

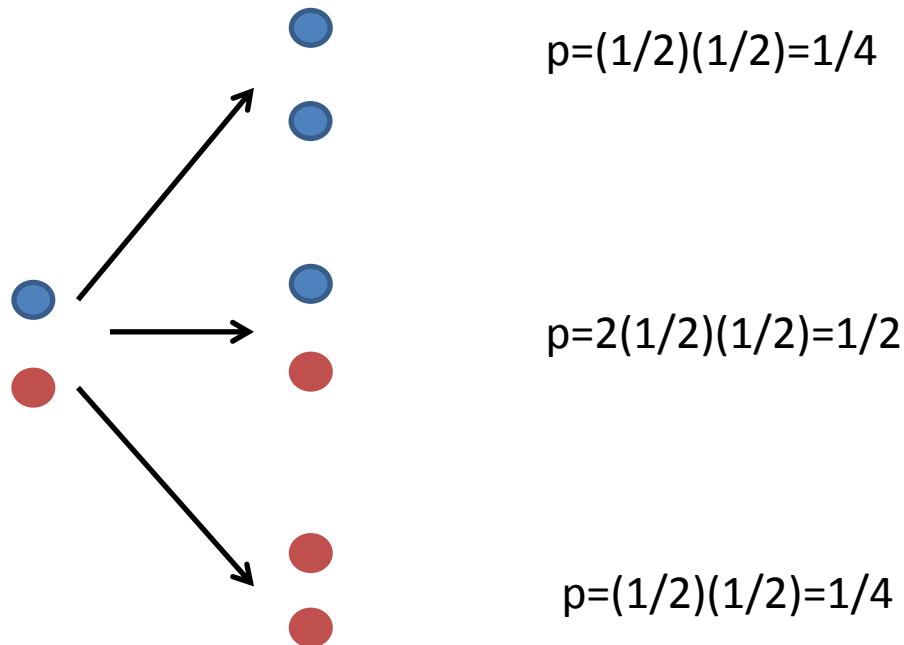
Variation: Genetic Drift

Genetic Drift

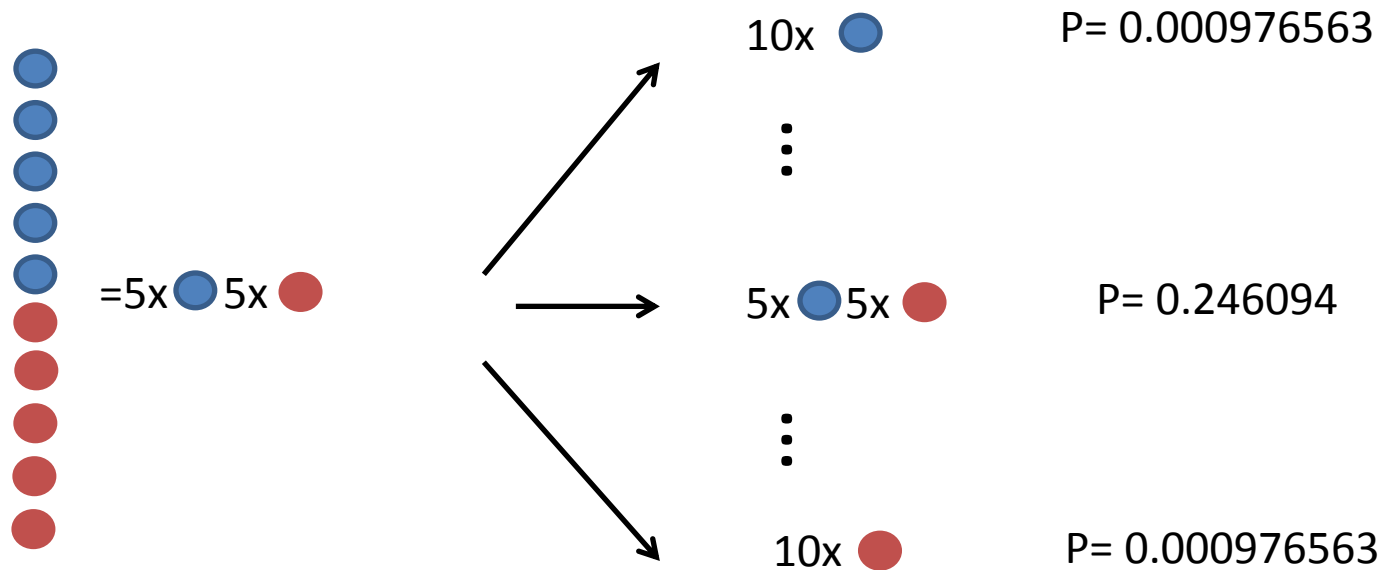
- Randomness will change gene frequencies, even if no other force acts on the population
- This randomness is caused by
 - Randomness in number of offspring
 - Randomness in mortality
- This process can be modeled by random sampling

Wright-Fisher model

Very small population sizes



Wright-Fisher model



$$P(k) = \binom{n}{k} (1-p)^{n-k} p^k$$

Wright Fisher Model

$$P(k) = \binom{n}{k} (1-p)^{n-k} p^k$$

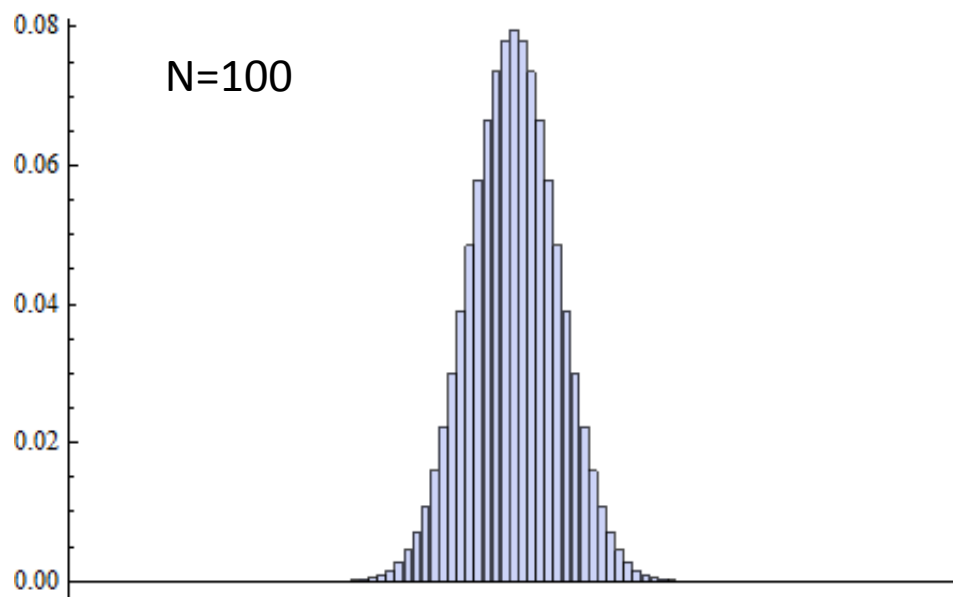
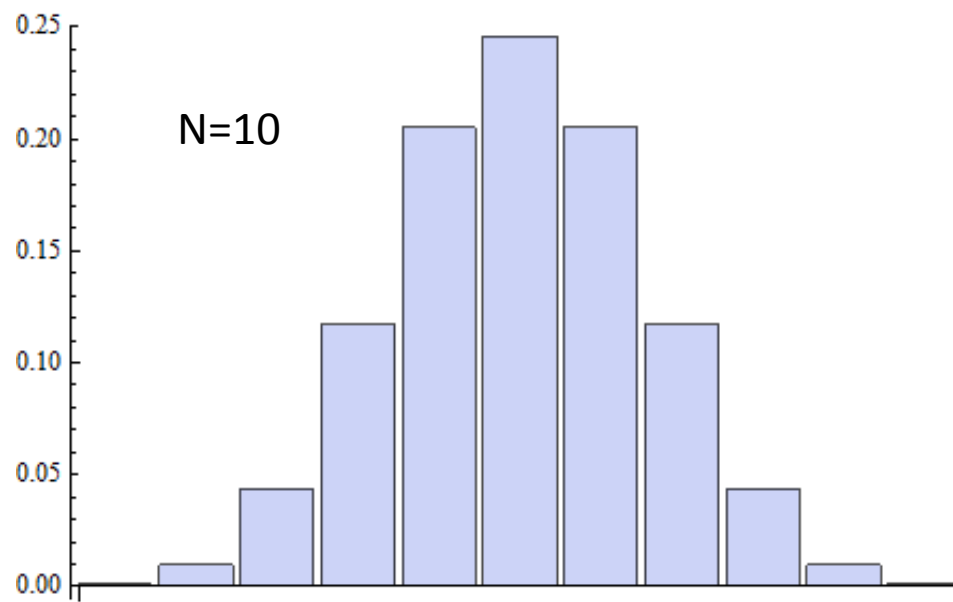
$$E[k] = np$$

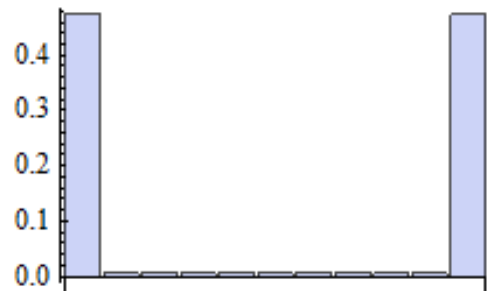
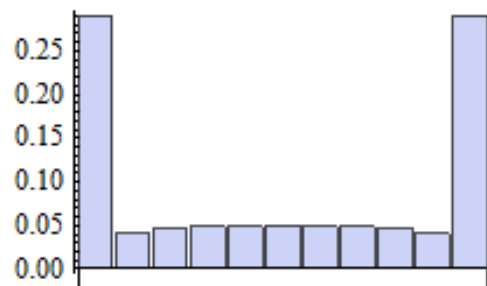
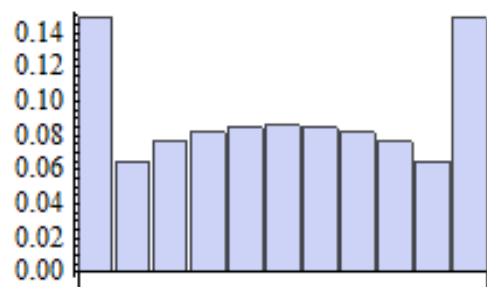
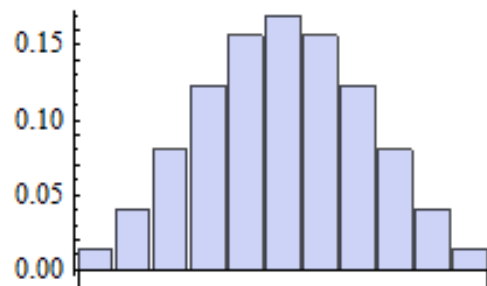
$$Var[k] = np(1-p)$$

For a neutral allele:

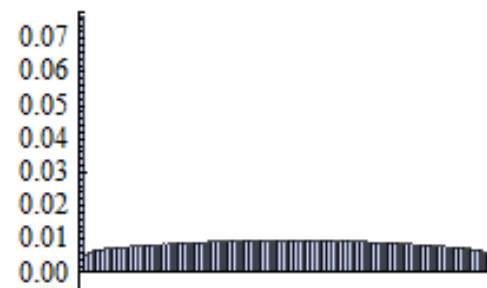
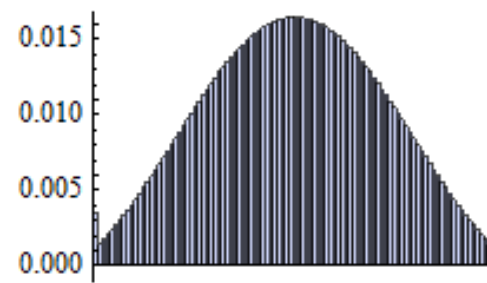
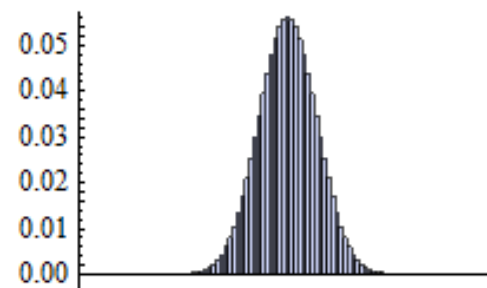
$$E[p_{t+1}] = p_t$$

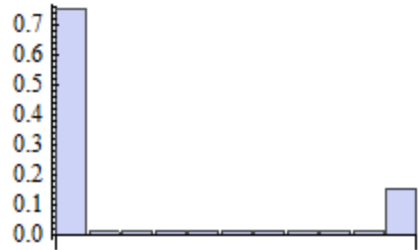
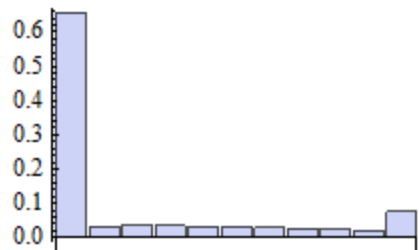
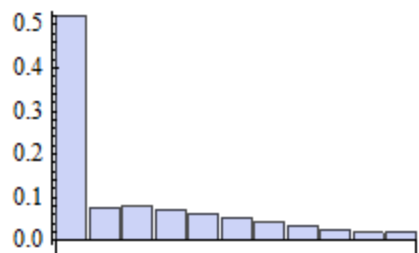
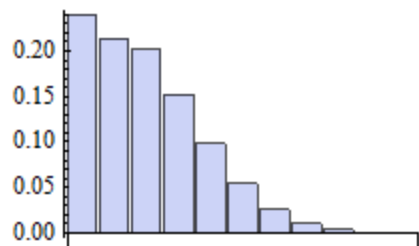
$$Var[p_{t+1}] = \frac{p_t(1-p_t)}{n}$$



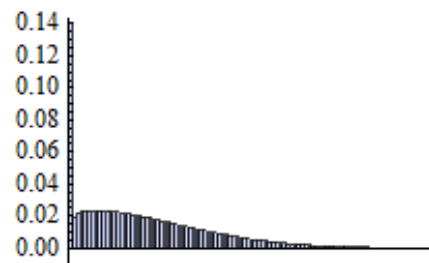
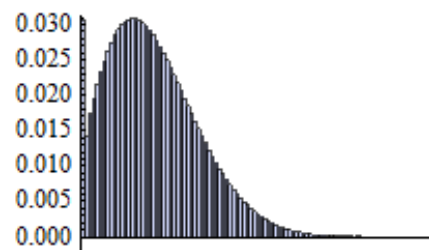
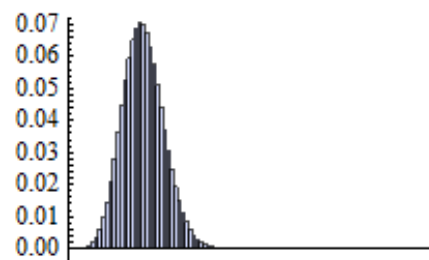


time

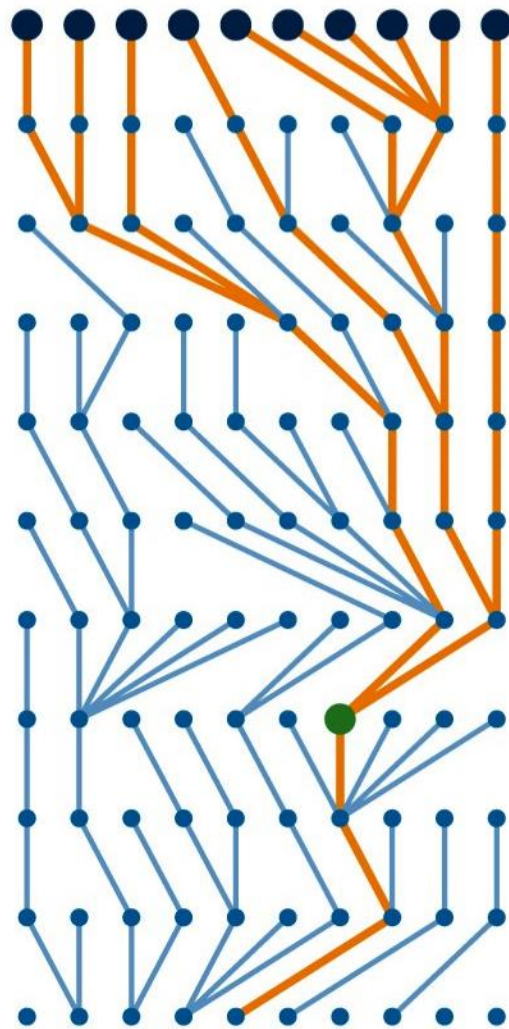




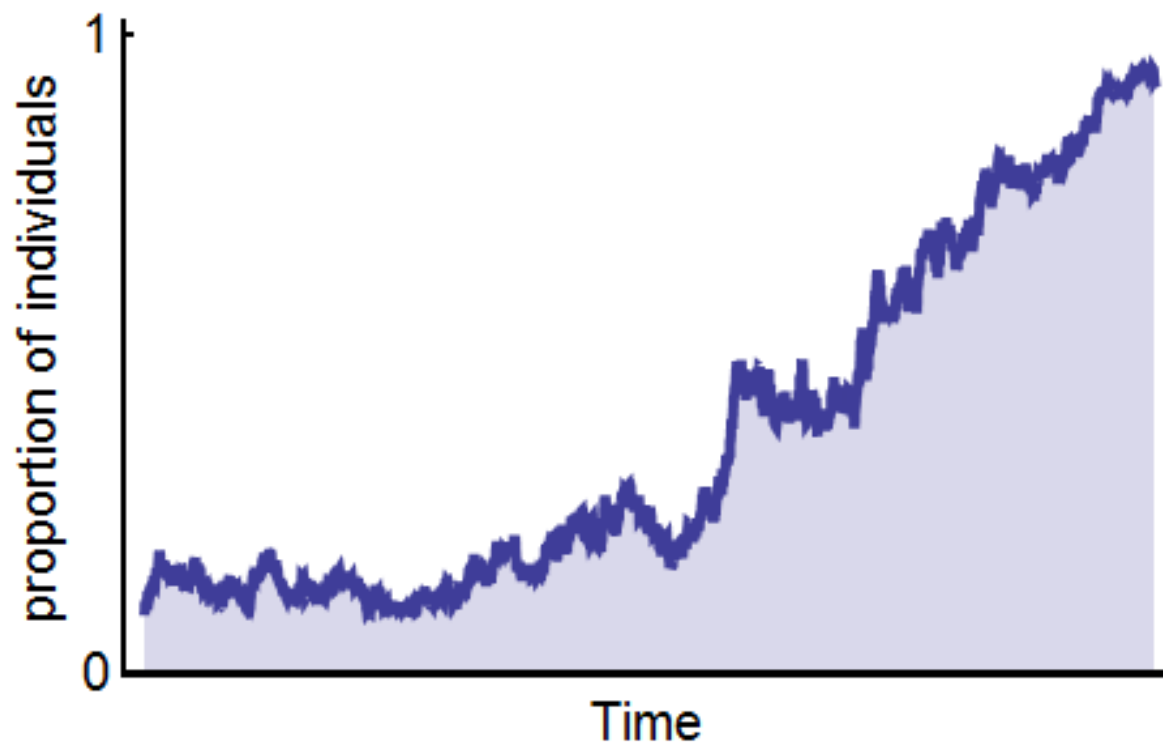
time



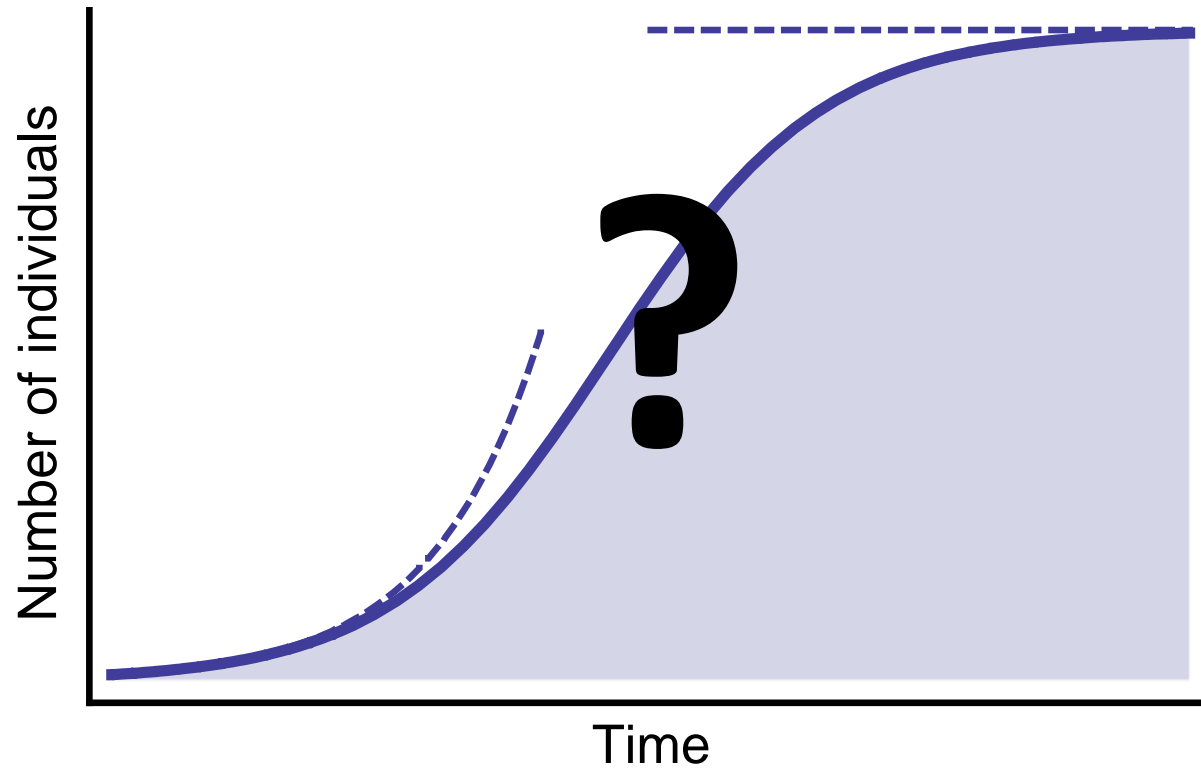
Present



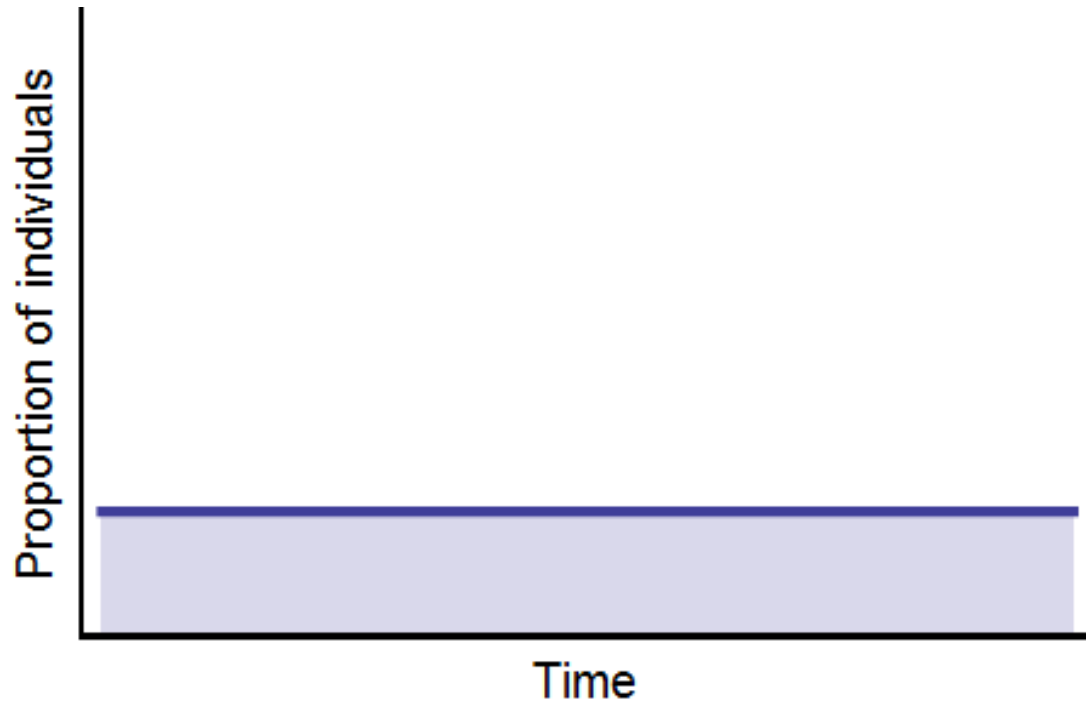
Genetic drift



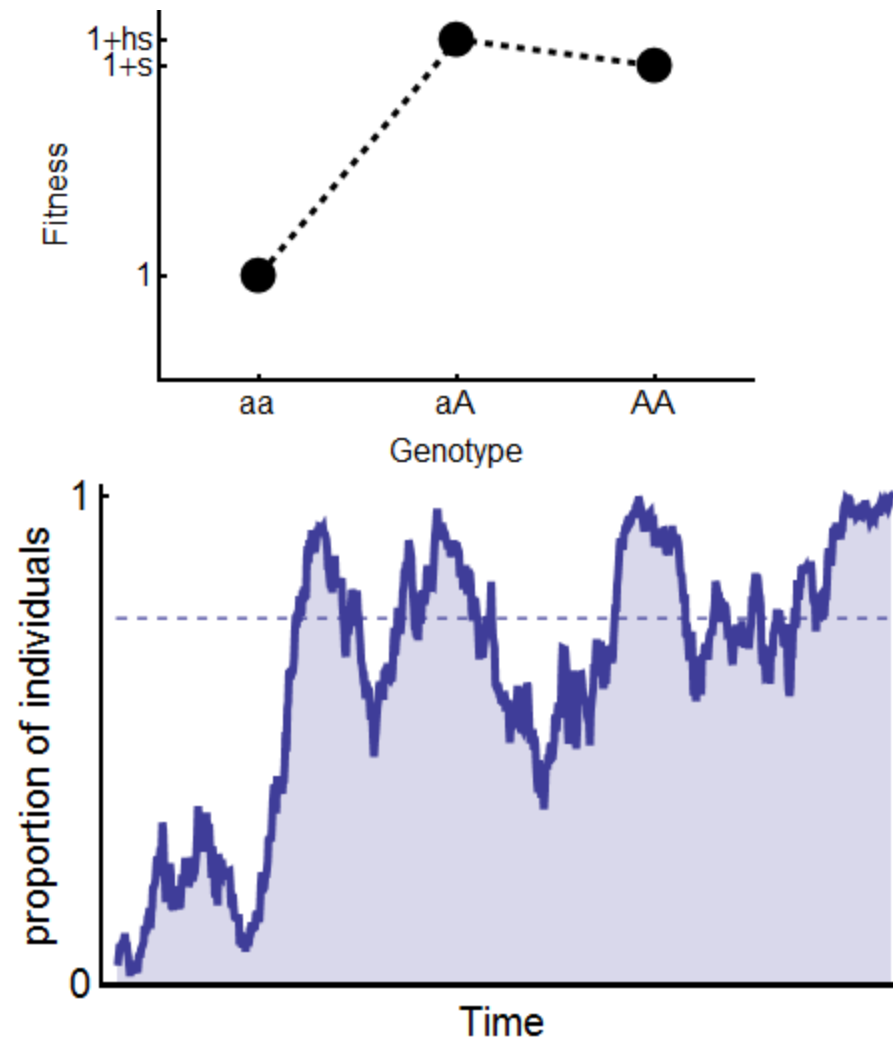
Deterministic limit?



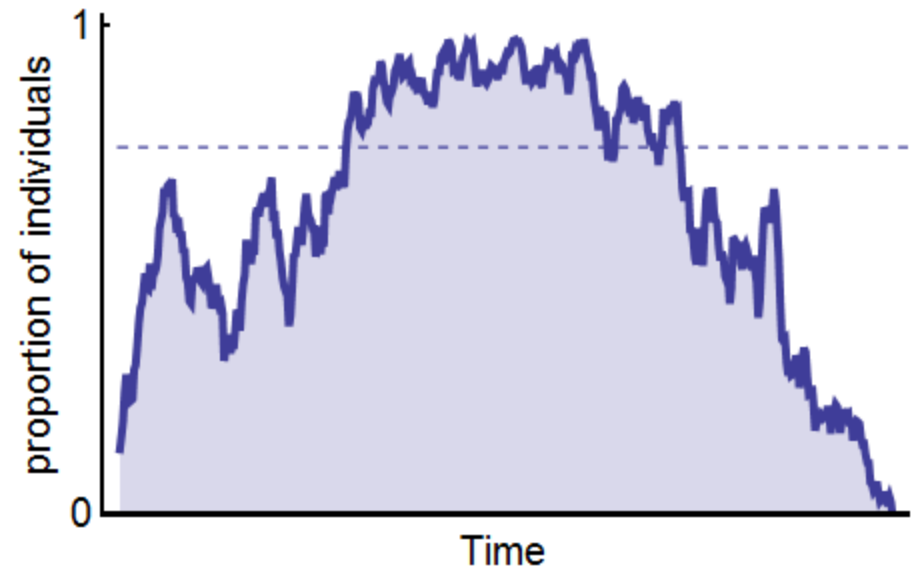
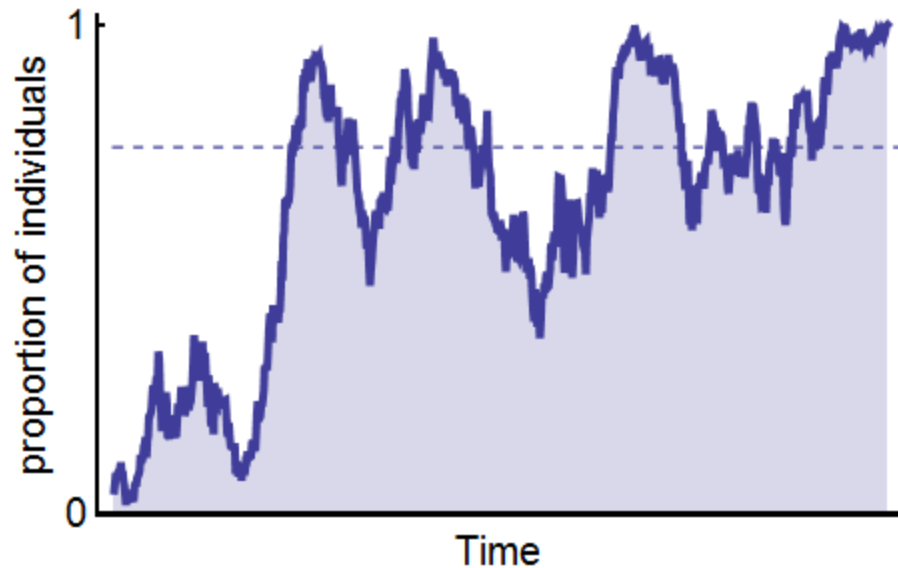
Deterministic Limit



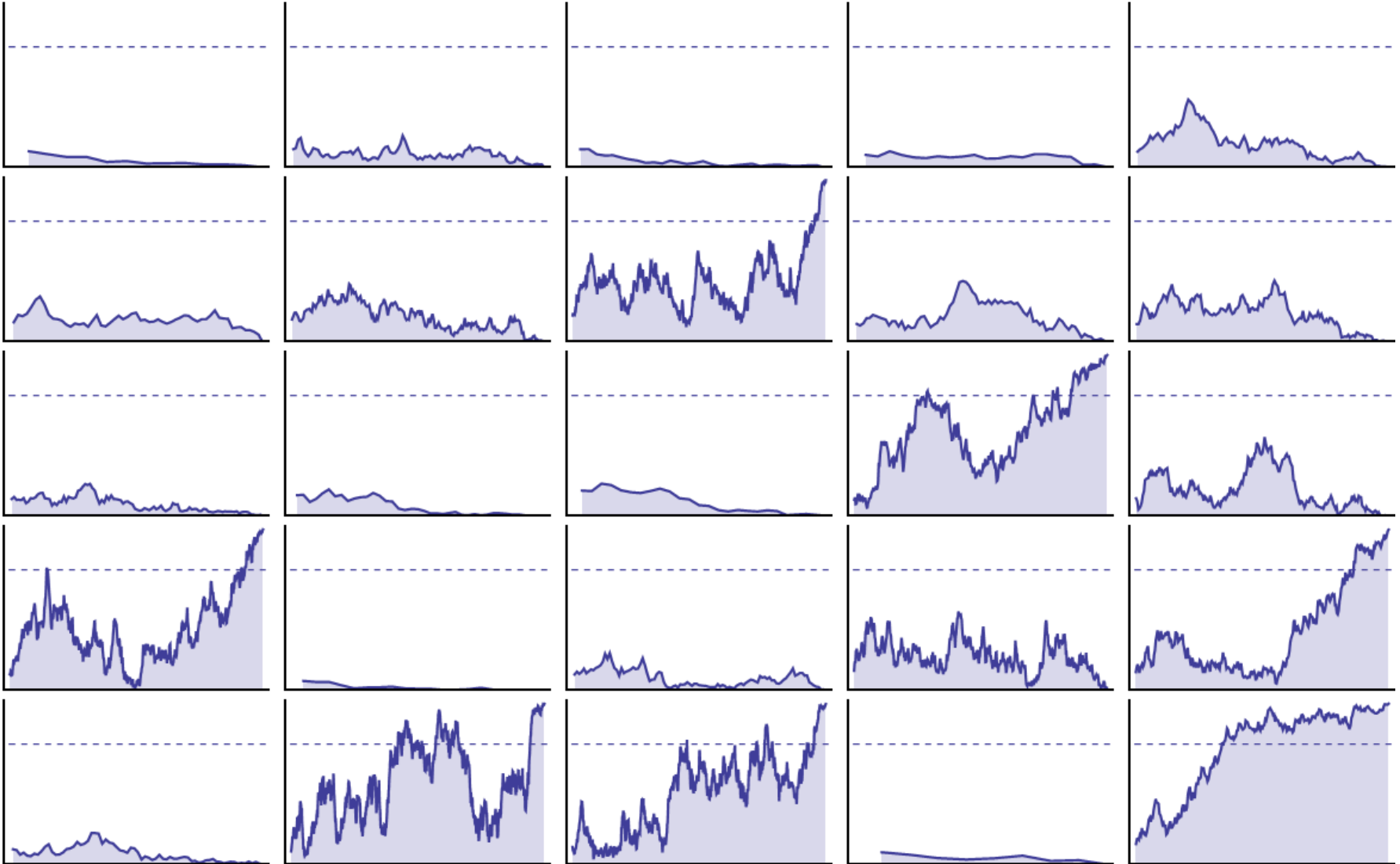
Drift decreases genetic variance within a population



Drift increases the variation between populations

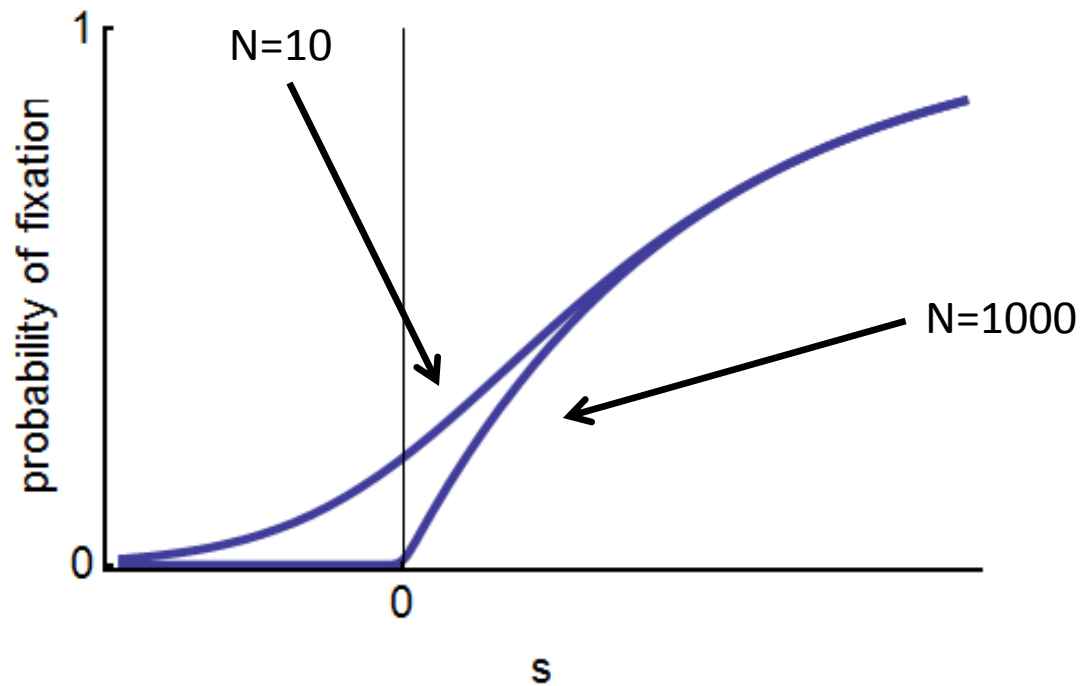


If this process happens over many populations (islands), then variation between islands will increase



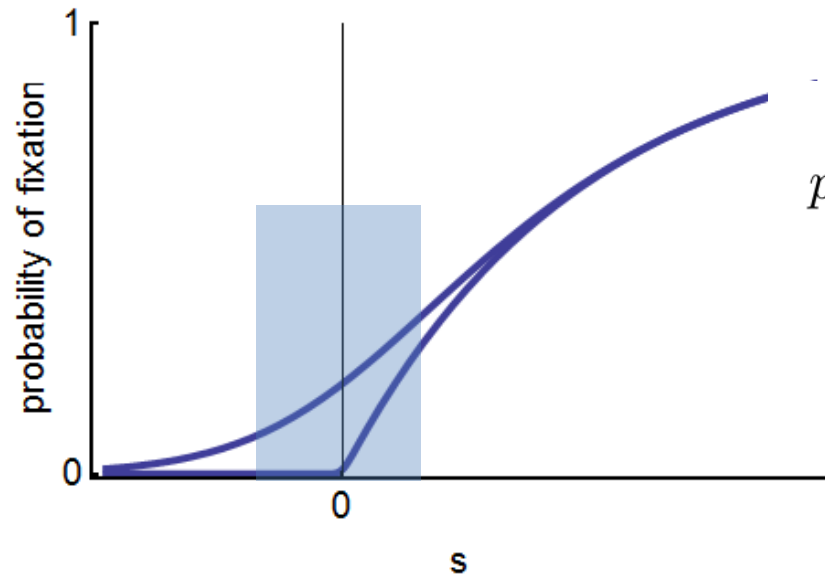
Probability of fixation of genes

$$p_{fix} = \frac{1 - e^{-4s}}{1 - e^{-4Ns}}$$

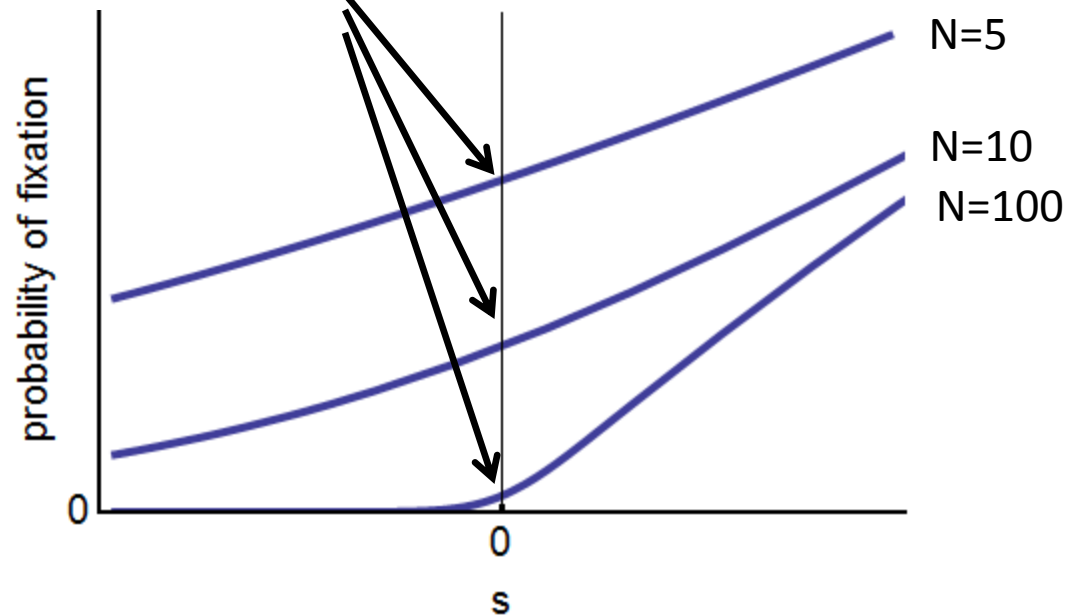


Fixation of neutral genes

$$p_{fix} = \frac{1 - e^{-4s}}{1 - e^{-4Ns}}$$



$$p_{fix}(s=0) = \frac{1}{N}$$



Neutral mutations and the molecular clock

Number of mutants per generation:

$$N\mu$$

Probability that a mutant will go to fixation:

$$\frac{1}{N}$$

Rate at which mutants go to fixation:

$$N\mu \times \frac{1}{N} = \mu$$

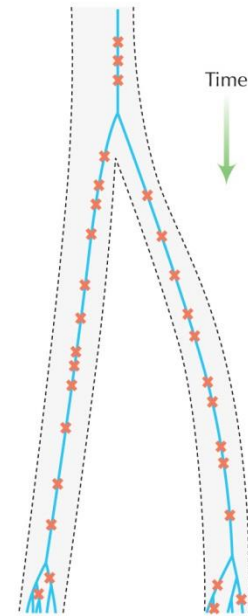
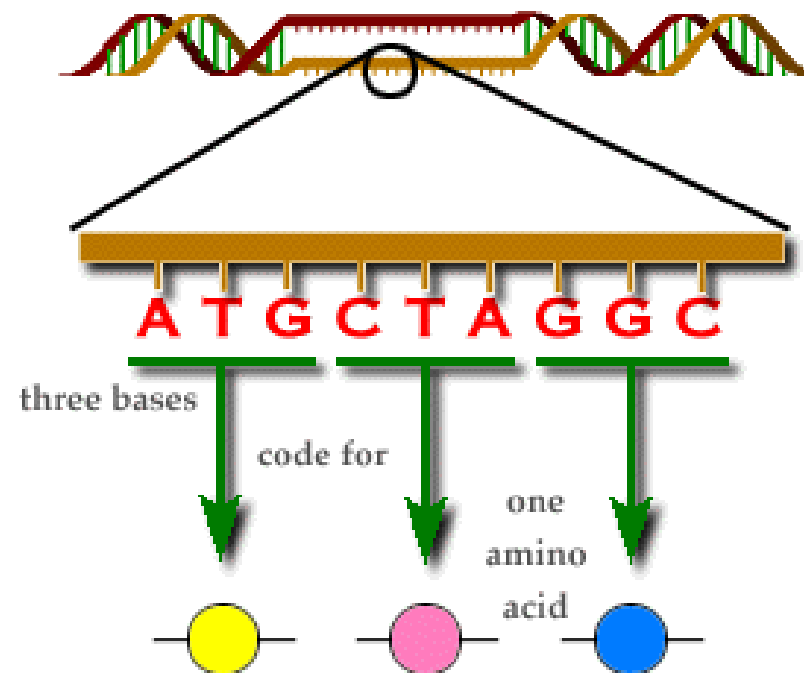


FIGURE 15.10. All the genes within a species descend from a single ancestral lineage, which traces back into the distant past. Thus, the rate at which two species diverge over time is equal to the rate at which their two ancestral lineages accumulate mutations. The *shaded area* shows two species, which descend from a single ancestral species (*left*), and the *solid lines* show the ancestry of all the genes presently in the two species. Mutations are indicated by *red crosses*.

Using neutral drift to detect selection

- Neutral mutations fix at a given rate
- Selected mutations go to fixation faster (if they are beneficial) or slower (if they are deleterious)
- Comparing number of mutations with mutations we are sure are (almost) neutral allows us to detect selection

The genetic code



Synonymous vs non-synonymous mutations

		Second letter					
		U	C	A	G		
First letter	U	UUU } Phe UUC } UUA } Leu UUG }	UCU } UCC } Ser UCA } UCG }	UAU } Tyr UAC } UAA Stop UAG Stop	UGU } Cys UGC } UGA Stop UGG Trp	U	C
	C	CUU } CUC } Leu CUA } CUG }	CCU } CCC } Pro CCA } CCG }	CAU } His CAC } CAA } Gln CAG }	CGU } CGC } Arg CGA } CGG }	U	C
	A	AUU } AUC } Ile AUA } AUG Met	ACU } ACC } Thr ACA } ACG }	AAU } Asn AAC } AAA } Lys AAG }	AGU } Ser AGC } AGA } Arg AGG }	U	C
	G	GUU } GUC } Val GUA } GUG }	GCU } GCC } Ala GCA } GCG }	GAU } Asp GAC } GAA } Glu GAG }	GGU } GGC } Gly GGA } GGG }	U	C
						Third letter	
						A	G

dN/dS ratios

- We can use the ratio of synonymous vs non-synonymous mutations to get a measure of selection on a gene
- If NS mutations are as frequent as S mutations:
 - $dN/dS = 1$ (neutral evolution)
- If NS mutations are more frequent than S mutations
 - $dN/dS > 1$ (positive selection)
- If NS mutations are less frequent than S mutations:
 - $dN/dS < 1$ (NS mutations are being selected against)
 - Stabilizing/purifying selection

Summary

- Finite populations make evolution less predictable
- Even deleterious mutations can go to fixation if the population is small
- Neutral mutations fix with probability $1/N$
- The rate at which neutral mutation appear and go to fixation is independent of the population size
- The ratio between non-synonymous and synonymous mutations can be used as a measure of selection