

BIO 390 - GENETICS
POPULATION GENETICS

OVERVIEW

- Populations contain a great deal of genetic variation.
- If no forces act to change gene frequencies, equilibrium is reached in one generation of random mating.
- Mutation, selection, migration, and random sampling can change allele frequencies.
- Changes in frequencies of phenotypes are consequence of changes in allele frequencies at several loci.

GENES IN POPULATIONS

- New alleles introduced by mutation
- Migration changes population composition
- Mating may be random or assortative and may involve inbreeding or outbreeding
- Recombination produces new combinations of alleles
- Random fluctuation in reproductive rates may result in genetic drift in allele frequencies
- Differential reproduction by different genotypes may result in natural selection

GENE FREQUENCIES

- Gene frequency refers to proportion of particular allelic form among all copies of gene in population
- Usually estimated by sampling population
 - diploid: 2 copies of gene
 - homozygotes: 2 copies of allele
 - heterozygotes: 1 copy of each allele
 - haploid: 1 copy of allele
- For two alleles, $p + q = 1$, where p and q are frequencies of the two alleles

CALCULATING GENE FREQUENCIES

- Consider a sample of genotypes with the following frequencies

$$A/A \quad 0.36$$

$$A/a \quad 0.48$$

$$a/a \quad 0.16$$

$$p = \text{frequency of } A = 0.36 + 0.48/2 = 0.6$$

$$\bullet p = f_{A/A} + \frac{1}{2}f_{A/a}$$

$$q = \text{frequency of } a = 0.16 + 0.48/2 = 0.4$$

$$\bullet q = f_{a/a} + \frac{1}{2}f_{A/a}$$

(note: calculations use all of the data)

$$p + q = 1$$

HETEROZYGOSITY

TABLE T7-1 Frequencies of Genotypes for Alleles at MN Blood Group Locus in Various Human Populations

Population	GENOTYPE			ALLELE FREQUENCIES	
	M / M	M / N	N / N	p(M)	q(N)
Eskimo	0.835	0.156	0.009	0.913	0.087
Australian Aborigine	0.024	0.304	0.672	0.176	0.824
Egyptian	0.278	0.489	0.233	0.523	0.477
German	0.297	0.307	0.196	0.530	0.450
Chinese	0.332	0.486	0.182	0.575	0.425
Nigerian	0.301	0.493	0.204	0.548	0.452

Source: W. C. Boyd, *Genetics and the Races of Man*, D. C. Heath, 1950.

- Total frequency of heterozygotes for gene in question
- Greatest when there are many alleles at equal frequencies
- Also measured from *haplotypes*
 - combinations of alleles at closely linked loci
 - greater than the average heterozygosity of separate loci because an individual is a haplotypic heterozygote if either of the two genes is heterozygous

POLYMORPHISM

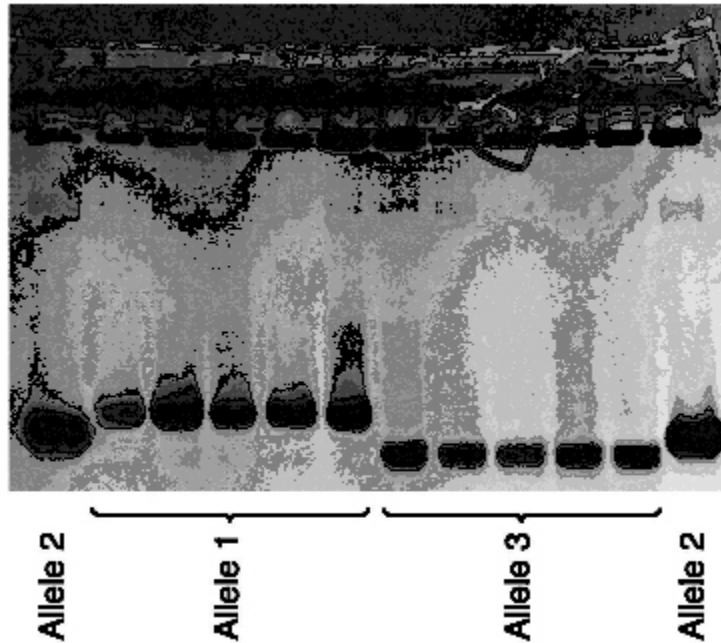
TABLE 17-3 Frequencies of the Alleles I^A , I^B , and i at the ABO Blood Group Locus in Various Human Populations

Population	I^A	I^B	i
Eskimo	0.333	0.026	0.641
Sioux	0.035	0.010	0.955
Belgian	0.257	0.058	0.684
Japanese	0.279	0.172	0.549
Pygmy	0.227	0.219	0.554

SOURCE: W. C. Boyd, *Genetics and the Races of Man*. D. C. Heath, 1950.

- Genetic variation occurs both within and between populations
- Basis for evolutionary change
- Most common variant is *wild-type*

POLYMORPHISM



- Protein polymorphism
 - immunologic: recognized by antibodies
 - amino acid sequence
 - deduced from DNA sequence
 - differences in electrophoretic mobility

DNA POLYMORPHISM

- Chromosome polymorphism
 - karyotype differences
 - supernumerary chromosomes
 - translocation and inversion heterozygotes

- Restriction fragment length polymorphism (RFLP)
 - mutation creates or abolishes restriction sites, resulting in different size fragments

- Variable number tandem repeats (VNTR)

- Complete sequence variation
 - SNP: single-nucleotide polymorphism
 - variation in both coding and noncoding regions

- At DNA level, some variation may have no visible effect

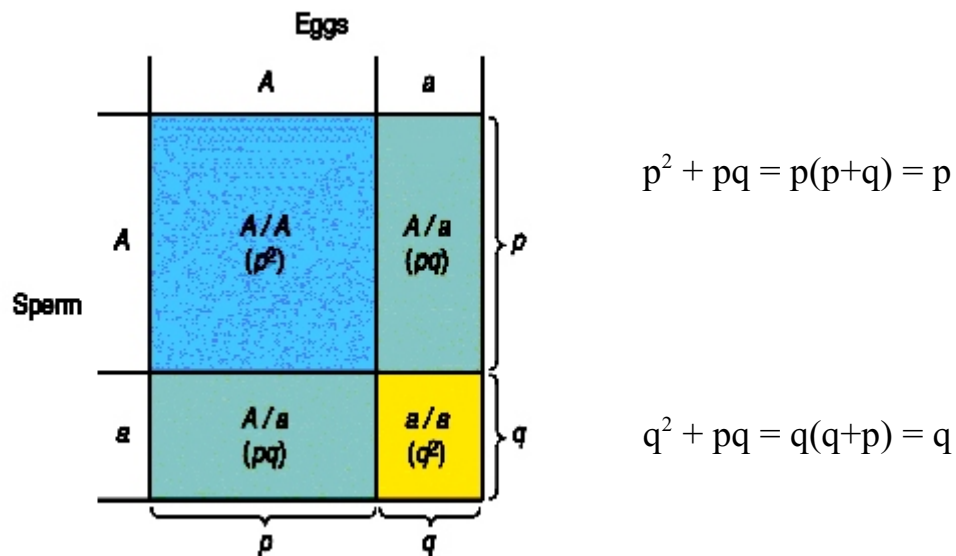
HARDY-WEINBERG EQUILIBRIUM

- In large randomly mating populations with no mutation, no migration, and no selection, allele frequencies will be in equilibrium

- At equilibrium, genotype and phenotype frequencies are function of allele frequencies

A/A	A/a	a/a
p^2	$2pq$	q^2

- Genetic variation remains constant over time



SOURCES OF VARIATION

- Mutation

- source of genetic variation
- mutation rate too low to drive evolutionary change
- if mutation rate (locus and species dependent) is 1/10,000
 - allele mutates
 - 0.01 change in original allele frequency (0.50 to 0.49) would require 200 generations
- mutation rate /generation X number of loci X n = change in allele frequency

$$10^{-4} \text{ locus/generation} \times \text{generation}/2 \text{ loci} \times n = 0.01$$
$$n = 0.01 \times 2 \text{ loci/generation} \times \text{generation}/10^{-4} \text{ locus} = \mathbf{200}$$

- Recombination

- linkage disequilibrium
 - nonrandom association of alleles
 - occurs with each new mutation
- repeated recombination randomizes combinations of alleles (haplotypes)
 - linkage equilibrium

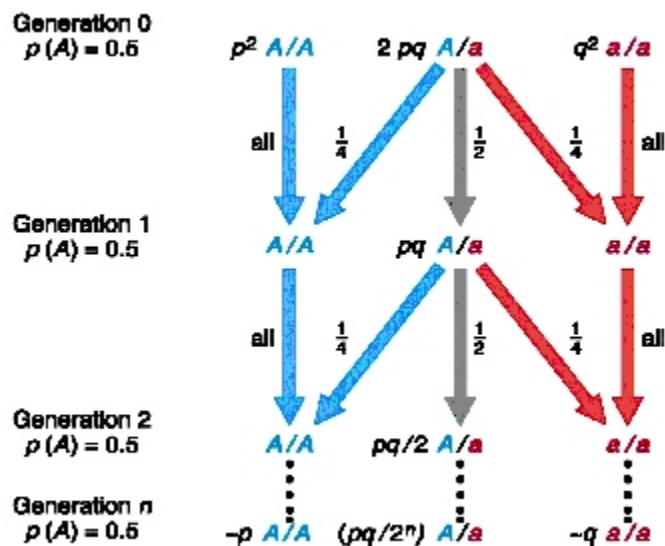
SOURCES OF VARIATION

- Migration

- immigration: migration into population
- emigration: migration from population
- if populations differ in gene frequencies, migration will alter frequencies

- Nonrandom mating

- inbreeding: mating between relatives
 - increased homozygosity



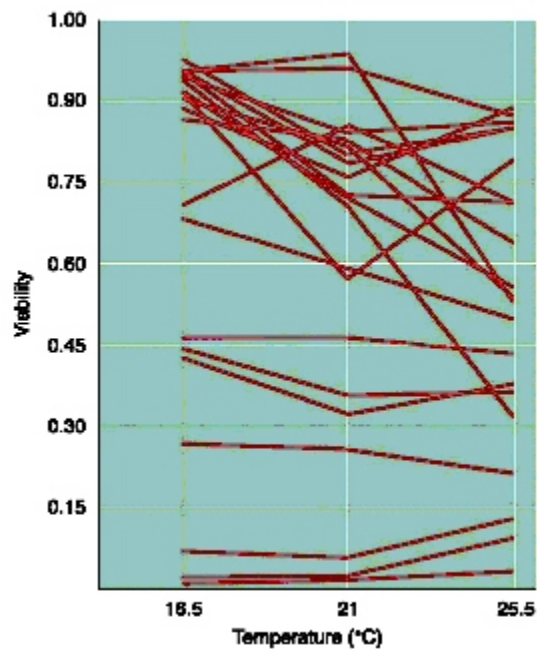
- outbreeding: mating between non-relatives
- positive assortative mating: mating between like individuals
- negative assortative mating: mating between unlike individuals

SELECTION

- Natural selection: differential rates of reproduction and survival among different genotypes
 - term used by Darwin by analogy with artificial selection
- Darwinian fitness: relative probability of survival and rate of reproduction
 - relative fitness of most reproductively successful variant is 1
 - relative fitness of a less successful variant that produces 30% as many offspring is 0.3 ($1 \times 30\% = 0.3$)
- consequence of relationship between phenotype and environment
- same genotype may have different fitness in different environments

SELECTION

- Frequency-independent selection
 - fitness of phenotype is independent of frequency of phenotypes
 - fixed property of individual's genotype
- Frequency-dependent selection
 - fitness of phenotype changes depending upon frequency of phenotype in population
- Fitness often measured as *viability*, the probability of survival to reproductive age



HOW SELECTION WORKS

- Differential reproduction of different genotypes, e.g., *a/a* lethal at maturity

genotype	<i>A/A</i>	<i>A/a</i>	<i>a/a</i>	<i>q</i>
born	0.81	0.18	0.01	0.1
mature	0.81	0.18	0.00	-
corrected	$\frac{0.81}{.99}$	$\frac{0.18}{.99}$	$\frac{0.00}{.99}$	
corrected	0.818	0.182	0.00	0.091 ($0 + \frac{1}{2} \frac{0.182}{2}$)

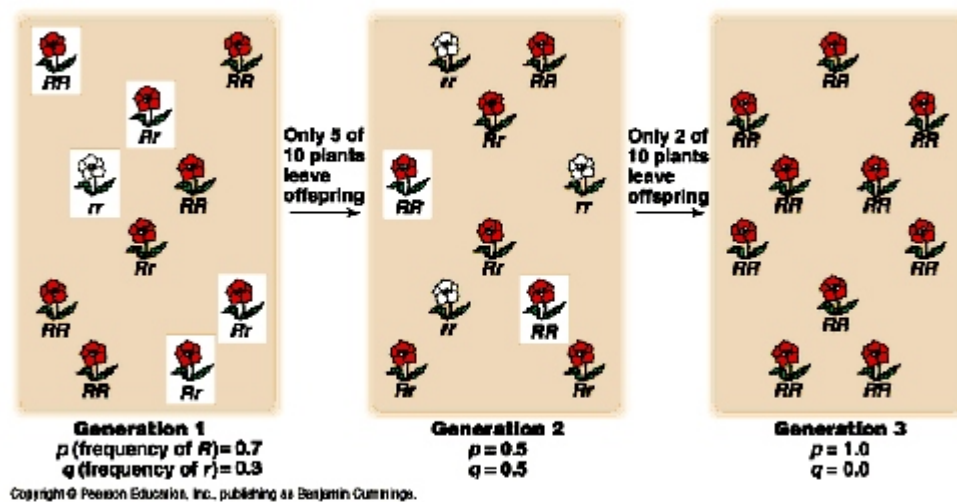
$$\Delta q = 0.091 - 0.100 = -0.019$$

RANDOM EVENTS

- Genetic drift

- change in gene frequency as a result of chance events from generation to generation
- most effective in small populations
- may result in fixation of allele ($p = 1$)

Figure 23.4 Genetic drift



- Founder effect

- small group breaks off from larger population
- founding group contains sample of alleles not necessarily in same frequency as parent population