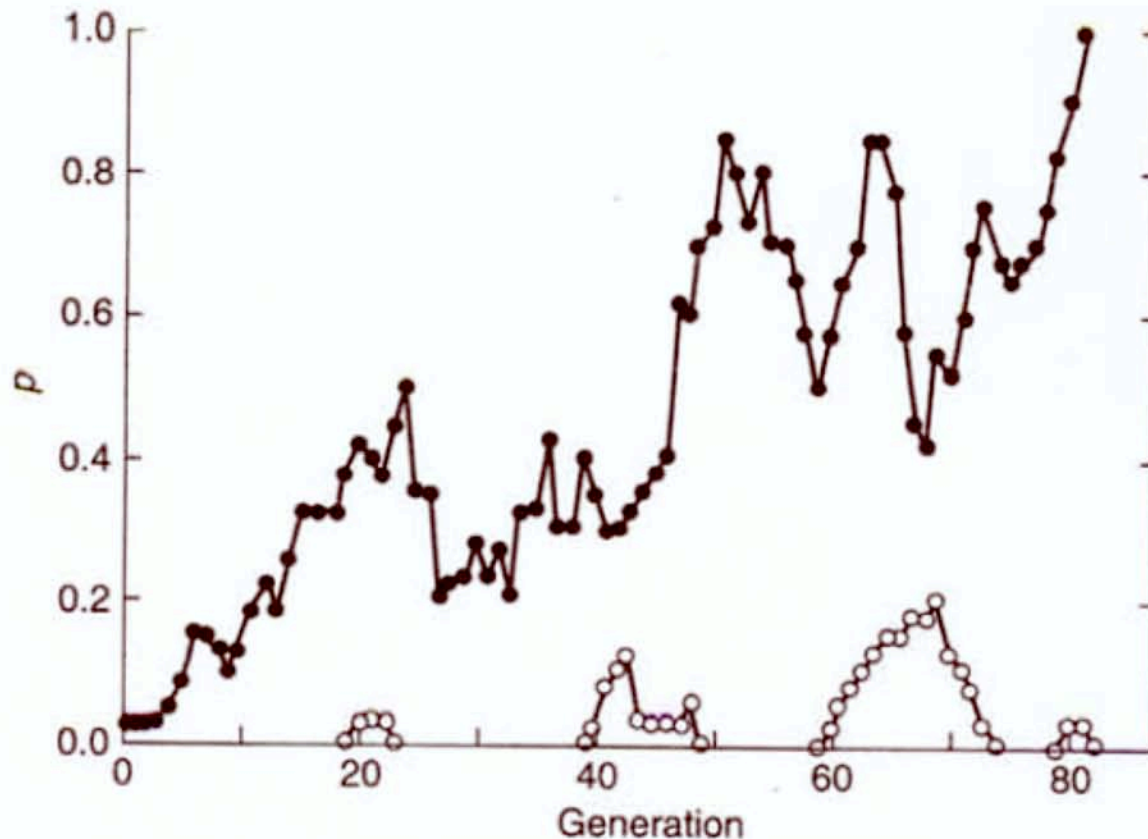


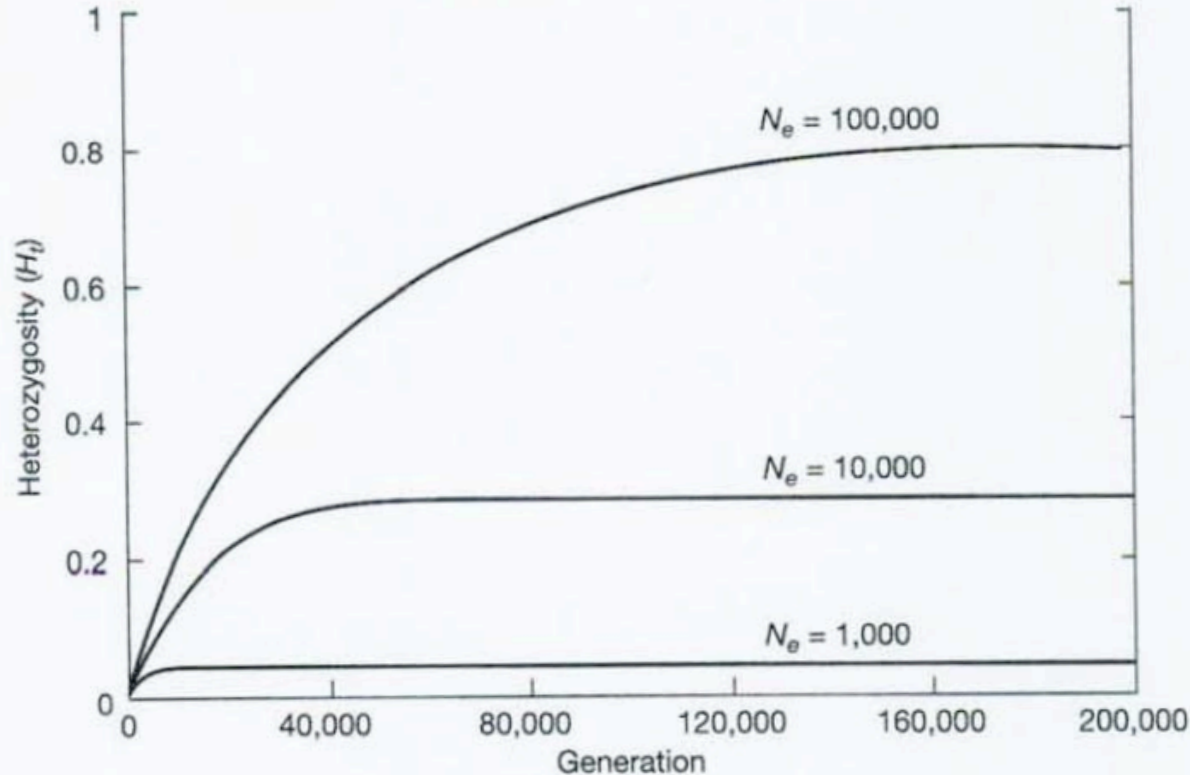
Figure 7.8. The change in allele frequency over time due to genetic drift for several mutants. One mutant (closed circles) eventually becomes fixed, whereas the others (open circles) are lost from the population. Note that the frequency of the ancestral allele is not given, and it is one minus the sum of the allele frequencies given.

For a new mutation, time to loss is short (since low initial frequency is close to zero).

Time to fixation is very long (since low initial frequency is far from 1)

Infinite allele model: each mutation assumed to lead to a new unique allele. Model finds the balance between increasing numbers of alleles due to mutation, and decreasing numbers of alleles due to drift.

Infinite allele model: balance exists between production of new alleles by mutation and the elimination of alleles by genetic drift due to finite population size



High N_e :
mutation
determines
heterozygosity

Low N_e : drift
determines
heterozygosity

Figure 7.9. The expected change in heterozygosity from mutation and genetic drift when $H_0 = 0$ and $u = 10^{-5}$ for three different effective population sizes.

Expected number of effective alleles:

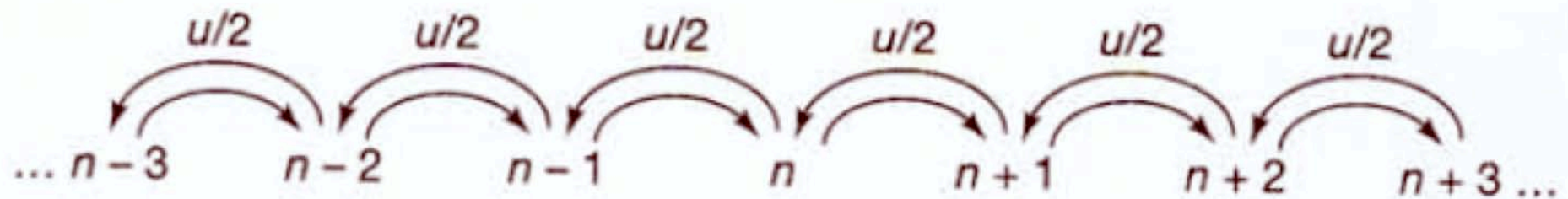
$$n_e = \frac{1}{1 - H_e}$$
$$= 4N_e u + 1$$

Theta, θ , is defined as $4N_e u$

When θ is high, mutation determines heterozygosity and genetic diversity is high.

When θ is low, genetic drift determines heterozygosity and genetic diversity is low.

Stepwise mutation model: applied to microsatellite data, assumes that mutation occurs only to adjacent states (ie one repeat higher or lower for the short tandem repeat)



But STRs (= microsatellites) may actually follow a **two-phase model** with some single-step and some larger step mutations.

After a bottleneck: reduced genetic diversity will increase over time due to mutation. Effects of the bottleneck will persist longer for genetic markers that mutate more slowly.

TABLE 7.4 The observed heterozygosity for three types of genetic variants in cheetahs, mountain lions, and African lions and the theoretical equilibrium values for two effective population sizes.

	<i>Allozymes</i>	<i>Minisatellites</i>	<i>Microsatellites</i>
Observed			
Cheetahs	0.0072	0.435	0.47
Mountain lions	0.018–0.067	0.579	0.35
African lions	0.037	0.481	0.47
Theoretical			
$N_e = 200$	0.0008		0.380
$N_e = 2000$	0.0079		0.757

Selection and mutation in finite populations:

Lethal or detrimental alleles pushed by selection to low frequencies will be removed by genetic drift (increased **purging**)

But if selection coefficient $s < 1/(2N)$ then deleterious alleles are fixed by drift as if they were neutral. **Mutation meltdown**: as population decreases, mutants with larger detrimental effects become effectively neutral and fixed, lowering population fitness.

Estimation of mutation rates:

For dominant or co-dominant mutants, in a single generation:

$$\hat{u} = \frac{x}{2N}$$

N is offspring examined, x is number of mutants

For recessive mutants, homozygote dominant and recessive individuals are crossed, with offspring examined for recessive phenotypes:

$$\hat{u} = \frac{x}{N}$$

Factors that influence mutation rate:

Mutations tend to be male-biased

More mutations with increased paternal age

Potential effect of generation time

Mutator genes: increase the general mutation rate across loci, eg genes involved in DNA replication or repair.