

LECTURE 11

Forces that change gene frequency

A. Mutation

1. Generally refers to spontaneous (rather than induced) mutations. There are two types relative to population genetics:
 - a) Recurrent -- mutations that occur repeatedly, generally at some characteristic frequency
 - b) Non-recurrent -- mutations that arise only once in the history of a lineage
2. Changes to gene (allele) frequencies are minimal:
 - a) Non-recurrent mutations are of little consequence relative to changing gene (allele) frequencies; most non-recurrent are deleterious and usually outnumbered by gazillions to one; the exception would be those that confer selective advantage (but then this is selection)
 - b) Recurrent mutations will change gene (allele) frequency as a function of the rate at which such mutations arise (minus the frequency of reverse or back mutation)
 - c) Mutation frequencies for coding genes are typically on the order of 10^{-5} - 10^{-8} per cell per generation, meaning that one may expect a new (recurrent) mutation at a gene to appear every 10^5 - 10^8 individuals; this is too low to change gene (allele) frequencies significantly unless one considers hundreds to thousands of generations
 - d) What this means is that mutation *alone* is extremely inefficient relative to promoting genetic change in a population
3. However, mutation is the *only* mechanism that generates “new” forms (alleles) of a gene; in concert with other “forces” (e.g., selection or drift), a new allele generated by mutation may increase significantly in frequency in a population, perhaps even to “fixation” in a very short period of time
4. Occurrence of “mutator” genes in natural populations reinforces the concept that mutation is an importance “force” in natural population when acting in concert with other “forces”

B. Selection (cursory treatment)

1. Best defined as non-random reproduction of different genotypes (phenotypes): important concepts are Darwinian fitness (not necessarily related to physical robustness) and reproduction of “fit” genotypes must have a temporal component
2. Best considered as a dynamic, ever-changing process that acts either to *change* or *maintain* gene (allele) frequencies in response to the environment
 - a) Gene (allele) frequencies can essentially “track” environmental change, in which case allele frequency change is typically “directional” in nature

- b) Alternatively, gene (allele) frequencies can remain constant if certain genotypes are those best “buffered” to environmental change
3. Types of selection (consider both genotypes and phenotypes):
- Directional selection → adaptive norm of a population changes in a directional fashion
 - Normalizing (stabilizing) selection → adaptive norm of a population is maintained
 - Disruptive selection → two or more “new” adaptive norms form following environmental disturbance – a component to several models of incipient speciation
4. The Classical Perspective (H. J. Müller)
- The view that there existed at each and every locus a “best” allele that provided optimal fitness; if the “best” allele was in high frequency in a population, selection simply removed (culled) deleterious alleles (the majority); in this case, selection was stabilizing
 - If the “best” allele was in low frequency (e.g., a newly arisen “favorable” mutation), selection operated to increase the frequency of this newly arisen allele by removing or eliminating individuals carrying other alleles; in this case, selection was directional

Corollary: There should always be a “drive” towards homozygosity for the “best” allele at each and every locus, with heterozygotes representing only a transient or intermediate stage in the process

- An example is provided by industrial melanism in the moth *Biston betularia*
 - selection originally was stabilizing -- the deleterious allele (for dark coloration) was continually removed from the population, maintaining a high frequency of the allele for light coloration
 - following industrialization, selection changed and became directional – the (now) deleterious allele for light coloration was continually removed from the population, promoting a high frequency of the allele for dark coloration
 - at a certain frequency, the population as a whole stabilizes in terms of allele frequencies at the “coloration” locus as *both morphologies (alleles) are maintained in the population* [more later]
 - this situation is best modeled as single locus, where selection is *against* a recessive

	AA	Aa	aa	
	p^2	$2pq$	q^2	$s =$ selection coefficient, ranging
fitness	1	1	$1-s$	from 0 to 1
selection	p^2	$2pq$	$q^2 - sq^2$	

- (v) the rate at which q decreases over time is a function of both the intensity of selection (value of s) and the initial value of q
- (a) if selection favors q alleles (actually, q^2 genotypes/phenotypes), the frequency of q alleles is high (the frequency of p alleles is low), the population is stable, and selection is perceived as stabilizing
 - (b) if selection changes to favor p alleles (i.e., is *against* q^2 genotypes/phenotypes), the change in allele frequency initially is rapid as most individuals are q^2 and are eliminated by selection; this results in a rapid drop in q and selection is perceived as directional
 - (c) once q alleles become very low in frequency, there are hardly any q^2 individuals that can be removed by selection, so selection once again is perceived as stabilizing
 - (d) thus, whether selection is perceived as directional or stabilizing depends primarily on the frequencies of the alleles – if q is initially high in frequency, selection against q generates a *directional* pattern; if q is low in frequency, selection against q generates a *stabilizing* pattern
- (vi) Can a recessive allele ever be eliminated from a population?

In theory, no!

- (a) the q allele can be hidden in heterozygotes and not “perceived” by selection
- (b) when the frequency of the q allele becomes low, q^2 (frequency of homozygous recessives against whom selection is acting) becomes *very* low and the drop in q alleles will be imperceptible
- (c) at some point, the reduction in q alleles due to selection will be equaled by the input of q alleles due to mutation

This is called the *mutation - selection* equilibrium. The equilibrium frequency of q can be estimated as

$$q = (\mu/s)^{1/2} \quad q \text{ is where} \quad q = 0$$

- (vii) What about selection against a dominant?
- (a) Rates of allele frequency change will depend primarily on penetrance and selection intensity
 - (b) At 100% penetrance and selection against a dominant, where selection intensity is one (i.e., $s = 1.0$), the frequency of the trait in the population will be the mutation rate to the allele