

Conifer Translational Genomics Network Coordinated Agricultural Project



Genomics in Tree Breeding and
Forest Ecosystem Management

Module 3 – Population Genetics



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Population genetics

- Population genetics is the study of genetic differences within and among populations of individuals, and how these differences change across generations
- In the classic view, it is the study of the amount and distribution of genetic variation in populations and species, and how it got that way
- Population genetics describes the mechanics of how evolution takes place



Why study genes in populations?

- In natural populations:
 - *Adaptation* – the ability to survive and exploit an environmental niche – involves the response of populations, not individuals
- In breeding populations:
 - *Genetic gain* – improving the average performance of populations for desired breeding objectives – depends on selecting and breeding parents with the best genetic potential

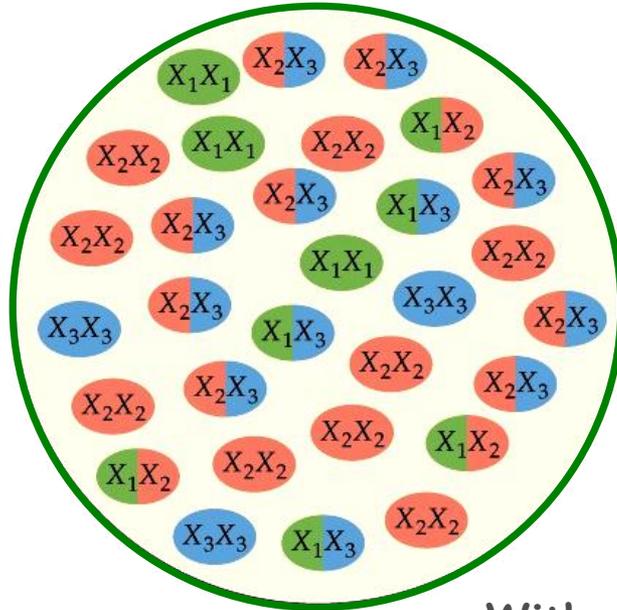
Population genetics addresses many topics

- How genetically diverse is a species or population?
 - *Contrast diversity in populations that differ in life-history traits, pop size, breeding structure, etc*
- Are different populations closely related to one another?
 - *Monitor diversity for conservation purposes*
- What is the potential for inbreeding depression?
 - *What is the minimum viable population size from a genetic standpoint?*
- How is genetic variation maintained?
- Which genes/alleles are responsible for phenotypic variation?
- How are species related (phylogenetics) and how did they acquire their current distribution (biogeography)?

What do population geneticists typically measure?

Typical descriptive statistics

Locus 'X' in pop #1



Allele

Frequency

A ₁	0.2
A ₂	0.5
A ₃	0.3

Total = 1.0

Genotype

Frequency

A ₁ A ₁	0.1
→ A ₁ A ₂	0.1
→ A ₁ A ₃	0.1
A ₂ A ₂	0.3
→ A ₂ A ₃	0.3
A ₃ A ₃	0.1

Sum = 1.0

A (# alleles) = 3

H_o (observed heterozygosity) = 0.5

With data from more loci, you can also calculate,
 P (% polymorphic loci) = % of loci with >1 allele

Figure Credit: Glenn Howe, Oregon State University

The Hardy-Weinberg principle

- The frequencies of alleles and genotypes in a population will **remain constant** over time (given certain assumptions which describe a static, or **non-evolving** population)
- The frequencies of alleles and genotypes can be described mathematically, where **p and q** are the frequencies of the alleles **A₁** and **A₂**

Freq. A₁A₁ homozygote

Freq. A₂A₂ homozygote

$$p^2 + 2pq + q^2 = 1.0$$

Freq. A₁A₂ heterozygote

Random mating restores HW proportions each generation

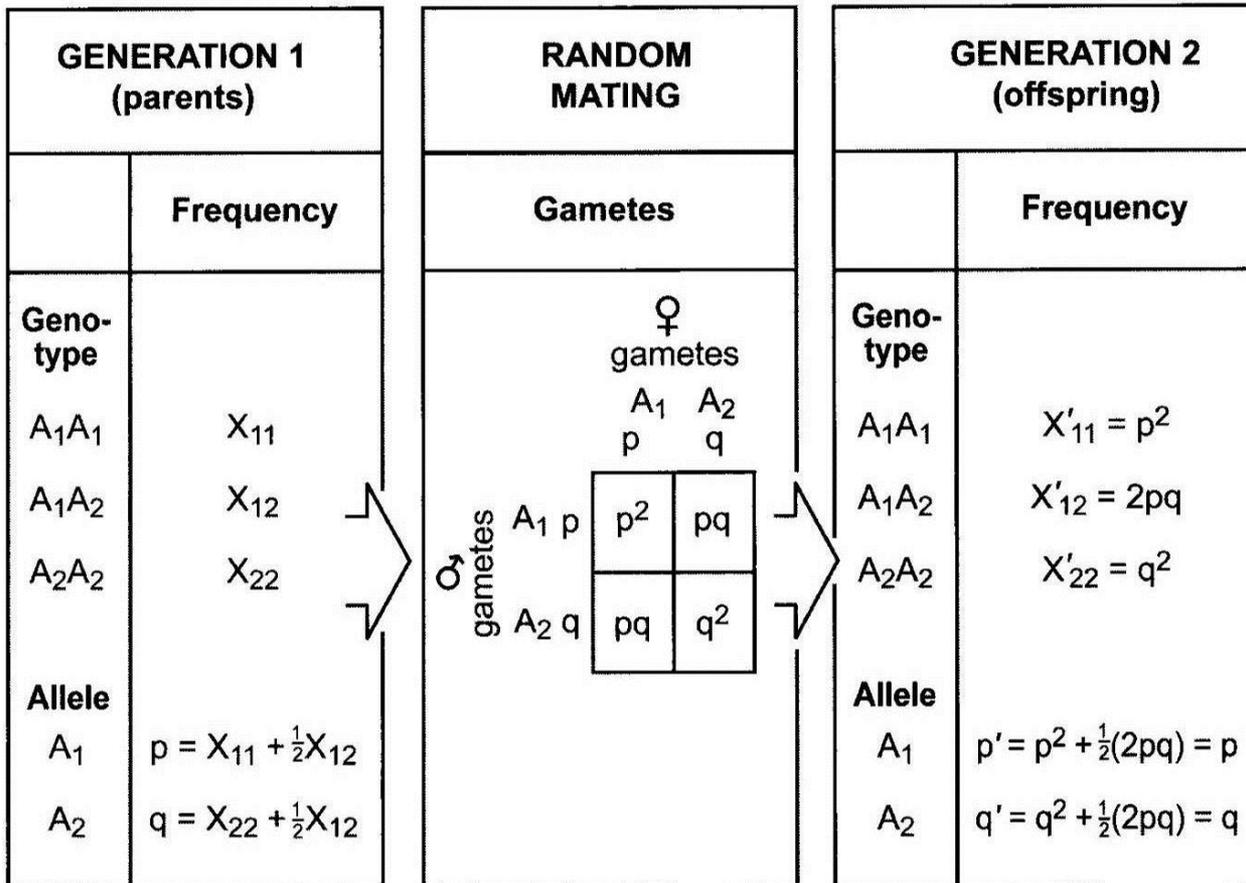


Figure Credit: White, T. L., W. T. Adams, and D. B. Neale. 2007. Forest genetics. CAB International, Wallingford, United Kingdom. Used with permission.

HW equilibrium conditions

- For Hardy-Weinberg equilibrium to exist, a number of assumptions must be met. For instance, the population under consideration must
 - *Be random mating (translation = all possible pairings of mates are equally likely)*
 - *Be infinitely large (translation = sampling with replacement)*
 - *Have no selection (which biases genotype frequencies)*
 - *Have no migration (since all alleles must be sampled from the same pool)*
 - *Have no mutation (which introduces new variants)*
- Obviously, such “ideal” populations rarely (if ever) exist
- Still, minor violations of assumptions generally have little impact

~~HW~~: Non-random mating

When individual genotypes do not mate randomly, HW equilibrium proportions are not observed among the offspring

-
- We'll look at two kinds of non-random mating
 - *Population substructure/admixture*
 - *Inbreeding (mating among related individuals)*

~~HW~~: Population admixture

- Consider mixing individuals from non-interbreeding subpopulations (e.g. alligator lizards from Washington and Idaho)
- Even if each subpopulation is in HW, the admixed group is not ($p_1 \neq p_2$)
- The admixed group will appear to have too many homozygotes
- This situation is called the Wahlund effect

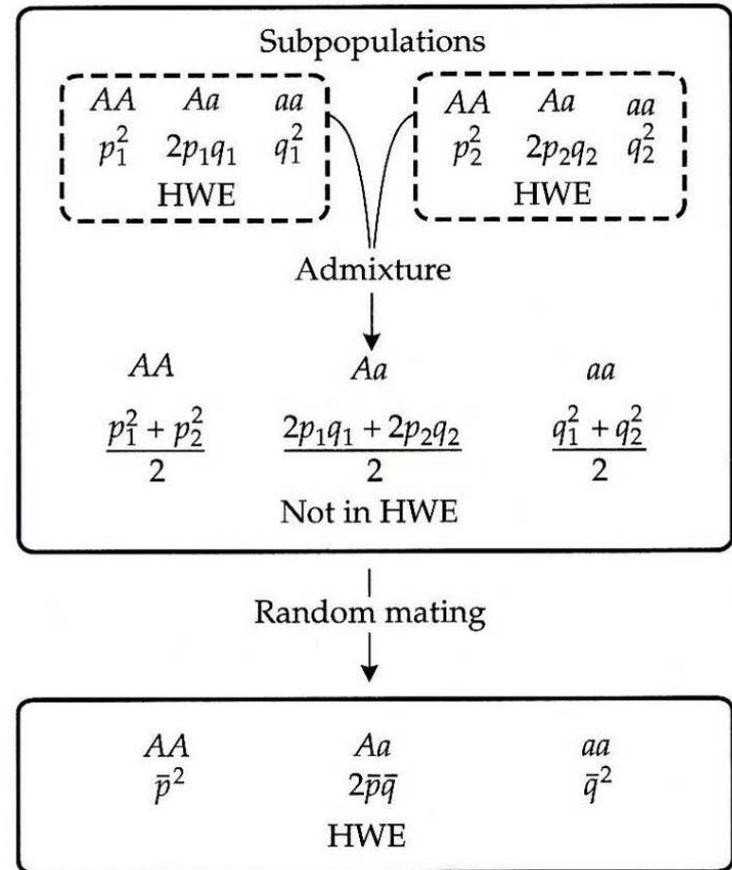


Figure Credit: Hartl. 2000. A primer of population genetics. Used with permission of Sinauer Associates.

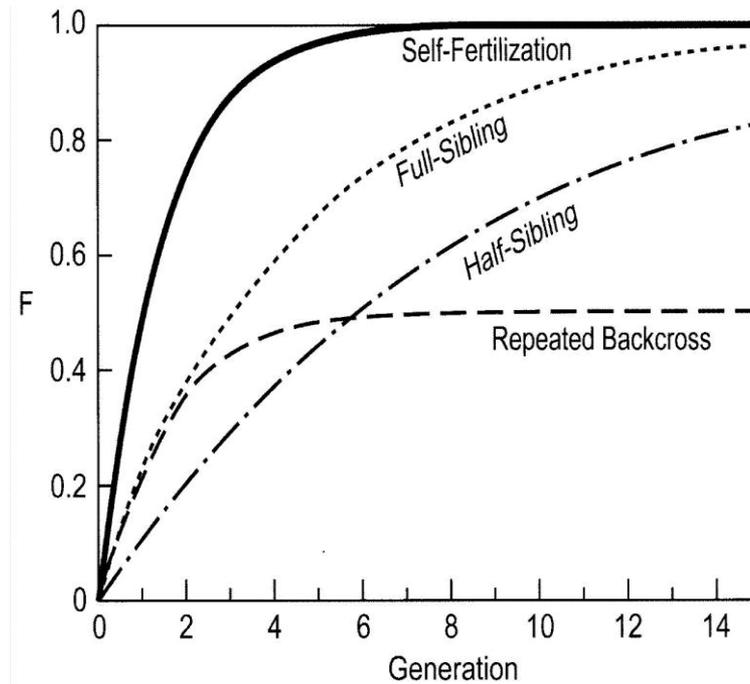
Population structure: Wahlund's effect

- **Wahlund's effect:** As long as allele frequencies vary among subpopulations, even if each subpopulation exhibits HW proportions, then more homozygotes will be observed than would be expected based on the allele frequency of the metapopulation
- The relative increase in homozygosity is proportional to the variance in allele frequencies among subpopulations, as measured by F (where $0 \leq F \leq 1$)
- F is commonly known as Wright's fixation index and may be most simply interpreted as $F = 1 - (H_{\text{obs}} / H_{\text{exp}})$, where the values represent observed and expected levels of heterozygosity

Inbreeding

- Inbreeding (mating among relatives) increases homozygosity relative to HW
 - *Rate is proportional to degree of relationship*
 - *Distant cousin < first cousin < half-sib < full-sib < self*
- Recurrent inbreeding leads to a build-up of homozygosity, and a corresponding reduction in heterozygosity
- Inbreeding affects genotype frequencies, but not allele frequencies
- How does inbreeding affect deleterious recessive alleles?

Inbreeding and homozygosity



- F reflects a proportional reduction in heterozygosity, and a build-up of genetic relatedness. HW implies $F = 0$. With recurrent selfing, F goes to 1

Figure Credit: White, T. L., W. T. Adams, and D. B. Neale. 2007. Forest genetics. CAB International, Wallingford, United Kingdom. Used with permission. (Table 5.1 in Falconer and Mackay, 1996)

Inbreeding depression

- Inbreeding often leads to reduced vitality (growth, fitness)
- Deleterious recessive alleles are made homozygous
- Outcrossing species are more likely to suffer higher inbreeding depression



Image Credit: White, T. L., W. T. Adams, and D. B. Neale. 2007. Forest genetics. CAB International, Wallingford, United Kingdom. Used with permission. (Photo courtesy of F. Sorensen, USFS, Pacific Northwest Research Station)

Evolutionary forces change allele frequencies

- **Mutation** – a random heritable change in the genetic material (DNA) – ultimate source of all new alleles
- **Migration (gene flow)** – the introduction of new alleles into a population via seeds, pollen, or vegetative propagules
- **Random genetic drift** – the random process whereby some alleles are not included in the next generation by chance alone
- **Natural selection** – the differential, non-random reproductive success of individuals that differ in hereditary characteristics

Mutation

- Mutations are the ultimate source of genetic variation on which other evolutionary forces act (e.g. natural selection)
- Mutations at any one locus are rare, but with sufficient time, cumulative effects can be large
- Heritable **changes in DNA** sequence alter allele frequencies as new alleles are formed
- **Effects on populations** – Mutations **promote differentiation** (but effects are gradual in the absence of other evolutionary forces)

Gene flow: Migration of alleles

- **Gene flow** – the movement of alleles among populations
- Movement may occur by individuals (via seed) or gametes (via pollen) between populations
- **Effects on populations** – gene flow **hinders differentiation**. It is a cohesive force which tends to bind populations together

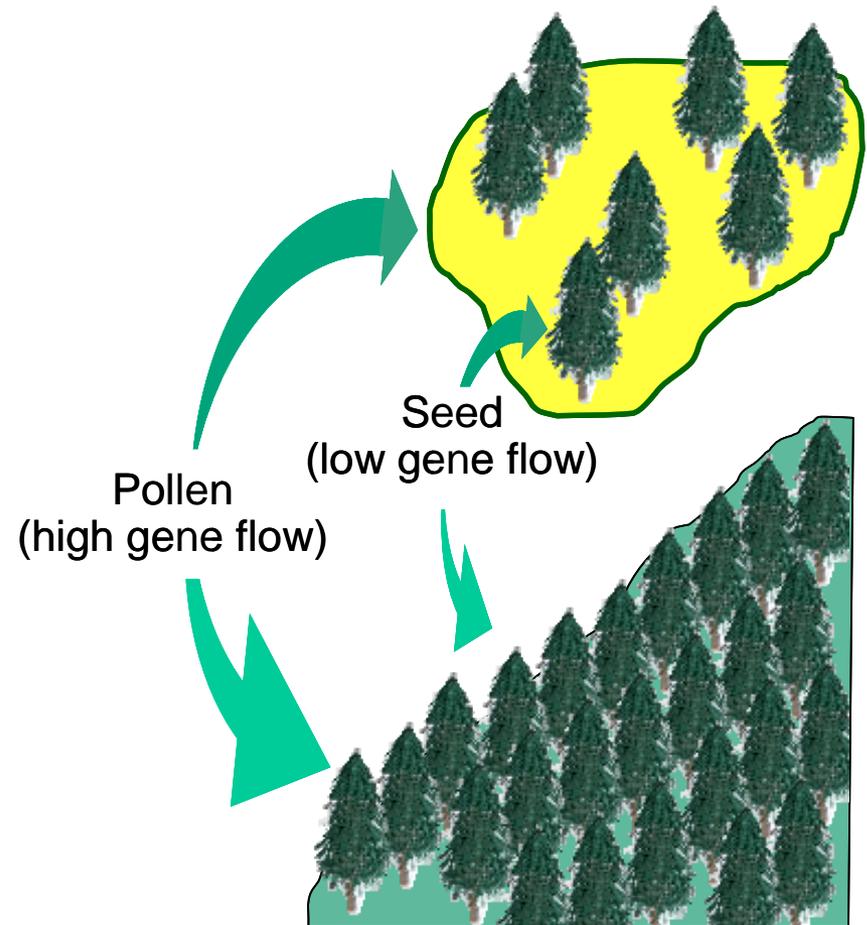


Image Credit: Glenn Howe, Oregon State University

Migration rates

- Modest migration rates will prevent divergence of populations
- The absolute number of migrants per generation affects F_{st} , the fixation index, independent of subpopulation size

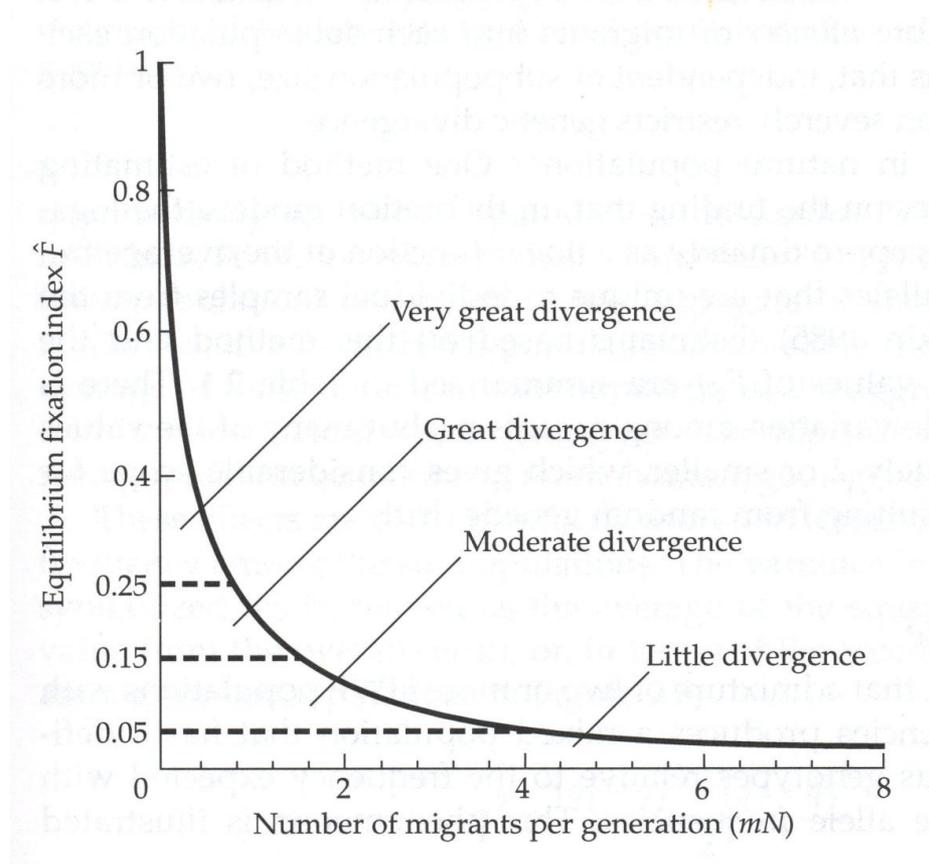


Figure Credit: Hartl. 2000. A primer of population genetics. Used with permission of Sinauer Associates.

Genetic drift

- Drift reflects sampling in small populations. Subgroups follow independent paths. Allele frequencies will vary among subgroups while frequencies in the metapopulation remain relatively stable. Major impacts of drift are:
- Reduced genetic diversity (loss of alleles).
- Reduced average heterozygosity.
- Increased genetic differentiation among populations.

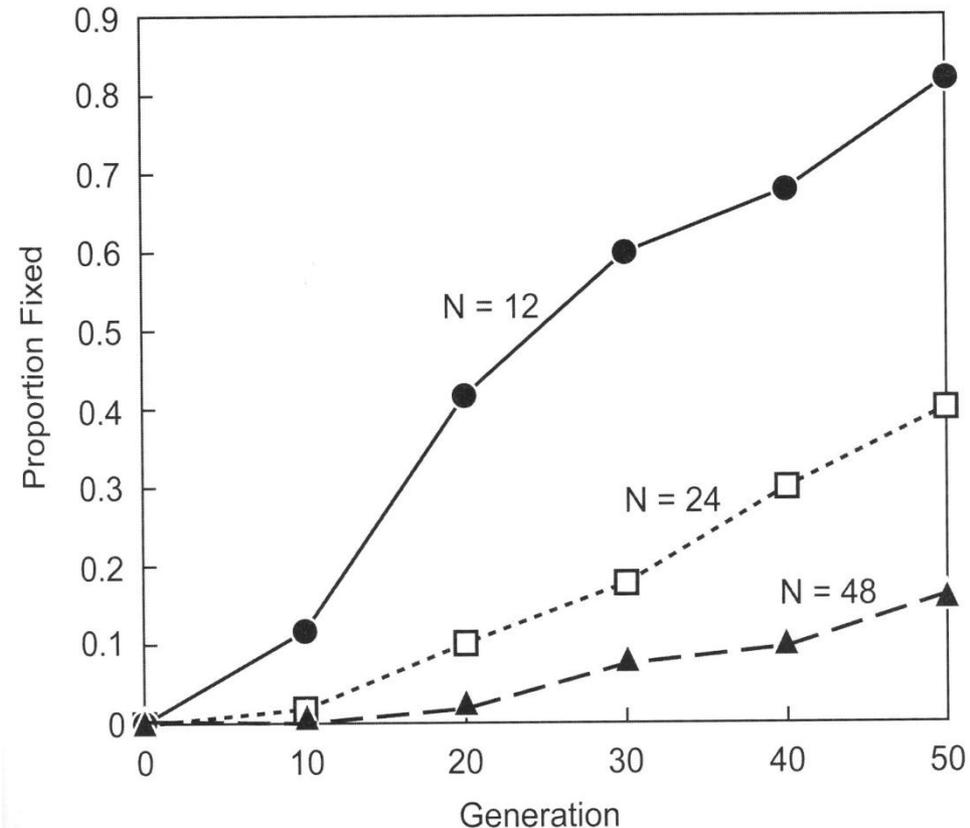


Figure Credit: Modified from White et al. Forest Genetics. 2007. Fig. 5.10

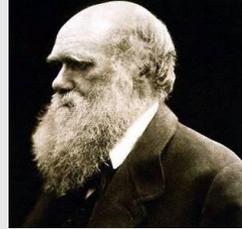
Random genetic drift: Bottlenecks



- **Bottleneck effect:** A type of genetic drift that occurs when a population is severely reduced in size such that the surviving population is no longer genetically representative of the original population

Figure credit: Nicholas Wheeler, Oregon State University

Natural selection



- **Natural selection** – First proposed by Charles Darwin in mid-1800s. The differential reproductive success of individuals **that differ in hereditary characteristics**
 - *Not all offspring survive and reproduce*
 - *Some individuals produce more offspring than others (mortality, disease, bad luck, etc)*
 - *Offspring differ in hereditary characteristics affecting their survival (genotype and reproduction are correlated)*
 - *Individuals that reproduce pass along their hereditary characteristics to the next generation*
 - *Favorable characteristics become more frequent in successive generations*
- **Effects on populations:**
 - **Promotes differentiation** between populations that inhabit dissimilar environments
 - **Hinders differentiation** between populations that inhabit similar environments

Relative fitness: Key considerations

- Which genotype has the largest relative fitness?
 - *Determines the direction in which allele frequencies will change*
- Are fitness differences large or small?
 - *Determines rate of change over generations – fast or slow*
- What is the fitness of the heterozygote compared to either homozygote?
 - *Reflects dominance*
 - *Complete (heterozygote identical to either homozygote)*
 - *No dominance (additive, heterozygote is intermediate)*
 - *Partial (heterozygote more closely resembles one homozygote)*
 - *Dominance influences how selection “sees” heterozygotes*
 - *Affects rate of change across generations*

Gene action: Additive vs. dominance

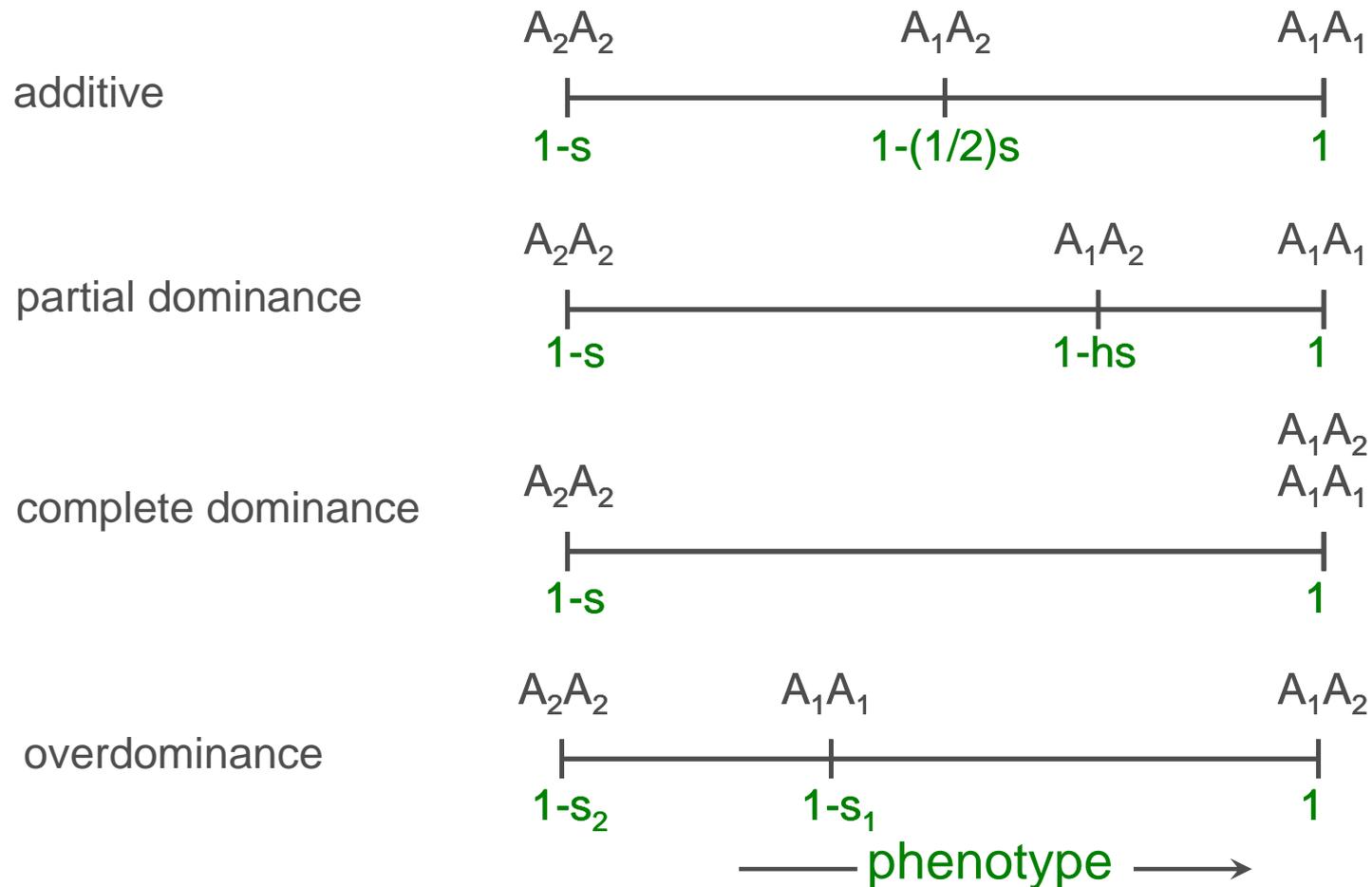


Figure Credit: Falconer and Mackay. 1996. Used with permission of Pearson Education.

Dominance and rate of change

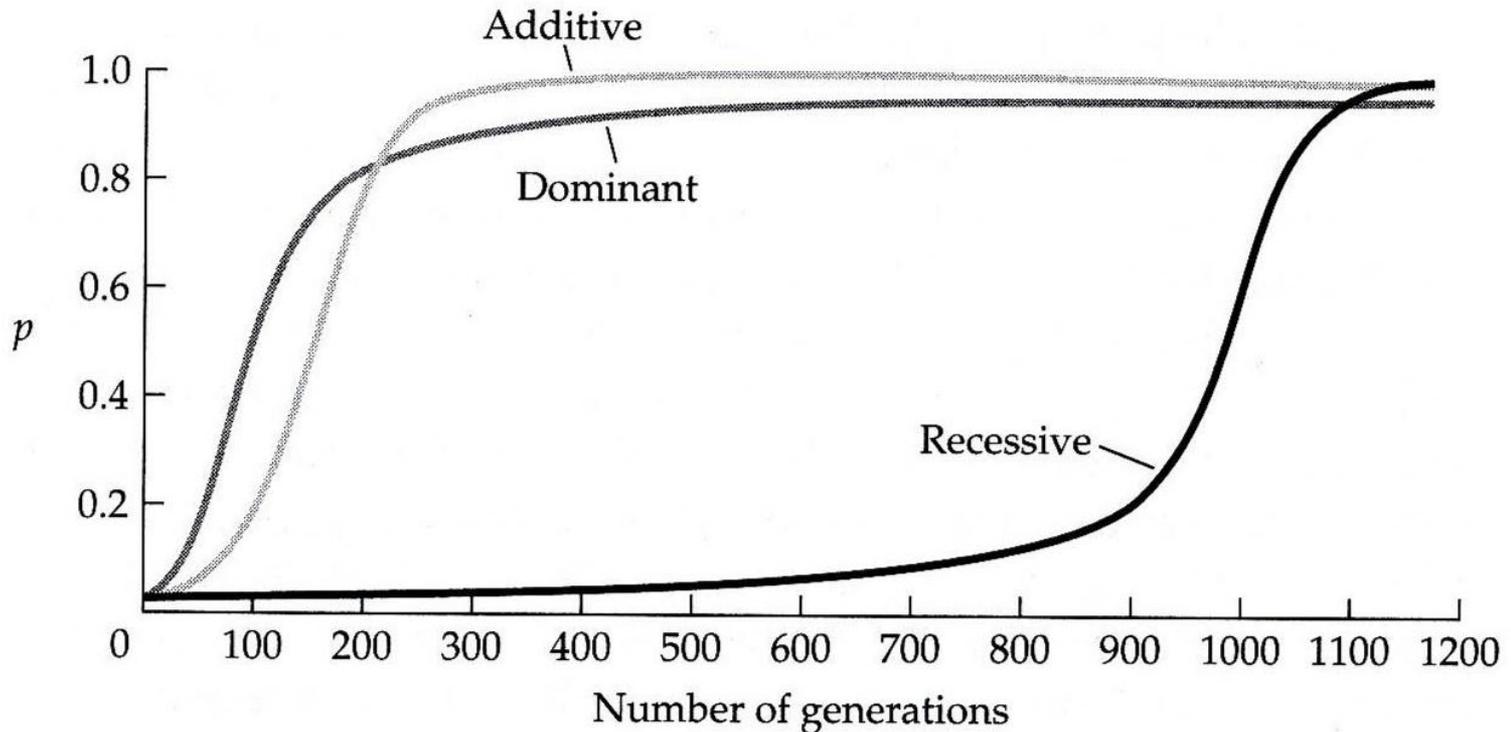


Figure 2.11 Change in frequency of a favored allele with dominant, additive, or recessive effects on fitness. In each case, there is a 5% difference in relative fitness between the homozygous genotypes.

Figure Credit: Hartl. 2000. A primer of population genetics. Used with permission of Sinauer Associates.

Selection: Numerical example

	Genotypes			Total
	A ₁ A ₁	A ₁ A ₂	A ₂ A ₂	
Initial frequency	0.360	0.480	0.160	1.000
Absolute viability (fitness)	0.80	0.80	0.20	
Relative viability (fitness) ^a	1	1	0.25	
Proportion after selection ^b	0.360	0.480	0.040	0.880
Frequency after selection ^c	0.409	0.546	0.045	1.000

Initial frequency of A₂ (q) = 0.160 + 1/2(0.480) = 0.400

Frequency of A₂ after selection (q₁) = 0.045 + 1/2(0.546) = 0.318

$\Delta q = q_1 - q = 0.318 - 0.400 = -0.082$

^a Relative viability is obtained as absolute viability divided by 0.80 which is absolute viability of the most viable genotype.

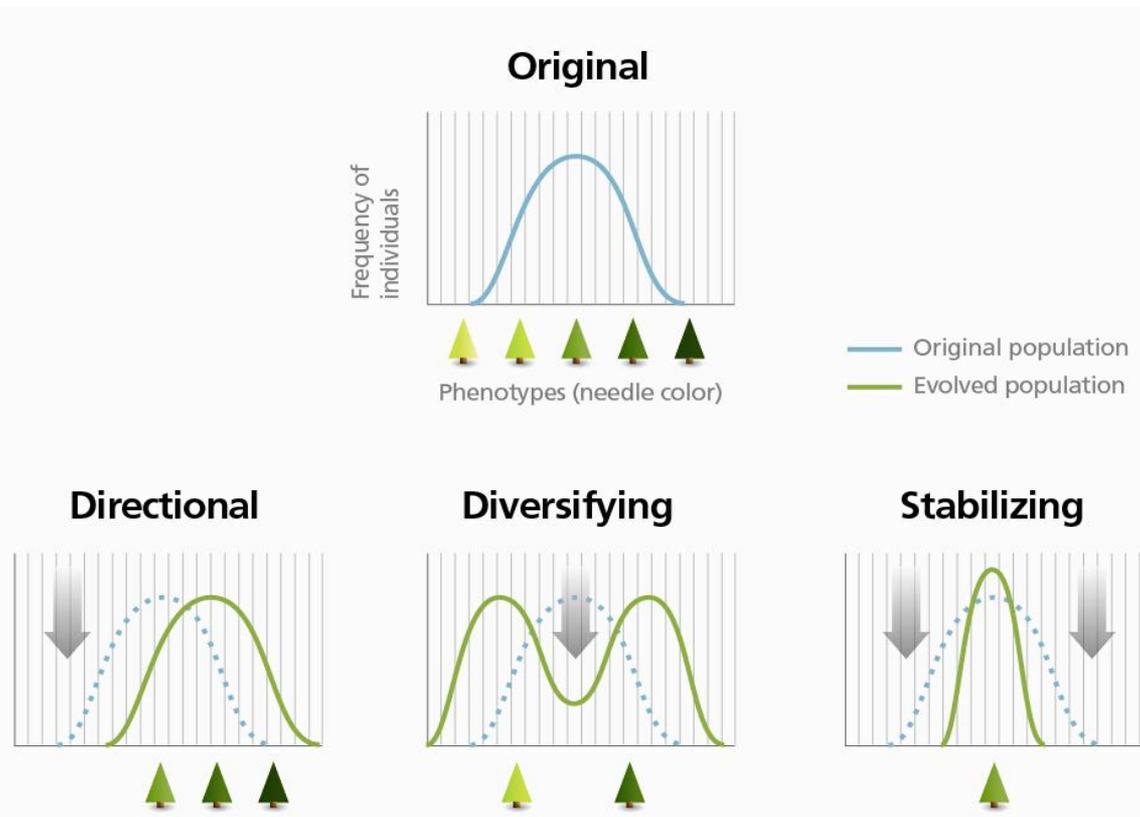
^b Proportion after selection is initial frequency times the relative viability.

^c Frequency after selection is proportion after selection divided by the sum of those proportions (*i.e.* divided by 0.88).

Table Credit: White, T. L, W. T. Adams, and D. B. Neale. 2007. Forest genetics. CAB International, Wallingford, United Kingdom. Used with permission.

Natural selection: Fitness and selection

- **Fitness:** The relative contribution an individual (genotypic class) makes to the gene pool of the next generation



What if selection is weak or absent?

- We've already seen that mutation can supply new variation that selection may act upon
- Most mutations are deleterious and are lost, but rarely, advantageous mutations can occur
- What about mutations that cause no effect either way?
- The neutral theory of evolution pertains to alleles that confer no difference in relative fitness – as if selection is oblivious to them

Population genetics: A final concept

Linkage disequilibrium (LD, also called gametic phase disequilibrium)

- Conceptually – LD is a correlation in allelic state among loci
- Numerically
 - *Expected haplotype (gamete) frequency is the product of the two allele frequencies, i.e. $f(AB) = f(A) \times f(B)$*
 - *If $f(AB) = f(A) \times f(B)$, then $LD = 0$*
 - *If $f(AB) \neq f(A) \times f(B)$, then $LD \neq 0$*
- LD may arise from factors such as
 - *Recent mutations*
 - *Historical selection (hitchhiking effect)*
 - *Population admixture*
- Recombination causes LD to decay over generations
- LD plays a major role in association genetics

A numeric example of LD

- Determine allele frequencies
- Ask whether $f(A) \times f(B) = f(AB)$
- Repeat for $f(Ab)$, $f(aB)$, and $f(ab)$
- Linkage disequilibrium (LD) reflects this difference

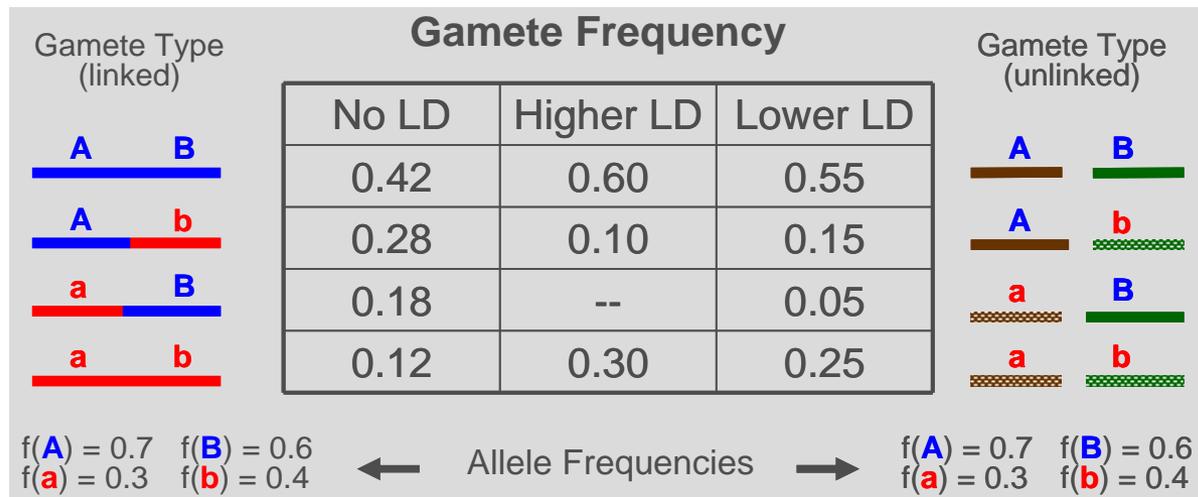


Image Credit: David Harry, Oregon State University

Some concluding remarks

- The central themes of population genetics remain
 - *How much genetic diversity is there?*
 - *How is it distributed?*
 - *How did it get that way?*
- The foundation of population genetics, identifying and quantifying genetic diversity, is no longer constrained by the lack of genetic markers. We can now measure diversity in literally thousands of genes simultaneously, and study how it is distributed
- Molecular population genetics

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External link

- Wikipedia contributors. 2011. Neutral theory of molecular evolution. Wikipedia, The Free Encyclopedia. Available at:
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Thank You.

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